Acidity and Basicity in Chemistry

Edited by: **Saeed Farrokhpay**

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LIST OF ABBREVIATIONS

AC	acetone
ADMET	absorption, distribution, metabolism, excretion, and toxicity
AFM	atomic force microscopy
ATP	adenosine triphosphate
BBB	blood-brain barrier
CAB	cellulose acetate butyrate
CNS	central nervous system
DAE	1,2-diaminoethane
DCM	dichloromethane
DLVO	Derjaguin–Landau–Verwey–Overbeek
EA	ethyl acetate
ESCA	electron spectroscopy for chemical analysis
HOMO	highest occupied molecular orbital
HPLC	high-performance liquid chromatography
IFM	interfacial force microscopy
IHP	inner Helmholtz plane
IRAS	infrared reflection absorption spectroscopy
ISFET	ion-sensitive field-effect transistor
LUMO	lowest unoccupied molecular orbital
mEq	milliequivalents
MW	molecular weight
NC	net charge
OHP	outer Helmholtz plane
PAHs	polycyclic aromatic hydrocarbons
PRALs	potential renal acid loads
PSA	polar surface area
PZC	point of zero charge
QAPPs	quality assurance procedures

TCM	trichloromethane
THF	tetrahydrofuran
Vd	volume of distribution
XPS	x-ray photoelectron spectroscopy

PREFACE

The issue of acidity and basicity is enormously valuable economically and technologically, and it continues to pose great scientific problems, with the potential for considerable technological advancements in the future. Historically, industrial advances in acidity/basicity have frequently anticipated scientific comprehension of the underlying processes, most notably in the petroleum sector, a major beneficiary and user of acidity principles. However, this procedure is prohibitively expensive and inefficient in comparison to advancements based on a basic grasp of the scientific phenomenon at hand. This has been realized throughout time, which explains why university, government, and industry laboratories have spent significant effort over the last 50 years to studying acidity (and, to a lesser extent, basicity) in order to obtain a technical edge. There is a vast amount of scientific literature on the issue. There have been a number of significant essays and books published on the subject that aim to critically analyze several individual contributions. Three events over the previous few years resulted in the creation of this book which are:

- Significant advances in the theory of acids and bases;
- Significant advances in the concept of acids and bases;
- The ASI's structure represented the convergence of these three forces.

This book contains detailed information about acids, bases, different types of alkaline and acidic materials and their applications. There are eight chapters in the book. Chapter 1 introduces the readers with fundamentals of acids and bases and their classifications. Chapter 2 focusses on the acid-bases properties of the surface.

Chapter 3 contains information regarding the measurement of pH and alkalinity of water. Chapter 4 illustrates the effects of pH variation on the properties and behavior of soil. Chapter 5 describes the historical developments in acid-base characteristics of food products.

Chapter 6 further expands the information about pH of food products by providing information about titratable acidity and pH in food products. Chapter 7 focuses on the applications of acidity and basicity in drug delivery and medical sciences. Finally, Chapter 8 sheds light on alkaline diet and its effects on human health.

The text of the book assumes no prior understanding of acidity of basicity beyond what would be taught in a standard secondary school. It is aimed for chemistry students who wish to learn more about the connections between acidity and basicity, as well as the macroscopic features of acidic and basic compounds.

CHAPTER 1

BASICS OF ACID-BASE CHEMISTRY

CONTENTS

1.1. INTRODUCTION

Acid, base, and salt are old notions that advanced chemistry has absorbed and developed. Bases and acids take part in a critical part in the lives of the humans and in the environment, through our body to the seas and minerals of the Earth. We have had bases and acids if we have ever sipped the juice of a lemon or used soap to wash our hands. Based on qualities like flavor and pH, researchers divide substances into bases (also known as alkali), acids, or neutral. Citric acid is a substance found in citrus fruits. Toothpaste is an ineffective starting point. Toothpaste preserves dental enamel by neutralizing the acids in meals (Ayers et al., 2015).

The bitter taste of acidic substances is typically a good indicator. An acid is a molecule that may give an H^+ ion as residual thermodynamically favorable after releasing H^+. Blue litmus can become red when uncovered to acids.

Bases, contrarily, have a sour flavor and a slick consistency. The word alkali represents a base that may be soluble in water. Salts are produced if such compounds react chemically with acids. Bases are reported to change red litmus to blue (Figure 1.1) (Shindy, 2012).

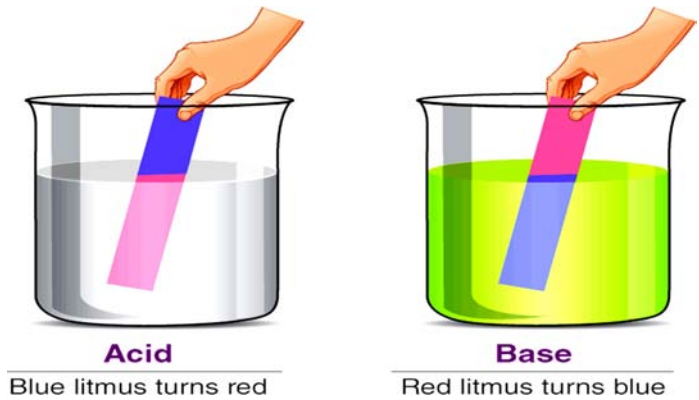

Figure 1.1. Litmus test of bases and acids.

Source: https://byjus.com/chemistry/acids-and-bases/.

1.2. ACIDS

The word acid was first utilized in the 17th century, and this word was derived through the Latin word ac-, which means “pointed,” like the taste of vinegar.

Acids are acknowledged as a unique class of chemicals with the following characteristics in their aqueous solutions (Figure 1.2) (Chen and Neibling, 2014):

- The ability to convert litmus from blue to red;
- A distinct bitter flavor;
- React with *bases* to produce water and sodium chloride;
- React with some metals to form hydrogen gas.

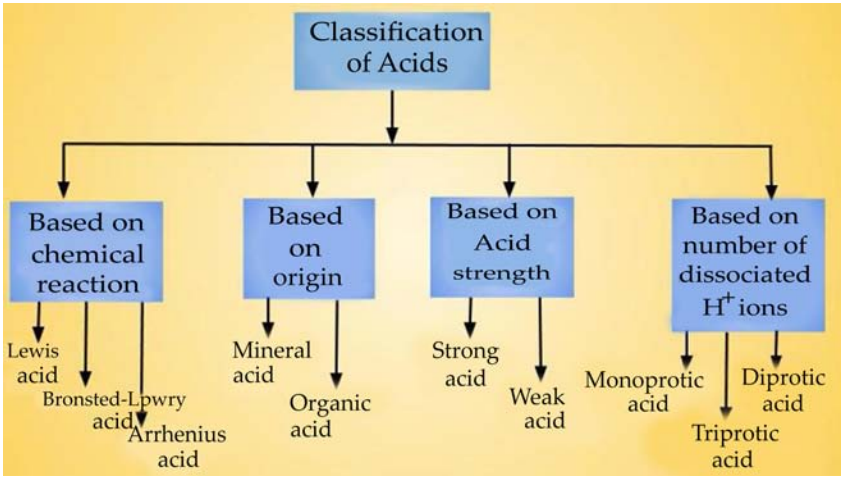

Figure 1.2. Categorization of acids.

Source: https://dewwool.com/10-types-of-acids/.

The initial chemical concept of acid was incorrect: in 1787, Antoine Lavoisier classified recognized acids like a distinct group of "complex substances" as a portion of his comprehensive taxonomy of compounds. He hypothesized that one's unique characteristics stemmed from the existence of a basic component that embodied the "acidity" concept, which he titled oxygen, after the Greek word for "acid former." Lavoisier was given this term to a novel gas element identified only a few years before by Joseph Priestly as the key ingredient which enables burning. Because several products of combustion (oxides) produce acidic solutions, and also most acids contain oxygen, Lavoisier's error is reasonable (McQuilton et al., 2012).

Humphrey Davy demonstrated in 1811 this muriatic (hydrochloric) acid (which Lavoisier was considered an element) doesn't really comprise oxygen and that only reassured a few that chlorine had been oxygen comprising

compound rather than an element. However, a few oxygen-free acids were identified by 1830, the hydrogen hypothesis of acids had not been broadly acknowledged till about 1840. Through this point, the misnomer oxygen had become too well-known to be altered (Brooks et al., 2005).

The importance of knowing acids (and also salts and bases) had to wait until Michael Faraday discovered the solutions of salt (called electrolytes) produce electricity in the mid-19th century. It suggests the presence of charged particles capable of migrating in response to an electric field. Such particles were given the name ions ("wanderers") by Faraday. The qualities we associated with acids are attributable to an overabundance of hydrogen ions in the solution, according to later investigations on electrolyte solution (Johnson, 2003).

Svante Arrhenius (1859–1927), a Swedish chemist, developed the 1st beneficial theory of acids in 1890: an acidic substance has at least 1 hydrogen atom which may dissociate, or ionize, once mixed with water, generating an anion and a hydrated hydrogen ion:

hydrochloric acid:	$HCl \longrightarrow H^+(aq) + Cl^-(aq)$
sulfuric acid:	$H_2SO_4 \longrightarrow H^+(aq) + HSO_4^-(aq)$
hydrogen sulfate ion:	$HSO_4^-(aq) \longrightarrow H^+(aq) + SO_4^{2+}(aq)$
acetic acid:	$H_3CCOOH \longrightarrow H^+(aq) + H_3CCOO^-(aq)$

To be considered an "Arrhenius acid," it should include hydrogen. Many compounds, on the other hand, don't really comprise hydrogen natively, however when mixed with water, they nonetheless produce hydrogen ions; the hydrogen ions are produced by the water on their own, as a result of the interaction with the material. To provide a very relevant operational concept of an acid, the preceding is provided (Titov, 2016):

When a chemical is mixed with water, it produces an oversupply of hydrogen ions, which is known as an acid.

When it comes to hydrogen in acids, there will be three critical aspects to remember. Although all Arrhenius acids comprise hydrogen atoms, not over all the atoms of hydrogen in a substance are vulnerable to detachment, hence the $–CH_3$ hydrogens in acetic acid are classified as "non-acidic."

- One of the most significant aspects of understanding chemistry is the ability to anticipate whether hydrogen atoms in a material would be capable to dissolve at what time. The hydrogen's that do dissolve may dissolve to varying degrees of intensity. Strong acids, like hydrochloric acid and nitric acid, are efficiently dissolved to a 100% degree in the solution they are in. A limited

percentage of mostly organic acids, like acetic acid, is dissolved in many solutions; hence, mostly organic acids are weak acids. Fluoric acid and HCN are instances of inorganic acids that are weak (Malhotra, 2018).

- Sulfuric acid and phosphoric acid are two popular instances of polyprotic acids that have a large number of ionizable hydrogen atoms are recognized as polyprotic acids. Ampholytes are intermediary types of protons that can both absorb and shed protons, like the HPO_4^{2-} molecule.

H_2SO_4 sulfuric acid	⟶	HSO_4^- hydrogen sulfate ion ("bisulfate")	⟶	SO_4^{2-} sulfate ion			
H_2S hydrosulfuric acid	⟶	HS^- hydrosulfide ion	⟶	S^{2-} sulfide ion			
H_3PO_4 phosphoric acid	⟶	$H_2PO_4^-$ dihydrogen phosphate ion	⟶	HPO_4^- hydrogen phosphate ion	⟶	PO_4^- phosphate ion	
HOOC-COOH oxalic acid	⟶	$HOOC–COO^-$ hydrogen oxalate ion	⟶	$^-OOC–COO^-$ oxalate ion			

1.3. BASES

The term "*base*" has often been connected with a group of substances its aqueous solutions have the following characteristics (Bruen and Bruen, 2010):

- A nasty flavor;
- A "*soapy*" texture if applied to the skin;
- The capability to return litmus to its natural blue color after it's been stained red through acids;
- The ability to produce salts when reacting with acids. The base is identical to the term "alkali." Since old times, woody ashes were the usual resource of the stronger base named as KOH; the basic name stems from the similar Latin term kalium (potash), which is also the source of the representation for potassium (K).

Whenever a base is mixed with water, it produces hydroxide ions, similar to when an acid releases hydrogen ions into solution (Pankaj et al., 2014):

$NaOH(s) \rightarrow Na^+(aq) + OH^-(aq)$

Since it includes OH^- ions, sodium-hydroxide (NaOH) is an Arrhenius base. Certain chemicals, on either hand, that don't possess hydroxide

ions but may make them by reacting with water are categorized as bases. Hydrogen compounds and metal oxides of some non-metals are two types of these compounds:

$$Na_2O + H_2O \rightarrow 2NaOH \rightarrow 2Na^+(aq) + 2OH^-(aq)$$

$$NH_3 + H_2O \rightarrow NH_4^+ + OH^-$$

1.4. NEUTRALIZATION

Bases and acids combine to form two items: an ionic and water molecule called salt. It is referred to as a neutralizing reaction (Sykes and Matza, 1957).

$$Na^+ + OH^- + H^+ + Cl^- \rightarrow H_2O + Na^+ + Cl^-$$

$$K^+ + OH^+ + H^+ + NO_3^- \rightarrow H_2O + K^+ + NO_3^-$$

Both such reactions are exothermic; while each employs various bases and acids, these both produce a similar quantity of heat (57.7 kilojoule) for one mole of hydrogen ion neutralized. It indicates that all neutralization reactions are equivalent to the following one (Maruna and Copes, 2005):

$$H^+(aq) + OH^-(aq) \rightarrow H_2O \quad (1)$$

In a neutralization process, the "salt" created is merely the cation and anion that already existed. Upon evaporating the water, the salt may be retrieved like a solid (Figure 1.3).

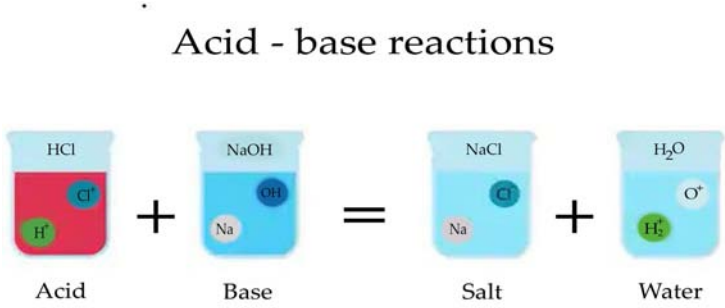

Figure 1.3. A typical reaction of acid and base.

Source: https://www.assignmentpoint.com/science/chemistry/an-acid.html.

1.5. DISSOCIATION OF WATER

Acids' capability to interact with bases is determined by the hydrogen ion's desire to mix with hydroxide ions to produce water. Due to the magnitude of such a propensity, the reaction in Eqn. (1) is almost completed. Furthermore, no reaction is fully completed; at equilibrium (while no additional net change in the quantities of substances occurs), there would always be the concentration of a very small reactant in the mixture. One more technique of putting it is that every reaction is reversible to some extent. It suggests that the reaction would occur to a little amount in distilled water (Feibelman, 2002):

$H_2O \rightarrow H^+(aq) + OH^-(aq)$

Experimental observations verify it: even the thoroughly distilled water prepared by chemists conducts electricity only minimally. Based upon the electrical conductivity, the optimum concentrations of both the hydrogen ion and hydroxide ions at 25°C are approximately precisely 1.00×10^7. This results in the dissociation of around one H_2O molecule per 50 million (Figure 1.4) (Sweeton et al., 1974).

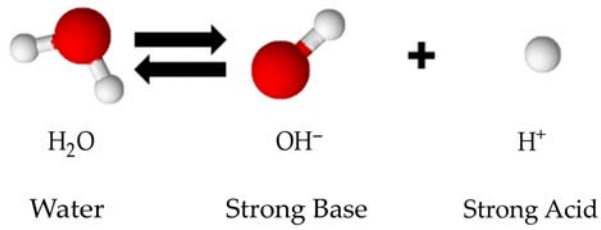

Figure 1.4. Water dissociation reaction.

Source: https://www.quora.com/What-is-the-pH-of-a-neutral-solution-Why-is-that-the-neutral-point.

Water's degree of separation is so minute that you may question why it is stated whatsoever. It is necessary is that the constant of equilibrium must be defined by using the concentrations of hydrogen ion and hydroxide ion in distilled water.

$[H^+][OH^-] = 10^{-7} \times 10^{-7} = Kw = 10^{-14}$

Constants of equilibrium and their computation are discussed further in-depth in a subsequent chapter. (Hundt et al., 2014).

At 25°C, the multiplication of the hydroxide ion and hydrogen ion concentrations in an aqueous medium of the solution is always 1.00×10^{14}.

In other terms, $[H^+][OH^-] = 1.00 \times 10^{-14}$ (2)

It is referred to as the multiplication of the ion of the water, and it relates to all aqueous mediums, not only distilled water. That has far-reaching implications since it indicates that even if the concentration of hydrogen ion is high, the concentration of hydroxide ion would be low, and conversely. It suggests that hydrogen ions exist in all water solutions, not only those that are acidic. As a result, the following critical concepts should be memorized (Zabolotskii et al., 1988):

- **Neutral Solution:** $[H^+] = [OH^-]$ (= 1.00×10^{-7} *M at* 25°C).
- **Alkaline Solution:** $[H^+] < [OH^-]$.
- **Acidic Solution:** $[H^+] > [OH^-]$.

1.6. THE PH SCALE

The probable values of $[OH^-]$ and $[H^+]$ in an aqueous medium of the solution range from around 10^{-1} to 10^{-15} magnitudes. As a result, it's easier to depict them on a compacted logarithmic scale. The *pH* scale is usually utilized to show the concentrations of hydrogen ions (Bjellqvist et al., 1993):

$pH = -\log_{10} [H^+]$

or on the contrary:

$[H^+] = 10^{-pH}$

you may describe also:

$pOH = -\log_{10} [OH^-]$

and

$pK_w = -\log K_w$

by Eqn. (2)

$pH + pOH = pK_w$ (= 14.0 in distilled water at 25°C) (3)

At 25°C, the value of the pH of a neutral solution is 7.0; a higher pH suggests a basic solution, while a lower pH indicates an acidic medium of the solution. A solution having $[H^+]$ = 1M has a pH of 0; a 0.00010M H+ solution has a pH of 4.0. A 0.00010M sodium hydroxide solution has a pOH of 4.0, and a pH of 10.0 as a result. You must have a thorough understanding of the pH scale and be able to transform $[H^+]$ or [OH] to pH in both directions (Figure 1.5) (Bosch et al., 1996).

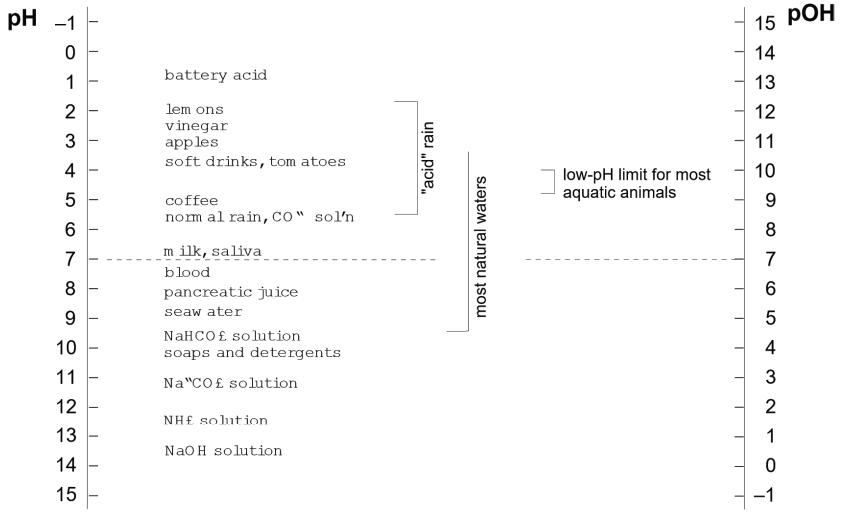

Figure 1.5. The pH scale.

Source: https://www.sciencenewsforstudents.org/article/scientists-say-ph.

As stated in further explanation on page 20, hydrogen ions don't exist independently in water, and hence the species denoted by "$[H^+]$" is a more complex one. Additionally, if the overall ions concentration of all types in the solution surpasses approximately 0.001 M, an important fraction would be linked into unbiased pairs like $H^+ \cdot Cl^-$, decreasing the concentration of "free" ion to the lower values we would then refer to as the efficient concentration. The efficient concentration of H^+ influences the level to which a solution is acidic, and that's what pH determination techniques measure. Consequently, the pH value is stated in terms of the H+ concentration that is most efficient. You don't have to worry about the details right now, but it's something to keep in mind later when doing acid-base balance calculations (Bjellqvist et al., 1994).

1.7. TITRATION

Because acids and bases rapidly react, that is fairly simple to determine the quantity of acid in a solution experimentally by estimating how many moles of the base is necessary to neutralize it. This procedure is known as titration, and you must be aware of it in your Lab research (Thordarson, 2011).

We may titrate an acid in the presence of a base or a base in the presence of an acid. The drug being titrated is the chemical whose concentration we are

evaluating; the chemical we are injecting in a specified titrant amount. The goal is to continue adding titrant till the solution is completely neutralized; at this stage, the number of titrant moles injected indicates the basic (or acid) concentration in the solution getting titrated (Figure 1.6) (Gaudette et al., 1974).

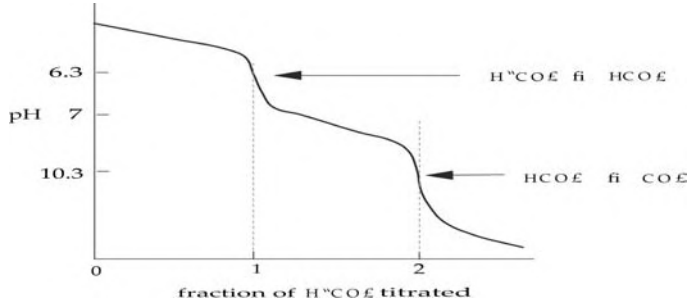

Figure 1.6. Na_2CO_3 titration curve in the presence of HCl.

Source: https://www.quora.com/What-are-reasons-for-getting-two-different-concentration-values-of-Na_2CO_3-when-it-was-titrated-with-HCL-using-Phenolphthalein-and-Methyl-Orange.

1.7.1. Titration Curves

Titration progress may be tracked by drawing the pH of the solution as the amount of titrant administered. Figure 1.6 shows two identical curves, first for a powerful acid (HCl) and the 2nd for a moderate acid, acetic acid (HAc). Notice how the pH varies extremely slowly until the acid is virtually neutralized when looking at the HCl curve first. Only one more drop of sodium hydroxide solution, as seen in the larger image at the top of Figure 1.6, would cause the pH to rise to a greater value – nearly as much as the pure sodium hydroxide solution (Tanford, 1963).

Comparing and contrasting the hydrochloric acid and HAc curves. The pH spike around the neutralization point is much less steep for a weak acid. It's also worth noting that the pH of the solution at the neutralization point exceeds seven. Such two properties of a weak acid's titration curve are critical to understanding (Tanford and Kirkwood, 1957).

There would be a pH spike for every proton titrated whereas if acid or base is polyprotic. The titration of a sodium carbonate solution with HCl is shown in Figure 1.6. The concentrations of both solutions are the same.

Because the CO_3^{2-} ion is a base, the pH of the solution begins to rise. CO_3^{2-} is converted to HCO^{3-} and then to carbonic acid, H_2CO_3 when protons are injected (Asuero and Kirkwood, 1957).

The vertical portions of the titration curve correspond to quantities of Hydrochloric acid that are equivalent to, as well as twice, the real volume of CO_3^{2-} solution (for example, identical numbers of moles due to equal concentrations of both solutions). The fact that one mole of carbonate ion takes two moles of hydrochloric acid to neutralize is demonstrated by the second equal point:

$2H^+ + CO_3^{2-} \rightarrow H_2CO_3$

1.7.2. Finding the Equivalence Point: Indicators

Whenever a sufficient amount of base is introduced to entirely react with the hydrogens in a monoprotic acid, the equilibrium is achieved. Titration having a stronger alkali and a stronger acid result in a pH of seven at the point of equilibrium. If the strength of the acid is weaker, then the pH would be more than seven; hence, the "neutralized" solution would not be pH neutral. Every titratable hydrogen in a polyprotic acid would have an equivalency point; they generally appear at pH levels four to five units separately (Mocchiutti and Zanuttini, 2007).

The secret to a good titration is determining the point of equivalency. The simplest technique to determine the equivalency point is to utilize an indicator dye; an indicator dye is a material whose color is pH-sensitive. However, one indicator that's also frequently seen in the lab is phenolphthalein; it is colorless in the solution of acidic medium however rapidly changes vividly red in alkaline solution. When acid is being titrated, only a small number of drops of phenolphthalein should be added to the solution before starting the titration. A local red color occurs as the titrant is introduced, however soon disappears as the solution is agitated. As the equilibrium is near, the color fades more gradually; the secret is to cease adding base until a solitary drop consequence in a persistently pink color solution (Checchetti and Lanzo, 2015).

Various indicators exhibit varying degrees of color change at certain pH levels. Because the pH of the equilibrium fluctuates as the concentration of the acid is titrated, one attempts to match the indicator to the specific acid. The titration of polyprotic acids may be accomplished via utilizing an appropriate mix of numerous indicators.

1.8. THE PROTON DONOR-ACCEPTOR CONCEPT OF ACIDS AND BASES

According to Arrhenius, bases, and acids are compounds that, upon dissociation, create hydroxide ions or hydrogen ions, respectively. Although it is a helpful notion, it's not been particularly helpful in communicating why NH_3, which does not comprise OH^- ions, is a base rather than an acid, why a solution of $FeCl_3$ appears acidic, or why a solution of Na_2S appears basic (He et al., 2000). Franklin, who devised a hypothesis in 1905 wherein the solvent performs a fundamental role in the establishment of acids and bases, is responsible for the broader working explanation of bases and acids that we've been utilizing. An acid is defined as a solute that produces a solubilized ion which is distinctive of the solvent, and a base is defined as a solute that produces a solubilized ion that is likewise typical of the solvent, according to the above interpretation. The analogous ions in water are always $OH^-(aq)$ and $H^+(aq)$ although in liquid ammonia, even though it is a suitable solvent, the comparable ions are NH^+_4 and NH^-_2 in the form of liquid ammonia. Because of the self-ionization reactions, it appears that the solvent may perform a specific role in the processes (Kiefer and Hynes, 2002);

$H_2O^- \rightarrow H^+(aq) + OH^-(aq)$

and

$2NH_3^- \rightarrow NH_2^- + NH_4^+$

As a result, Franklin broadened the scope of the acid-base notion to include non-aqueous solvents and generalized it somewhat (Figure 1.7).

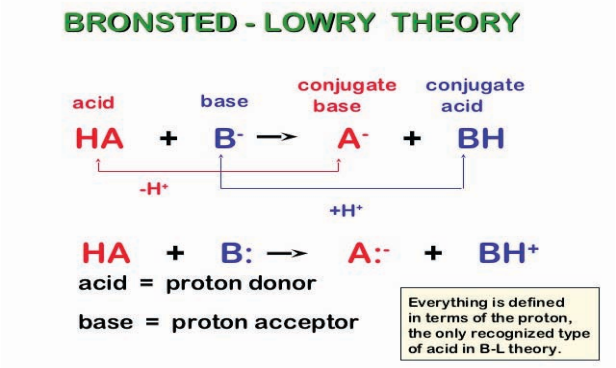

Figure 1.7. In acids and bases, the Bronsted-Lower theory includes the idea of proton donor-acceptor.

Source: https://www.quora.com/Why-are-bases-called-proton-acceptors.

Consequently, it wasn't until 1923 that J.N. Bronsted, a Danish scientist, offered a hypothesis that would be both simple and more universal.

A proton donor is an acid, while a proton acceptor is a base (Zubatyuk et al., 2009). As a result of such definitions, there is an extremely significant implication: a substance may not behave like acid exclusive of the existence of alkali to take the proton, and conversely.

A proton exchange reaction occurs when an acid reacts with an alkali; if the acid is designated by AH and the base is designated by B, so we may express a universal base and acid reaction as:

$AH + B^- \rightarrow A^- + BH^+$

However, because the result BH^+ is now able of releasing its newly gained proton to some other acceptor, it may be another acid (Orlandi and Schulten, 1979):

$acid_1 + base_2 - \rightarrow base_1 + acid_2$

Base$_1$ is conjugated to *acid*$_1$, and *acid*$_2$ is conjugated to *base*$_2$. Conjugate signifies "linked with," implying that every entity and its conjugate entity are linked by the release or gain of a single proton. The conjugate pairings of some common acid and base systems are shown in Table 1.1 (Kyrychenko et al., 1999).

- **Amphiprotic Species:** Numerous chemicals, for instance, HCO_3^-, $H_2PO_4^-$, H_2O and NH_3, may both give and take protons. These chemicals are referred to as *amphiprotic*, and the dissolved species are referred to as *ampholytes*.
- **Acid-base Reactions:** Within the Arrhenius principle, the only form of the reaction base and acid that may happen is the neutralization of H^+ by OH^-. The Bronsted idea expands our perspective by including a diverse range of reactions that have the property of proton transfer from a donor to an acceptor (Table 1.2) (Ovalle and Waegele, 2021).

Table 1.1. Some of the Most Frequent Acid-Base Conjugate Pairs

Substance	Conjugate Base	Acid
Acetic acid	$CH_3CH_2COO^-$	CH_3CH_2COOH
Hydrochloric acid	Cl^-	HCl
Potassium-dihydrogen phosphate	HPO_4^-	$H_2PO_4^-$

Nitric acid	NO_3^-	HNO_3
Sodium sulfide	S^-	HS^-
Sodium hydrogen sulfate	SO_4^{2-}	HSO_4^-
Iron(III) chloride	$Fe(H_2O)5OH_2^+$	$Fe(H_2O)^{3+}$
Ammonium chloride	NH_3	NH_4^+
Hydronium ion	H_2O	H_3O^+
Water	OH^-	H_2O

1.8.1. The Hydronium Ion

An acid, according to the Arrhenius definition, is a chemical that ionizes in water to form the ion of hydrogen. Moreover, there may be a significant flaw in this logic: the ion of hydrogen is nothing greater than a proton, or a bare nucleus, in nature. Although one electron carries just one unit of positive charge, this charge is condensed into a volume of space only 100 millionth the size of the volume covered by the smallest of all conceivable atoms. Because of its exceedingly tiny size, the proton would be drawn to every component of a neighboring molecule or atom that has an increase in negative charge due to its exceedingly tiny size (Guo et al., 2020). This type of location may be found on every atom which contains non-bonding electrons, and it is at this location that protons link themselves to the acceptor atom through the formation of a shared-electron (coordinate) bond having the single pair of electrons. As the strength of the link between the proton and acceptor increases, so does the strength of the acid, and vice versa. As a result, the species H_2O, NH_3 and F^- are all considered bases. As a result, the hydrogen ion can't present as an independent particle in an aqueous medium because the latter of such species constitutes the vast majority of the species in all of these solutions (Wang et al., 2017).

Table 1.2. Instances of Proton Donor and Acceptor Reactions

Reaction	**$Base_1$**	**$Acid_2$**	**$Base_2$**	**$Acid_1$**
Ionization of HCN	CN^-	H_3O^+	H_2O	HCN
Ionization of H_2O	OH^-	H_3O^+	H_2O	H_2O
Hydrolysis of NH_4Cl	NH_3	H_3O^+	H_2O	NH_4^+
Ionization of NH_3	OH^-	NH_4^+	H_2O	NH_3

Neutralization of HCl through NaOH	H_2O	H_2O	OH^-	H_3O^+
Hydrolysis of $CH_3COO^-Na^+$	OH^-	CH_3COOH	CH_3COO^-	H_2O
Dissolution of BiOCl through HCl	$2H_2O + Cl^-$	$Bi(H_2O)^{3+}$	BiOCl	$2H_3O^+$
Displacement of NH_3 through $Ca(OH)_2$	NH_3	H_2O	OH^-	NH_4^+
Neutralization of NH_3 through acetic acid	CH_3COO^-	NH_4^+	NH_3	CH_3COOH
Displacement of HCN through CH_3COOH	CH_3COO^-	HCN	CN^-	CH_3COOH
Decomposition of $Ag(NH_3)^+_2$ through HNO_3	$3H_2O + Ag^+$	NH_4^+	$Ag(NH_3)$	$2H_3O^+$

While molecules of water are somewhat strongly attached to other types of dissolved ions, the contact between water and H^+ is really strong as expressing " $H^+(aq)$" scarcely does that justice. Alternatively, we regard the species H_3O^+ to be the acidic solution's defining species. This is called hydronium ion.

According to the Bronsted principle, the acid HA can donate a proton to a water molecule, forming H_3O^+ while keeping the anion A as the conjugate base (Begemann et al., 1983):

$$HA + H_2O^- \rightarrow A^- + H_3O^+ \qquad (4)$$

Since the molecule of water takes a proton, H_2O acts as a base in this situation. As a result, what Arrhenius will have considered a simply ionization of HA is today considered a reaction between an acid and a base in and of itself. While Eqn. (4) comes closer to expressing what occurs $HA \rightarrow H^+ + A^-$, the latter equation is very easy to write those scientists often utilize it to depict acid-base reactions in situations when the proton acceptor-donor mechanism isn't important. So long as you recall that "hydrogen ions" as well as the formula "H^+" weren't to be regarded literally in the situation of the aqueous medium, we nevertheless talked regarding "hydrogen ions" and utilize the formula " H^+" in composing chemical equations (Balsiger et al., 1995).

Experiments show that the proton doesn't cling to one molecule of water, but rather switches partners several times every second. The proton's

molecular promiscuity, which is a result of its tiny mass and size, enables it to traverse through the solution by swiftly bouncing from one molecule of water to another, forming a novel H_3O^+ ion along the way. The total action is identical to that of a moving H_3O^+ ion. Likewise, a hydroxide ion that may be thought of as a "proton hole" in H_2O acts as a land spot for a proton from other molecules of water, causing the OH^- ion to bounce about (Kovalevsky et al., 2011).

Solutions that are alkaline or acidic have unusually higher electrical conductivities since hydroxide ions and hydronium may "move with no moving," and hence do not have to plow their technique through the solution via pushing away the molecules of water and so do others also (Zhao and Zhang, 2004).

1.8.2. Acid Strengths and the Role of Water

The reactions base and acid are simply proton contests between two acceptors (bases). Whenever we state that HCl is a powerful acid in the water, we're referring to the fact that water is a significantly powerful base than Cl^-. In water, HCN is a weaker acid since the proton may more efficiently exchange the cyanide ion: CN^- one pair electrons than it may with H_2O. As a result, the reaction only develops to a very minor amount (Liu et al., 2006).

$HCN + H_2O \leftrightarrow H_3O^+ + CN^-$

But Although what exactly does this mean when we say "acid power"? The proton coordination just with the pair of electrons gets more electrons nearer to even more nuclei, resulting in a decrease in potential energy, as with all bond formation. When we suppose that the proton would prefer to "fall" towards its least potential condition, a basic graphic like the one shown in Figure 1.8 may assist us to grasp this notion. Here are some potential acid-base pairings connected by horizontal lines. That picture may be thought of as a "proton ladder": the high the pair of acids and base on the figure, the more likely the proton would descend from such acid to a base at a lesser level (Grifoni et al., 2021). If the solution contains two or several bases, the protons would first drop into the lower-lying (stronger) base earlier than interacting with the high one. The vertical distance (energy) that a proton may descend in a proton transfer process determines the likelihood of that reaction occurring.

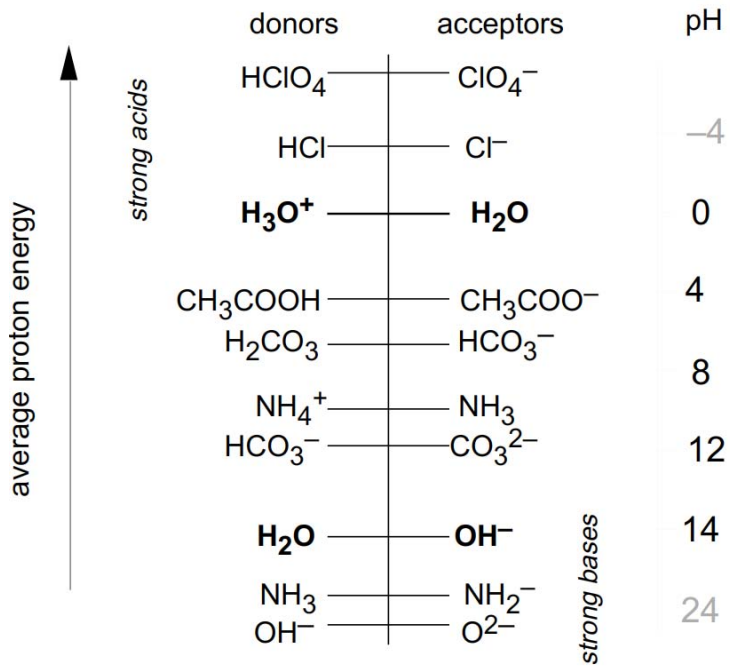

Figure 1.8. The "proton ladder" shows the relative strengths of bases and acids.

Source: https://pdf4pro.com/amp/view/introduction-to-acid-base-chemistry-57a6af.html.

It's worth noting that H_2O appears twice in this figure. It's the conjugate base of H_3O^+ towards the top, whereas an acid whose conjugate base is OH^- close to the bottom. Since protons may fall from HCl to H_2O, generating H_3O^+, HCl behaves like a powerful acid in H_2O. That potentially advantageous decline is why we term HCl a "strong" acid; a *1M* solution of hydrochloric acid is a *1M* solution of H_3O^+ (Zhang et al., 2015).

Comparing or contrasting the cases of HCN and HCl. The HCN or CN^- pair is located below the H_2O or H_3O^+ line, and for HCN to transfer a proton to H_2O, energy input is required to get the proton up to the degree of the H_2O and H_3O^+ and CN^- are produced because of the reaction.

$HCN + H_2O - \rightarrow H_3O^+ + CN^-$

This indicates that the reaction is inefficient in terms of energy. Besides a limited number of thermally produced interactions which sometimes

provide enough energy for one molecule to traverse the gap, the reaction will not happen at all. As just a consequence, just a trace amount of the HCl molecules in H_2O react; this is why HCN is referred to as a rather weak acid (Soler et al., 2018).

While hydrocyanic acid is a weaker acid in distilled H_2O, it may be titrated using sodium hydroxide solution due to the low-energy (strong) OH^- (at the bottom of the picture). That's why we employ a stronger base as a titrating agent, like NaOH; even just a comparatively "weak" acid would interact with a base as strong as a hydroxide ion.

The double opening water in Figure 1.8 shows the detail that H_2O performs a more active role in acid and alkaline chemistry than that of a solvent. Water participates directly in either proton transfer process that occurs in an aqueous medium, and its conjugate acid H_3O^+ and base OH^- are the strongest acids and bases that may present in an aqueous medium, correspondingly (Record et al., 1978).

- **The Leveling Effect:** Considering the hydrochloric acid or nitric acid, both are unquestionably strong acids than H_3O^+ based on their position on the acid-base ladder. However, because they are over H_3O^+, they are also beyond its conjugate base H_2O, and therefore both acids would transfer protons to H_2O, resulting in a solution with H_3O^+ as the sole surviving acid (donor of the proton). Likewise, the amide ion NH_2^- is a more powerful base than the hydroxide ion OH^-. However, if NH_2 is mixed with water, the NH_2^- would absorb the proton from an equal amount of H_2O molecules, releasing OH^- as the solution's strong base (Han et al., 2020):

$$NH_2^- + H_2O \rightarrow NH_3 + 2OH^-$$

The leveling effect is a theory which states that in an aqueous medium, all acids stronger than H_3O^+ as well as all bases stronger than OH^- seem to be uniformly powerful (such that, completely dissociated). It is also possible to describe the similar concept in the following manner: the distinction amongst degrees of dissociation of 99%, 99.9%, and 99.99% is hardly statistically significant (Han et al., 2014).

- **The pK_a and the Acid Dissociation Constant:** We express the constant of equilibrium for the reaction in Eqn. (4) to indicate the strength of an acid quantitatively:

$$K_a = \frac{[H^+][A^-]}{[HA]} \quad (5)$$

Where the bracketed terms indicate the individual species' equilibrium concentrations It would be obvious that the higher the K_a value, the more thorough the dissociation of HA. As K_a is unity or more, acid is called "strong." (Davis, 1962).

It is usual practice to represent the strength of acid as $pK_a \equiv -\log K_a$ for the similar reasons that this is practical to describe the concentration of H^+ on the log pH scale. The pK_as of strong acids are zero or less, whereas the pK_as of weak acids are +ve (Akbour et al., 2013).

1.8.3. Autoprotolysis

Autoprotolysis is a process in which neutral molecules which are amphiprotic and which may reside like liquids experience what Arrhenius will have named "self-ionization." The autoprotolysis reaction of water, wherein one H_2O acts like an acid and the other as a base, is very significant for humans since it is very ubiquitous. One H_2O serves as the acid, while the other serves as the base (Table 1.3) (Rondinini et al., 1987).

$2H_2O^- \rightarrow H_3O^+ + OH^-$

Table 1.3. Certain Typical Acids' Strengths and Conjugate Bases

Name	K_a	Base	Acid
Hydriodic acid	(>100)	I^-	HI
Perchloric acid	(>100)	ClO^{4-}	$HClO_4$
Sulfuric acid	(>100)	HSO^{4-}	H_2SO_4
Hydrobromic acid	(>100)	Br^-	HBr
Nitric acid	(>100)	NO^{3-}	HNO_3
Hydrochloric acid	(>100)	Cl^-	HCl
Oxalic acid	0.056	$HOOC–COO^-$	HOOC–COOH
Hydronium ion	1	H_2O	H_3O^+
Hydrogen sulfate ion	0.012	SO_4^{2+}	HSO^{4-}
Sulfurous acid	0.017	HSO^{3-}	H_2SO_3
Phosphoric acid	0.0071	H_2PO^{4-}	H_3PO_4
Chlorous acid	0.011	ClO^{2-}	$HClO_2$
Hydrofluoric acid	$6.8E^{-4}$	F^-	HF

Iron(III) ion	0.0068	$FeOH(H_2O)^{2+}_5$	$Fe(H_2O)_6^{3+}$
Oxalate ion	$1.7E^{-4}$	$C_2O_4^{2-}$	$HOOC–COO^-$
Carbonic acid	$1.7E^{-4}$	HCO^{-3}	H_2CO_3
Aluminum(III)	$1.1E^{-5}$	$AlOH(H_2O)^{2+}_5$	$Al(H_2O)_6^{3+}$
Acetic acid	$1.8E^{-5}$	CH_3COO^-	CH_3COOH
Dihydrogen phosphate ion	$6.3E^{-8}$	HPO_4^{2-}	H_2PO^{4-}
Hydrosulfuric acid	$8.9E^{-8}$	HS^-	H_2S
Hypochlorous acid	$6.0E^{-8}$	ClO^-	HClO
Hydrogen sulfite ion	$6.2E^{-8}$	SO_3^{2-}	HSO^{3-}
Ammonium ion	$5.9E^{-10}$	NH_3	NH_4^+
Copper(II) ion	$1.0E^{-8}$	$CuOH(H_2O)^+_3$	$Cu(H_2O)_2^{+4}$
Zinc(II) ion	$1.5E^{-10}$	$ZnOH(H_2O)^+_5$	$Zn(H_2O)_6^{2+}$
Hydrocyanic acid	$4.8E^{-10}$	CN^-	HCN
Hydrogen peroxide	$2.6E^{-12}$	HO^{2-}	H_2O_2
Water	$1.0E^{-14}$	OH^-	H_3O^+
Hydrogen carbonate ion	$4.8E^{-11}$	CO_2^{3+}	HCO^{3-}
Hydrosulfide ion	$1.3E^{-13}$	$S2^-$	HS^-
Monohydrogen phosphate ion	$4.4E^{-13}$	PO_4^{3-}	HPO_4^{2-}

It's simple to understand why such a reaction just occurs to a limited degree in the perspective of Figure 1.8 – for water to operate as just acid in distilled H_2O, its proton should be increased from the H_2O or OH^- – a level close to the bottom of the figure up to the H_3O^+ or H_2O level close to the top. Because of the large energy difference, the multiplication of the ion concentrations is just approximately 10^{-14}.

- **Non-Aqueous Acid and Base Systems:** Although water is essential in the acid and base chemistry of an aqueous medium, it is feasible to have alternative families of bases and acids wherein various solvents perform a function equivalent to those of water in the absence of water. The liquid ammonia setup is the most commonly seen of them. Ammonia is amphiprotic, much like water, and can participate in autoprotolysis:

$2NH_3^- \rightarrow NH_2^- + NH_4^-$

Every acid that is stronger as compared to the ammonium ion is classified as "strong" (completely dissociated), and the ion of amide is classified as the strongest base in liquid ammonia (Kiliç and Aslan, 2005).

Solvent	Kautoprot.	Formula	Conj. Base	Conj. Acid
Methanol	10–16.7	CH_3OH	CH_3O^-	$CH_3OH_2^+$
Ammonia	10–33	NH_3	NH_2^-	NH_4^+
Sulfuric acid	10–3.8	$SO(OH)_3$	$SO_2(OH)^{2-}$	$S(OH)_4^+$
Formic acid	10–6	HCOOH	$HCOO^-$	$HC(OH)_2^+$

Likewise, purified liquid sulfuric acid has a little proclivity to receive a proton:

$SO(OH)_3 + H^+ \rightarrow S(OH)^+_4$

Because H_2SO_4 is a significantly weak base as compared to water, although strong acids like hydrochloric acid and HNO_3 are completely ionized in water and thus appeared to be equally powerful, they are only partly ionized in liquid sulfuric acid, wherein Hydrochloric acid is 100 times more powerful than HNO_3.

1.9. CLASSIFICATION OF ACIDS AND BASES

You would have noted that not each chemical containing hydrogen atoms is acidic; NH_3 is a base, for instance. Likewise, certain molecules with the –OH group are alkaline, while others are acidic. Recognizing which chemicals would display acidic and alkaline characteristics in an aqueous medium is a critical component of knowing chemistry. Luckily, the majority of typical acids and alkalies fit into a limited amount of very well-known groups, making this task quite straightforward (Pearson, 1966).

1.9.1. Hydrides as Acids and Bases

Technically, the term hydride refers to ionic compounds composed of electropositive metals that make up the hydride ion; H. The term is often used in a wider meaning to refer to any binary compound XHn, where X stands for any element (Table 1.4).

The hydride ion is an excellent proton acceptor:

$H^- + H^+ - \rightarrow H_2$

Table 1.4. Approximate Acid Strengths for Some Binary Hydrogen Compounds

CH_4	10^{-46}	NH_3	10^{-35}	H_2O	10^{-16}	HF	10^{-3}
PH_3	10^{-27}	H_2S	10^{-7}	HCl	10^{7}		
H_2Se	10^{-4}	HBr	10^{9}				
H_2Te	10^{-3}	HI	10^{10}				

The H^- ion can't survive in an aqueous medium as it is a stronger base as compared to H_2O and removes protons from H_2O:

$$H^- + H_2O^- \rightarrow H_2(g) + OH^-(aq)$$

As a result, ionic hydrides are alkaline; molecules like NaH and CaH_2 dissolve in the water to release hydrogen gas, resulting in a basic solution (Balarew and Duhlev, 1984).

The covalent hydrides are acidic, except very weakly. Certainly, such as H_2O and NH_3, have alkaline qualities as well; nevertheless, the alkaline property predominates in ammonia.

Non-metallic hydrides' acidity grows in proportion to the number of protons in the element to which they are linked. As the element M moves from the left side to the right side of the periodic table or down within such a group, the acids MH become more powerful (Table 1.4).

Efforts to describe such tendencies using a single metric, like M's electronegativity, are usually ineffective. The problem is that various factors determine the acid's strength, such as the strength of the M-H bond and the energy expended when the resultant ions become hydrated in solution. It's better to just study the rule at this point (Lu et al., 2020).

We normally conceive of NH_3 as a base instead of acid; it is amphoteric, like H_2O, however, the basic qualities prevail in an aqueous medium. Just a proportion of the NH_3 molecules in water would take protons since ammonia is a weak alkali:

$$NH_3 + H_2O^- \rightarrow NH_4^+(aq) + OH^-(aq) \qquad (6)$$

Ammonium hydroxide is the name given to an aqueous medium of NH_3. That misunderstanding stems from the necessity to presuppose the presence of a material NH_4OH that may ionize regarding Arrhenius' theory to produce the products of Eqn. (6) in pre-Bronsted periods. Though there's no bodily proof for the presence of NH_4OH, the term appears to be permanently inscribed on reagent bottles in the chemistry lab (Carvalho, 1951).

NH_3 generates the amide ion NH_2^- whenever it interacts like an acid.

$NH_3^- \rightarrow NH_2^- + H^+$ (7)

Because NH_3 is a weaker acid, the conjugate base it forms is a powerful acceptor of the proton. Because it has a stronger base as compared to hydroxide ion, and so on, similarly the H^- ion, can't reside in water:

$NH_2^- + H_2O^- \rightarrow NH_3(aq) + OH^-(aq)$ (8)

When solid $NaNH_2$, is mixed with H_2O, it produces a basic solution with a powerful ammonia odor. As a result, ammonia's acidic character may only be manifested in a solvent apart from water.

1.9.2. Hydroxy Compounds Like Acids and Alkaline

The organic acids (covered separately further on) are the biggest classification of acids, with compounds bearing the group –OH being the biggest group of acids. Among the most prevalent bases are also found in M–OH complexes.

The final examination of the comparative strengths of the M–O and O–H bonds determines that a compound of the common class M–O–H would operate like an acid or a basic. If the M–O link is weak, the –OH component of the molecule would keep its uniqueness and behave like a hydroxide ion. The MO– portion of the molecule would stay intact if the O–H bond is weak, and the material would be acidic (Niemelä, 1990).

1.9.3. Metal –OH Compounds

As a rule, if element M is a metal element, the MOH compound would be alkaline. It is worth noting that the strongly electropositive elements of Groups 1 and 2 are unique in that their solid MOH compounds are joining two structures of metal cations as well as the ions of OH^-; therefore, those which solubilize quickly in water form strongly basic solutions; NaOH and KOH, on the other hand, are popular instances of strong alkalies. From the perspective of Brønsted, several "bases" are simply diverse reservoirs of the one powerful base hydroxide ion.

As one progresses through Group 2 of the periodic table, the M-OH compounds have lesser solubility; as a result, a saturated solution of $Ca(OH)_2$ is only moderately basic. It is so difficult to dissolve the OH^- of p-block metal elements as well as transition metals in the water that their solutions are not basic. Nonetheless, because such solids are soluble quickly in an acidic medium to generate salt and water, they are classified as basic in the formal sense (Xu et al., 2018).

1.9.4. –OH Compounds of the Non-metals

Because the electronegative central atom displaces the –ve charge from the hydroxylic oxygen atom in such compounds, which are generally called oxyacids, they have an acidic nature. The total result is that the oxygen becomes somewhat more +ve, allowing the hydrogen to leave the cell as H^+ to leave more easily.

It is important to note that the existence of additional electron gaining groups on the central atom has a significant impact on the strength of an oxyacid compound. The oxygen atom that has formed a double bond is very significant. Excluding the halogen halides, all of the typical strong acids, such as $NO_2(OH)$, $SO_2(OH)$, and $PO(OH)_3$, include several of these oxygens. Generally, the strength of such acids is determined by the number of oxygen atoms present rather than by any other factor, therefore periodic patterns are not particularly significant. As it occurs, Cl is the only halogen by which all 4 oxyacids have been identified, and the K_a values for such a series demonstrate how significantly the Cl–O oxygen atoms influence the strength of the acid (Yang et al., 2007).

Acid	Formula	K_a Value
Hypochlorous acid	ClOH	10–7.2
Chlorous acid	ClO(OH)	0.011
Chloric acid	$ClO_2(OH)$	10
Perchloric acid	$ClO_3(OH)$	≈ 1,010

1.9.5. Organic Acids

The carboxyl group –CO(OH) is the organic acids' distinctive functional group. The carboxylic hydrogen atoms acidity is nearly completely owing to the withdrawal of electrons by the non-hydroxylic oxygen atom; if it weren't, we'd contain alcohol –COH, which has acidity still low as compared to the water. This partial electron removal through a single atom might affect not just the atom next to it, as well as the atom next to it. As a result, the bonding environment of the carbon atom with that it is attached would impact the strength of a carboxylic acid. The inductive effect is a very significant concept in organic chemistry because it propagates partial electron removal to multiple nearby atoms. Contrasting the acetic acid strength and the increasingly more strongly substituted chloroacetic acids provides a nice illustration of the inductive effect induced by chlorine (a very powerful electronegative atom) (Jones, 1998):

Acid	Formula	Strength
Acetic acid	CH_3–COOH	1.8×10^{-5}
Monochloroacetic acid	$ClCH_2$–COOH	0.0014
Dichloroacetic acid	Cl_2CH–COOH	0.055
Trichloroacetic acid	Cl_3–COOH	0.63

- **Phenols:** The increased acidity of the –OH group as impacted through the 2nd atom of the oxygen which composes the –COOH group results in the carboxyl group's acidic nature. Because the benzene ring has a comparable but lesser withdrawing of electron function, hydroxyl groups connected to benzene rings behave as acids too. Phenol, C_6H_5OH, is a very well instance of an acid. Phenolic acids are weaker in comparison to carboxylic acids (Ricke, 2003):

Acid	Formula	Strength
Acetic acid	CH_3–COOH	1.8×10^{-5}
Benzoic acid	C_6H_5–COOH	6.3×10^{-5}
Phenol	C_6H_5OH	1.1×10^{-10}

1.9.6. Organic Bases and Amines

Given that we contain just examined organic acids, maybe a brief mention of organic bases are in order. Because the –OH group is acidic instead of basic when attached to carbon, alcohols aren't analogs of inorganic hydroxy compounds. Amines are a very abundant class of organic alkalies. They are composed of the $–NH_2$ group coupled to a carbon atom. In water, amines form weak alkaline solutions:

$$CH_3NH_2 + H_2O^- \rightarrow CH \quad 2NH_3 + OH^-(aq) \qquad (9)$$

Amines are the byproducts of microorganisms degrading nitrogenous organic compounds like proteins. They frequently smell strong like "rotten fish." This is not coincidental, since seafood includes a high concentration of nitrogen-containing chemicals that degrade rapidly. Methylamine, CH_3NH_2, is particularly suitable to make itself known to humans since it is a gas at room temperature. When lemon juice or another acidic material is added to fish, the methylamine is converted to the methylammonium ion $CH_3NH^+_3$. Since ions are non-volatile, they contain no fragrance (Greenberg, 1966).

1.9.7. Oxides as Acids and Bases

The separation of oxygen compounds into acidic and basic oxygen compounds is broadly analogous to the divide of –OH compounds. The compounds of oxygen of the Groups 1–2 highly electropositive metals have the O^{2-} ion. Such ion is another example of a proton acceptor which is strong as compared to OH^- and hence can't reside in water. As a result, ionic oxides tend to produce extremely basic solutions:

$$O_2^- + H_2O^- \rightarrow 2OH^-(aq) \quad (10)$$

In other circumstances, like MgO, the solid is sufficiently insoluble that it causes a minimal change in pH when added to water. Furthermore, CaO, often referred to as *quicklime*, is enough soluble to create a highly alkaline solution when adequate heat is generated; the result is the somewhat dissolvable *slaked lime*, $Ca(OH)_2$ (Pearson and Songstad, 1967).

Transition metal-oxygen compounds are often insoluble solids with relatively complicated comprehensive lattices. While certain would soluble in acids, they are not acidic when dissolved in H_2O.

1.9.8. Acid Anhydrides

When the binary oxygen compounds of the non-metallic elements are introduced to water, they tend to form acidic solutions. Acid anhydrides are compounds like SO_3, CO_2, and P_4O_6 that are occasionally used to describe a group of compounds (acids having no water).

$$SO_3 + H_2O^- \rightarrow H_2SO_4 \quad (11)$$

$$P_4O_{10} + 6H_2O^- \rightarrow 4H_3PO_4 \quad (12)$$

$$CO_2 + H_2O^- \rightarrow H_2CO_3 \quad (13)$$

In certain circumstances, the reaction entails more than the incorporation of water's constituents. Consequently, NO_2, which is utilized in the commercial manufacture of NH_3, is not strictly an anhydride:

$$3NO_2 + H_2O \rightarrow 2HNO_3 + NO \quad (14)$$

1.9.9. Amphoteric Oxides and Hydroxides

The hydroxides and oxides of Group 3 and above metals are typically very mildly basic, and the majority is amphoteric. The majority of such compounds are so water-insoluble that their acidity or alkalinity properties become apparent only when they react with strong acids or alkalies.

By and large, such compounds are more basic as compared to acidic; for example, the hydroxides and oxides of iron, aluminum, and zinc are all soluble in concentrated acid (Pearson, 1963):

$Al(OH)_3 + 3H^+ \longrightarrow Al^{3+}(aq) + 3H_2O$ (15)

$Zn(OH)_2 + 3H^+ \longrightarrow Zn^{2+}(aq) + 2H_2O$ (16)

$ZnO + 2H^+ \longrightarrow Zn^{2+}(aq) + 2H_2O$ (17)

$FeO(OH) + 3H^+ \longrightarrow Fe^{3+}(aq) + 3H_2O$ (18)

Furthermore, in concentrated OH^- solutions, such compounds create anionic species that are the oxide or hydroxide's conjugate bases:

$Al(OH)_3(s) + OH^- \longrightarrow Al(OH)^-_3\,(aq)$ (19)

$Zn(OH)_2(s) + 2OH^- \longrightarrow Zn(OH)_4^{3-}(aq) + 2H_2O$ (20)

$Fe_2O_3(s) + 3OH^- \longrightarrow 2FeO_4^{2+}(aq) + 3H_2O$ (21)

These are referred to as the ferrate, aluminate, and zincate ion. Additional products are generated in which just a portion of the –OH groups of the parent OH^- are deprotonated, resulting in a sequence of such oxyanions for the majority of metals.

1.9.10. Salts

In distilled water, sodium chloride is completely neutral because the chloride ion, being the conjugate base of a very strong acid, is a very weak proton acceptor. When a specific amount of sodium acetate $CH_3COO^-\ Na^+$ is solubilized in water, the solution turns basic. Because HF and CH_3COOH are both weak acids, their conjugate bases $F^-(aq)$ and $CH_3COO^-(aq)$ would be good proton acceptors (Pearson, 1987).

At the very least, they are powerful enough to behave as weak bases in H_2O:

$F^-(aq) + H_2O \longrightarrow HF(aq) + OH^-$ (22)

$CH_3COO^- + H_2O \longrightarrow CH_3COOH + OH^-$ (23)

Consequently, the rule (that you should be familiar with) states that a water solution of a salt of a weak acid would be basic. This activity is occasionally referred to as hydrolysis, a throwback to a time when the notion of proton transfer acid-base reactions gained acceptance.

When the salt has the ammonium ion as its cation, hydrolysis would result in an acidic solution when no weak-acid anions are present to counteract the effect. Therefore, an ammonium sulfate solution would be acidic (Hundelshausen, 1971):

$NH_4(aq) + H_2O^- \rightarrow NH_3(aq) + H_3O^+(aq)$ (24)

1.9.11. Metal Cations

Iron(III) chloride is a bright orange solid that soluble readily in water to form a highly acidic solution. How is that possible? Because neither the Cl^- nor the Fe^{3+} ions possess protons, how are they able to give protons to H_2O to form H_3O^+?

The protons originate from the water molecules in the metal cation's main hydration shell. These are the water molecules, typically 6 in number, which is most closely connected to the cation via ion-dipole attraction. If the cation has a charge of +2 or more, the electric field intensity near the hydration shell's edge is sufficient to encourage the release of a hydrogen ion from one of the H_2O molecules (Duhlev et al., 1991):

$Fe(H_2O)_6^{3+} + H_2O \; Fe(H_2O)_5(OH)^{2+} + H_3O^+$ (25)

A solution of $FeCl_3$ is a stronger acid as compared to an equimolar solution of acetic acid as a result of this reaction. A $FeCl_2$ solution, on the other hand, would be a lot weaker acid; the +2 charge would be much lesser helpful in reducing proton loss. Alkali metals and ions like $Ag^+(aq)$ have very little acidity; in general, the smaller and more strongly charged the cation, the more acidic it is.

Ion	In^{3+}	Bi^{3+}	Fe^{3+}	Sn^{2+}	Fe^{2+}	Cu^{2+}	Mg^{2+}
Acid Constant	0.6	0.01	0.007	1E–4	5E–9	5E–9	1.6E–13

A hydrated cation must be capable of losing more than one proton. An $Al(H_2O)3+6$ ion, for instance, must produce the following species in order:

$AlOH(H_2O)_5^{2+} \rightarrow Al(OH)_2(H_2O)_4^+ \rightarrow Al(OH)_3(H_2O)_3^0 \rightarrow Al(OH)_4(H_2O)^{2-} - \rightarrow Al(OH)_5(H_2O)^{2-} - \rightarrow Al(OH)_6^{3-}$

Furthermore, when the charge declines from a high +ve to a –ve value, the elimination of protons becomes more difficult; the final three species have not been observed in solution. The main species in dilute aluminum chloride solutions are Al^{3+} and $AlOH^{2+}$ (such as $Al(H_2O)^{3+}_6$ and $AlOH(H_2O)^{2+}_5$).

The issue is compounded in highly concentrated solutions by processes in which two or more hydroxylations polymerize form multi-center complexes. In concentrated aluminum ion solutions, for instance, the two aluminum species stated above are mostly $Al_4(OH)^{2+}_{10}$ and $Al_6(OH)^{3+}_{15}$. Likewise, the major ions in bismuth salt solutions are $BiOH^{2+}$, Bi^{3+}, and $Bi_6(OH)^{6+}_{12}$; $Bi(OH)^+_2$ is not present (Brown and Duhlev, 1991).

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CHAPTER 2

ACID-BASE PROPERTIES OF SURFACES

CONTENTS

2.1. INTRODUCTION

This chapter describes a few experimental approaches for assessing the acid-base characteristics of solid surfaces, with a concentration about description of smooth surfaces, that is documented in less quality as compared to those particles. Because a surface is composed of many chemical species, their acidobasicity is determined by the accessibility, density, and strength of the individual places. As a result, it varies depending on the measuring method utilized. In practice, the technique of choosing is frequently determined by the intended scale of description (local or general).

2.2. GENERAL METHODS

2.2.1. Wettability

Due to the ease with which the wettability technique may be implemented and the huge body of literature devoted to this since Young's study in 1805, it is the most often utilized methodology in a variety of areas. Only one or more than one liquid sessile drop technique is used to conduct measurements on a flat substrate. Both procedures may be used to find the adhesion work and, in removing the dispersive component, to get the amount of the acid-base component. The single liquid approach is optimal for materials with less energy of surface (polymers), whereas the two liquid way is optimal for solids along a large energy of surface (metals, oxides, etc.). The reader may relate to these two methodologies, as well as the ideas upon which they are built. While molecular groups on the surface of a solid may be ionized (e.g., hydrated groups Me-OH on the surface of a metal), a mixture of electrocapillarity and wettability techniques could be utilized in order for the evaluation of a surface's acid-base nature.

2.2.2. Electrokinetic Method

Electrokinetic measurements provide information on the charged solution/particle interface features. This technique was originally established for the solid oxide particles and was later extended to the flat surfaces.

2.2.2.1. Double Electrochemical Layer

When a flat surface or particle or is submerged in a fluid, it gets an induced surface charge as a result of ionization or ionic adsorption of the charged groups on a surface. Due to which counter ions collect towards the surface,

forming a "double electric layer" contact between both the liquid and solid. Helmholtz proposed modeling this double layer in 1853 using a condenser for whom the capacity is completely determined by the electrolyte's dielectric constant and the width of the double-layer (Helmholtz, 1853) (see Figure 2.1). Thus, the potential inside this layer changes proportional to the charged surface's zero value Ψ_0 to the electrolyte's zero value (Figure 2.1).

Chapman expanded on this model in 1913 (Chapman, 1913), by incorporating a charge distribution inside of diffuse layer (double layer). As a result, the capacity inside this layer ranges proportional to Ψ_0 to zero (Figure 2.2). The Debye length is indeed a thickness of the diffuse layer.

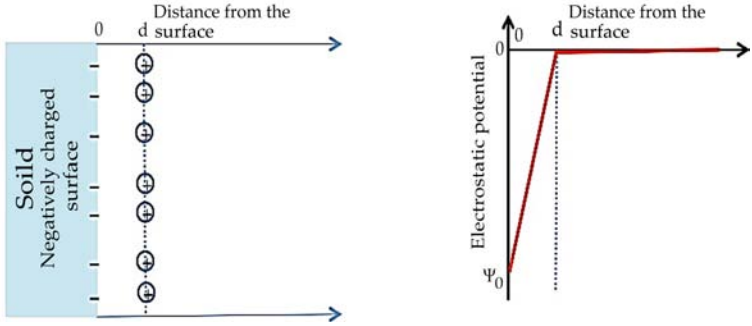

Figure 2.1. With a potential of Ψ_0 and an electrolyte solution, Helmholtz model of interface among negative charged surface.

Source: https://onlinelibrary.wiley.com/doi/book/10.1002/9781119145387.

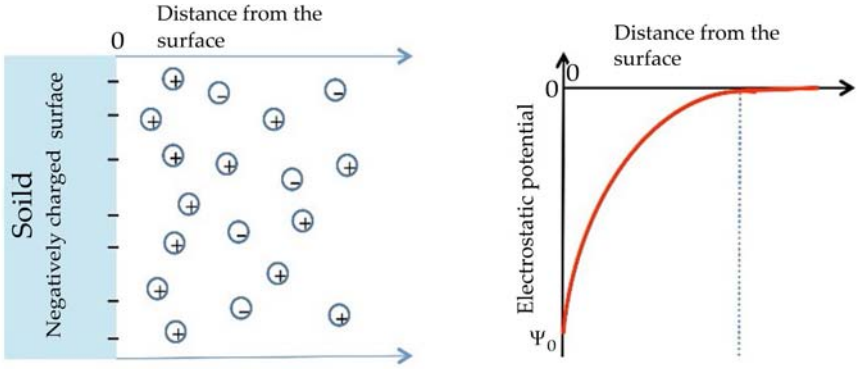

Figure 2.2. The Gouy–Chapman model of the interface among a negative charged surface with a potential Ψ_0 and an electrolyte solution.

Source: https://www.sciencedirect.com/topics/engineering/helmholtz-layer.

According to the Chapman model, ions are distinct points, and the solvent is a dielectric continuum. In order to consider for the ions' finite size, the solid–electrolyte interface be divided into two sections: (a) compact layer devoid of ions; (d) with a thickness equal to ions' least approach distance and modeled by a condenser of constant capacity C, and a diffuse layer with identical features to the Chapman layer (see Figure 2.3). A stern plane is a plane that separates a dense layer from a diffuse layer. Thus, the potential differs linearly from Ψ_0 to Ψ_d, as well as afterwards exponentially to zero.

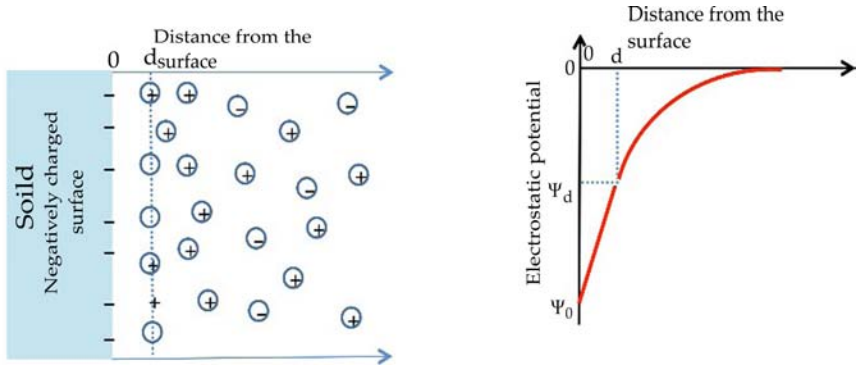

Figure 2.3. Stern interface model among a negative charged surface with a potential of Ψ_0 and an electrolyte solution.

Source: https://www.mdpi.com/1424-8220/19/15/3425/htm.

The Stern model analyzes just Coulomb interactions and ignores the chemical affinity that a few ions may have for surface sites. In 1947 Grahame proposed that the Stern layer be divided into two sublayers to account for these unique adsorption processes (Grahame, 1947). Three layers are obtained as a result of this procedure (Figure 2.4). The primary layer, which is in touch with a surface, includes ions that have been specially adsorbed. It can be compared to a continual capacity condenser Ci. Another layer is composed of hydrated ions and it could be absorbed into a second condenser of constant capacity Ce. The diffuse layer is represented by the third layer. The primary and secondary layers are divided by the inner Helmholtz plane (IHP), whereas a third as well as fourth layers are distinguished by outer Helmholtz plane (OHP), which is comparable to the Stern plane in prior model. Thus, the potential typically differs across Ψ_0 and Ψ_i then exponentially among Ψ_i and Ψ_d, and eventually to zero.

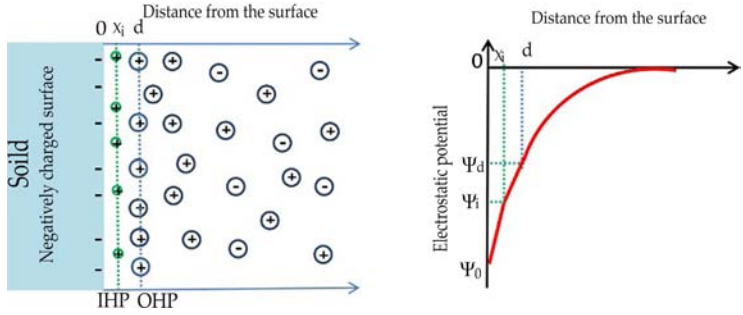

Figure 2.4. Grahame's interface concept among a negatively charged surface with a potential of Ψ_0 and an electrolyte surface.

Source: https://onlinelibrary.wiley.com/doi/book/10.1002/9781119145387.

2.2.2.2. Zeta Potential – Point of Zero Charge (PZC)

When an electric field is applied to a suspension of charged particles, it causes them to move. Ions that have an exact affinity for the particle's surface migrate with the particle within the double layer, while the other ions flow back from the surface. The hydrodynamic shear plane, which would be typically quite near to the OHP, is formed by these changes in behavior. The potential Ψ in this plane is identical to the electrokinetic potential or potential ς (zeta). Its value is determined by the ion concentration, which determines the solution potential. The point of zero charge (PZC), or the value where the electrical surface charge is zero, is defined by an intensity at where it cancels itself out.

2.2.2.3. Measurement of the Streaming Potential

To evaluate the potential ς and, particularly, the PZC or the IEP, electrokinetic techniques can be applied. These approaches, which were originally devised to research oxide powders, are now routinely applied to investigate colloids and biological cells. Electrophoresis, which would be the measurement of particle displacement speed beneath the effect of an electric field, is the most extensively used approach. A current review published paper beneath the guidelines of the IUPAC (International Union of Pure and Applied Chemistry) (Delgado et al., 2007) can be consulted by anybody concerned about the theory and execution of these methods to find the electrical characteristics of particle–liquid interfaces. We will solely discuss the application of these measurements to flat surfaces in this book.

The determination of the streaming potential is used to determine the PZC of flat surfaces. The graphic in Figure 2.5 depicts the idea.

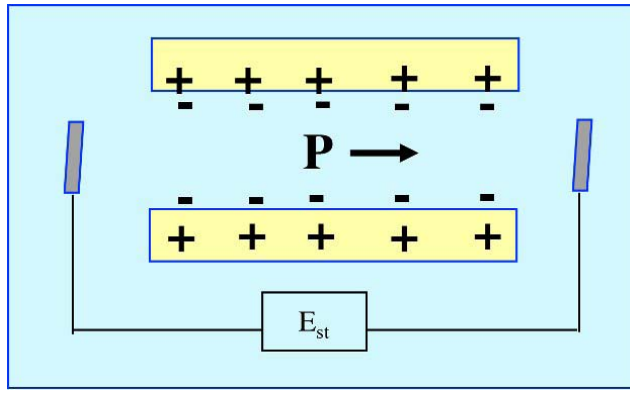

Figure 2.5. The principle of calculating the streaming potential E.

Source: https://www.researchgate.net/figure/Principle-of-streaming-potential-measurements-in-the-SurPASS-elctrokinetic-analyzer_fig13_41463463.

In an electrolytic cell, two plates formed of the solid being investigated are arranged parallel to each other, with surfaces to be described facing each other. The electrolyte solution is carried parallel to the plates through a cell under the influence of a pressure difference P in the range of 10–500 mbar. The solution's moveable charges, particularly those who are on Gouy surface, are referred to as counter-charges; they are displaced by the streaming among the plates, while the solution's core charges do not generate any current (electroneutrality). The addition of those counter-charges results in a stream or convection current, as well as a differential in potential 'E' at the plates' edges, dubbed the streaming potential. Due to the conductivity of the liquid, a conduction current emerges in the opposite direction of the previous current. In equilibrium, these two currents are comparable. The creation of a relative speed as a result of counter-charge movement creates a shear plane or hydrodynamic breach in the double electric layer, where the streaming remains stationary and the potential ζ. remains constant. The following equation establishes a relationship between the streaming potential E and the potential ζ:

$$\zeta = \frac{\eta}{\varepsilon\varepsilon_0}\left(\lambda_{sol} + \frac{L_{surf}}{b}\right)\frac{E}{P} \qquad (1)$$

where; the viscosity, absolute, and relative permittivity, and conductance of the solution are represented by η, ε, ε_0, and λ_{sol}, respectively. L_{surf} denotes the surface's specific conductance, b the half-distance in among plates, E the potential difference at the plates' edges, and P the applied pressure.

It is feasible to produce conditions such that L_{surf}/b is insignificant when compared to λ_{sol} by making an appropriate choice of solution properties. As a result, Eqn. (1) may be reduced to:

$$\zeta = \frac{\eta}{\varepsilon\varepsilon_0}\lambda_{sol}\frac{E}{P} \qquad (2)$$

In practice, the streaming potential is frequently determined by the flow direction. Compute the potential ζ by adjusting the pressure P in the two flow path as well as using the slope E/P attained via linear regression. Helmholtz–SmoluchoWski equation is used to calculate the potential:

$$\zeta = \frac{\eta}{\varepsilon\varepsilon_0}\lambda_{sol}\frac{\Delta E}{\Delta P} \qquad (3)$$

It's worth noting that this connection only applies to laminar and stationary flows. It is thus feasible to create the curve ζ=f(pH) by determining ζ for numerous parameters of the solution pH. The convergence of that curve with the origin of the ordinates axis (ζ =0) yields the PZC or IEP value.

In a trial setting, quantities are obtained with a zeta-meter, the principle of that is depicted in Figure 2.6.

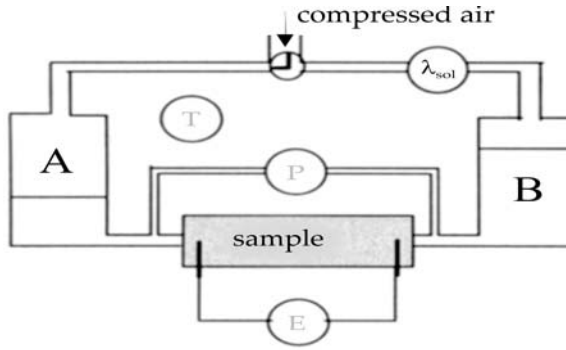

Figure 2.6. Diagram showing the principle of a zeta-meter (based on (CHE 02)).

Source: https://www.theses.fr/2002PA112172.

Figure 2.7, adapted on the Boulangé-Petermann et al. (1995) study, shows in what way the IEP of an AISI 304 steel surface calculates. An annealing treatment in a hydrogen-rich environment was performed on this surface previously (bright annealed).

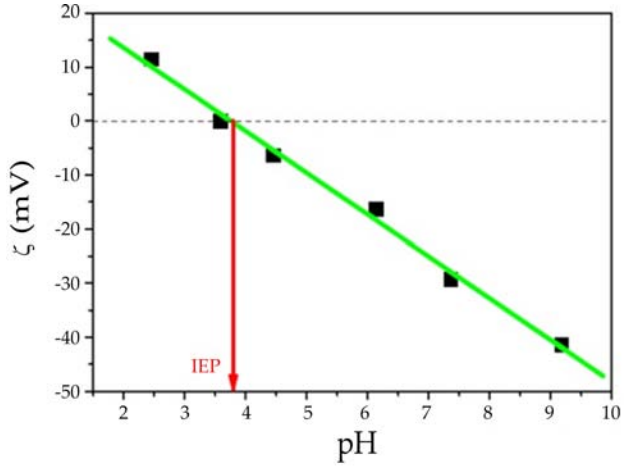

Figure 2.7. In what way is the IEP of an AISI 304 steel sheet that has been bright annealed calculated. In a 0.01 M NaCl solution, measurements were taken (Boulangé-Petermann et al., 1995).

Source: https://www.sciencedirect.com/science/article/abs/pii/S0021979785711654.

2.2.3. Scanning Probe Microscopies

2.2.3.1. Atomic Force Microscopy (AFM)

The analysis of interactions among a nanometric tip and the surface of a model is a basis for atomic force microscopy (AFM), which was first invented through Binnig et al. (1985) to produce topographic pictures of surfaces. The graphic in Figure 2.8(a) depicts the method's premise. The tip is attached to the elastic cantilever and the model is placed on a piezoelectric tripod that allows for XYZ movement. An attractive or repulsive force among the tip and the surface generates a deflection of the lever d proportionate to a force of contact, that may be measured by means of a mechanism connecting the reflection of the laser beam upon a backside of a cantilever to the four-quadrant photodiode detector.

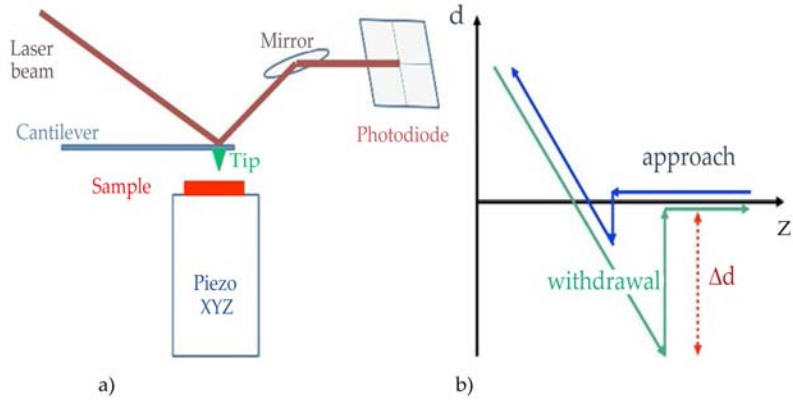

Figure 2.8. *(*a) AFM fundamental shown in diagram; (b) fundamentals for measurement of force of adhesion utilizing force-distance curves.

Source: https://www.researchgate.net/figure/AFM-diagram-left-and-the-principle-of-force-distance-curve-measurement-right_fig4_298641652.

The adhesion force among the probe as well as the surface may also be measured using this instrument. While the sample is placed closer to (approach stage) and subsequently moved back from (withdrawal phase) the tip, changes of the deflection d of the lever are evaluated as a function of the distance z among the sample and the tip, whereas x and y stay stationary. The curve produced is depicted in Figure 2.8(b).

The force of adhesion, as a first approximation, relates to a withdrawal force and may be stated as follows:

$$F = k.\,\Delta d \qquad (4)$$

where; k is a cantilever's stiffness coefficient.

If k doesn't change (utilizing the same measurement device), the acid-base properties of q surface can be determined by a measurement of variants in a force of interaction among the tip and the surface submerged in an electrolyte solution with factor pH, as suggested by Lin et al. (1993). This method is depended on Derjaguin–Landau–Verwey–Overbeek (DLVO) theory, that gives the idea of the interaction Fdl among a sphere of radius R at a distance d from a surface deep in an aquatic electrolyte solution (Israelachvili and Berman, 1995):

$$F_{dl} / R = 4 \Pi \varepsilon \varepsilon_0 \phi_1 \phi_2 e^{-d/\lambda} / \lambda \qquad (5)$$

where; Φ_1 and Φ_2 are the surface potential of a sphere and plane, correspondingly, and λ is the length of electrolyte's Debye, and ε and ε_0 are the relative permittivity of the electrolyte and the vacuum absolute permittivity.

When Φ_1 and Φ_2 have the same or opposite signs, the sign of F_{dl} is derived from the sign of the product $\Phi_1\Phi_2$ and relates to repulsive or attractive interactions. As a result, the isoelectric point is where the sign changes.

Lin et al. (1993) demonstrated that the IEPs of a tip and the flat surface (IEP1 and IEP2) could be derived from the fluctuations of F_{dl} with the pH of the electrolyte by the measurement of the forces of contact among a flat surface and a tip-in electrolytes of varied pH for a static distance 'd' (Figure 2.9).

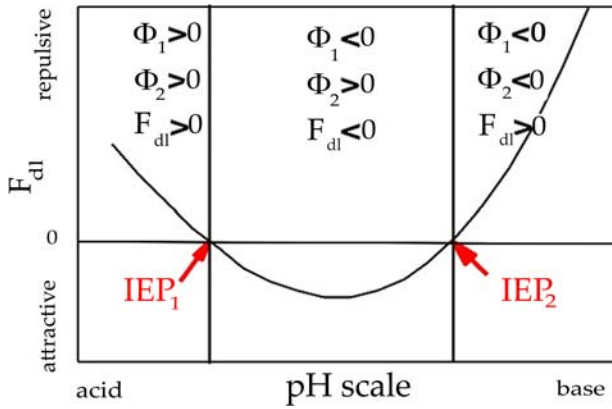

Figure 2.9. Evaluating the isoelectric points among a tip (IEP1) as well qs the plane surface (IEP2) (extracted from: Lin et al., 1993).

Source: https://pubs.acs.org/doi/abs/10.1021/j100130a025.

Dubois and Joud used a similar method to determine the isoelectric point of passive films grown upon polished chromium specimen submerged in water, that is calculated for the value of pH related to the change in the symbol of F (IEP = 8.1 in the case shown in Figure 2.10) (Dubois, 2000).

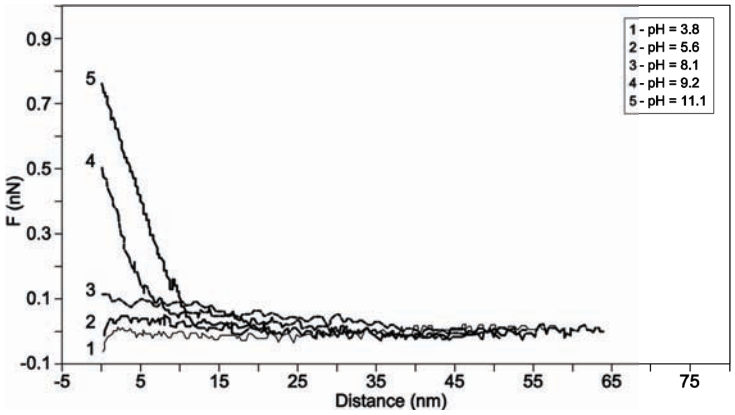

Figure 2.10. Force-distance curves gained on oxidized chromium surfaces by means of a silicon tip covered with SiO_2.

Source: https://www.researchgate.net/publication/283563750_Influence_of_Alkali_Ions_on_Tribological_Properties_of_Silicon_Surface.

2.2.3.2. Interfacial Force Microscopy (IFM)

Joyce and Houston (1991) developed interfacial force microscopy (IFM) to eliminate the mechanical instability associated with AFM measurements at the time of the approaches or withdrawals of the cantilever.

This mechanism (see Figure 2.11) secures the sample to the piezoelectric tripod that allows for XYZ movement. The tip is attached to torsion bars through a coefficient of infinite stiffness (zero compliance) support. Whenever the model is placed in adjacent proximity to a tip, a repulsive or else attracting force among the model and the tip spins the solid support along a torsion bar axis. Torsion is compensated to providing a direct current to two capacity C_1 and C_2 positioned beneath either side of the torsion axis support. Thus, the magnitude of the voltage required to re-establish equilibrium gives the direct measure of the interfacial force. When the model is placed closer to (arriving curve) or removed from the tip(withdrawal curve), force-displacement curves can be generated. This sort of instrument is capable of measuring forces in an order of 10–50 μN along a precision of greater than 1 nN and lateral displacement resolution of a range of 1. As a result, this method may be utilized to notice both weak (van der Waals) and strong interactions (for example, acid-base connections) at the molecular level.

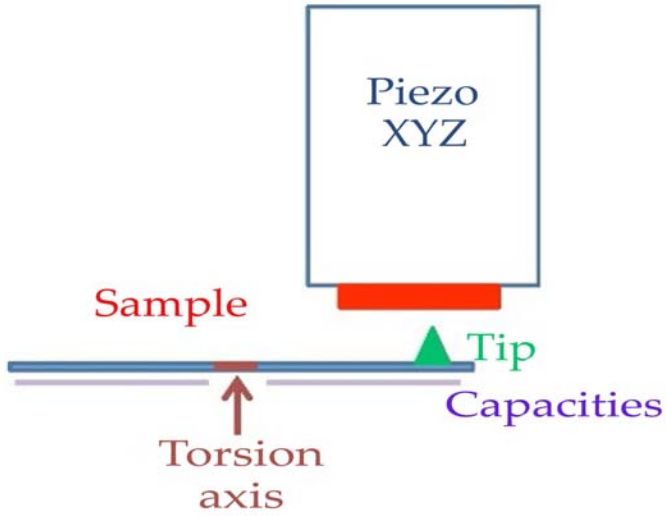

Figure 2.11. Schematic illustration of an operation of the interfacial force microscope.

Source: https://www.researchgate.net/figure/Schematic-drawing-of-the-atomic-force-microscope_fig1_326721617.

The adhesion work W_A among the tip and the sample surface is provided by the following equation:

$$W_A = \frac{-L_c}{\pi CR} \quad (6)$$

where; L_c denotes a serious charge (as well as the highest attraction force on to the withdrawal); R denotes the tip radius (as a parabola); and C denotes a constant that varies according to the model chosen (C = 3/2 in the Johnson, Kendall, and Roberts model (JKR; Johnson et al., 1971), and C = 2 in the Derjaguin, Muller, and Toporov model (Derjaguin et al., 1975).

Figure 2.12 shows a case of a force (normalized to the diameter of the tip) displacement plot during arrival (unfilled circles) or withdrawal (crosses) among a sample and a gold-coated tip functionalized with COOH-terminal thiols or NH_2-terminal thiols, correspondingly. The work of adhesion estimated from these curves is W_A = 90,783 mJ/m^2 and is mostly attributable to hydrogen bonding by the authors.

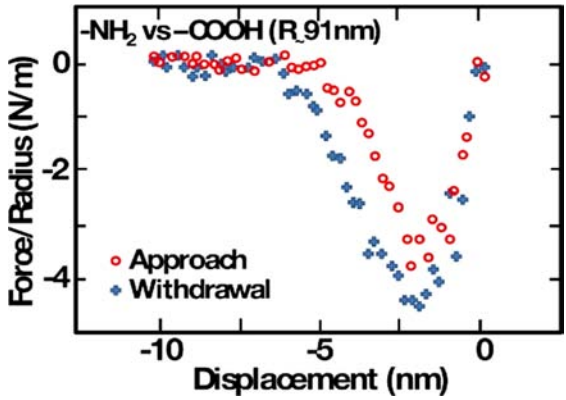

Figure 2.12. Force displacement plots (normalized to the tip radius) comparing a sample functionalized with thiol alkanes with COOH terminal groups and a tip functionalized with a layer of NH_2-terminal thiols.

Source: https://pubs.acs.org/doi/pdf/10.1021/ja00118a019.

2.2.4. Inverse Gas Chromatography at Infinite Dilution Conditions

IGC-ID (inverse gas chromatography at infinite dilution) could be utilized to analyze polar and dispersive interactions among a solid material and molecular probes, which are model chemical compounds (or adsorbable or solute molecules). It's mostly utilized to describe separated solids, nonetheless similarly, it may be used to describe fibers. Figure 2.13(a) shows the solid being placed into a chromatographic column. Gaseous probe molecules are inserted inside the column on extremely small amounts using a carrier gas, obviating the requirement to account probe–probe interactions. The chromatogram (Figure 2.13(b)) is defined by the amount of molecules removed from the column like the function of the time every probe needs to pass the column (retention time). Each probe has a unique retention duration that is determined by its affinity for the solid surface, resulting in a distinct signal in the detector. Alkanes (to detect dispersive reactions) and polar molecules (to find polar reactions) are examples of molecules with well-defined characteristics (to find acido-basicity). The fluctuation in energy of free adsorption among the molecule as well as the solid, that is linked to the adhesion energy, may be calculated using thermodynamic rules.

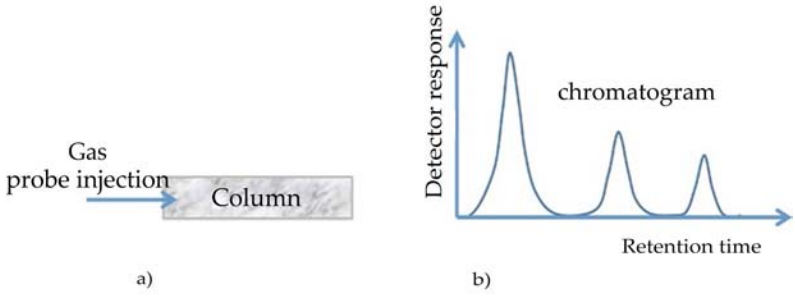

Figure 2.13. The principle of chromatography of inverse gas.

Source: https://www.semanticscholar.org/paper/A-Review-of-Inverse-Gas-Chromatography-and-its-as-a-Ho-Heng/30e1085b1b1f270c9bb686244d242fc2379cea45.

The surface energy-dispersive element, γ_S^d, may be computed utilizing linear alkanes, but the particular elements, γ_S^{sp}, and acid and basic constants, K_A, and K_D, can be calculated using acid or base molecules.

In infinite dilution circumstances, the following relation provides the retention's net volume of Vn (i.e., the volume of carrier gas necessary to allow the probe molecule to transit a column, adjusted for dead volume, and it is the volume of column's volume not taken by the solid):

$$V_n = K.s \quad (7)$$

wherein; K is the Henry constant (also called the partition constant) and s is the probe's accessible surface (which represents the partition of probe molecules between the adsorbed and gaseous phases).

The net volume of retention Vn is proportional to the change in the free enthalpy of adsorption ΔG_a related to the transition of the molecule from a gas to an adsorbed state:

$$-\Delta G_a = RT \ln V_n + C \quad (8)$$

wherein; R is an ideal gas constant; T is a temperature in Kelvin; and C is a constant that based upon adsorbed probe's reference state.

Furthermore, given that the dispersive and particular interactions are both present, G_a may be stated as follows:

$$\Delta G_a = \Delta G_a^d + \Delta G_a^{sp} \quad (9)$$

Subtracting the dispersive component G_a^d (found with non-polar probes) from the overall value G_a^{sp} may therefore be used to derive the particular

component ΔG_a (found with polar probes). The acid-base interactions dominate the particular interactions, allowing for a characterization of the solid's acid-base characteristics.

Dorris and Gray demonstrated that the adsorption's free enthalpy changes linearly with a number of carbon atoms n in the probe when linear alkane molecules are injected (n-alkanes) (DOR 80). This linear performance may extend to additional chemical descriptors (for example, the injected probe's vapor pressure), yielding a "n-alkanes reference line." The points belonging to polar probes that contact more strongly with a polar surface, are situated above the n-alkanes reference line in the line displaying ΔG_a as a function of this chemical descriptor. The difference is due to the contribution of particular connections to free enthalpy variation ΔG_a^{sp} (Figure 2.14).

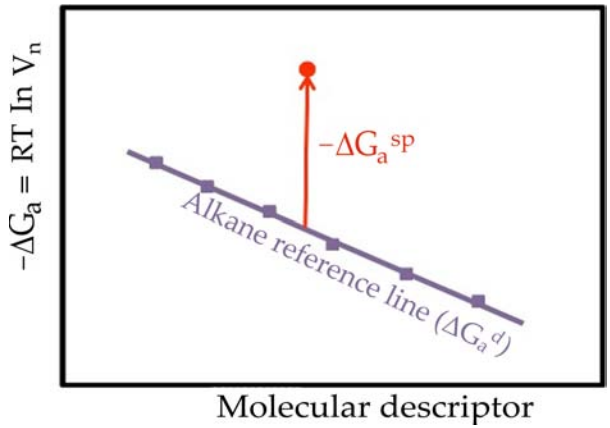

Figure 2.14. Determining the particular component gasp of the free enthalpy of adsorption.

Source: https://onlinelibrary.wiley.com/doi/10.1002/9781119145387.ch6.

The polar probe is integrated to the molecule that will interchange a similar dispersive connection as an alkane along the similar chemical description in this representation. As a result, the value of ΔG_a^{sp} is determined by the chemical description used to establish the comparison scale. Several hypotheses have been presented to describe such hypothetical molecule. This book just gives a basic description of them. Brendlé and Papirer's review paper (Brendlé and Papirer, 1997) is a good place to start for anybody interested in this topic.

The primary two models offered are depended on variables that reproduce the probe molecules' intermolecular connections in a liquid state. Saint-Flour and Papirer (1983) suggested the first in 1983. The logarithm of the probe molecules' saturation vapor pressures at the column's temperature, $\log P^0$, is used to describe them in this model. This is the most often used strategy since P^0 values are widely obtainable from the literature. For materials with high surface energy, however, it creates a variety of issues. Schultz et al. (1987) then proposed utilizing the product $a(\gamma_1^d)^{1/2}$, where a is the area of the adsorbed molecule and γ_1^d is the dispersive component of a probe's surface energy in a liquid state, as calculated by means of Fowkes' work of adhesion (Schultz et al., 1987). The key challenge with that approach is calculating the value of a, which is affected by the composition of a substance upon which the molecule is adsorbed as well as the temperature. Furthermore, at the temperatures utilized in IGC, the values of γ_1^d are not always attainable.

The models built after that are dependent on the probes' molecular properties. Dong et al. (1989); and Donnet et al. (1991) recommended utilizing the product $\alpha_0\sqrt{h\nu}$ where α_0 represents the probe's polarizability, *h* Planck's constant, and the probe's electronic frequency characteristic. Regrettably, the values of α_0 are rarely found in the literature.

Eventually, Brendlé and Papirer suggested applying the X_T topological index, which considers the molecule's shape as well as the local electrical density associated with the existence of heteroatoms (Brendlé and Papirer, 1997). The number of carbon atoms in a hypothetical hydrocarbon molecule that will contact with the surface in a same way as the molecule it mimics is represented by this metric. It has the benefit of being directly determined using Wiener indices for both polar and non-polar molecules.

On a molecular scale, it is critical to emphasize that the basic procedures provided above are only relevant for flat and homogenous surfaces. Other models, which are outside the scope of this book, have been created to account for the roughness or heterogeneity of the bulk of solid surfaces. The review study by Balard et al. (2000) is recommended for everyone interested in this topic.

To quantitatively define the acid or basic composition of a solid surface, several methodologies have been proposed. We will just touch on the Gutmann model (1978), and it's the most widely utilized in IGC-ID, in this section.

Mukhopadhyay and Schreiber's review work (Mukhopadhyay et al., 1995) is recommended for anybody interested in this topic.

The Lewis acido-basicity of a solid surface is defined in the Gutmann model (1978) by two parameters K_A and K_D, which reflect the solid's acid and base constants, respectively, and are connected to the donor (DN) and acceptor (AN*) numbers of a probe by a given relation:

$$\Delta H_a^{sp} = K_A\, DN + K_D\, AN^* \quad (10)$$

where; ΔH_a^{sp} denotes the adsorption specific enthalpy, which is connected to ΔG_a^{sp}, the free enthalpy; and ΔS_a^{sp}, the specific entropy, by the following relationship:

$$\Delta G_a^{sp} = \Delta H_a^{sp} - T\,\Delta S_a^{sp} \quad (11)$$

In practice, the slope of the linear plot $\Delta G_a^{sp}/T = f(1/T)$.) is used to determine the value of ΔH_a^{sp}. By analyzing the interactions of probe with the reference base (triethyl phosphine, Et3PO) and a reference acid, the donor DN and acceptor AN* values may be obtained experimentally (antimony pentafluoride, SbCl5).

In the literature, DN, and AN* are readily available. The linear plot $\Delta H_a^{sp}/AN^* = f(DN/AN^*)$ is used to calculate K_A and K_D visually. The slope of the plot is denoted by K_A, while the ordinate at the origin is denoted by K_D.

The given application scenario is based on Reddi Rani et al. (2011) research. Cellulose acetate butyrate (CAB) is a cellulose thermoplastic that is widely used in blister packaging, tool handles, eyeglasses, as well as automobile interior trim.

Figure 2.15(a) presents the $-\Delta G_a$ values obtained at 333.15 K with non-polar n-alkane probes (n = 5–8) and polar probes: dichloromethane (DCM), trichloromethane (TCM), acetone (AC), ethyl acetate (EA), and tetrahydrofuran (THF). Schultz et al. (1987) established the molecular descriptor model that was employed for the scale comparison. As with DCM, the values of ΔG_a^{sp} are calculated.

By considering the slope of the plot $\Delta G_a^{sp}/T = f(1/T)$, same observations in 10 K increments in the temperature of order 333.15–393.15 K helped to calculate ΔH_a^{sp}. The acid constant K_A=0.126 and the base constant K_D = 1.109 calculated from Figure 2.15(b) indicate that the surface has a base character, that the authors ascribe to the CAB's ester groups.

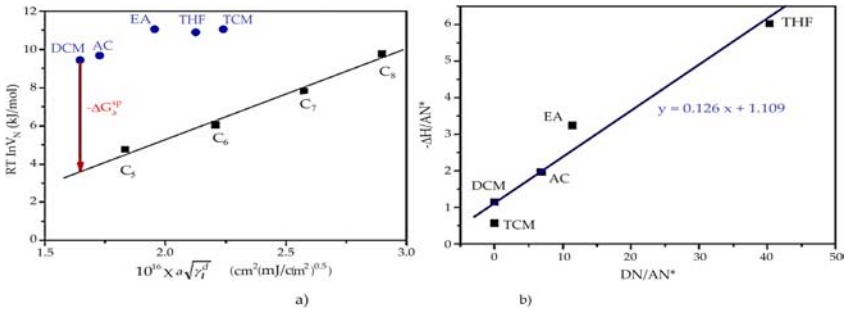

Figure 2.15. (a) Differences in the free enthalpy of adsorption Ga on a cellulose acetate butyrate (CAB) surface (b). The linear plot Hasp/AN = f(DN/AN) yields the values of KA (slope) and KD (ordinate at the origin).

Note: Non-polar (n-alkanes with n = 5 to 8) or polar probes: dichloromethane (DCM); trichloromethane (TCM); acetone (AC); ethyl acetate (EA); and tetrahydrofuran (THF). In the case of the DCM, the value of the particular component of the free energy ***ΔGa*** is show.

Source: https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/abs/10.1002/sia.3514.

2.2.5. X-Ray Photoelectron Spectroscopy (XPS)

2.2.5.1. The Principle of XPS

The photoelectric effect lies at the heart of X-ray photoelectron spectroscopy (XPS), also termed as electron spectroscopy for chemical analysis (ESCA). This technology dates back to the 1960s, when researchers discovered the ability to provide data on the chemical condition of materials.

The connection of a photon X of energy hv with an atom or molecule results in ionization of the atom or molecule and the emission of a photoelectron with kinetic energy $E_K = h - E_1$ from the energy level E_1 (see Figure 2.16). The photon's hole is filled with energy E_2 by an electron from an upper level. The excess energy (E_1–E_2) can be relaxed in two methods: either a photon is emitted with the characteristic energy $h' = E_1–E_2$ (fluorescence phenomenon), or an Auger electron is released from an outer layer (of energy E_3) with the kinetic energy $E_A = E_1 – E_2 – E_3$* (*considering an existence of a hole in the emitting atom).

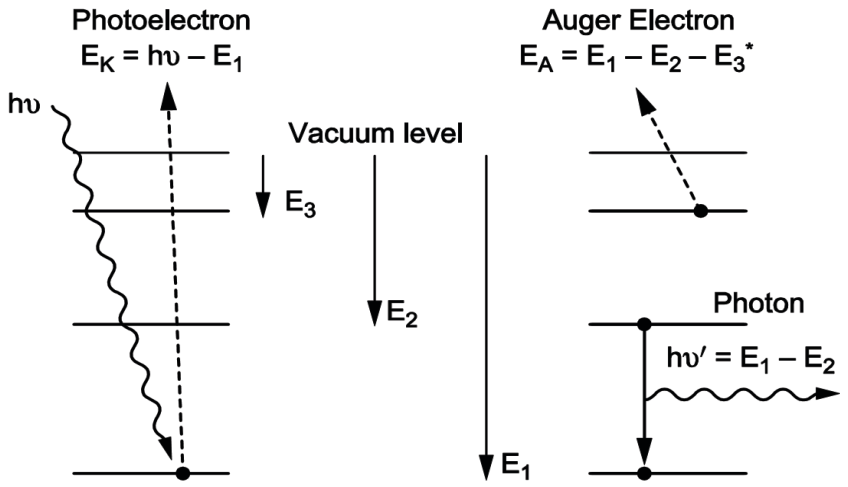

Figure 2.16. Principle of photoemission.

Source: https://www.frontiersin.org/articles/10.3389/fchem.2019.00377/full.

The kinetic energy of a photoelectron is determined exclusively by the energy of an incoming photon h and the binding energy of the expelled electron E1 and is hence distinctive to the emitting element.

The photoelectric transitions are defined by a level from which the photoelectron originates: 1s, 2s, $2p_{1/2}$, $2p_{3/2}$, and so on.

X-ray induced photoelectron spectroscopy (or XPS) depends on the measurement of the energy distribution of electrons released by a surface assaulted with an X-ray beam of energy on the range of keV. As a result, it notices both photoelectrons and Auger electrons. The energy of the photoelectron can be described regarding kinetic energy E_K or binding energy E_B, with those two values connected by the given relation:

$$E_B = h\nu - E_K - \Phi_{sp} \quad (12)$$

where; 'sp' denotes the spectrometer's work function.

Figure 2.17 illustrates a typical XPS spectrum (XPS spectrum of copper). The XPS peaks associated with the most intense core levels (Cu2p and Cu3s) are indexed and look alongside the valence band spectra in the 0–30 eV range and the Auger transitions Cu LMM.

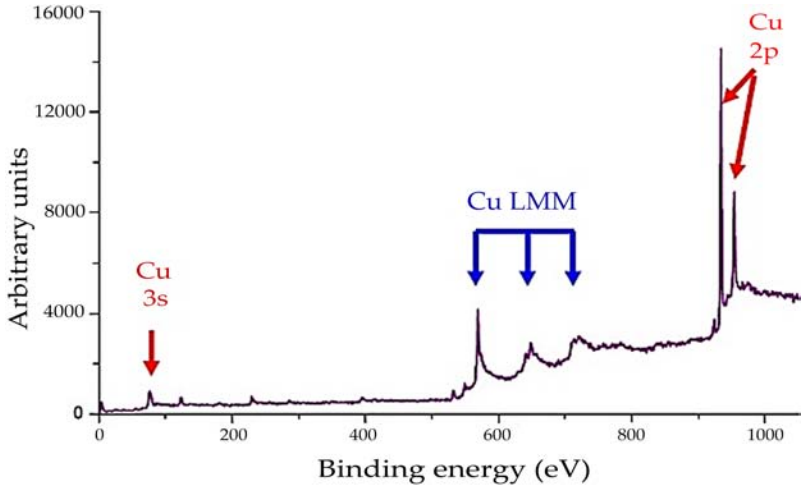

Figure 2.17. XPS spectrum of copper.

Source: https://www.researchgate.net/figure/The-XPS-spectra-of-CuNi-NWs-Cu-2p-a-and-Ni-2p-b_fig2_316748799.

The studied depth is exactly proportional to the mean free route of released electrons, and consequently to their kinetic energy. This depth is generally approximately several nm in XPS. It should be noticed that raising the angle among the analyzer and the normal to the surface might lower this depth (and therefore enhance the sensitivity of the surface) (angular analysis).

2.2.5.2. Correlations between Electronic Structure and Acid-Base Properties

XPS may be used to assess the acid-base properties of a solid surface since the band structure of a solid is equivalent to the molecule's molecular orbitals.

Liu described acid-base interactions for the first time in terms of electrical structure, by assuming an acid to be an electron acceptor and a base to be a donor (Liu et al., 2003). Mulliken (1951) and later Klopman (1968) extended Lewis' concept by defining the chemical bond between two molecules as a distribution of electrons between the base's highest occupied molecular orbital (HOMO) and the acid's lowest unoccupied molecular orbital (LUMO), resulting in the development of the adducts bonding and antibonding molecular orbitals (see Figure 2.18).

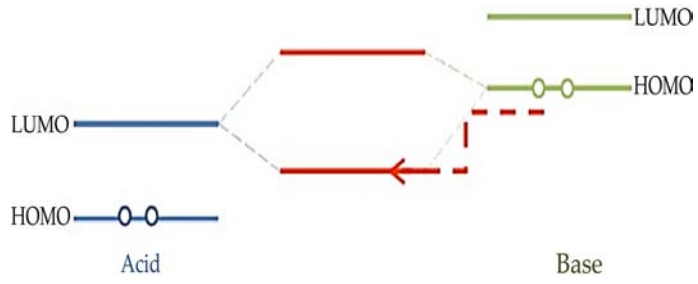

Figure 2.18. The concept of an acid-base reaction involving the sharing of an electron pair.

Source: https://onlinelibrary.wiley.com/doi/10.1002/9781119145387.ch6.

Thus, in this concept, a species' acid or basic nature is completely determined by the relative locations of its HOMO and LUMO levels in comparison to some of other classes. Whenever the distance among the LUMO and HOMO orbitals becomes too large, orbital contact becomes impossible, and total electronic transfer results in the redox phenomena (Sato, 1989).

Though this model doesn't account for the energy variations among HOMO and LUMO among different species nor the changing because of the orbital overlapping, it has been expanded to solid surfaces by assimilation of the HOMO and LUMO orbitals with the valence band and conduction band at 0K, respectively. Thus, the Lewis acidity of the surface may be calculated from the binding energy E_b at the core levels detected using XPS.

Mullins and Averbach's early method (Mullins and Averbach, 1988) connected the oxide's surface acid-base nature to the binding energy of an oxide components' core levels. Casamassima et al. (1991) took this technique, which is based on the given expression:

$$E_B = -\varepsilon_F + E_R + E_{F0} \quad (13)$$

where; $-\varepsilon_F$ is the energy of the Hartree–Fock orbital associated with an electron released in its basic state; E_R is the relaxation energy associated with reorganization however after photoemission; and E_{F0} is the Fermi level energy associated with a vacuum level.

While the chemical environment of studied atom changes, a resulting change in a concentration of valence electrons alters the screening of the core levels, resulting in a displacement ΔE_B of the binding energy as follows:

$$\Delta E_B = -\Delta\varepsilon_F + \Delta E_R + \Delta E_{F0} \quad (14)$$

Generally, the last two components are ignored, and the observed differences are ascribed to the solitary modification of the energy of the core level caused by changes in the chemical environment (chemical shift).

Mullins and Averbach suggested as because the local electronic density about ions is the same for the same oxides, the change in energy of electronic levels is minimal (Mullins and Averbach, 1988). Thus, the ΔE_B changes found in XPS are due to a Fermi level displacement with respect to the valence band bottom and are similar for all of the same photopeaks. The greater the Fermi level energy EF in comparison to the valence band, the more acidic the surface is in this scenario. This explanation is based on the observed agreement among the binding energy fluctuations estimated from the XPS spectrum and the PZC measurements obtained for Mg-Al-Si oxide powders with varying cation concentrations (see Figure 2.19).

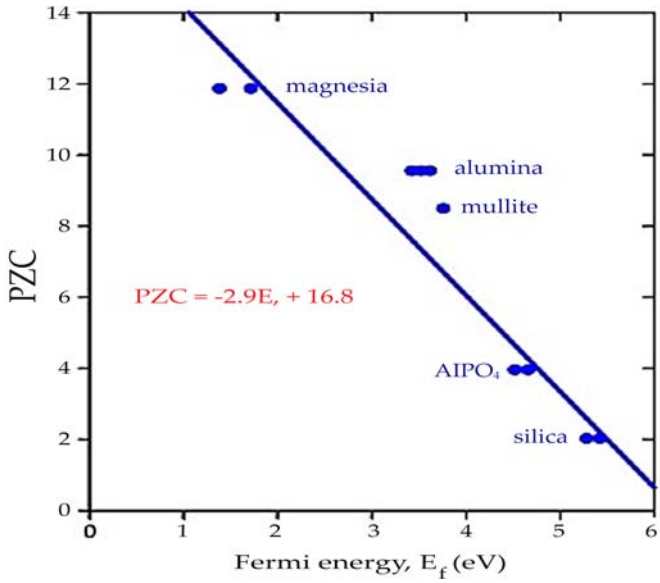

Figure 2.19. Relationship between the PZC and variance in the Fermi level determined from binding energy measurements in XPS.

Source: https://www.sciencedirect.com/science/article/abs/pii/0039602888900131.

Nonetheless, Mullins, and Averbach's explanation, which attributes the change in binding energy to differences in the Fermi level, looks dubious. Indeed, in the rigid band model proposed by Mullins and Averbach, the rise

in the Fermi level (related to the bottom of the valence band) is a direct outcome of a rise in the population of the conduction band (or of localized states in the oxide gap, as suggested by Baroux and Gorse (1994)), i.e., an increment in the density of electronic donor states. It should consequently correlate to a rise in the surface's Lewis basicity, relatively than its acidity, as Mullins and Averbach postulated. Likewise, Butler and Ginley (1978); and Labib and Williams (1984) previously established a link between the inherent rise in the Fermi level and a rise in basicity.

This apparent inconsistency arises because the spectrometer/analyzer set is electrically linked to an ultra-high vacuum chamber, i.e., to a ground, during the acquisition of an XPS spectrum. Thus, the sample's Fermi level is not basic, but arises from a balance with the spectrometer's Fermi level. Indeed, Debontridder (2001) demonstrated that the displacements analyzed after charge effect correction are not straight measurements of the intrinsic Fermi level's displacement, then of the variation among the difference in the energy of the core levels and the intrinsic Fermi level's energy variation comparative to the vacuum level. According to Debontridder's hypothesis, an increment in the energy of core levels is connected with the reduction in energy of the Fermi level compared to the vacuum level, and hence with an increment in the acidity of the surface, as Lewis' theory predicts.

While an explanation of the changes in the core level peaks vary, a number of writers have identified a link among the binding energies and acid-base characteristics. The binding energies could be utilized to describe the acid-base characteristics of polymer surfaces as well; readers have interest in this field can see Chehimi et al. reviews study (Chehimi, 2000).

The contrast between the energy levels observed on different surfaces may thus be used to classify the acid-base nature of these surfaces, as seen in the following example from Debontridder's (2001) study.

Aluminum coupons of extremely high purity (99.999%) were polished to a mirror finish and then treated with one of the following methods:

- Thermal annealing: 300°C for 24 hours (TT300) or 500°C for 24 hours (TT500);
- Anodization in a solution of 0.1M H_3BO_3 + 0.01M $Na_2B_4O_7$ at a pH of 8.2. There were two types of anodization: at 25°C on a polished and degreased surface (AN25) and at the temperature of 95°C following a flash heat treatment at 600°C for 10 minutes (AN95);

- Hydrothermal (Boehmitage), by submerging a polished and degreased surface for 10 minutes in distilled boiling water (16 M.cm) (BOEH).

The fluctuation in the binding energy of the O1s peak component relative to oxidized aluminum like function of the binding energy of the Al2p peak component relative to oxidized aluminum (Al2pox) after an adjustment for the charge effect is shown in Figure 2.20. This graph illustrates a linear relationship among O1s and $Al2p^{ox}$. A line with a slope of 1.2 is obtained (represented by the solid line on the graph), which is near to the theoretic line (represented by the dotted line) attained with a slope 1 regression, allowing the planes to be categorized in order of rising acidity:

BOEH < TT300 < TT 500 < AN25 ≤ AN95

The BOEH treatment created the maximum basic surface, whilst the anodic oxides (AN95 and AN25) generated the most acidic surface.

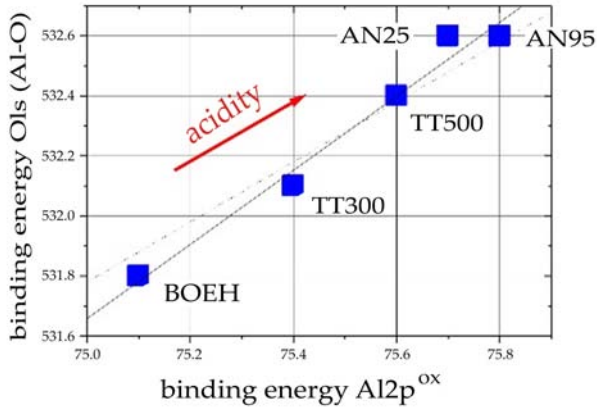

Figure 2.20. Variation in the binding energies of components of peaks O1s and Al2p related to Al-O bonds on pure aluminum surfaces following various treatments. (01 DEB).

Source: https://www.theses.fr/2001PA112123.

2.2.5.3. Other Uses of XPS

Exchange reactions among surface sites and one or more species respond selectively with specific sites may also be utilized to evaluate the acid-base composition of a surface. XPS may be used to detect and measure these exchange processes because it is essentially a surface analysis tool. Simmons

and Beard (1987) introduced this approach to measure the intensity of the acid character of the hydroxyls located at the surface of hydrated iron samples. The approach is depend on finding the equilibrium constants K_1 and K_2 in aqueous conditions for the following reactions:

$$–FeOH_2^+ \leftrightarrow –FeOH + H^+ \text{ (constant } K_1) \quad (15)$$

$$–FeOH \leftrightarrow –FeO^- + H^+ \text{ (constant } K_2) \quad (16)$$

The fluctuations in the proportion of hydroxyls about that hydrogen was exchanged with a cation (anion) is a function of the pH of the solution can be used to calculate the values of K_1 (K_2). For example, for a potassium ion exchange, the given relation can be used:

$$pH = pK_2 - log\frac{\theta}{1-\theta} \quad (17)$$

The solution pH for which $pK_2 = 0.5$ corresponds to the value of pK_2. Simmons and Beard's measurements yielded $pK_1 = 8.5$ and $pK_2 = 11.5$, permitting the value of the isoelectric point IEP to be calculated by means of the given relation:

$$IEP = \frac{1}{2}(pK_1 + pK_2) \quad (18)$$

Other authors have applied this approach successfully to determine the isoelectric points of metals coated in oxide layers (Kurbatov et al., 1992, 1993).

2.3. LOCAL METHODS

The methods presented in the preceding section provide a broad description of a surface's acid-base characteristics regarding point of charge having zero value, surface charge, or isoelectric point. Solid surfaces, on the other hand, have altogether bases and acids sites, and their total acido-basicity is a outcome of the type, strength, and spreading of these distinct sites. In many situations, a more local description is required to establish a few properties. This kind of local explanation can be accomplished directly by applying a method that is proportional to the acid-base composition of the surface sites or passively upon analyzing the adsorption of surface probe molecules to be described.

2.3.1. Infrared Spectroscopy

2.3.1.1. Principle of Infrared Spectroscopy

In a molecule, atoms vibrate continuously across a mean position, while lengths and angles of the bonds continually change, producing an oscillating electric field. Absorption happens, when the frequency of this electric field becomes equivalent to a frequency of the incoming infrared radiation's electrical component. As a result, a molecule can absorb only radiation with the same frequency as the vibration frequency that produces a change in its dipole moment. Infrared spectroscopy is used to analyze molecular vibrations, with wavelengths in the order from 4,000 cm^{-1} to 400 cm^{-1} (equivalent to 2.5–25 m wavelengths).

Each absorption produces a high characteristic of a particular bond in a spectrum, allowing the chemical set to be recognized because its wavenumber is nearly independent of a molecule with which it relates. As a result, it is likely to detect chemical groups (defined by their wavenumber) as well as estimate their concentrations (evaluating the absorption peak's size). Table 2.1 lists many vibrational frequencies associated with molecular groupings. It would be observed that the values for an absorbed molecule on a solid surface are often a little unlike from those related to the similar molecule in the gas phase.

Table 2.1. Characteristic Vibration Frequencies of a Few Molecular Groups

Type of Bond Elongations	**Group**	**Wavenumbers (cm^{-1})**
C-H	C_{sp3}-H	2,800–3,000
	C_{sp2}-H	3,000–3,100
	C_{sp}-H	3,300
C-C	C-C	1,150–1,250
	C=C	1,600–1,670
	C≡C	2,100–2,260
C-N	C-N	1,030–1,230
	C=N	1,640–1,690
	C≡N	2,210–2,260
C-O	C-O	1,020–1,275
	C=O	1,650–1,800

N-H	RNH_2, R_2NH	3,400–3,500
	RNH_3^+, $R_2NH_2^+$, R_3NH^+	2,250–3,000
O-H	ROH	3,610–3,640 (free) 3,200–3,400 (H bonds)

Several types of infrared spectroscopy may be used to investigate adsorption processes and so define the acid-base characteristics of solid planes. Most approaches, on the other hand, can be just utilized to analyze elements. This book only covers infrared reflection absorption spectroscopy (IRAS), a technique for studying solid/smooth surfaces with a less specific surface area. Any of the student looking to learn more about the other strategies can consult specialist literature.

2.3.1.2. Infrared Reflection Absorption Spectroscopy (IRAS)

IRAS depends upon the analysis of the specular reflection of an infrared beam on the reflecting surface, which was first established by Francis and Ellison (1959). It's mostly utilized to investigate thin films or molecular systems that have been deposited on flat metal surfaces.

Figure 2.21 depicts the concept in action. from the normal surface, the infrared beam puts impact directly on the surface with the incidence angle Φ. A vertical part (polarized s) and a horizontal component (polarized p) can be split to the plane of incidence with the help of the incoming electric field. Only one part horizontal to the surface makes up the polarized component 's' (represented as 'S' on the figure). The polarized factor p (abbreviated as P) could be divided into two parts: one horizontal to the surface (P_t) and the other vertical to the surface (P_n).

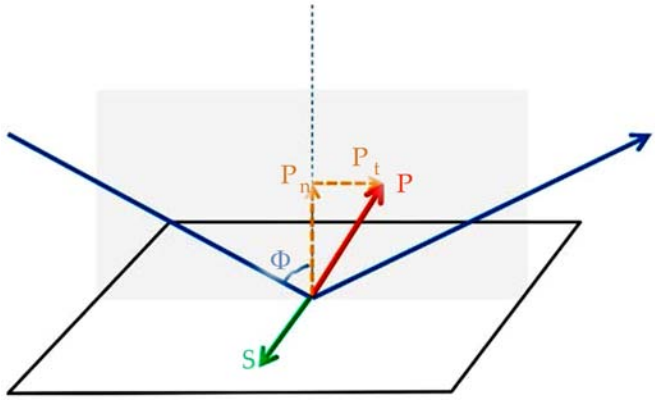

Figure 2.21. An electric field is reflected at the metal surface.

Source: https://en.wikipedia.org/wiki/Fresnel_equations.

In the situation of a metallic substrate, it is clear that reflection onto the surface results in destructive interference for components parallel to the plane, but results in constructive interference for components orthogonal to the surface. The absence of an electric field corresponding to the surface that may link with the dipole moment of a corresponding vibration mode describes the rule of surface selection, which is tight in the scenario of metals, and stipulates that only vibration modes orthogonal to the surface are detectable. Additionally, graze incidence (φ about 80–90°) aids in signal optimization.

The IRAS spectrum represents the difference in reflectance between the adsorbed layer and the bare substrate, which is used as a reference:

$$\Delta R/R_0 = (R_0 - R)/R_0 \quad (19)$$

where; R denotes the reflectance of the adsorbed layer; and R_0 is the reflectance of the bare substrate; and $R_i = r_i^2$ denotes the reflection coefficient. Sensitivity is dictated by changes in R/R_0, which are typically minor (10^{-1} to 10^{-3}) but maybe enough to distinguish single layer fractions in molecules with significant dipole moment fluctuations. A considerable improvement in sensitivity may be gained by rapidly varying the polarization of the incoming beam among the polarizations p and s using a photoelastic modulator (polarization modulation–infrared reflection absorption spectroscopy (PM-IRAS)). Due to the surface selection principles, this technique may also be used to determine the direction of groups of molecules present on the surface.

The vibration frequency of various molecular groups is frequently used to estimate the kind and intensity of reactive sites for a given molecule. For example, when the ability toward proton dissociation diminishes (or rises), the frequency of extension of isolated OH groups on an oxide surface rises (or falls), equivalent to the increment in a basicity (or acidity) of these groups. However, because the majority of characterizations are done with probe molecules, the acid-base properties are influenced by the probe applied. As a result, establishing a general rule of acidity (or basicity) for solid surfaces is impossible.

Furthermore, the numerical implementation of that approach is depended on the suggestion that R/R_0 changes proportionally with the concentration of the adsorption chemical group. In practice, it is frequently required to perform a calibration using a different approach.

The given application example comes from Freund's group's research (Boscoboinik et al., 2013). D_2O was utilized to partially oxidize a two-dimensional (2D) alumino-silicate layer that had been deposited on a (0001) ruthenium surface. On the surface of this film, which may be described as a zeolite model, are bridged families Si-OD-Al. These bridging groups have a high Bronsted acidity and may interact with both weak and strong bases (for example, ethylene or carbon monoxide) (such as pyridine or ammonia). In Figure 2.22, the IRAS spectrum obtained after CO adsorption is divided by the spectrum obtained before to CO exposure. The positive (negative) peaks indicate the removal (reappearance) of the corresponding chemical groups. Figure 2.22 illustrates the vibrations of the extension of the bridged OD groups, which arise at 2,652 cm^{-1} on a smooth surface and shift to 2,409 cm^{-1} during CO adsorption. The OD groups' redshift is caused by the formation of a CO and OD complex among both the molecule and the bridging OD groups. The amplitude of the shift (243 cm^{-1}, similar to values seen in zeolites) shows that the OD sites in the two-dimensional alumino-silicate film are strong acids. Additionally, the high characteristic of CO vibrations is seen at 2,183 cm^{-1}, which corresponds to a blue shift of 40 cm^{-1} when compared to the CO molecule in its gaseous state, showing that this molecule interacts with a surface. Finally, since IRAS can only see dipole moments with a part perpendicular to the surface, the appearance of a peak corresponding to CO vibrations implies that this molecule is not deposited parallel to the surface. The DFT-derived values are displayed in the top band of Figure 2.22, which verifies the preceding findings.

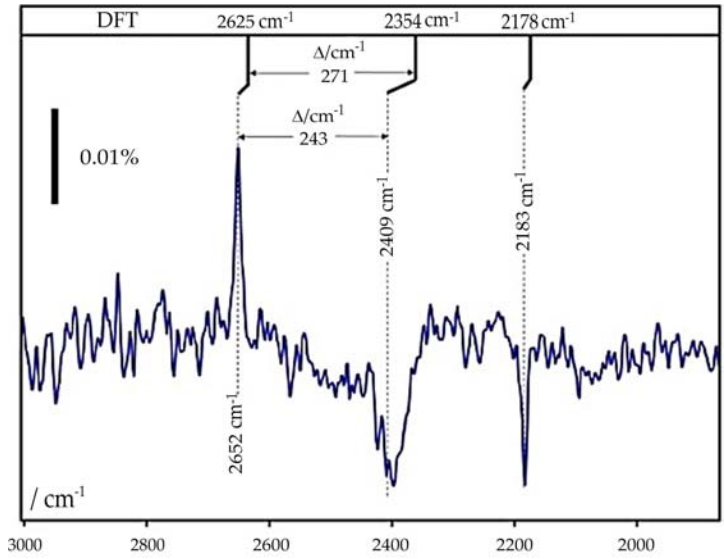

Figure 2.22. IRAS spectrum of CO adsorption on a two-dimensional zeolite model placed on a Ru (0001) surface.

Source: https://pubs.acs.org/doi/10.1021/jp405533s.

2.3.2. X-Ray Photoelectron Spectroscopy (XPS)

Section 2.2.5 discussed the fundamentals of XPS. Additionally, Section 2.2.5 demonstrated that It is feasible to classify surfaces according to their acido-basicity by examining variations in the interaction energy of a distinctive peak location in the XPS spectrum for materials with similar chemical compositions. As with infrared spectroscopy, probing molecules might be utilized to explain the kind and density of active sites.

That strategy is dependent on the idea that whenever probe molecule interreacts with various types of surface places, changes in the probe-reactive site interactions result in a difference in the probe molecule reactive group's binding energy (see Figure 2.23(a)). Primarily utilized to the investigation of the reactive sites in scattered solids like the zeolites, that technique was later expanded to flat solid surfaces (Defosse et al., 1978).

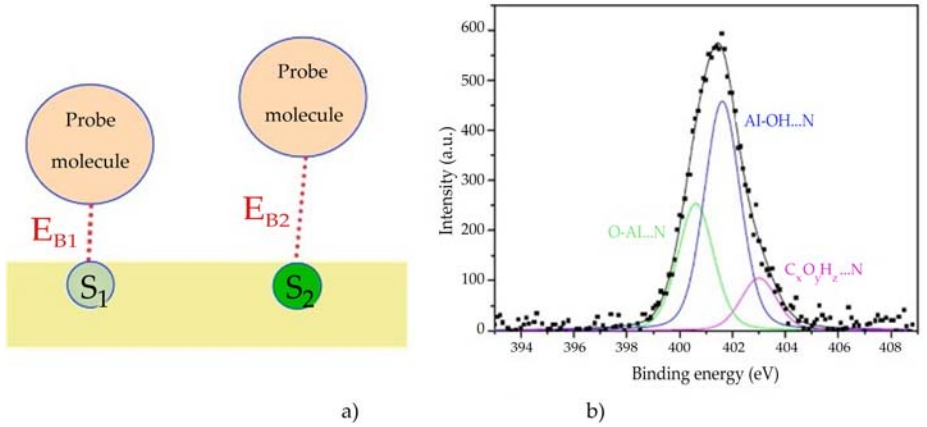

Figure 2.23. *(*a) The concept of interactions among a probe molecule and two distinct types of surface sites. (b) The N1s peak components obtained after immersing a 1050 aluminum alloy plate in a xylene solution that contains 0.1 mol L^{-1} DAE.

Source: https://www.researchgate.net/publication/229129894_Interaction_of_amines_with_native_aluminum_oxide_layers_in_non-aqueous_environment_Application_to_the_understanding_of_the_formation_of_epoxy-aminemetal_interphases.

The interface between amines and native aluminum oxide layers in a non-aqueous environment is studied in order to get a better understanding of how epoxy-amine metal interphases arise.

The majority of probe molecules utilized react through carbon, nitrogen, oxygen, fluorine, or sulfur atoms. The binding energies of these atoms' central electrons range from several tenths to a few electron volts, depending on the kind of contact at that they are included. By observing, with the use of XPS, the adsorbing of a probe molecule with a defined acid or basic nature, one may identify the acid-base properties of the sites on the surface with which it interacts. For instance, Figure 2.23(b) depicts the N1s peak found when a 1050 aluminum alloy plate is immersed in a xylene solution containing 0.1 mol L^{-1} 1,2-diaminoethane (DAE), a strong base. The existence of reactive sites of rising acidity on the aluminum surface is demonstrated by the development of three parts in the N1s peak, each respective to the three different kinds of interaction. The peak at 400.5 eV can be qualified to Lewis-like interactions among the lone pair of nitrogen and the aluminum cations through O-Al…N donor-acceptor interactions

(Lewis acids). The highest point at 401.6 eV is caused by the surface hydroxyls (Bronsted acids) protonating the amine terminal of the molecule, forming Al-OH…N complexes. Lastly, the peak at 402.6 eV is a result of the amine termination being protonated by carbon hydroxyls derived from the carbonaceous pollution, that are likewise Bronsted acids and produce CxOyHz…N complexes. The greater binding energy revealed for polluted hydroxyl interactions implies that these hydroxyls have a higher Bronsted acidity than the surface hydroxyls, which should be noted. The related intensities of the three measured parts may also be used to calculate each reactive site type's relative concentration. Finally, the evolution of these relative intensities through time offers insight into the relative stability of those interactions. Figure 2.24 depicts the final two parts. Interactions with Bronsted acid sites (surface hydroxyls and contaminant hydroxyls) account for almost 75% of all interactions when XPS is done immediately after DAE adsorption. After seven days of aging in ultra-high vacuum, these linkages account for less than 60% of the total, suggesting that Lewis acid site interactions have become more stable (metal cations).

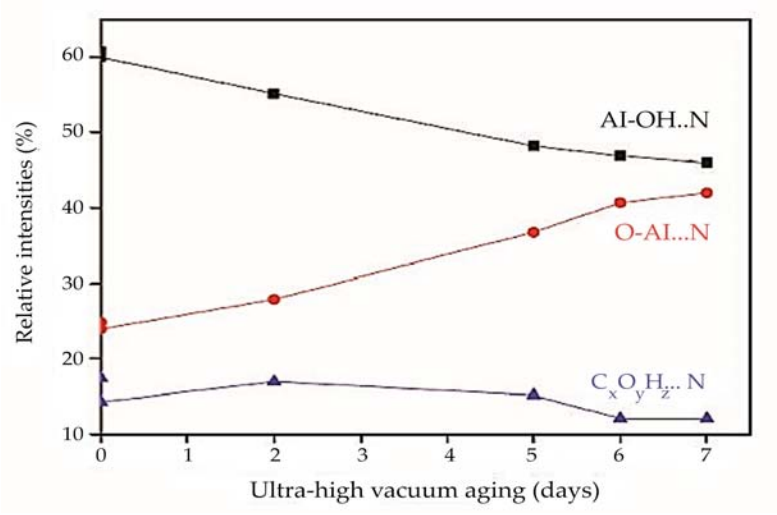

Figure 2.24. The consequence of ultra-high vacuum aging on the relative intensities of the different components of the N1s peak observed following immersion of 1050 aluminum alloy plates in a xylene solution containing 0.1 mol L^{-1}.

Source: https://inis.iaea.org/search/search.aspx?orig_q=RN:40033626.

2.4. APPLICATION EXAMPLES

Despite the fact that the term "acido-basicity" was introduced to describe a process in the aquatic environment, the acid-base properties of solid surfaces have influenced a solid's interactions with its surroundings and are thus related in a wide range of application areas such as catalysis, adhesion, bioadhesion, soil sciences, corrosions, and so on. The next section contains examples from several areas.

2.4.1. Bonding Ability of Aluminum Sheets

Adhesion is a complicated process involving a number of forces of interfaces. Fowkes recognized the relevance of acid-base interaction in adhesion phenomena in the 1960s (Fowkes, 1964), and it has since been the subject of various theoretical and experimental research. The following example is based on Lopez's work (1997).

Lopez's research aimed to link the acid-base qualities of aluminum alloy plate surfaces to their capability to connect with an organic covering.

Lopez applied numerous grades of alloys in his research because of the wide range of industrial applications of aluminum (automobiles, aerospace, food, electronics, building, and so on). Only the data for grades AA 1198 and AA 5182, which are frequently utilized in the food sector or whose chemical composition (in mass percent) is reported in Table 2.2, will be presented here.

Table 2.2. Chemical Composition (in mass%) of AA 1198 and AA 5182 Alloys

	Si	**Fe**	**Cu**	**Mn**	**Mg**	**Cr**	**Zn**	**Ti**	**Al**
AA 1198	0.01	0.006	0.006	0.006	–	–	0.01	0.006	>99.98
AA 5182	0.2	0.35	0.15	0 . 2 – 0.5	4–5	0.1	0.25	0.1	rest

Chemical brightening of Grade AA 1198 samples was proceeded by several surface treatments:

- **T1:** Sodium hydroxide degreasing (15 seconds absorption in a 1 M NaOH deionized water solution at normal temperature, followed by washing with deionized water);

- **T2:** degreasing with alkaline detergent (10 seconds soaking in 35 g L^{-1} OakiteTM in deionized water at 65°C, followed by rinsing with deionized water);
- **T4:** T1 proceeded by a ten-minute immersion in hot deionized water;
- **T5:** T1 proceeded by thermal treatment (four hours of heating at 420°C in a muffle furnace);
- **T7:** T1 proceeded by phosphoric acid anodization (40 g L^{-1} H_3PO_4 in deionized water; 20 V DC on 1199 aluminum foil (Al > 99.9%) for 25 minutes at room temperature, followed by washing with deionized water).

As-rolled samples of grade AA 5182 were subjected to a specialized industrial annealing procedure (Figure 2.25).

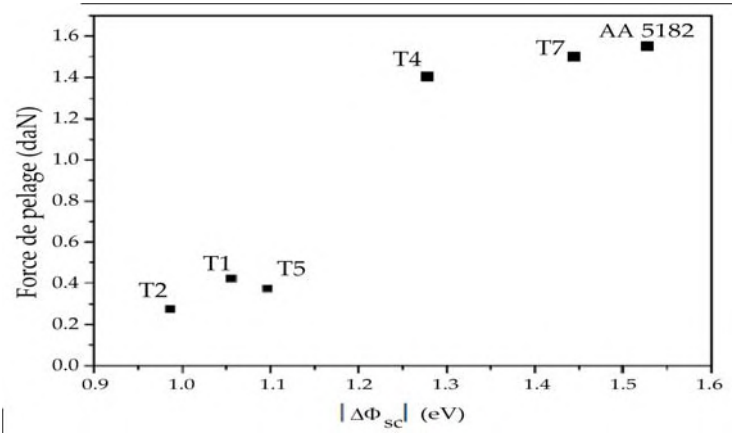

Figure 2.25. Relationship among the band bending of AA 1198 aluminum sheets (after various surface treatments) and AA 5182 aluminum sheets (following various surface treatments) and the peel force of an adhesive tape. T1: degreasing with sodium hydroxide; T2: degreasing with an alkaline detergent; T4: hydrothermal treatment; T5: thermal treatment; T7: anodizing.

Source: https://www.theses.fr/1997INPG0145.

2.4.2. Mechanism of Formation of the Interphase in Metal–Polymer Joints

Epoxy-amine–metal couplings are widely applied, particularly in the aerospace and automotive industries.

A metal bond with polymer assemblage may be seen as a cross-layered structure, as shown in Figure 2.26. Aside from gold, every metallic substrate (zone) is covered with an oxy-hydroxide coating (zone) that forms as a result of spontaneous interactions along the environment or specific surface treatments under normal working conditions. The interphase (zone) is a complex polymeric zone that occurs near to the metallic surface and has a chemical composition and heterogeneity morphology that differs substantially from the adhesive zone (zone).

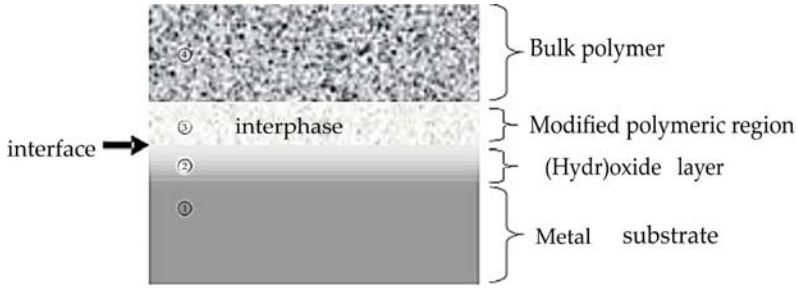

Figure 2.26. A polymer/metal connection is seen schematically.

Source: https://www.wiley.com/en-us/Physical+Chemistry+and+Acid+Base+Properties+of+Surfaces-p-9781848218437.

The type and features of an interphase play a critical role in the eventual bond functioning (durability, mechanical properties, practical adhesion, and so on), therefore a thorough knowledge of the events that lead to its formation is essential. Several studies have discovered an amine hardener enrichment in the vicinity of the metal surface in epoxy-amine adhesives, indicating that this hardener may play a unique role in the interphase formation.

Mercier et al. (2008) investigated the interactions between a 1050 aluminum sheet with a high aluminum content (>99.5 mass percent) and a molecule with an only one amine function (propylamine CH_3-CH_2-CH_2NH_2, PA) or even a molecule with two amine functions (NH_2CH_2-CH_2-NH_2, DAE) that can model a diamine hardener.

Figure 2.27 illustrates the atomic emission spectroscopy measurements of the aluminum content in a xylene solution having 0.5 mol.L^{-1} PA or DAE as a function of contact time with the 1050 aluminum surface (ICP-AES). The partial disintegration of the oxy-hydroxide coating covering the aluminum substrate is responsible for the appearance of aluminum in the DAE solution. Though the two molecules (PA and DAE) interface with

the reactive surface sites in the same way, only the DAE has the ability to disintegrate the surface. The dissolving method is thus related to the occurrence of two amine terminations on the molecule aids in the formation of a bidentate-mononuclear complex (i.e., a complex tends to result from the adsorbent of both amine terminations of the molecule on the similar metal cation), weakening the cation's bonds with the oxide matrix and allowing it to pass into solution. It's worth noting that amine hardeners utilized in adhesives often include at least two amine functionalities.

The same dissolution processes related with the formation of chelate complexes among a surface and the ligands attached to it might also be suggested to analyze corrosion mechanisms (passive film dissolution) or geochemistry (dissolution of minerals in natural water).

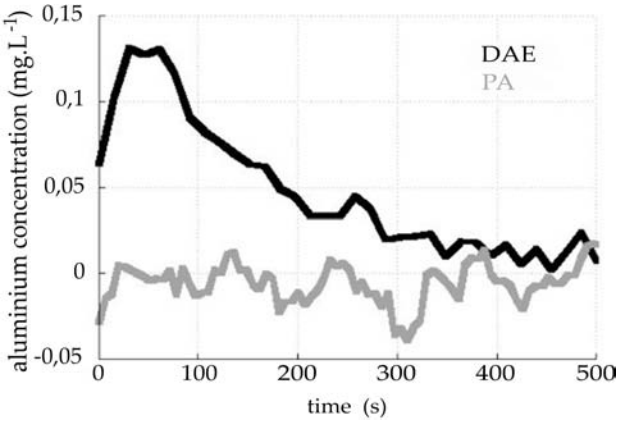

Figure 2.27. The evolution of aluminum concentration in a xylene solution having 0.5 mol.L^{-1} PA or DAE as a function of contact time with the 1050 aluminum surface in a xylene solution having 0.5 mol.L^{-1} PA or DAE (Mercier et al., 2008).

Source: https://www.infona.pl/resource/bwmeta1.element.elsevier-969056d7-e621-36aa-bc54-ca2ebff8a42e.

2.4.3. Heterogeneous Catalysis

For decades, the acid-base concept has broadly been used in the area of heterogeneous catalysis. Solid acid catalyzers, for example, are crucial in the refinement process. Despite their lack of widespread use, solid base catalyzers are important in the transformation of biomass, for instance.

Bi-functional catalyzers are employed in a number of industrial processes because they have either acid or base surface locations. As a consequence, their interactions with various kinds of surface sites may occur simultaneously or sequentially, involving one or even more molecules. Dehydration of 1-butanol on alumina doped with Na is shown in Figure 2.28 as an example of a single-molecule simultaneous process. One of the hydrogens in the $–CH_2–$ group would connect with the base surface sites (B), whereas the oxygen's electron pair would interact with the acid surface sites (A).

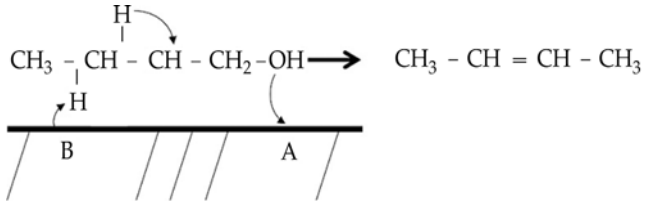

Figure 2.28. The mechanism by which 1-butanol dehydrates on sodium-doped alumina.

Source: https://onlinelibrary.wiley.com/doi/book/10.1002/9781119145387.

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CHAPTER 3

MONITORING PH AND ALKALINITY OF WATER

CONTENTS

3.1. INTRODUCTION

pH and alkalinity are two important chemical characteristics of river mouths that are being examined to expand our knowledge of the water's health, and they are discussed in this chapter. In ensuring the survival of most aquatic animals and plants, pH levels must be monitored as part of practically every water quality checking program. The inspection is simple and quick, and it can provide a vital standard of information that can be used to better understand unforeseen changes in the quality of drinking water.

The total alkalinity of water samples is measured to determine the water's ability to neutralize acidic substances. An essential part of establishing the estuary's potential to neutralize acidic pollutants from wastewater rainfall is to conduct this test (Björnsson et al., 2001; Yadav and Kumar, 2011).

Every estuary contributes to the carbon cycle in some way. As carbon dioxide is removed from the atmosphere, it is taken up by animal and plant tissue as well as aquatic bodies. Several variables such as pH, acidity, alkalinity, total hardness, and inorganic carbon are all connected and are all components of the inorganic carbon compound. The interrelationships between these components are quite intriguing to see. For instance, the quantity of CO_2 in the water impacts the pH and the rate of photosynthesis in the environment (Anderson and Robinson, 1946; Adhikari et al., 2006).

3.2. WHY MONITOR ALKALINITY AND PH?

Monitoring a waterbody on a regular basis should offer baseline information on typical pH and alkalinity levels in the waterbody. Acid rain, overflow from acidic soils, and pollution through agricultural pesticides all have the potential to cause unexpected pH drops. If the pH of the water is found to be beyond the normal range of 5.0 to 10.0, it should be suspected to be the result of industrial contamination or a natural disaster of some sort. An extensive collection of alkalinity readings, on the other hand, allows scientists to sense changes in the chemical composition of estuarine waters over time (Wurts and Durborow, 1992; Cao et al., 2011).

The pH of a solution is a measure of how basic or acidic it is. H+ activity in a solution is measured using this method, which is represented as a negative logarithm in the equation. The pH readings are presented on a scale ranging from 0.0 to 14.0 (neutral). Pure water contains a pH of 7.0 and is considered neutral; water having a pH < 7.0 is considered acidic, while water having a pH >7.0 is considered basic or alkaline. Conditions

containing pH levels ranging from around 6.5 to 8.5 are preferred by most estuary species (Bae et al., 2020; Boyd, 2020).

pH values are expressed on a logarithmic scale, which means that for every one-unit change in pH, acidity or alkalinity increases or decreases by a factor of ten; for example, a pH of 5.0 is 10 times more acidic than a pH of 6.0 and 100 times more acidic than a pH of 7.0. The pH of a solution is 7 when the hydroxyl and hydrogen ions are mixed in sufficient amounts (this is known as the neutral point).

3.3. THE ROLE OF PH IN THE ESTUARINE ECOSYSTEM

It is possible for plants and animals to change the pH of water by photosynthesis and respiration, as well as by the minerals dispersed in the dust, aerosols, and water from the human-made pollutants and air. Human activities that result in substantial, long-term acidification of a waterbody or short-term variations in pH are extremely detrimental to the environment. For example, algal blooms, which are frequently triggered by an excess of nutrients, may affect pH levels to change substantially over a short period of time, putting a significant amount of stress on nearby species. It is possible that acid precipitation in the higher freshwater goes of an estuary will reduce the existing rate of eggs laid by breeding fish in that area (Figure 3.1) (Jarvis et al., 2006; Boyd et al., 2011).

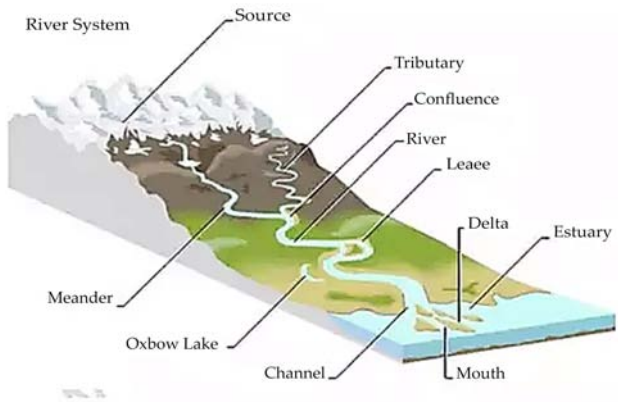

Figure 3.1. Estuarine ecosystem.

Source: https://unacademy.com/lesson/estuarine-ecosystem/Y1FL6LFP.

- The pH of water is also determined by several other variables, including:
- Water turbulence;
- Bacterial activity;
- Chemical components in runoff flow into the waterbody;
- Manure spread out; and
- Other human activities both inside and beyond the drainage basin have an influence.

The pH of the estuarine water ranges from 7.0 to 7.5 in the fresher portions to 8.0 to 8.6 in the saltier areas. The natural buffering of bicarbonate and carbonate dissolved in the water gives seawater a slightly alkaline pH (Monteith and Evans, 2005; Riley and Mayes, 2015).

Several aquatic animals and plants rely on the pH of their water to survive. Many organisms struggle to survive when pH values fall below 5.0 or climb beyond 9.0. Other components of the water's chemistry can be affected by changes in pH, typically to the harm of indigenous species. Minor changes in the pH of water can impact the solubility of metals like copper and iron. If the pH levels in the estuary's silt are decreased, harmful metals in the sand can be resuspended in the water column, affecting aquatic life indirectly. Many aquatic animals may be harmed because of this (Moss et al., 1996; Jantsch and Mattiasson, 2003).

3.4. SAMPLING CONSIDERATIONS

Several considerations should be considered when establishing monitoring locations, where to monitor, and when to monitor. A few pH monitoring factors are discussed here (Nacht, 1983; Yao and Byrne, 1998).

3.4.1. When to Sample

The fact that pH levels fluctuate during the day and over the season is well recognized; consequently, a single pH measurement taken throughout the day may not offer an accurate picture of the estuary's long-term pH conditions if taken daily. Photosynthesis, which occurs in aquatic plants, eliminates CO_2 from the water, causing the pH of the water to rise significantly. It will be different from a pH value recorded at dawn in a place with many aquatic plants and one obtained six hours later in the same area when the plants are actively photosynthesizing. The same may be said for waterways with plant life, which may see an increase in pH throughout the growing season.

Therefore, if you wish to compare your conclusions to those from previous measurements, you should check pH levels at the same time of day every time. It is also required to monitor pH values for an extended period in order to obtain useful information. The specific time period for pH testing will be chosen by local conditions as well as the monitoring objectives of the volunteer program (Nilsson and Edwall, 1983; Klobucar et al., 2017).

3.4.2. Choosing a Sampling Method

A typical study performed in volunteer estuary monitoring projects is the pH test. In general, citizen programs employ either the colorimetric approach or electronic meters to measure pH. Because the pH of a water sample can fluctuate fast owing to chemical and biological processes, both require measurements to be conducted in the field (Wages et al., 1986).

Color comparator field kits (also known as "colorimetric") are simple to use, affordable, and accurate enough to meet the demands of most applications. An electronic colorimeter can also be utilized with the colorimetric approach. More costly electronic pH meters Bleach offers exceedingly accurate readings if very exact measurements are necessary. Because test paper strips do not yield reliable measurements in saltwater, they are not suited for use in estuary environments. The sections that follow describe how to use the two most prevalent approaches (Figure 3.2) (Nelson and Ward, 1980; Rose and Long, 1988).

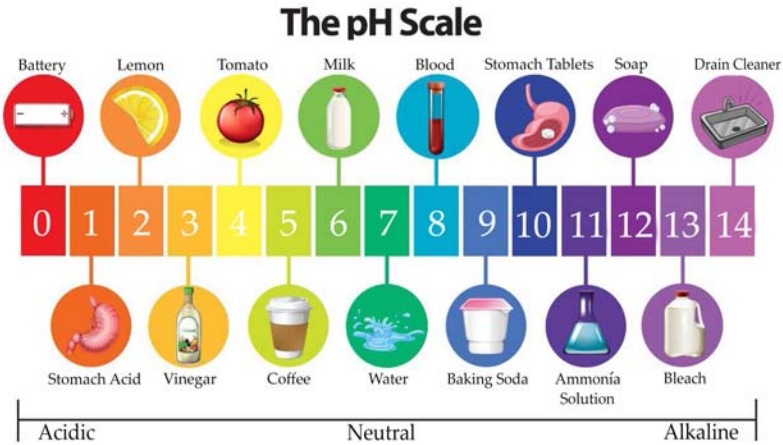

Figure 3.2. pH range scale.

Source: https://blog.jencoi.com/what-is-ph-in-water-testing.

3.4.2.1. Colorimetric Method

"To measure color" is what colorimetric implies. Reagents are applied to a water sample in a colorimetric test procedure, and a reaction occurs, resulting in color. Visually or electronically, the color can be measured. This procedure will not work with water that contains colorful elements like dissolved organic compounds or algae. A meter is recommended for colored water samples (Abbaspour et al., 2006; Rérolle et al., 2016).

- **Visual Technique to Measure Color:** Field kits are available in a variety of pH levels. They range in price from $15 to $50, based on the variety of pH values that will be measured. These kits are comprised of a number of color standards that are either incorporated into printed-on cards or plastic housing units. Following the addition of reagents in accordance with the guidance, the volunteer matches the color of the test tube to the standards to calculate its pH value. Identify a kit that contains the typical pH values of the estuary within its area of sensitivity if these values are known. If not, choose a kit that does. The use of a wide-range kit that includes pH values ranging from 3.0 to 10.0 is preferred by certain programs till the observed range of standards for that waterbody has been determined. After ascertaining the real variety over several sea sessions, move to a smaller range kit to improve accuracy and precision. Check to see if the kits have been verified against the appropriate pH standards (Figure 3.3) (Kim et al., 2017).

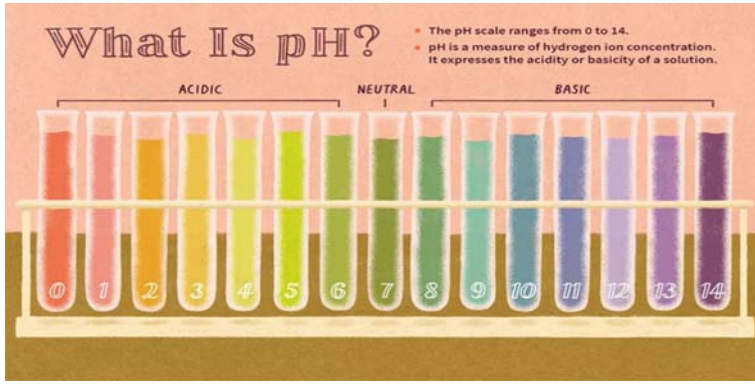

Figure 3.3. pH values based on color.

Source: https://www.thoughtco.com/definition-of-ph-in-chemistry-604605.

- **Electronic Method to Measure Color:** When light passes through a reaction sample, an electronic colorimeter detects the quantity of light that passes over it and transforms the measurement to an analog or digital signal (LaMotte et al., 1999). Using a test tube, add the reagent to the water sample before placing it into the colorimeter. Typically, electronic colorimeters can assess a variety of water quality parameters at the same time (Figure 3.4) (Sedjil et al., 1998).

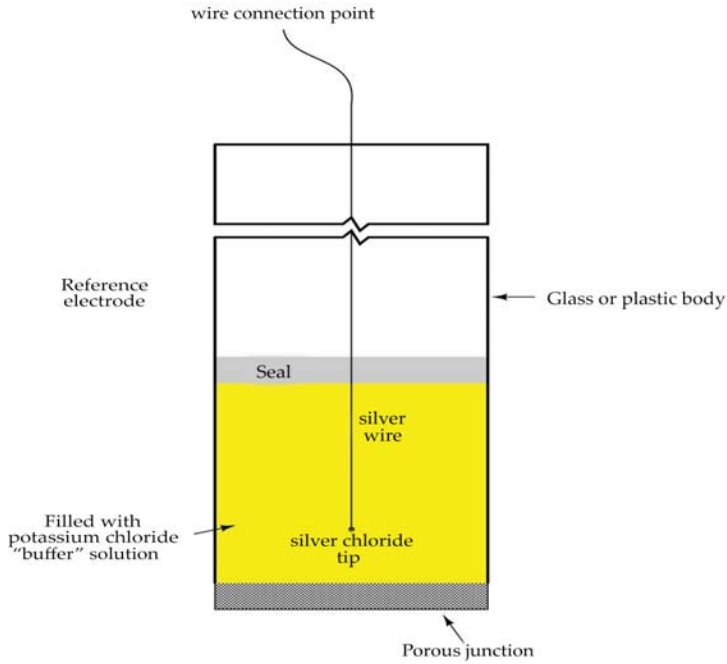

Figure 3.4. Potentiometric method to measure pH.

Source: https://control.com/textbook/continuous-analytical-measurement/ph-measurement/.

3.4.2.2. pH Meters

pH meters are more costly than colorimetric field kits, but they provide exceptionally precise readings across a wide pH range. The more affordable pH testers are around $40. Some more costly meters ($75-$750) also show the water temperature, and a few meters come with wires so you can get readings all the way down the water column. Meters may be used even

though the water is murky or tinted, unlike the colorimetric approach (Figure 3.5) (River Watch Network, 1992; Environment Federation, 1998).

Figure 3.5. SevenCompact™ S220 benchtop pH meter.

Source: https://www.carlroth.com/com/en/benchtop-ph-meters/benchtop-ph-meters-sevencompact%E2%84%A2-s220-uni-kit-version/p/ta10.1.

3.4.3. pH Calibration Standards

Calibration standards are used to guarantee that your apparatus is correct, whether you're using a field kit, pH meter, or colorimeter device. pH 10.00, pH 7.00, and pH 4.00 are the most often used standards. They're available as a liquid or a powder. These pH standards range in price from $5 to $25 per unit, based on the number of measurements you'll be doing (USEPA, 1997; Godfrey, 1988).

The subsequent is information on buffers:

- Since buffer pH readings fluctuate with temperature, you should calibrate the meter with the buffer solutions at room temperature. pH equipment may usually be calibrated at home a few hours before use. Consult the instructions provided by the manufacturer.
- After the expiration date of a buffer, do not utilize it.
- To avoid contamination, always cap the buffers while storing them.
- Buffer solutions should not be reused!

3.5. HOW TO MEASURE PH VALUES?

Generally speaking, the protocols for measuring pH provided in this section are intended to serve as general guidelines only; they do not apply to all sampling processes. Monitors should refer to the user manuals that accompany their sample and analyzing tools for more information. When presenting data to water quality authorities, those who are interested in doing so should confer with the agencies in order to identify suitable equipment, techniques, quality control measures, and data quality targets.

Before traveling to the monitoring location, it is vital to check the monitoring site, day, and time; to ensure that the relevant monitoring apparatus and personal protective equipment are on hand and to be aware of any safety precautions. When volunteers arrive at the monitoring location, they should take notes on general observations about the place. The following procedures must be followed in order to determine the pH values (Ehlers et al., 2001):

- **Check Equipment:** The volunteer should bring additional items to each sample session as well as the regular sampling equipment and attire (Figure 3.6):
- Field pH colorimetric kit; or
- pH meter with temperature sensor built-in; or
- Reagents and colorimeter unit.

Figure 3.6. Inspection of calorimeter units with reagents.

Source: https://fdocuments.in/reader/full/chapter-11-ph-and-alkalinity-voluntary-estuary-document-is-chapter-11-of-the.

- **Collect the Sample:** The pH test tube can be filled by lowering it into the water if you are employing the colorimetric technique to determine the pH. The meter may occasionally be placed right in the water, so you don't have to gather any water samples if you're using one. In contrast, while doing water quality monitoring from a boat or pier, you will be required to store a water sample utilizing screw-cap bottles, water bottles, or Whirl-Pak bags.

1. **Measure pH Values:**

i. **Colorimetric Technique:** The colorimetric techniques make use of indicators that change color in response to the solution's pH being tested. Observe the instructions provided with your colorimetric kit.

Because the colorimetric tests' test tube is so small, it is helpful to use a clean eyedropper to meet the tube together with the appropriate quantity of sample water as you fill the tube. The use of colorimetric kits involves the addition of a chemical or two to a water sample, followed by a comparison of the color of the water sample to color standards representing different pH levels. The use of white paper in the backdrop of the tube while using the field kits, which rely on visual evaluations, is beneficial since it draws the eye's attention to any color changes, especially when the sample's color is faint. Make a note of the pH value of the specification that is very carefully matched to the hue of the sample. Examine the quality assurance project strategy for your software if the sample hue is in the middle of two criteria (QAPP). You may be required to average the readings of the two nearest requirements and report this figure as the pH in some QAPPs (quality assurance procedures). In some cases, you will be required to choose the nearest value and will not be able to average the numbers.

- **pH Meter:** Measurement of equipment on a regular basis will guarantee that high-quality data is collected. According to the recommendations in the meter handbook, the pH meter should be regulated before sample assessment after every 25 samples. Use two standard pH buffer solutions. Put the electrode in the water sample after calibration and record the pH. To guarantee accurate results in the future, the glass electrode on these meters must be properly washed with deionized water when every usage (Moore et al., 1921; Olin Neal, 2001).
- **Send Off Data and Clean Up:** All equipment should be carefully cleaned by volunteers.

Check that the data-sheet is comprehensive, clear, and correct and that all samples are included. In the event that the original data sheet is lost, volunteers should create a copy of it before submitting it to the authorized person or agency.

3.6. TOTAL ALKALINITY

The capacity of water to neutralize acids is measured by alkalinity (also known as "buffer capacity"). Alkaline chemicals like bicarbonates, carbonates, and hydroxides remove hydrogen ions from the water, lowering its acidity (thereby increasing pH). They normally achieve this by forming new molecules by interacting with hydrogen ions (Ehlers et al., 2001; Yamamoto et al., 2021).

Rocks and soils, salts, some plant activities, as well as certain industrial effluent discharge all impact alkalinity. Even though some water is on the acid side of the pH scale, it has a high alkalinity rating! This indicates that, although being acidic, the water has the ability to buffer or neutralize acids (Dickson, 1981; Wolf-Gladrow et al., 2007).

The quantity of acid (e.g., sulfuric acid) required to get the sample to a pH of 4.2 is used to determine total alkalinity. All of the alkaline chemicals in the test are "used up" at this pH. The result is expressed in milligrams of calcium carbonate per liter (mg/l $CaCO_3$).

3.6.1. In the Estuarine Ecosystem – The Role of Alkalinity

The ability of an estuary to neutralize acidic pollutants from rainfall or wastewater is determined in part by the alkalinity of the water. If a body of water did not have this acid-neutralizing ability, any acid that was introduced would cause a shift in pH to occur immediately. Water's buffering capacity, or its ability to tolerate changes in pH, is crucial to the survival of aquatic organisms. The capacity of the estuary to neutralize acids will differ between the freshwater stretches of the river and the areas of the estuary that have greater salt levels (Zhang and Pang, 1999; Takahashi et al., 2018).

3.7. SAMPLING FACTORS

A double termination titration employing a pH meter and a numerical titrator is advised for the determination of total alkalinity. This can be carried out in the area or in the laboratory setting. If you intend to do an alkalinity analysis in the field, it is advised that you utilize a numerical titrator to make

your measurements. A burette is another instrument that may be used to measure alkalinity. Since digital titrators are transportable, cost less money, take a lesser amount of time, and feature easy-to-read terminations, using a numerical titrator is suggested overusing a buret for volunteer programs (results).

In this approach, titration is performed by adding small, exact amounts of sulfuric acid to the sample till it sample achieves a certain pH value, which is then recorded (the endpoint). This is because the sum of acid employed is proportional to the overall alkalinity of the sample (Ellett, 1993; Green, 1998).

3.8. HOW TO MEASURE ALKALINITY?

Digital titrators are equipped with counters that display numerical values. The titrator works by forcing a plunger into a container holding the reagent by twisting a knob on the unit. The counter varies in amount to the amount of reagent that has been used as the handle is turned. The alkalinity is then determined depending on the amount of alkalinity that was utilized. It costs roughly $100 to purchase a digital titrator and approximately $36 to purchase the reagents (chemicals) necessary to conduct total alkalinity assays. Furthermore, alkalinity standards are required for the purpose of performing accuracy checks.

A computerized titrator was used to construct the alkalinity technique depicted below, which was produced by the Acid Rain Monitoring Project of the University of Massachusetts Water Resources Research Center. The method is explained below (River Watch Network, 1992):

1. **Check Equipment:** The volunteer should carry the following materials to the location for each sample session, along with the usual sampling equipment and clothes (Kwon et al., 2013):

i. 250-ml beaker;
ii. 100-ml graduated cylinder;
iii. Numerical titrator;
iv. pH meter with temperature sensor built-in;
v. Reagent;
vi. 0.500 N standard alkalinity containers for accuracy check; and
vii. To rinse the pH meter electrode, fill a container with deionized water.

2. **Collect the Sample:** Complete these collection and storage methods if you wish to evaluate a water test for alkalinity in the

lab (Buck et al., 2002):

i. Employ glass bottles or 100 ml plastic;
ii. Label the bottle with the name of the data collector, the date, the time, the place, and the analysis that will be done;
iii. Submerge the bottle in the water while wearing gloves. Fill the bottle to the brim and secure the lid;
iv. Excessive agitation and extended air exposure should be avoided;
v. Put the bottle in the refrigerator. Samples should be tested once feasible; however, they can be kept for however 24 hours if kept at 4°C or lower.

3(a). Measure Total Alkalinity: Sulfuric acid and a computerized titrator are typically used to determine alkalinity. In the field or in the lab, stick to the instructions below. Wear latex or rubber gloves at all times.

To convert the three primary alkaline chemicals to carbonic acid, combine sulfuric acid to the water sample in determining proportions. If there is hydroxide present, it interacts with it to generate water at pH 10. Carbonate is transformed to bicarbonate at pH 8.3. Both bicarbonate and carbonate are transformed to carbonic acid at pH 4.5. The water is unable to neutralize the sulfuric acid below this pH, and the amount of sulfuric acid supplied to the sample, and the change in the pH of the sample are proportional. As a result, additional sulfuric acid is given to the sample, lowering the pH to 4.2 by exactly 0.3 pH units. However, the exact pH, or total alkalinity, at which the transformation of these bases occurred is unclear.

To calculate total alkalinity, use the following equation to extend back to the quantity of sulfuric acid used to convert all of the bases to carbonic acid. The total alkalinity is then converted to mg/l of calcium carbonate using a multiplier (0.1). ($CaCO_3$). Follow these instructions to measure the alkalinity of your sample (Federman et al., 2006):

i. Samples should be warmed to room temperature before analyzing;
ii. Insert a clean delivery tube into the 0.16 N sulfuric acid titration cartridge and attach the cartridge to the titrator body;
iii. Hold the titrator over a sink or garbage container with the module tip pointing up. To discharge air and a few

drops of titrant, use the delivery knob. Wipe the tip and reset the counter to 0;

iv. Measure the pH of the sample using a pH meter;

v. In the beaker sample holder, place the delivery tube. When the pH meter reads 4.5, turn the delivery knob even though magnetically agitating the beaker. Keep track of how many numbers it took you to get to this pH. Keep the counter from being reset;

vi. Maintain titrating until the pH reaches 4.2 and keep track of the numbers;

vii. Use the subsequent equation:

Alkalinity (as mg/l $CaCO_3$) = (2a – b) × 0.1.

where; a is the titrant digits to achieve pH 4.5; b is the titrant digits to achieve pH 4.2.

0.1 = For a 0.16 titration pad and a 100 ml sample, use a digit multiplier.

Example:

The pH of the sample is 6.5 at the start.

To get a pH of 4.5, you must turn 108 times.

It takes another five rounds to reach pH 4.2, bringing the total number of turns to 113.

Alkalinity = [(2 × 108) – 113] × 0.1

= 10.3 mg/l

- On the datasheet, write alkalinity as mg/l $CaCO_3$.
- Before the next sample, rinse the beaker using distilled water.

3(b). Measure Total Alkalinity: If your water sample's pH is less than 4.5, before titration, continue as sees:

i. Place the supply tube in the beaker with the sample;

ii. While rotating the beaker, turn the supplied knob until the pH meter reads precisely 0.3 pH units lower than the sample's original pH;

iii. Keep track of how many digits were required to get this pH;

iv. Use the same equation as previously, but with a = 0 and b = the number of digits necessary to lower the original pH to exactly 0.3 pH units.

Example:

The pH of the sample is 4.53 at the start.

Titrate to a pH that is 0.3 unit lower than the starting pH; in this example, 4.0.

To get to 4.0, you'll need 10 digits.

Alkalinity = (0 – 10) x 0.1

Alkalinity = –1.0

i. On the datasheet, write alkalinity as mg/l $CaCO_3$.

ii. Before the next sample, wash the beaker using distilled water.

4. Perform an Accuracy Check: This accuracy check should be done on the first field sample that has been titrated, then midway across the line of work samples, and finally at the last field sample. After every 10 samples, compare the pH meter to the pH 7.00 and 4.00 buffers.

i. Split the neck off an alkalinity ampule standard, 0.500 N, or pour a few milliliters of the standard solution into a clean beaker if employing a standard solution from a bottle.

ii. 0.1 mL of the standard should be pipetted into the titrated sample. Return to the pH 4.2 endpoint and titrate again. Keep track of how many digits you'll need.

iii. Repeat with two additional 0.1 ml additions of standard. After each addition, adjust the pH to 4.2. 250 digits of 0.16 N titrant should be added to each 0.1 ml addition of standard.

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CHAPTER 4

EFFECT OF BASICITY AND ACIDITY ON SOIL REMEDIATION AND PLANT NUTRITION

CONTENTS

4.1. INTRODUCTION

For several people, the pH of the soil is solely important for vitality and soil chemistry. Furthermore, recognizing soil activities other than plant nutrient delivery and the significance of soil like a media for plant development necessitated a multidisciplinary examination of soil as well as its features because of larger ecological processes. It allows researchers to see procedures at all scales, from the landscape to the local and worldwide. Soil biogeochemistry, which examines biogeochemical procedures, is an example of a holistic approach to soil research. Soil biogeochemical activities that are linked across chemically, biologically, and geologically procedures, have a strong relationship with ecological processes of soil to a certain degree (Dahlgren, 2006). The soil is an important component of life support networks since it provides a variety of ecosystems services, including carbon stocking, water control, soil fertility, and meal production, all of which have an impact on human health (FAO, 2015). Maintaining, supplying, cultural, and controlling services are some of the ecosystems services. The supplying and controlling functions, as per the Millennium Ecosystem Evaluation, have the largest influence on the constituents of human well-fair for security purposes, the fundamental substance for decent health, life, and healthy social relations (Carpenter et al., 2009).

The soil pH has a huge impact on soil biogeochemical procedures in the natural world. As a result, the pH of the soil is referred to as the "key soil factor" because it affects the wide range of physical, biological, and chemical qualities and procedures which impact the development of plants and the output of biomass (Minasny et al., 2016). Throughout medical diagnostics, the pH of the soil is related to a patient's temperature since it immediately reveals the condition of the soil and the predicted direction of numerous soil activities (declaration of the lecture, Emeritus Prof. Eric Van Ranst, Ghent University). For example, the pH of the soil is regulated by the leachate of basic cations like Calcium, Magnesium, Potassium, and Sodium far beyond their discharge from weathered nutrients, releasing Hydrogen ion and Aluminum ions as the predominate exchangeable cations; the disintegration of H_2CO_3 in groundwater, that also generates carbonic acid, that ionizes and discharges Hydrogen ion; humic byproducts from the

humic substances of soil organisms, that generate higher density phenolic and carboxy groups that ionize and discharges Hydrogen ion, on either hand, regulates soil biology and also biological activities. As a result, in ecological systems, especially in the soil, there is a bidirectional interaction among the pH of the soil and biogeochemical procedures. As seen in Figure 4.1, the pH of the soil controls numerous biogeochemical procedures, while certain biogeochemical procedures, in return, affect the pH of the soil to a certain degree.

4.2. THE PH OF THE SOIL INFLUENCES PROCEDURES BIOGEOCHEMICAL

4.2.1. Translocation of Substance

Likewise, physicochemical procedures such as precipitation, dissolution, dilution, adsorption, volatilization, as well as others impact leaching quality in response to biochemical variations (Kulikowska and Klimiuk, 2008).

4.2.1.1. Mobility of Trace Element

The bioavailability, mobility, and solubility of trace minerals are all influenced by the pH of the soil that determines its transportation in plants. Thus, pH-dependent variation in organic and mineral soil components is mostly reliant on the partitioning of components among liquid and solid soil stages via dissolution-precipitation procedures (Rieuwerts et al., 1998). The –ve charges, for example, predominate at higher pH, while +ve charges predominate at lower pH. The amount of dissolvable organic carbon in the soil, that determines the accessibility of trace minerals, is likewise influenced by the pH of the soil. Due to poor absorption and rapid desorption, trace elements are frequently accessible at lower pH. Inside a small pH range known as the pH-adsorption edge, the tendency of trace element adsorption rises from essentially no adsorption to almost full adsorption at medium pH. The elements are entirely absorbed from this stage to onward (Bradl, 2004). For example, Bradl (2004) discovered that at pH of 5.3, Cadmium, Copper, and Zinc adsorption onto a sedimentary composite made up of Fe, Al, and Si-oxides was 62%, 60%, and 53%, correspondingly.

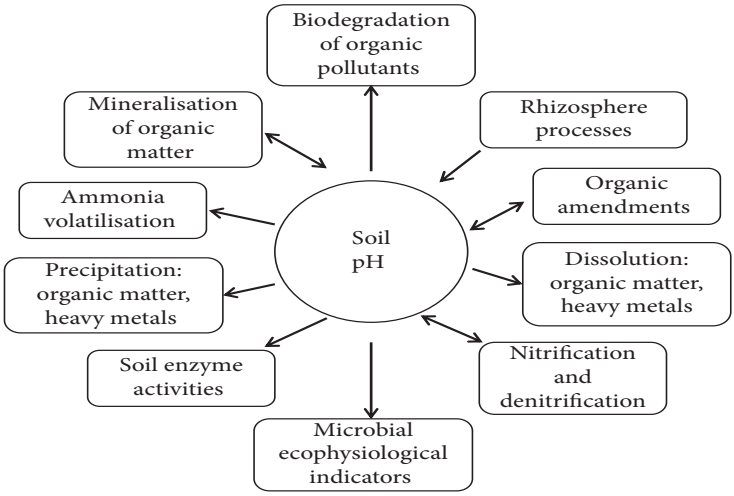

Figure 4.1. The relationship between the pH of the soil and several biogeochemical procedures.

Source: https://www.researchgate.net/figure/Some-biogeochemical-processes-and-their-relations-with-soil-pH_fig1_338357168.

On contrarily, they discovered that among pH 4.8 to 4.9, 50% of Cadmium and Zinc was sorbed on humic acids (Bradl, 2004). Besides the pH of the soil, the destiny of easily available trace elements is determined by the characteristics of its species(ionic) generated in the soil solution as well as the chemical setup of the soil. According to a study, when the pH of the soil rises, the solubility of most trace elements decreases, resulting in lower amounts in the solution of the soil. Any change in the pH of the soil has an impact on the solubility of metals. It's likely to be dependent on the pH change's direction and the metals' ionic species. Rengel (2001) discovered that the solubility of divalent metals reduces by a factor of 100, whereas that of trivalent metals reduces by a factor of 1,000. Baldock (2007) discovered that a one-unit reduction in the pH of the soil resulted in 10 times rise in metal solubility. In one experiment, they discovered that only around 1 mg $Zn \cdot L^{-}$ of the total Zn content of 1,200 $mg \cdot kg^{-1}$ was available in the solution of the soil at the pH of seven. At the pH of six, the concentration was a 100 milligrams $Zn \cdot L^{-}$, but at the pH of five, it was 40 milligrams $Zn \cdot L^{-}$.

4.2.1.2. Soil Mobility of Organic Fractions

Various fractions of soil organic matter are present, ranging from basic molecules like monomeric carbohydrates and amino acids to polymeric molecules like lignin, cellulose, and protein. These are found among partially degraded and nondecomposed microbial and plant remnants (Figure 4.2) (Baldock, 2007).

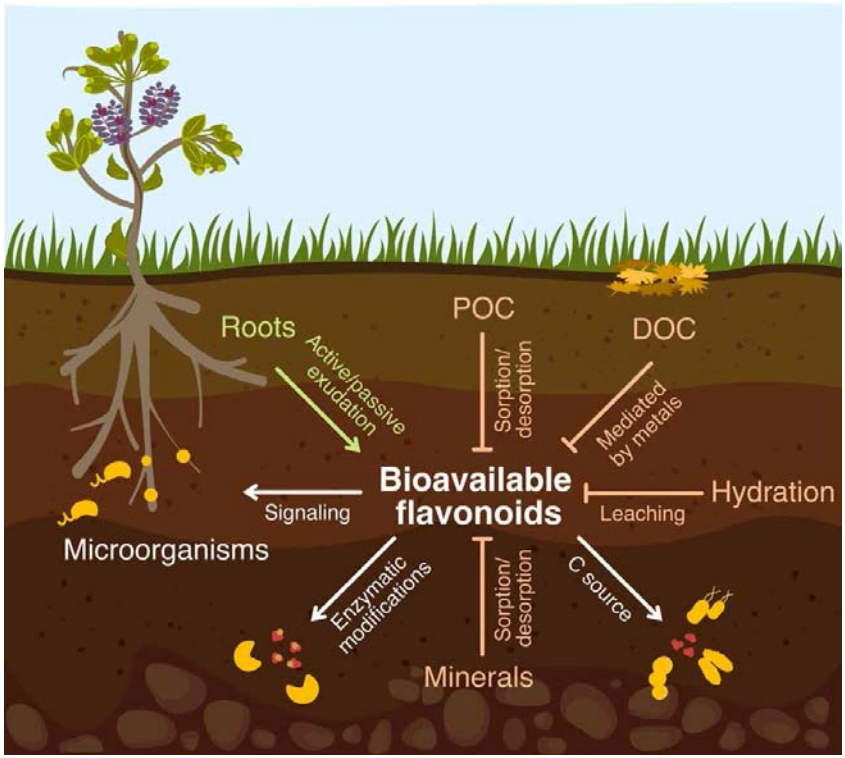

Figure 4.2. Flavonoid bioavailability in soils is influenced by environmental factors.

Source: https://www.science.org/doi/10.1126/sciadv.aax8254.

The fractions' mobility and solubility fluctuate after and during degradation, which might lead to soluble organic C and N leakage in certain soils. The proportion of organic material which flows through a 0.45 mm diameter filter is described as soluble organic carbon. The pH of the soil enhances the solubility of the organic matter of the soil via enhancing acid functional group ionization and decreasing the interactions among organic

components and clay minerals (Andersson et al., 2000). As a result, the amount of soluble organic matter in the soil rises, as does the amount of mineralizable nitrogen and carbon. This illustrates why the basic pH of the soil conditions have such a large influence on the drainage of soluble organic nitrogen and soluble organic carbon in several soils with significant organic matter (Andersson et al., 2000; Evans et al., 2012). The soluble organic carbon content in peatland soils has been observed in a similar way. Above the pH of six, the pH dependency of liquid organic carbon content becomes stronger (Curtin et al., 2016).

4.2.2. The Biological Procedures of Soil

4.2.2.1. Microbial Ecophysiological Indicators

Ecophysiology is the study of the relationship between environmental variables and cell-physiological functioning (Anderson, 2003). It is calculated utilizing the metabolic quotient ($_qCO_2$) like an indicator to demonstrate the effectiveness of soil microorganisms in utilizing organic material under various circumstances. Reduced bacterial communities metabolism provides more carbon accessible for biomass synthesis, resulting in greater biomass/unit (Anderson and Domsch, 1986). As a result, the metabolic quotient is defined as a cell-physiological component that mediates variations in climate. That means that the index would signal any shift in climate circumstances to an undesirable condition (Anderson, 2003). This is commanded through the pH of the soil. The effect of pH of the soil on the bacterial communities, as well as the society's maintaining requirements, is a driving factor for microorganisms ecophysical indicators, and it was one of the forecasters of the metabolic quotient (Neina et al., 2016). In the soils of lower pH, the metabolic quotient had been reported to be 2.5 times greater than in neutral pH soils. It's been linked to a pH difference between the interior cell pH (typically about 6.0) and the external pH circumstances, which raises maintenance costs and lowers overall bacterial biomass production (Anderson, 2003).

4.2.2.2. Soil Enzyme Activities

Soil microbes generate various enzymes for the biogeochemical nutrient cycle (Pietri and Brookes, 2008). The pH of the soil is necessary for appropriate enzymatic action in the soil, and it can indirectly influence enzymes by affecting the bacteria that create them (Sinsabaugh et al., 2008).

Biological setups, on the other hand, have a plethora of enzymes that aid in the conversion of numerous substances. Furthermore, enzymes come from various sources and have various levels of stability on solid surfaces. As a result, the pH upon which it achieves its peak activity (optimum pH) is varied (Figure 4.3) (Pietri and Brookes, 2008).

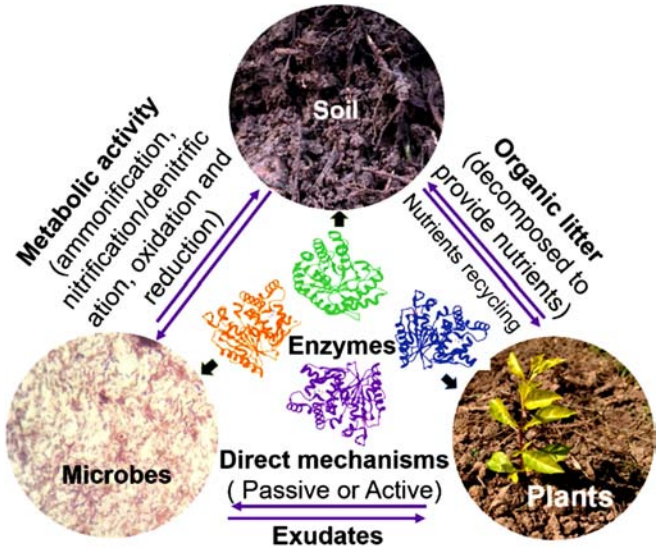

Figure 4.3. The significance of enzymatic actions and soil microbiome in plant development nutrition.

Source: https://link.springer.com/chapter/10.1007/978-981-13-9117-0_5.

It's amazing how enzymes that function on similar substrates can have vastly different pH at optimal conditions. It's obvious in phosphorous enzymes that have base and acid operating windows in the pH ranges of 8.5 to 11.5 and 3 to 5.5, respectively. Researchers categorized enzymes into 3 categories based on their optimum pH discovered in the soils in research on the optimal pH for particular enzymatic activity in soils from 7 wet tropical forests in the Center of Panama. These included enzymes with constant acidic optimal pH across soils, enzymes with variable optimal pH acidic across soils, and enzymes with optimal pH in both alkaline and acidic soil pH. Organo-phosphorus hydrolase activity is highest at high pH, according to Singh and Walker (2006). Glycosidases, for example, have an ideal pH range of four to six, whereas oxidative and proteolytic enzymes have an optimum pH range of seven to nine (Sinsabaugh et al., 2008). If distinct

microorganism species need low nutritional concentrations to create biomass or have enzymes with varied nutrient affinities, changes in the composition of microorganism communities might impact enzyme synthesis (Allison et al., 2007).

4.2.2.3. Biodegradation

The engineers of the Ecosystem, microbes of soil are engaged in the conversion of chemicals in the soil. Biodegradation is one of these conversions, wherein bacteria change xenobiotics and hazardous chemicals into less or more harmful forms to repair polluted soils. The chemical disintegration of inorganic and organic contaminants by microbes or biological agents is known as microbial degradation. The pH of the soil impacts microbial degradation, as it does several other biological procedures in the soil, by influencing bacterial growth, microbial population and biodiversity, enzymes that help in the decomposition procedure, and the characteristics of the compounds to be destroyed. In the breakdown of atrazine, the most relevant soil characteristic was pH (Singh et al., 2003). Microbial degradation is often aided by basic or mildly acid pH of the soil, but microbial degradation is hampered by acidic settings (Singh and Walker, 2006). For oil breakdown, pH levels around 6.5 and 8.0 are generally regarded as an ideal. Distinct enzymes operate within a specific pH spectrum within this range. The herbicide fenamiphos, for example, deteriorated in 2 soils in the U.K with higher pH (greater than 7.7) and 2 soils in Australia pH with the range from 6.7 to 6.8; in 3 acidic U.K soils (with pH range from 4.7 to 6.7). Around 90 days after inoculation, the microbial gradation procedures slowed significantly (Singh et al., 2003). In a degradation experiment having polycyclic aromatic hydrocarbons (PAHs), half of the PAHs deteriorated at the pH of 7.5 within 7 days, showing the highest value deteriorated. Xu (2012) discovered that certain bacteria isolated from petroleum-contaminated land in north China were able to degrade over 7% of petroleum at the pH of seven and nine. This was shown to be linked to most bacterial communities. Moreover, Zebarth et al. (2015) discovered that higher the pH of soil caused enhanced atrazine breakdown in Canadian and French soils. They found that soil respiration was greatest in atrazine-contaminated soils having pH values more than 6.5, as opposed to those with pH values lower than six, wherein metabolites were collected.

4.2.2.4. Mineralization of Organic Matter

Microbial activity frequently results in the mineralization of organic materials like nitrogen, carbon, sulfur, and phosphorus. For its direct influence on the bacterial community and its actions, the pH of the soil regulates mineralization in soils. It has ramifications for extracellular enzymes that assist in the bacterial respiration of organic substances. Furthermore, since the link among clays and organic components is weakened at increased pH of the soil, the extractable portions of Nitrogen and Carbon rise. ŠImek et al. (2002) discovered that pH of the soil and Carbon/Nitrogen fraction was responsible for 61% of the biodegradation rate in various upland subtropical soils supplemented with various organic substances, with corresponding raises in Carbon dioxide effluxes, total Nitrogen mineralization, and total nitrification in basic soil as compared to the acid soils. Sun et al. (2012) had previously achieved identical findings.

4.3. BIOGENIC REGULATION OF SOIL PH

Variations in the pH of soil are caused by biological activities involving live species and biochemical reactions using the remnants of deceased organisms. It may happen either via indirect and direct impacts of imposed organic wastes, whether in unburnt, completely burned, or charred formation, and also their biodegradation, or via indirect and direct impacts of biochemical procedures happening in living things in the soil setup, mostly via rhizosphere procedures.

4.3.1. Rhizosphere Procedures

The rhizosphere is the amount of soil around roots that are impacted by root and microbial activity (Hinsinger et al., 2003). From the root mat, it is a radial and longitudinal gradient, spanning from zero to two millimeters (Gahoonia and Nielsen, 1992). Roots absorb mineral nutrients and H_2O, perform root growth, emit excess fluid, breathe, and hence have increased bacterial activity in this tiny volume of the soil. Plant roots have the potential to produce pH variations in the rhizosphere through certain of such biological activities, whether by discharging protons (H^+) or hydroxyl ions (OH^-) to sustain ion equilibrium (Riley and Barber, 1969), based upon the nutritional state of the plants. As a result, rhizosphere pH may rise or fall based upon the predominant mechanism and ions discharge particular procedures and variables like (1) ion absorption paired with the discharge of inorganic ions which sustain electrical neutrality, (2) the removal of anions

of organic acid, (3) root desorption and breathing, (4) reduction-oxidation coupled procedures, (5) microorganisms manufacturing of acids after the integration of discharged root carbon, and (6) plant genotype regulate plant root-induced pH of soil variation in the rhizosphere. Interestingly, roots show a stronger propensity to increase instead of drop the rhizosphere pH. Plant intake of nutrients in the format of anions and cations, principally owing to plant absorption of the two main forms of nitrogen source (NO_3^- and NH_4^+), that is normally absorbed in significant amounts, is the key mechanism accountable for pH alterations in the rhizosphere. Plants absorb nitrogen in three states which are (1) ammonium, (2) nitrate, and (3) molecular nitrogen, while amino acids may also be absorbed (Hinsinger et al., 2003). To sustain electrical neutrality in the rhizosphere, the intake of each of the three states of nitrogen is accompanied by the discharge of matching ions. Plants should discharge hydroxyl ions and bicarbonate to sustain electroneutrality around the soil-root interface whenever nitrate predominate in soil whenever its absorption prevails, leading to a rise in the pH of the rhizosphere (Hinsinger et al., 2003). Plants, on the other hand, discharge protons in reaction to ammonium ion absorption, lowering the pH of the rhizosphere (Riley and Barber, 1969). It's been discovered that 15, 6, and 0% correspondingly, of the ammonium ion from the net Nitrogen contained in the soil, is necessary to reduce the pH of the rhizosphere by 1.2 pH units and to sustain, or enhance the pH of the rhizosphere by 0.4 pH units (Gahoonia and Nielsen, 1992).

The amount to which the mechanisms and variables that influence rhizosphere pH variation affect the species of plant and development levels varies. For example, Rukshana et al. (2012) discovered variations in rhizosphere acidification in beans (*Phaseolus vulgaris L.*) and maize (*Zea mays L.)* in research on rhizosphere acidification reactions. Maize acidified the rhizosphere at first, then basic it with time, whereas beans had the reverse impact. Researchers discovered a reaction impact of the two plant species on the pH variation of the rhizosphere, in which the extent of alkalization or acidification was weak when roots developed close to each other than whenever roots developed far apart. Moreover, as a result of changing nitrogen ion intake, species of plants, and plant development phases, the rhizosphere pH fluctuates throughout time. Metzger (1928) discovered the highest (HCO_3^-) in the rhizosphere during the blossoms and fruit development phases (Figure 4.2) in an experiment on apple fruit trees (*Malus pumila Miller*), corn (*Zea mays L.*), buckwheat (*Fagopyrum esculentum Moench*), kaffir lime (*Citrus hystrix DC.*), and cowpeas (*Vigna unguiculata (L) Walp*) and lettuce (*Lactuca sativa* L.). The (HCO_3^-) in the

rhizospheres of the plants were as follows: lettuce buckwheat>pine>apple>k affir>cowpeas>corn>wheat. Such values were significantly less than any of those found in the soybean rhizosphere (*Glycine max (L.) Merr.*) (Riley and Barber, 1969). Gregory (2010) discovered that between April–September, a Douglas fir (*Pseudotsuga menziesii* (Mirb.) Franco) stand absorbed 93% of NO_3-N, compared to 83% during October to March. It most likely raised rhizosphere pH, implying that during times of weak nitrate absorption, the pH of soil may drop owing to buffering or as a reaction to NH_4^- absorption.

4.3.2. Raw and Combusted Organic Materials

The pH rises to a high and then drops when unburned organic matter or raw plant remains are introduced to the soil. For example, whenever Forjan et al. (2014) introduced a blend of slurry from a bleach factory, metropolitan waste products, and mining wastes, as well as a blend of waste from a purifying plant, woody biomass, and agri-food industry leftovers to the soil, they discovered early rises in the pH of soil. furthermore, adding young Kikuyu (*Pennisetum clandestinum L.*) branches raised the pH of soil by approximately 1 pH unit. The main causes of this pH variation are (1) the discharge of surplus residual alkalinity attributed to alkaline cations like Calcium, Potassium, Magnesium, and Sodium; (2) decarboxylation of organic anions which happens during Carbon mineralization, usually causes protons to be consumed and hydroxide ion to be released; (3) ammonification of the residual nitrogen; (4) nitrogen fixation of mineralized residual nitrogen; and (v) ionization or non-ionization of organic substances. Such procedures are influenced by the amount of fertilizer used as well as the soil and ambient variables (Xu et al., 2006). The primary processes involved in organic anion-induced pH of soil elevation, as per Xu et al. (2006), include direct chemical reactions and oxidation of organic anions throughout residual breakdown. Furthermore, Hydrogen ions may form associations with organic anions as well as other negatively charged chemical functional groups found in organic materials (Xu et al., 2006).

The quantity of alkalinity available, residual quality (Carbon to Nitrogen ratio), the velocity of residual administration and degradation, the starting pH, and soil buffering capability all influence the rise in the pH of soil following residual utilization (Xu et al., 2006). The chemical and biological contents of distinct residuals govern the mechanisms that cause the pH of soil variation. It was discovered in an incubating experiment with three soils and three distinct residual kinds, wherein soil pH rose as lucerne>chickpea>medic>high-N wheat>low-N wheat (Figure 4.4) (Xu et al., 2006).

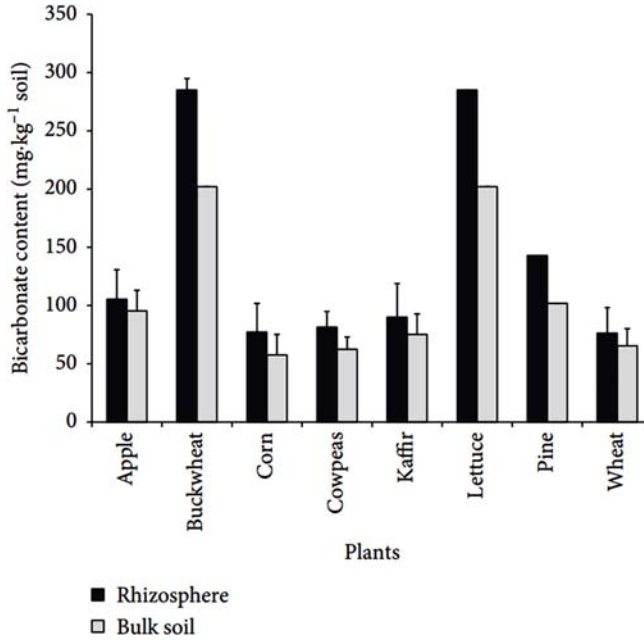

Figure 4.4. The bicarbonate compositions are detected in the rhizosphere and massive soil of various greenhouse-grown plants. The standard deviation is shown by the error bars (n 2 to 34). Pine and lettuce each had just one piece of data, therefore error bars were not possible to provide (Metzger, 1928).

Source: https://journals.lww.com/soilsci/Citation/1928/04000/THE_EFFECT_OF_GROWING_PLANTS_ON_SOLUBILITY_OF_SOIL.3.aspx.

Moreover, it was discovered that the amount of soil pH rise after residual replenishment was in the sequence chickpea>canola>wheat in a 59-day laboratory incubation and field tests (Butterly et al., 2013). The pH rises were caused by 40% to 62% dissolved alkalinity in chickpea and canola residuals, according to the researchers. The residual of dicots, especially legumes, have significant alkalinity and cause bigger impacts on soil pH change than monocots, as shown in this and several other studies. As a result of nitrification, the pH rise following residual addition generally reaches a high and then drops. Low carbon-nitrogen ratio residuals are generally linked with a dramatic pH fall over a while, the amount of which changes with the type of soil and soil buffering capability (Xu et al., 2006; Butterly et al., 2013), while high carbon-nitrogen ratio residuals generate a lesser pH rise if any at all (Xu et al., 2006).

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CHAPTER 5

HISTORICAL DEVELOPMENTS IN ACID-BASE CHEMISTRY OF FOOD PRODUCTS

CONTENTS

5.1. INTRODUCTION

It was around the 17th century that the notions of nutrition and food began to shift in northern European countries. Salts were first discovered as a result of a reaction between acids and bases, according to early scientific research. Digestion was no longer considered as a cooking process but rather as a series of fermentation that was regulated by a balanced generation of acids and alkalis instead. The balance of alkalis and acids appeared to be essential for survival.

Food was first thoroughly studied for the amount of energy and macronutrients in the 19th century, and the first scientifically based nutritional guidelines were developed. The most popular use for processed foods (Astrup, 1986).

The introduction of new foods into the market has resulted in an epidemic of nutritional problems. Acidosis seems to be a likely pathogenic component in this situation. Practitioners developed holistic philosophies that included the notion of acid-base balance as well as the recommendation of foods that included an abundance of alkali.

New micro methods for determining the concentration of electrolytes and the acid-base state of the blood have been developed.

In the 1960s, the American Heart Association encouraged scientific and medical trials into acid-base metabolism. The link between blood acid-base status and excretion or net acid consumption was, though, improperly easy in the new physiologically-based language of systemic acid-base status, which was developed to replace the previous nomenclature. Patients on chemically specified diets and receiving parenteral nourishment were found to be suffering from metabolic acidosis in the 1970s. Data from complete acid-base balance investigations were utilized to develop calculations that estimated renal net acid excretion from nutrient intake and predicted the possible renal acid load posed by particular meals (Laudan, 2000).

5.2. HISTORICAL PERSPECTIVES OF ACIDS AND BASES

Nowadays, we have a solid grasp of acids and bases, thanks to advances in contemporary chemistry (also called alkalis). In our daily lives, acids and bases are present everywhere, from the laboratory to the kitchen. These critical compounds are employed as industrial catalysts, laboratory reagents, culinary additives, and cleaning products, among other applications.

However, during the course of the history of chemistry, it has taken centuries to get a complete understanding of these compounds.

5.2.1. Ancient Science: Vinegar and Soap

The characteristics of acids and bases were only hazily known through the time of the Ancient Greeks. A number of tests were employed to differentiate compounds throughout their endeavors to categorize substances as well as to bring perfection, harmony, and balance to the cosmos. One of them was taste, and they classified items based on whether they were bitter, sour, salty, or sweet (or a combination of these; Figure 5.1) (Astrup et al., 1995).

Figure 5.1. Ancient soap with inscriptions.

Source: https://www.sciencefocus.com/science/who-invented-soap/.

Because of the decline of Greek influence in the Roman world and the transmission of their expertise to the Romans, sour substances such as vinegar and lemon juice came to be referred to as acids. “Acid” and “acetic” are both come from the Latin term for “sour-tasting,” acere, and are used to describe a variety of substances. Bases, on the other hand, were not as thoroughly investigated, despite the fact that they were recognized as substances capable of neutralizing acids, which corresponded well with the ancients’ aim to achieve harmony and balance in all things. Making bases was the simplest method for the ancients, and it was a procedure that was well-known to the Greeks, who used ashes in conjunction with animal fat to produce soap, among other things. Several Greeks still employ a similar

procedure to manufacture great handmade soap, which involves combining ashes with olive oil. Aside from bases, alkalis are also used to refer to them, a term that comes from the Arabic word for 'roasting;' however, it is unknown why they were later referred to as bases. Both terms are totally appropriate and are frequently used in the same sentence (Sörensen, 1909).

5.2.2. Acids and Bases: The Playthings of Alchemists

As science progressed during the Islamic Golden Age and the Modern, alchemists began to gain a better understanding of acids, realizing that stronger solutions could accelerate the corrosion of metals and dissolve specific types of minerals. Alchemists throughout the Middle Ages and Islamic times had a wide variety of alkalis and acids to choose from:

- Ammonia;
- Potash (potassium carbonate);
- Soda (sodium carbonate);
- Acetic acid;
- Hydrochloric acid;
- Sulfuric acid;
- Sulfuric acid;
- Citric acid;
- Aqua regia is a combination of nitric and hydrochloric acids that is capable of dissolving even precious metals such as gold.

Arnaldus de Villa Nova, a Spanish scholar, first used litmus to examine acids and bases around 1,300. This lichen-derived substance had been employed as a dye since at least the Viking era, but he was the first known academic to employ it as an acidity test. Robert Boyle, who discovered that many plant-derived chemicals changed color in the presence of acids or bases, elaborated on this theory. The syrup of violets, for example, is blue in a pH-neutral environment but becomes green when subjected to bases and red when combined with an acid. Chemists could figure out what percentage of acids and bases would neutralize each other using these testing chemicals, allowing them to evaluate the relative strengths of these substances in a primitive way. The belief that heat was a distinct element contained inside combustible materials was popular for most of the 18th century, whenever the thermodynamic Theory of Phlogiston reigned supreme. Georg Ernst Stahl argued that all acids were produced from sulfur and that the strength was determined by the amount of phlogiston; however, before the end of the

century, this theory would be debunked (Hasselbalch, 1917).

5.2.3. The Enlightenment: Classifying Acids and Alkalis

A more systematic study of bases and acids did not begin till the time of Antoine Lavoisier, a great French chemist who strove to categorize elements and comprehend the nature of heat. Bases were defined by chemists at this time as compounds that could neutralize acids to produce water and salt. Lavoisier attempted to isolate the molecule in acids essential for their peculiar qualities in 1776, prompted by investigations into the features of gases. He incorrectly assumed that a chemical called oxygen was to blame, but his discoveries prompted more research (Figure 5.2).

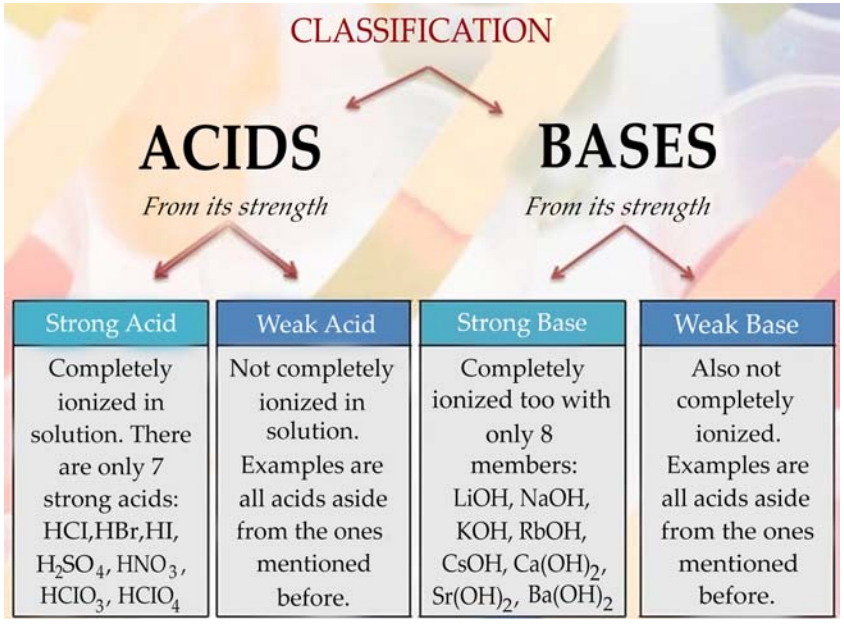

Figure 5.2. Typical classification of acids and bases.

Source: https://www.slideshare.net/annisahayatunnufus/acid-base-physical-chemistry-presentation.

Humphrey Davy (1778–1829), was a British scientist most renowned for his studies of gases, but Lavoisier's ideas to the test determined that oxygen was not the ingredient responsible for acid characteristics. Because many acids lacked oxygen, he reasoned that maybe something was at work. Scholars from many different nations contributed to the rise in scientific

activity throughout the Age of Enlightenment, and the study of acids was no exception. Another inventive scientist in Germany, Justus Freiherr von Liebig (1803–1873), isolated hydrogen as the responsible ingredient, arguing that it was the single element common to all acids. Svante Arrhenius (1859–1927), a Swedish chemist, was the next to examine acids and bases, claiming that acids and bases acquire their characteristics as a result of ion activity in the solution. Despite being dismissed by his contemporaries as a lunatic, he was given the Nobel Prize in 1903, demonstrating how fringe scientists may have a significant impact on paradigm changes. One of Stockholm University's buildings is named for this famous scientist, which is an appropriate homage. Acids, according to Arrhenius, are chemicals that add hydrogen cations, H^+, to water. Hydrochloric acid, for example, adds H^+ and Cl^- ions to water. Alkalis, on the other hand, add hydroxyl ions, OH-. Sodium hydroxide, for example, contributes OH^- and Na^+ to water. Since the H^+ and OH^- ions combine to generate water, leaving salts behind, acids, and bases balance each other out: $HCl + NaOH \leftrightarrow NaCl$ (Table Salt) + H_2O This was a reasonable definition, and study into these compounds proceeded (Darrow, 1950).

5.3. ACIDS AND ALKALIS IN EVERYDAY LIFE

5.3.1. Alkali and Acids in Alchemy

Several chemicals that are now recognized as bases and acids were known in ancient times. Strong acids piqued the curiosity of medieval alchemists hunting for the knowledge of how to produce gold. The initial stage in converting metal to gold seems to be dissolving it in sulfuric or nitric acid (Astrup, 1986). Acid is most likely originated from the sour taste. The name alkali alludes to its source, vegetable ash. The Arabian name for ash is "al qali."

5.3.2. The Change from Old-Fashioned to Modern Diet in the 17th Century

The highest classes of the Islamic and Christian worlds ate similar foods until the 17th century: thick purees with loads of sour sauces, cooked vegetables, sweets, and spices, and warming wines (Laudan, 2000). This custom was carried on by Spanish America and the Islamic world. This may be seen in India's modern curries and Mexico's moles. This food and

nutrition concept dates back to Greco-Roman antiquity (Laudan, 2000). Cooking was considered to be a sort of digestion. The balance of the four physiological fluids – blood, phlegm, yellow bile, and black bile – related to the four elements – air, water, fire, and earth – was sustained by a healthy diet. Differences in heat and dryness were used to allocate food. Pepper and beef, for example, were associated with yellow bile and fire as dry and hot, whereas milk was associated with blood and air as damp and hot. Northern Europe's aristocracy began to adjust their diet around the middle of the 17th century. Using alchemy's expertise with distillation, Paracelsus categorized matter into three elements around the start of the 16th century (Laudan, 2000). Mercury was the volatile portion of the plant that contained the essence, scent, or perfume.

Sulfur was the name given to the oily component that carried the moistness and sweetness. Salt is the solid residue of food that gives it flavor and firmness.

These terminologies bear little resemblance to modern chemistry terminology. The process of digestion was thought to involve a series of fermentation. Fruits and vegetables deteriorate quickly. As a result, heating was not required for pre-digestion. Vegetables and fresh greens were therefore appreciated. Sauces made with fat and salad dressings made with oil became popular. Sulfur-containing vegetable oils or butter were blended with salt-containing flour and salt-containing salt, as well as mercury-containing vine or bouillon. As dessert, sweets, and sugar were pushed to the edge of the menu. The essence appeared as gas bubbles in certain dishes. As a result, sparkling mineral waters became increasingly popular, and sparkling cava was first manufactured.

5.3.3. Salt: A Compound of Alkali and Acid

In the natural sciences, the exploration of the nature of gases and "salts" was a popular topic in the 17th century, particularly in Europe. As a result of his experiments with table salt and sulfuric acid, Rudolph Glauber (1627–1691) discovered sodium sulfate, a miraculous laxative that was commercially successful in the brand name "Sal Mirabile"(Astrup et al., 1995). His research helped to establish the theory that salts are formed by the reaction of acids and alkalis.

5.3.4. Life: An Equilibrium of "Alkali and Acids"

Francis de la Boé Sylvius thought that the decomposition of food in the alimental canal, which was caused by a sequence of fermentations, was regulated by the generation of an equal amount of acids and alkalis in the digestive tract. Scientist Jan Baptista van Helmont from the Netherlands had established that stomach juice, as well as regular urine, was very acidic. He imagined acids as sharp rodlets dispersing stuff that was impervious to all other alkalis and liquids as rings that prevented the sharpness of the rodlets from dissolving substances (Figure 5.3).

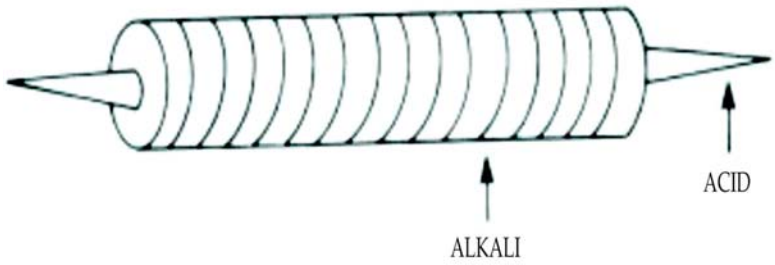

Figure 5.3. As per Jan Baptista van Helmont (1577–1644), salt is a composite of acid and alkali.

Source: https://www.dovepress.com/facing-acidndashbase-disorders-in-the-third-millennium-ndash-the-stewa-peer-reviewed-fulltext-article-IJNRD.

According to this theory, diseases were thought to be the consequence of aberrant fermentation, which resulted in the creation of an alkaline surplus or acid in bodily fluids. An excess of acids should be addressed with alkali, and vice versa, in order to preserve equilibrium in the system. This extremely speculative holistic notion of Life as a balance of alkalis and acids had a major impact on the development of the mind in Europe, particularly in the Middle Ages and Renaissance (Figure 5.4) (Dill and Fölling, 1928).

Figure 5.4. Common examples of household acids and bases.

Source: https://sciencenotes.org/household-acids-and-bases/.

5.4. DEVELOPMENTS OF ACID-BASE CHEMISTRY IN THE 18TH CENTURY

For the purpose of dissolving bladder stones, Joseph Black (1728–1799) discovered that chalk lost weight through calcination and concurrently generated a gas known today as CO_2, which was also included in terminated air and fire smoke at the time. The ordinary air, according to Antoine Laurent Lavoisier (1743–1794), contained an additional gas that was respirable, fed combustion, and could be coupled with metallic elements. He named it "oyxgène," which comes from the Greek words for "acid" and "to form," since, in his opinion, the new gas represented the universal principle of acidity that applied to all acids. He also demonstrated that water was not a basic element but rather a mixture of oxygen and hydrogen molecules. Mineral alkalis were referred to as "la soude," vegetable alkalis were referred to as "la potasse," and volatile alkalis were referred to as "l' ammoniaque" in his new chemical nomenclature (Hasselbalch, 1917).

5.5. ORGANIC CHEMISTRY AND THE RELATION OF ACID-BASE METABOLISM AND NUTRITION IN THE 19TH AND 20TH CENTURY

Jöns Jacob Berzelius (1779–1848) concentrated on the chemical composition and activities of animals, whereas Justus von Liebig (1803–1873) concentrated on the chemical processes and combination of plants, drawing on the growing body of knowledge in inorganic chemistry. Organic acids are being investigated for their chemical makeup. Acids, according to Liebig, are compounds whose hydrogen content may be substituted by the presence of a metal. William Prout (1785–1850) identified free acid in rabbit gastric juice, which had roughly one-third the chloride concentration of normal rabbit gastric juice. Henry Bence Jones made meticulous observations of the changes in the acidity of urine that occurred in response to food ingestion. He hypothesized that the conversion of oxygen to carbon dioxide results in the production of acid in the body and, as a result, suggested drinking alkaline water. Liebig demonstrated that herbivores discharged urine that was alkaline in pH (Figure 5.5) (Gamble and Najjar, 1954).

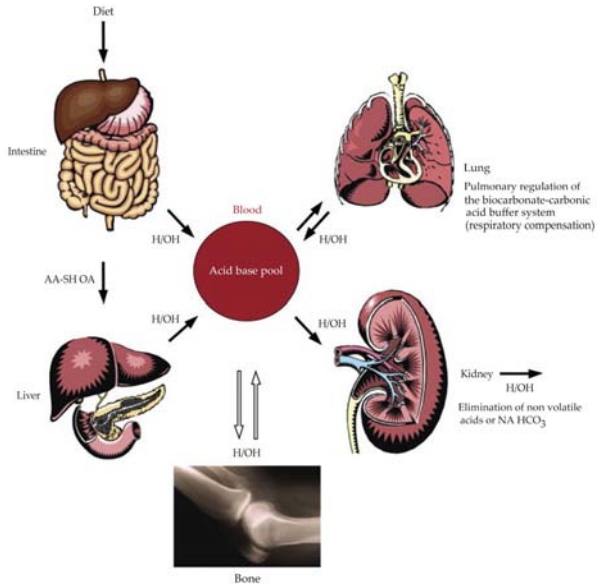

Figure 5.5. Acid-base metabolism in the human body.

Source: https://www.sciencedirect.com/topics/medicine-and-dentistry/acid-base-homeostasis.

5.5.1. Heroic Treatment of Cholera Patients

Dietetics and balneology were two of the most well-regarded medical remedies during the 19th century. Thomas Aitchison Latta (1796–1833), a young, unfamiliar Scottish practitioner, administered an intravenous solution comprising 0.5% sodium chloride and 0.2% sodium bicarbonate to a 50-year-old woman suffering from cholera in 1832, which was the first effective and most remarkable treatment of a mineral disparity and an acid-base disturbance (Greig, 1946). Despite the excellent experiences of other physicians, Latta's treatment notion was not embraced by the scientific community. It was in direct contradiction to Galen's prevailing therapeutic philosophy, according to which "the evil" was ejected by bloodletting or the use of strong emetics such as mineral acids, calomel, and antimony. Body fluid salt and chloride concentrations were inaccurately measured, and there was no fundamental physiological comprehension of what was going on in the body. The notion was tarnished by widely fluctuating amounts of sodium bicarbonate and sodium chloride, as well as by volume estimates that were frequently too low.

5.5.2. The Discovery of the Ionic Structure of Water and Salts

The notion of ions has had a significant impact on our knowledge of acid-base physiology. A link between chemical reactivity and conductivity was discovered by Svante August Arrhenius (1859–1927) in different salt solutions, and he developed the dissociation hypothesis as a result. Wilhelm Ostwald (1853–1932) discovered that water has the capacity to dissociate, resulting in the formation of OH– and H^+ ions. During his lifetime, Soren Peter Lauritz Sorensen pioneered the concept of pH and showed its critical significance in the regulation of enzyme activity (Sörensen, 1909). Both Karl Albert Hasselbalch and Lawrence Joseph Henderson conducted research on buffer systems in biological fluids, namely the carbonic acid/bicarbonate system, and developed the "Henderson-Hasselbalch equation as a result (Ill and Fölling, 1928).

5.5.3. The Beginning of Nutritional Science in the 19th Century

William Beaumont (1785–1853) noted that the digestion of varied meals always ended in an acidic chyme in a patient who had a gastric fistula as a consequence of a gunshot wound in one of his patients. He thought that all meals included only one nutrient, or "ailment," which is dispersed in the stomach and absorbed afterward in the digestive process. Nutrition

developed a topic of discussion in the new disciplines of biochemistry and physiology in the second part of the 19th century. A thorough analysis of food was carried out to determine the number of macronutrients and energy it contained, and nutritional guidelines were developed. For example, an adult man weighing 70–75 kg should consume 3,000 kcal, 118 g–500 g carbs, and protein, 56 g fat per day. The new understanding served as the foundation for a fast-developing food sector that resulted in the introduction of a new type of food, known as processed food (Howland and Marriott, 1916).

5.5.4. Clinical Study of Acid-Base Metabolism from 1850–1950

Before 1950, medical trials in acid-base metabolism were impeded by the necessity for huge volumes of biological material and the need for sensitive and time-consuming analytical processes, such as blood analysis, which needed more than 20 ml of blood for one sample (Droese and Stolley, 1964). Emil Heinrich du Bois-Reymond was the first person to notice the creation of lactic acid throughout muscle contraction. Intensive research into the relationship between lactic acid production, carbohydrate conversion, oxygen delivery, and decreasing blood alkalinity began at that point. Among the symptoms of diabetic comas, Adolf Kussmaul noted the presence of heavy, deep breathing, and Bernhard Naunyn (1839–1925) noted the presence of high levels of beta-oxybutyric acid and acidity in the blood as well as a high excretion of ammonium in the urine. In his 1855–1947 book Uremic Acidosis, Rudolph von Jaksch hypothesized that uremic acidosis was caused by poisoning through organic acids as a result of the retention of urea. As a result, ketoacidosis is potentially lethal. According to Adalbert Marianus Czerny (1863–1941), who published his views in 1897, acidosis might potentially be a contributing factor to infantile diarrhea. This was demonstrated explicitly in 1916 by Williams McKim Marriott and John Howland, who worked together. They employed pricey new analytical procedures with blood samples ranging from 1–2 ml in volume (Howland and Marriott, 1916).

5.6. NON-ACADEMIC DOCTRINES OF NUTRITION AND LIFESTYLE INCORPORATING THE CONCEPT OF AN EQUILIBRIUM OF BASES AND ACIDS

Numerous practitioners have reported that a diet comprising of a vast range of raw fruits and vegetables, rather than a consistent diet of managed food products, has helped them or their patients to recover from illnesses.

This was in stark contrast to the scientific conceptions of the time period. Consequently, they established new holistic health and lifestyle ideologies that went far past the principles of nutrition and incorporated the theory that has been in existence since the 17th century – that Life is a delicate balance of alkalis and acids – As the creator of the macrobiotic ideology, Sagen Ishizuka (1851–1910) brought together the European concept of acid-alkaline balance with the Chinese concept of Yin and Yang (Aihara et al., 1988). Howard Hay argued for a diet high in alkali and a diet in which carbs and proteins were consumed in different portions (Heintze, 2012). When Franz Xaver Mayr advocated for an alkali-dominated vegetable diet, he developed his concept of intestinal autotoxication, which is still in use today (Rauch, 1991).

The current state of physiological understanding backed the theory that the novel nutritional outbreaks were produced by acidification of the body's pH level in the blood. It was commonly recognized that vegetables and fruits have a large alkali surplus as compared to other foods, such as meat. However, dietary guidance from academic institutions and the food sector failed to account for variations in mineral content. When it came to the meal tables, mineral deposits were not mentioned. The prevalent diet of greens ended in alkaline urine, whereas the predominant intake of meat was caused in acid urine. At the end of the day, carbohydrate metabolism was associated with the formation of large quantities of diabetic ketoacidosis, and organic acids, the cause of which was yet unknown, was a potentially fatal condition. It is possible to illustrate the apocalyptic vision of certain adherents of these writers by the retranslated German title "Cultural sickliness and death of acidosis, proper nutrition a decisive matter for the white race" of Alfred McCann's American book "The science of eating" (McCann, 1929).

5.6.1. Acidified Formulas in Infant Nutrition

Mariott discovered that newborns fed acidified cow's milk preparations grew faster than those fed non-acidified cow's milk preparations in 1919 (Marriott, 1923). In newborns with hypocalcemic tetany, acidification by hydrochloric acid, calcium chloride, or ammonium chloride has proven to be an efficient therapy (Freudenberg and György, 1922; Scheer et al., 1924). Due to the antibacterial action and an estimated enhancement in bioavailability of various elements, cow's milk products acidified with citric or lactic acid developed quite popular in the following years. The

enhanced bioavailability could not be proven in the 1960s (Droese and Stolley, 1964). Furthermore, systematic clinical monitoring of blood acid-base status showed late metabolic acidosis in certain newborns and babies because of a discrepancy among a high renal acid load from acidified cow's milk formulae and the age-related poor renal ability for net acid excretion (Kildeberg, 1964). Acidified cow's milk formulae were phased out in favor of humanized formulas by the end of the 1960s.

5.6.2. Routine Micro Methods for the Analysis of Blood Acid-Base Status and Serum Electrolytes

In the 1950s and 1960s, two novel analytical methods made routine monitoring of acid-base metabolism possible in clinical practice. Flame photometry enabled the systematic detection of potassium and sodium in tiny amounts of biological material in a rapid, affordable, and exact manner (Lundegårdh and Burström, 1933). The essential relevance of proper pH management in artificial respiration was proven in 1952 in Copenhagen during a polio outbreak with a high prevalence of patients requiring synthetic respiration.

As a result, Poul Astrup, a young doctor, devised a micro method for determining acid-base balance in the blood.

It was depended on three blood pH measurements, one earlier equilibration and the other two after equilibration at two distinct CO_2 pressures. The novel micro method was quickly adopted as a standard clinical procedure, resulting in a surge in acid-base metabolism medical research.

A consensus meeting in 1964 agreed on a standard language for blood acid-base status (Manz, 2001). A variation of blood pH value of 7.4 was labeled " alkalosis " or " acidosis " by those who preferred a physiological explanation. The respiratory component, measured by pCO_2, and an undefined metabolic factor, characterized through plasma bicarbonate concentration or standard base excess, might both be to blame. In easy disturbances, the words alkalosis or acidosis can be adjusted with the adjectives " metabolic " or " respiratory " to describe the influence of the main etiologic component, and with the additional adjectives " compensated " or " secondary " if the other cause had enough time to compensate. In reflection, this phrase revealed two major flaws: To begin with, pH 7.4 is not the preferred reference signal of the body's controller for determining the physiologic optimal hydrogen ion concentration. Second, pCO_2, pH, and

base surplus are all measurements of concentration. They can, but not must, be linked to turnover rates (Kildeberg, 1964).

5.7. RELATIONSHIP BETWEEN RENAL NET ACID EXCRETION AND BLOOD ACID-BASE STATUS

Bicarbonate and acid loading studies were undertaken in the 1940s and 1950s (Pitts et al., 1949). At a plasma bicarbonate level of around 25 mmol/l, renal net acid secretion was around 40% of severe maximal renal net acid excretion in patients eating a western-style diet. The maximum amount of renal acid stimulation was around 18 mmol/l. This is roughly 9 mmol/l lower than the plasma bicarbonate level at zero renal net acid excretion, or, to put it another way, at the acid-base balance of the kidney. There is no physiological limit to the amount of bicarbonate excreted by the kidneys. Absorption and production in the intestines restrict it (Figure 5.6).

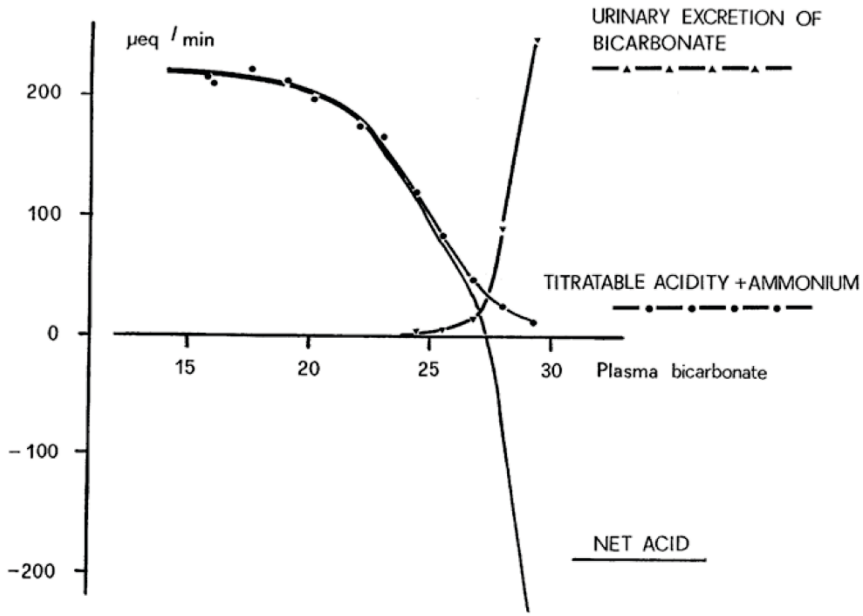

Figure 5.6. Relationship between plasma bicarbonate level in an adult and renal net acid excretion.

Source: https://pubmed.ncbi.nlm.nih.gov/16695657/.

Despite these findings, in a sample of babies with either pyloric stenosis or acute gastroenteritis, a linear association between blood base excess and renal net acid excretion was hypothesized (Kildeberg et al., 1969). This is an instance of the evocative power of the consensus conference's interpretations and definitions in 1964, which linked acidosis of the blood to the concept of a net acid load of the body and alkalosis to the concept of a net baseload. In the context of a significant metabolic alkalosis, several individuals with pyloric stenosis had an acidic urine pH (Kildeberg et al., 1969). This appeared to be an irreconcilable mixture of evidence; thus, it was dubbed "paradoxical aciduria" by the consensus conference.

Dumas (1970) described the findings of three bicarbonate loading tests in a seven-year-old kid with genetic chloride diarrhea at three levels of extracellular volume, intestinal chloride loss, and sodium chloride intake in 1970.

Extracellular volume, blood pCO_2, serum potassium, parathormone, and calcium all influence plasma bicarbonate levels at the renal acid-base balance (Manz et al., 1997).

5.8. TRADITIONAL INPUT-OUTPUT ACID-BASE EQUILIBRIUM STUDIES

Traditional input-output acid-base stability tests in healthy persons and patients with chronic renal acidosis were done for the first time in the 1960s (Goodman et al., 1965). Four nonmetabolizable cations and two nonmetabolizable anions of consumption, urine, and stool, as well as urinary data of three renal metabolites of renal net acid excretion and two metabolic end-products were included in the balance data (titratable acidity, ammonium, bicarbonate). The net hydrogen balance of the body may be determined using individual preservation rates of the key nutritional ions, as well as urine excretion of organic acids, sulfate, and net acid excretion. Hydrogen retention was nil in healthy persons. Regular net acid retention was around 50% of daily renal net acid excretion in individuals with persistent renal failure and metabolic acidosis (Goodman et al., 1965).

5.8.1. Potential Renal Acid Load

The role of the stomach, the liver, and development in acid-base metabolism has been hotly contested over the last 30 years, and the results have been a source of much controversy. Kildeberg postulated that intestinal

ion absorption was governed by an overall active regulatory system that maintained a substantial surplus of absorbed cations (Lennon et al., 1966). Specific absorption rates of all main ions, on the other hand, do not need the implementation of a comprehensive regulatory mechanism. Häussinger and Bourke hypothesized that the liver performs a major role in acid-base metabolism by focusing on a specific portion of acid-base metabolism (Remer and Manz, 1995). During the process of growing, a vast alkali pool is formed in the skeleton (Figure 5.7).

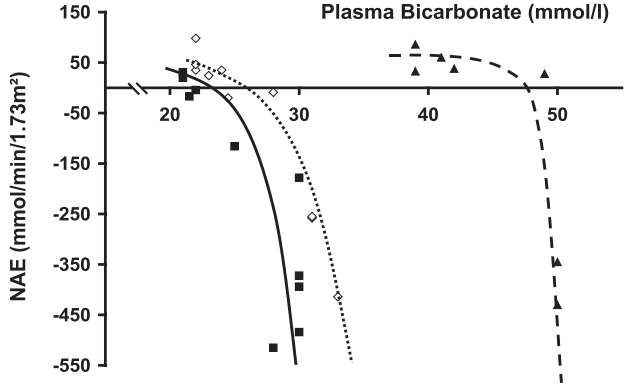

Figure 5.7. Correlation among plasma bicarbonate and renal net acid excretion in a patient with congenital chloride deficit at dietary chloride intakes of 0.2, 3.5, and 10 mmol kg/d (Dumas et al., 1970).

According to several writers, increasing skeletal development is attributed to an increase in the acid load on the kidneys. It is common for enhanced protein Ca absorption to be accompanied by increased intestine organic acid absorption as well. Approximately 0.92 mmol of nonmetabolizable base and 0.92 mmol of protons are released into the surrounding fluid for every mol of calcium deposited in hydroxyapatite. Organic acids essentially metabolize these protons, rendering them inert. When nonmetabolizable cations are consumed in the gut, the net gain of alkali in the skeleton compensates for the loss of acid excretion in the kidney. In contrast, an increase in extracellular is executed in an increase in the amount of acid excreted by the kidneys. The amounts of chloride and sodium consumed are relatively comparable. Both ions have been virtually fully absorbed by the body. In the presence of greater salt retention, a correspondingly unaltered urine chloride excretion results in a larger renal acid load (Remer and Manz, 1995).

A physiologically based computation approach for estimating renal net acid excretion has just been confirmed and it is expected to be widely used.

The mineral and protein content of diets, as well as the average intestinal absorption rates of the various nutrients, sulfur metabolism, and urine excretion of organic acids, were all taken into consideration in the calculating model.

5.8.2. Metabolic Acidosis in Parenteral Nutrition and Chemically Defined Diets

The maximal renal net acid excretion in normal persons is frequently greater than the maximum nutritional renal acid load. The chemical industry in the 1960s has managed to synthesize all of the amino acids at a reasonable cost due to technological advances. As a result, low-quality protein hydrolysates were substituted with precisely intended amino acid combinations or chemically specified diets to improve the overall quality of the protein. Surprisingly, metabolic acidosis was found in a high proportion of patients receiving parenteral nourishment, suffering from chronic renal failure, or having congenital metabolic disorders (Heird et al., 1972). This elevated renal acid load was the result of a number of contributing variables. The chloride salts of the basic amino acids were used to represent them. Another source came from the hydrolysis of phospholipids. As a reference protein, egg protein with a high amount of cysteine and methionine was utilized, resulting in a high synthesis of sulfate and a high excretion of sulfate in the urine (Manz et al., 1977). Several amino acid combinations were sold as nitrogen enhancements, but the mineral content was not taken into consideration. As a result of the low mineral content of the basic low protein diet, the primary cation excess of the basic diet was likewise low (Manz et al., 1977).

5.8.3. Long-Term Impacts of a Nutritional Chronic High Acid Load

A girl having phenylketonuria was given an inadvertently acidic, low phenylalanine diet for 29 months, which she did not want to do. Urolithiasis and temporary growth retardation were two of the immediate consequences of chronic acid loading, with acute caries following as a late result. As a result, persistent dietary acid overload might result in significant adverse effects.

5.8.4. Long-Term Causes of Dietary Chloride Deficiency Syndrome with Metabolic Alkalosis

Two batches of soy-based baby formula were introduced in the United States around the end of the 1970s, and one batch of a cow's milk formula was supplied in Spain, both of which had accidentally very low chloride amounts (Grossman et al., 1980). Psychomotor delay, growth failure, hypokalemia, microhematuria, hypercalciuria, and hypochloremic metabolic alkalosis were all observed in infants who were exclusively given these formulas over a period of several weeks. At 2 to 4 years of age, researchers discovered a negative dose-response connection between previous formula consumption and developing outcomes. The youngsters demonstrated catch-up development between the ages of 7 and 10 years. There was, on the other hand, a significant risk of language and learning skills deficiencies (Malloy et al., 1991).

5.8.4.1. Benefits of a Historical Approach?

An understanding of topics and contradictions in nomenclature may be enhanced by reading this historical study. The physiology of acid-base metabolism appears to be one of the least popular disciplines in medicine due to the complex nature and the horrendous usage of several ideas and nomenclatures at the same time, according to the public. Although the "so-called" great transatlantic acid-base dispute has been going on for 37 years, is it truly over (Gao et al., 1988)?

German non-academic society has a strong advantage in the link between diet and acid-base metabolism, and this interest has grown in recent years.

For example, in the previous 40 years, 750,000 copies of Hay's dietary advice have been marketed in Austria, Switzerland, and Germany alone. The original definition of the word diet, derived from the ancient term 'diaita,' which recommended, among other things, proper drinking and eating, a good balance of activity and inactivity, and a balanced tempo of sleep and restlessness, has lost none of its appeals. It provides a sense of direction, inner significance, and a sense of security. For several people, the term acid-base equilibrium refers to a modern, scientifically designed functional equivalent of the ancient Greek term 'diaita' (acid-base balance). In many cases, the commercial success of alkalizing measures is dependent less on the alleviation of a specific clinical ailment and more on the expectation of the customer that his or her unquenchable yearning for inner security and meaning will be satisfied.

The extrapolation method, as the last step, allows for the conjecture of future changes in nutrition and acid-base metabolism (Greenhaff et al., 1987).

5.8.5. Elements of Regulation of Blood Acid-Base Status and Renal Net Acid Excretion

Illustration of the ingredients involved in maintaining a normal acid-base balance in the blood as well as renal net acid excretion. Renal net acid output is derived from three sources in a constant state: There are three major causes of organic acid excretion: 1) the surplus of ingested nonmetabolizable cations on the nonmetabolizable anions in the gut, 2) sulfate synthesis, and 3) urine secretion of organic acids (Figure 5.8) (Manz et al., 1997).

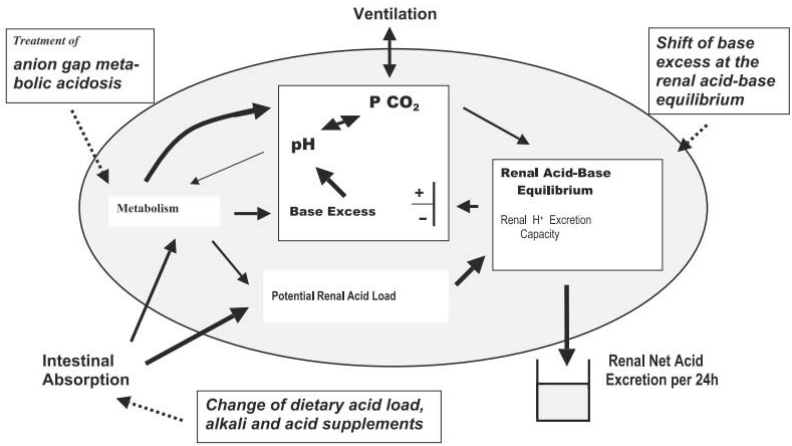

Figure 5.8. Management of blood acid-base status, net acid in- and output, and sites of voluntary and/or therapeutic actions to manage blood base excess and renal net acid excretion.

Source: https://pubmed.ncbi.nlm.nih.gov/11842944/.

Renal hydrogen excretion is stimulated by a drop in blood base excess when the amount of blood base surplus at the acid-base balance of the kidney is slightly below that level. In addition to renal management of hydrogen ion excretion, delta base excess is also dependent on the real renal acid load. As lactic acid is produced in excess quantities, it has the effect of temporarily decreasing the level of blood base surplus without affecting renal net acid excretion. This is due to practically total tubular absorption of the organic acid at physiological serum levels (Bourke and Häussinger, 1992).

5.9. FUNCTIONAL MEDICINE IN ACID-BASE AND NUTRITION METABOLISM

In the following several years, functional medicine is likely to be the most popular issue in the fields of acid-base and nutrition metabolism. A number of strategies for manipulating the acid-base state of the organism or for treating diseases of acid-base metabolism are discussed in the following section.

During high-intensity exercises, acidosis is assumed to be the cause of weariness and exhaustion in the muscles that are engaged in the activity. Productivity in interval swimming was increased by administering a bicarbonate supplement before exercise (Greenhaff et al., 1987). This was accomplished by delaying the onset of tiredness. As a result, an increase in the body's buffer capacity leads to an improvement in muscle performance. In contrast, alkali enhancements as adjuvant therapy may be used in the treatment of other organs that are at risk of developing local metabolic acidosis, such as the treatment of angina pectoris, the treatment of pain or the treatment of skeletal mineralization. Alkali supplements are required to compensate for significant extrarenal bicarbonate losses in individuals suffering from urine diversion, diarrhea, or intestinal malabsorption (McConnell et al., 1979).

Pathologic urine outflow of amino acids is seen in numerous tubulopathies and hereditary metabolic diseases, resulting in an increase in renal net acid excretion. Alkali treatment should be explored in cases of metabolic acidosis or when urine pH levels are consistently less than 5.4, suggesting that the kidneys are excreting the maximum amount of acid possible. A ketogenic diet, which is frequently accompanied by metabolic acidosis, has been shown to minimize the risk of seizures in children with refractory seizure disorders (Gasch, 1990). The anticonvulsant activity of ketoacids appears to be mediated by an increase in their brain metabolism. Because on a ketogenic diet, acidosis enhances the likelihood of urolithiasis and reduces the creation and blood levels of ketone bodies in patients with refractory seizure disorders, it is important to determine the optimal acid-base status in these patients (McConnell et al., 1979, Gasch, 1990). Acidosis is associated with an increased hazard of urolithiasis and decreased creation and blood levels of ketone bodies. In the future, it is possible that the acid-base state of patients who are fasting may receive greater attention as well.

Low urine pH values caused by acid loading in patients with catheterization in the bladder or infection stones reduce the incidence of

recurrence of urolithiasis and catheter incrustation (Bach, 1985). The production of new stones is inhibited in people with uric acid stones when the pH of their urine is greater than 6.5.

Patients with renal tubular acidosis kinds 1, 3, and 4, as well as preterm neonates, elderly, patients with renal tubular acidosis type 1 and 2, and patients with chronic renal failure, have a decreased renal hydrogen ion excretion capability. These individuals' regular Western-style diet outcomes in reasonably high or even maximal renal acid stimulus with less or no metabolic acidosis (but the usual Eastern-style diet does not. It is recommended or required that people in these categories consume a diet that has a low acid renal acid burden.

Patients receiving parenteral nutrition using chemically specified meals or synthetic amino acid solutions were shown to have metabolic acidosis in the 1970s (Röckel et al., 1976). It was established by this secondary impact that these products must have an upper limit on the possible renal acid load they might cause. In 1983, the German government issued a guideline specifying the structure of chemically defined meals, which specified that the number of minerals in the diet should be calculated in relation to the general impact on renal net acid excretion (Grossklaus, 2003). In 1995, the EU set a restriction of 5% for the amount of ammonium chloride that may be found in confectionery goods (Populin et al., 2007). This is the first time that a functional diet has been shown to have an upper acceptance level for a possible renal acid load. When it comes to the dispersion of renal net acid excretion in healthy people, there are no epidemiological data available. Consequently, we are unaware of the proportion of healthy persons who have experienced maximal renal acid stimulus, as shown by urine pH values lower than 5.4 in 24-hour urine samples at this time. In view of the much lower renal net acid load in ancient human diets and the age-related trend to metabolic acidosis in people consuming a Western-style diet it is reasonable to assume that the net acid load in human ancestral diets is lower, it is reasonable to accept that the mean and 97.5% percentile of renal net acid excretion in a population could become significant data in determining the nutritional quality of a diet.

Volume contraction, hypercapnia, hypokalemia, and hypercalcemia are all known to cause the blood base surplus at the acid-base balance of the kidney to be moved to higher levels (Manz et al., 1997).

Hyperkalemia, hypocapnia, volume expansion, proximal renal tubular acidosis, and hyperparathyroidism are all known to cause it to be moved to

lower (negative) levels (Manz et al., 1997). Therapeutic interventions must be targeted at correcting the underlying cause of the shift.

When it comes to preterm babies, a number of factors frequently come into play at the same time. Hypercapnia and volume expansion, for example, can cause an excess of the base in the bloodstream, which may be considered normal in some cases. By way of exception, in patients with severe renal tubular diseases, including proximal renal tubular acidosis, the pathologic shift to lower blood base excess levels may be partially balanced by giving hydrochlorothiazide to reduce volume expansion (Rampini et al., 1968). Dietary acid load is commonly overlooked in individuals with complicated abnormalities of acid-base metabolism, and this has serious consequences. When preterm babies with a low optimum renal hydrogen ion excretion capability are given a prenatal formula with a high renal acid load, urinary net acid excretion is often around the maximum. If these children acquire hypercapnia as a result of bronchopulmonary dysplasia, their blood base surplus does not grow at the same time because the kidneys are unable to eliminate the increased acid load required to raise the extracellular bicarbonate pool in their bodies. It is common for these youngsters to have urine pH values that are below 5.4. Alkali treatment is required to reduce the stress caused by the functional condition of an initial late metabolic acidosis in preterm newborns, which might cause them to be born prematurely.

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CHAPTER 6

TITRATABLE ACIDITY AND PH IN FOOD PRODUCTS

CONTENTS

6.1. INTRODUCTION

For the examination of foodstuff, two conceptions relate to acidity: which are *titratable acidity* and *pH*. Each of such variables is analyzed in its method, and each gives a unique perception of the quality of foodstuff.

The overall acid content in a foodstuff is measured by *titratable acidity*. Comprehensive titration of fundamental acids having a common base is used to evaluate the amount. Titratable acidity, instead of pH, is a stronger forecaster of acid's taste influence. Titratable acidity, although, doesn't provide complete critical data about a product. For example, a microorganism's capacity to flourish in a certain diet is determined by the concentration of freed H_3O^+ ion, instead of titratable acidity (Kou et al., 1993). Such H_3O^+ ions form in the aqueous medium of the solution when H_2O is combined using hydrogen ions separated from acids. A necessity to determine solely the quantity of freed hydronium ions guides to the 2nd key notion of acidity, pH (known as active acidity). The –ve logarithm (with the base 10) of the H^+ concentration is used to calculate pH, which has a value of 14 times greater. This depends upon the kind and quantity of acids contained in meals, as well as the concentration of ionized acid analogs (its conjugated bases). A mechanism may be characterized as a reservoir when the components have existed in equal proportions.

Its data on evaluating the titratable acidity and the pH, in general, and concerning particular foodstuff (Liu and Stafford, 1995; Dubascoux et al., 2015). For determining the titratable acidity and pH of different foodstuffs (Joslyn, 1970).

6.2. CALCULATION AND CONVERSION FOR NEUTRALIZATION REACTIONS

6.2.1. Concentration Units

This section covers the practice and theoretical concept of calculating and determining pH and titratable acidity. For the evaluation of the constituents of food statistically, mixtures should be made to precise concentrations and diluted into the requisite range of working.

It's a good idea to examine the typical words for concentration in the evaluation of meals. The most frequent SI (International Scientific) words utilized in the evaluation of meals are normality (N) and molarity (M),

however, solutions may also be stated as percentage. The expert must be capable of converting between the two systems (Redwan et al., 2017).

The number of moles of the solute for one liter of solution is measured in *Molarity* (M). The *Normality* (N) unit of concentration defines the number of solute equivalents (Eq) for one liter of the solution. In the solutions of base and acid, normality refers to the concentration of hydroxide ion or hydrogen ion for one liter that would be interchanged during a neutralization reaction. For redox reagents, the normality specifies the density of moles or electrons per liter that would be interchanged upon the finalization of the reaction. Several instances of normality versus molarity (equivalents) are as follows (Eary and Williamson, 2006):

1. Acid-Base Reactions:
   - One *Molarity of* sulfuric acid is equal to two *Normality of* H_2SO_4

Two equivalents of hydrogen ion for one mole of sulfuric acid

   - One *Molarity of* sodium hydroxide is equal to one *Normality of* NaOH

One equivalent of hydroxide ion for one mole of sodium hydroxide

   - One *Molarity of* acetic acid is equal to one *Normality of* CH_3COOH

One equivalent of hydrogen ion for one mole of acetic acid

   - One *Molarity of* malic acid is equal to two *Normality of* $C_4H_6O_5$

Two equivalents of hydrogen ion for one mole of malic acid

2. Redox Reactions:

$$HSO_3^- + I_2 + H_2O \rightleftarrows SO_4^{2-} + 2I^- + 3H^+$$

   - One *Molarity of* iodine is equal to two times *Normality of* I_2

Two equivalents of electrons gained for one mole of iodine

   - One *Molarity of* HSO_3^- is equal to two times *Normality of* bisulfite

Two equivalents of electrons released for one mole of bisulfite

Numerous systematic procedures in the evaluation of meals utilize the idea of equivalents to evaluate the equivalence or normality of an unspecified solution. These tests utilize stoichiometry or the complete number of fractions of atoms that interact to form a certain substance. Maybe the most well-

known of such reactions is the *neutralization reaction*, which involves the interchange of H+ ions and may be measured by stoichiometric neutralization with a usual base. The titration of acid and base is used in a variety of food tests, including the assessment of nitrogen in the assessment of Kjeldahl protein, the assessment of benzoic acid in sodas, and then calculating the percentage of titratable acidity. Equivalents are indeed utilized to measure unidentified analytes proficient in the straight transfer of electrons in red-ox situations (Verdone and De Filippis, 2006).

In chemical reactions, the *equivalent weight* is expressed as molecular mass is divided by the number of equivalents. Sulfuric acid has a molecular mass of 98.08 grams because sulfuric acid has two equivalents for one mol; the corresponding weight is 49.04 grams (Walters et al., 2018).

The molecular and relative masses of acids in the evaluation of foodstuff are listed in Table 6.1. The word *milli-equivalents* (mEq) are commonly used when dealing with normality. The relative masses are divided by 1,000 to get milli-equivalent mass (Liu et al., 2000).

Table 6.1. Molecular and Relative Masses of Common Foodstuff Acids

Acid	Chemical Formula	Molecular Weight	Equivalent Weight	Equivalents per Mole
Citric (hydrous)	$H_3C_6H_5O_7 \cdot H_2O$	210.14	70.05	3
Citric (anhydrous)	$H_3C_6H_5O_7$	192.12	64.04	3
Lactic	$HC_3H_5O_3$	90.08	90.08	1
Acetic	$HC_2H_3O_2$	60.06	60.05	1
Oxalic	$H_2C_2O_4$	90.04	45.02	2
Malic	$H_2C_4H_4O_5$	134.09	67.05	2
Ascorbic	$H_2C_6H_6O_6$	176.12	88.06	2
Tartaric	$H_2C_4H_4O_6$	150.09	75.05	2
Sulfuric	H_2SO_4	98.08	49.04	2
Hydrochloric	HCl	36.47	36.47	1
Potassium acid phthalate	$KHC_8H_4O_4$	204.22	204.22	1
Phosphoric	H_3PO_4	98.00	32.67	3

The weight quantity of solute for 100 milliliters or 100 grams of material is expressed in percentage concentration. Dissimilar molarity, normality, and equivalents, percentage concentrations do not need or offer information about a reaction's stoichiometry. On the base of volume (v) or the base of mass (m), the percentage may be represented for the solution volume or the weight of solids (w). Consequently, a specific rationale is usually provided. In all circumstances when the particular gravities of the 2 factors are not similar, 10% (weight/volume), 10% (volume/volume), and 10% (weight/weight) represent distinct concentrations. *Parts per trillion* (ppt), *Parts per billion* (ppb), and even though *parts per million* (ppm) are commonly selected whenever the proportion is lower than 1%. If the weight of the solute for one mass or volume of specimen is a 100, then parts per million are a similar fraction of mass of solute per mass of specimen 1,000,000 (Harrison and Kitto, 1992).

6.2.2. The Equation for Dilution and Neutralization

There may be a few general guidelines for analyzing equilibrium reactions that apply in the majority of cases. At the point of complete neutralization, the equivalents of the first reactant equate to the equivalents of the second reactant. It may be mathematically stated following:

(vol of X) (N of X) = (vol of Y) (N of Y) (1)

Eqn. (1) may be utilized to address issues involving dilution, wherein Y indicates the working solution and X indicates the stock solution. While solving the dilution issues by using Eqn. (1), whatever concentration value (grams, moles, parts per million, etc.), maybe replaced for normality. Units must be noted for each number, as canceling units gives a fast verification of the problem's appropriate setting (Schneider and Stoessel, 2005).

6.3. PH

6.3.1. Acid and Base Equilibrium

The Lowry-Brønsted theory of acid-base reaction is dependent on the given below concepts of base and acid:

- **Acid:** A material able to give protons. In the systems of meals, the only important proton source is the HO_3^+ ion.
- **Base:** A material able of receiving protons.

Neutralization is the interaction of a base with an acid to generate a salt as indicated in the following reaction:

$$HCl + NaOH \leftrightarrow NaCl + HO_2 \quad (2)$$

In the solutions of an aqueous medium, acids produce hydrated protons termed hydronium ions, while bases produce hydroxide ions:

$$HO_3^+ + OH^- \leftrightarrow 2HO_2 \quad (3)$$

The *constant of ion product for H_2O (K_w)* is the multiplication of the molar concentrations (moles/liter) of hydronium ion (remember: molar concentrations are generally represented by brackets) and Hydroxide ion at every temperature:

$$(HO_3^+)\,(OH) = K_w \quad (4)$$

K_w varies as the temperature varies. For instance, at 25°C, $K_w = 1.04 \times 10^{-14}$ however at 100°C, $K_w = 58.2 \times 10^{-14}$.

The preceding discussion of K_w poses the question of what concentration of hydronium ion and the concentrations of hydroxide ion are in distilled H_2O. At 25°C, the concentration of hydronium ion is about 1.0×10^{-7} Molarity, as is the concentration of hydroxide ion. Due to the similar quantities of such ions, distilled H_2O is known as unbiased (Zuo et al., 1999).

Consider adding a droplet of acid to clean H_2O. The concentration of hydronium ions must rise. K_w, on the other hand, must stay constant (1.0×10^{-14}), indicating a decline in the concentration of hydroxide ions. If a droplet of the base is introduced to distilled H_2O, the concentration of hydronium ion decreases and the concentrations of hydroxide ion increase, keeping the K_w constant at 1.0×10^{-14} at 25°C (Yamaguchi et al., 2011).

How did the word pH come to be associated with the aforementioned considerations? To address this question, one should examine the concentrations of hydronium ion and concentrations of hydroxide ion in numerous meals, as given in Table 6.2. The calculated values for the concentrations of hydronium ion and the concentrations of hydroxide ion in Table 6.2 are cumbersome, which inspired a Swedish scientist, S.L.P. Srensen, to design the pH method in 1909.

The log of the inverse of the (OH^-) is described as *pH*, which is equivalent to the –ve logarithm of the (OH) molar concentration (Eriksen et al., 1985).

$$pH = -\log(H^+) \quad (5)$$

Therefore, the concentrations of hydronium ion value of 1×10^{-6} are easily represented as pH 6. The concentration of hydroxide ion is represented as pOH, which in this example must be pOH 8, as indicated in Table 6.3.

Calculation of [H+] of a beer with pH 4.30:

Step 1. Substitute numbers into the pH equation:

$$pH = -\log\left[H^+\right]$$
$$4.30 = -\log\left[H^+\right]$$
$$-4.30 = \log\left[H^+\right]$$
$$-4.30 = 0.70 - 5 = \log\left[H^+\right]$$

Step 2. Calculate the antilog of –4.30: $\left[H^+\right] = 5 \times 10^{-5} M$

Table 6.2. (H_3O^+) and (OH^-) in Different Meals at 25°C (Pecsok et al., 1970)

Food	K_w	$(H_3O^+)^a$	$(OH^-)^a$
Grape juice	1×10^{-14}	5.62×10^{-4}	1.78×10^{-11}
Cola	1×10^{-14}	2.24×10^{-3}	4.66×10^{-12}
Schlitz beer	1×10^{-14}	7.95×10^{-5}	1.26×10^{-10}
Seven-up	1×10^{-14}	3.55×10^{-4}	2.82×10^{-11}
Milk of magnesia	1×10^{-14}	7.94×10^{-11}	1.26×10^{-4}
Tap water	1×10^{-14}	4.78×10^{-9}	2.09×10^{-6}
Pure water	1×10^{-14}	1.00×10^{-7}	1.00×10^{-7}

Table 6.3. Correlation of the Concentration of Hydrogen Ion vs. pH and the Concentration of Hydroxide Ion vs. pOH at 25°C (Pecsok et al., 1970)

pOH	pH	$(H^+)1$	$(OH^-)^a$
14	0	1×10^{0}	1×10^{-14}
13	1	10^{-1}	10^{-13}
12	2	10^{-2}	10^{-12}
11	3	10^{-3}	10^{-11}
10	4	10^{-4}	10^{-10}
9	5	10^{-5}	10^{-9}
8	6	10^{-6}	10^{-8}
7	7	10^{-7}	10^{-7}
6	8	10^{-8}	10^{-6}
5	9	10^{-9}	10^{-5}

4	10	10^{-10}	10^{-4}
3	11	10^{-11}	10^{-3}
2	12	10^{-12}	10^{-2}
1	13	10^{-13}	10^{-1}
0	14	10^{-14}	10^{0}

It is worth noting that the product of $(H^+)(OH^-)$ is often 1×10^{-14}

Despite utilizing pH representation being easier numerically, that is a perplexing idea for many pupils. Note that it must be a log number and that 1 pH unit changes the concentration of hydronium ion 10 times (Fontes et al., 2020).

That's critical to distinguish between titratable acidity and pH. Chlorine, sulfuric, and nitric acids are nearly ionized at one pH. Dietary acids like malic, citric, tartaric, acetic, etc.), seldom ionize in solution. Compare the pH of 0.1 normality HCl and CH_3COOH solutions to demonstrate that idea.

$$CH_3COOH \leftrightarrow H^+ + CH_3COO \quad (6)$$

$$HCl \leftrightarrow H^+ + Cl^- \quad (7)$$

At 25°C, the hydrochloric acid completely ionized in solution, resulting in a pH of 1.02. At 25°C, however, only around 1% of acetic acid is ionized, resulting in a substantially high pH of 2.89 (Joo et al., 2013).

6.3.2. pH Meter

6.3.2.1. Activity versus Concentration

The idea of concentration versus activity should be addressed while utilizing pH electrodes. *Concentration* is a measurement among all types (loose and bonded) of ions in solution, whereas *activity* is a measurement of actual chemical reactivity. The efficient activity and concentration are often less than the real concentration due to ion reactions together and with the solvent, yet concentration and activity tend to approximate each other at limitless dilution. The given equation connects activity with concentration (McBryde, 1969):

$$A\,C = g \quad (8)$$

In which; A is the activity coefficient; *C* is the activity; g = concentration.

The strength of the ion affects the *coefficient of activity*. The concentration and charge of all ions in the solution determine the strength of the ion. Hydronium ions under pH one and OH^- at pH 13 and above might cause

substantial activity problems. Since these severe pH levels are uncommon in food science, the strength of the ion can be elevated, necessitating the utilization of alternative equations (Sigel et al., 1991).

6.3.2.2. General Principles

The A pH meter is an excellent illustration of a *potentiometer* (a gadget that computes the voltage at the infinitesimal flow of current). Potentiometry's fundamental premise (an electrochemical technique of voltammetry with no current) is based on the utilization of an electrolytic cell made of 2 electrodes submerged in a sample solution. A voltage is generated that is proportional to the solution's concentration of ions. Since the presence of current may modify the concentration of nearby ions or cause irreversible processes, that voltage is calculated under settings that draw an infinitesimal current (1,012 amperes or less) (Moore, 1968).

The pH system requires four essential components: a voltmeter or amplifier able of detecting tiny voltage variations in a loop with extremely higher resistance, a pH-sensitive indication electrode, a citation electrode, and a specimen to be studied (Figure 6.1). For simplicity, the majority of modern pH electrodes include both the reference and signifier electrodes into a single housing. Every one of the two electrodes used in the test is cautiously engineered to generate a stable, repeatable voltage. As a result, when no additional ions are present, the potential difference between the two electrodes is constant and readily computed. Furthermore, hydronium ions in solution add a fresh potential around the signifying electrode's ion-selective glass membrane. This modifies the potential difference amongst the two electrodes in a proportionate manner to the concentration of hydronium ion. The novel potential created by combining all of the separate potentials is referred to as the potential of the electrode, and it is easily converted to pH measurements (Rodil et al., 2001).

The potential difference that arises among the two electrodes is used to assess the (H^+) (or more precisely, activity).

The Nernst equation establishes a relationship between the electrode that responds to the activity, in which:

$$E = E_o + 2.303 \frac{RT}{zF} \log A \qquad (9)$$

where; E_o denotes the standard potential of the electrode, a constant representing the sum of the individual potentials in the system at the electrode

composition, ion concentration, and a standard temperature; *E* denotes the calculated potential of the electrode; *F* denotes the constant of Faraday, 96,490 coulombs (C) per mole; *R* denotes the constant of universal gas, 8.313 *J*/mol.*K*; *A* denotes the ionic activity being calculated; *z* denotes the number of charges on an ion; *T* denotes the absolute temperature in Kelvin (K).

For monovalent ions (for example, the HO_3^+) at 20°C, the association of 2.303 RT/*F* is measured to be 0.0591, as follows:

$$\frac{2.303 \times 8.316 \times 298}{96490} = 0.0591 \quad (10)$$

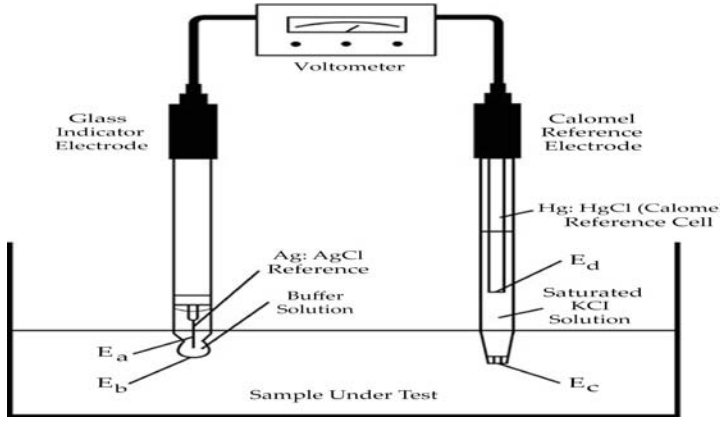

Figure 6.1. The measurement circuit of the system of potentiometric.

Note: E_a The contact potential between the inner liquid and the Ag/AgCl electrode is E_a. E_a is not affected by the pH of the sample solution, however, it is affected by temperature. The pH-sensitive glass membrane formed an E_b potential. E_b is affected by the pH of the sample solution as well as the temperature. Moreover, to the E_b potential, the glass electrode creates an asymmetrical potential that is determined by the glass membrane's content and structure. This also varies with the duration of the electrode. Among a saturated solution of potassium chloride and a sample solution, E_c is the diffusion potential. E_c is unaffected by the sample solution. The contact potential between the calomel section of the electrode and the potassium chloride salt bridge is known as E_d. E_d is unaffected by the sample solution and is affected by temperature (Walters et al., 2018).

Source: https://www.sciencedirect.com/science/article/abs/pii/S0925400502003015.

6.3.2.3. Reference Electrode

Inside the pH setup, the reference electrode is expected to implement the circuit. Amongst the very difficult sections of the pH meter is the half-cell. A defective reference electrode is frequently blamed for difficulties in getting pH values.

The saturated Potassium chloride salt bridge's E_o at 25°C is +0.2444 Volt versus a conventional hydrogen electrode; the equation of the Nernst for the process is:

$E = E_0 - 0.059/2 \text{ logarithm } (Cl^-)$ (11)

The most frequent reference electrode is a *saturated calomel electrode* (Figure 6.1). This is dependent on the repeatable process described below:

$Hg_2Cl_2 + 2e^- \leftrightarrow 2Hg + 2Cl^-$ (12)

As a result, the potential is proportional to the (Cl^-) that may be readily controlled by using a saturated Potassium Chloride solution in the electrode.

A calomel reference electrode consists of three main components: First, a platinum cable coated with a calomel (Hg_2Cl_2) combination, Second, a filled solution (saturated with Potassium Chloride), and Third, a porous junction whereby the filling solution gradually relocates into the specimen as evaluated. Porcelain or filamentous material is used for junctions. Such connections frequently block, resulting in a delayed, unsteady reaction and erroneous findings (Figure 6.2) (Irving and Rossotti, 1954).

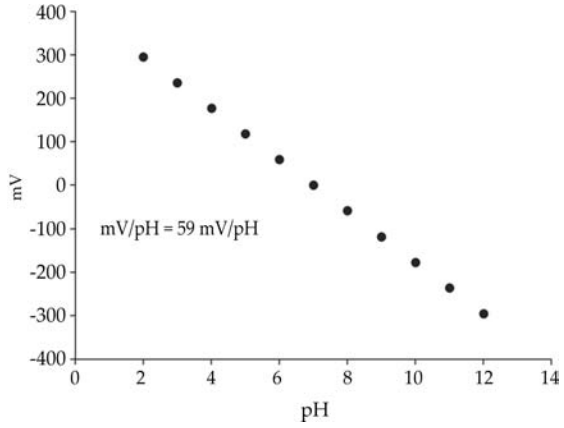

Figure 6.2. At 25°C, the relation among pH and millivolts for a monoprotic acid.

Source: https://link.springer.com/chapter/10.1007%2F978-3-319-45776-5_22.

The Ag-Ag chloride electrode is a low commonly utilized reference electrode. An Ag-Ag chloride electrode should be employed for this purpose since the calomel electrode is not stable at a higher temp (80°C) or in strongly basic materials (pH > 9). Depending on the aforementioned response, this is a fairly repeatable electrode:

$$AgCl_{(s)} + e^{-} \leftrightarrow Ag_{(s)} + Cl^{-} \qquad (13)$$

An Ag-coated platinum cable serves as the inner component, with the exterior Ag being transformed to AgCl by hydrolysis in HCl. The stuffing solution is a combination of four Molarity of Potassium Chloride and Silver Chloride, which is employed to keep the inner component's Silver Chloride surface from solubilizing. The perforated leaky connection is the most common form. This electrode clogs very easily as compared to the calomel reference electrode because of the insolubility of Silver Chloride. A double-junction electrode design is much typically utilized, wherein the Silver/Silver Chloride inner component electrolyte and porcelain junction are held in a distinct body's internal. The internal body is separated from the specimen by an exterior body carrying a 2nd electrolyte and a connection (Wang et al., 2018).

6.3.2.4. Indicator Electrode

The *glass electrode* is the most often utilized indicator electrode for detecting pH nowadays. The *indication electrode* (Figure 6.1) comprises three sections, such as the reference electrode: First, a mercury-connected AgCl electrode; Second, a buffer solution of 0.01 NHCl, 0.09 NKCl, and acetate buffer utilized to keep the pH (E_a) constant; and Third, a tiny pH-sensitive glass membrane whose potential (E_o) fluctuates with the pH of the sample solution. The observed voltage (determined against the calomel electrode) is exactly proportionate to the pH, $E = E_0 - 0.059$ pH (Liu et al., 2014).

Glass electrodes are suited for measuring pH 1–9. With sodium ions existence, that electrode is responsive to increased pH. Recent glass electrodes with a sodium ion inaccuracy are less than 0.01 pH at 25°C have been created by instrument makers.

6.3.2.5. Combination Electrodes

Nowadays, several meal testing labs now employ composite electrodes which incorporate pH, reference electrodes, and temp detecting probes into a single device. Such combo electrodes come in a variety of forms and dimensions, from microprobes to horizontal surface investigations, in plastic or glass, with uncovered or crimped electrode tips. Microprobes can test pH within a cell or a solution on a microscope slide. Electrodes with a horizontal surface may test pH in semisolids (for example, cheese, meat, agar plates) and little volumes (less than 10 µl) (Wang et al., 2018).

6.3.2.6. Guidelines for the Use of pH Meter

The pH meter must be used and sustained appropriately. Constantly obey the manufacturer's exact recommendations. Centralize the meter with at least two buffers for maximum accuracy (*2-point calibration*). Choose two mediums with pH values approximately three pH points distant. The very often utilized standardizing buffers in labs are pH 9.0, pH 7.0, and pH 4.0 (at 25°C). Yellow, blue, and pink solutions are commonly encountered near pH meters in labs (Ridout et al., 1988).

Obey the manufacturer's *one-point calibration* directions; wash completely with pure water and towel dry. Insert electrode in 2nd buffer (such as pH 4) and standardize again. The pH meter gradient control is being used to adjust the measurement for the 2nd buffer. Redo such two processes till the 2nd buffer's pH value is inside 0.1 pH unit of the first. If that's not possible, the equipment is broken.

Inspect the electrodes, keeping in mind that the reference electrode is much more likely to demand attention. When storing a pH electrode, carefully obey the instructions provided by the electrode maker. As a result, the pH meter is always prepared to utilize, and the electrodes' lifespan is extended. A calomel reference electrode is one caution which must be observed. To avoid storage solution diffusion into the electrode, the storage solution level ought to be at least two centimeters underneath the saturated Potassium chloride solution level in the electrode (Figure 6.3) (Ghosh et al., 2013).

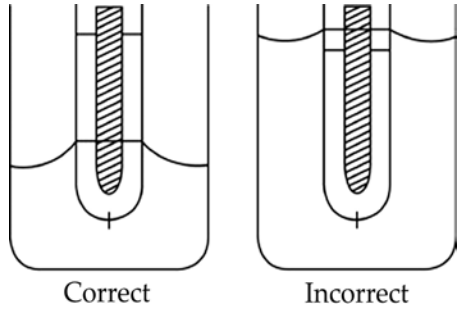

Figure 6.3. Both right and wrong depth of the electrodes of calomel in solutions (Pecsok et al., 1970).

Source: https://www.amazon.com/Modern-Chemical-Technology-al-Pecsok/dp/0841204926.

6.4. TITRATABLE ACIDITY

6.4.1. Principle and Summary

The overall acid content of a meal is measured by titratable acidity. Acetic, lactic, malic, tartaric, and citric acids are the often-frequent organic acids found in foods. Inorganic acids like carbonic (derived from CO_2 in solutions) acids and phosphoric, on the other hand, frequently play a significant, if not dominating, part of food acidulation. Organic acids in meals affect taste (malty flavor), color (because of its influence on anthocyanin as well as other pH-influenced colors), microbiological stability (because of organisms' intrinsic pH-sensitivity traits), and quality preservation. Fruits' titratable acidity, coupled with their sugar level, are utilized to determine their ripeness. Organic acids can be found naturally in foods, but they can also be created by fermentation or incorporated as part of its core meal recipe (Reardon et al., 1951).

Titratable acidity is evaluated by employing a standard base to neutralize the acid that exists in a specific amount (mass or volumes) of a meal specimen. A specific pH or the color shift of a pH-sensitive dye, such as phenolphthalein, is frequently used as the titration endpoint. The titratable acidity, defined in terms of the major organic acid, is calculated using the volume of titrant employed, the normality of the alkali, and the volume (or mass) of the specimen (De Marchi et al., 2009).

6.4.2. Universal Thoughts

Several dietary qualities are more closely related to pH as compared to acid content. A base and acid titration's conclusion are also determined by the pH. A pH meter may be used to determine the pH, although it's more typical to use a pH-sensitive pigment. The method pH varies throughout titration might sometimes cause minor issues. To completely comprehend titration and recognize the rare issues that may develop certain knowledge of acid theory is required (Johnson and Chandler, 1982).

6.4.2.1. Buffering

While pH may theoretically vary between –1 and 14, observations under one are uncertain due to +H ions ionization at higher acid concentrations. At 0.1 Normality, it is expected that strong acids are completely ionized. Thus, in titrations employing strong acids, totally ionized acid is retained at all titrant doses; the pH at every moment during the titration is equivalent to the residual acid's (H^+) (Figure 6.4).

On contrary to strong acid titration, whenever weak acids are titrated using a strong base, the system contains a combination of the acid as well as its conjugate base. It has the effect of cushioning the solution against sudden pH fluctuations. The ability of a solution to withstand pH variation is referred to as *buffering*. If a weaker acid, as well as its conjugate base, are existed in a similar medium, buffering happens. Due to buffering, the graph of pH versus titrant concentration for weaker acids is very complicated as compared to stronger acids. Although, the Henderson-Hasselbalch equation may be used to approximate this correlation (Tarakçi and Kucukoner, 2003):

$$\mathrm{pH} = \mathrm{pKa} + \log\frac{[A-]}{[\mathrm{HA}]} \qquad (14)$$

where; (HA) is the non-ionized acid concentration; (A^-) is the conjugate base concentration; pK_a is the pH when non-ionized acid and conjugate base are equivalent. The equation says maximal buffering capacity is reached when pH = pK_a. It is illustrated by a graph of 0.1 Normality acetic acid titration with 0.1 Normality sodium hydroxide (Figure 6.5).

Di- and triprotic acids have 2 and 3 buffering areas, correspondingly. Figure 6.6 shows a pH versus citric acid titrant curve. The Henderson-Hasselbalch equation may forecast the plateau correlating to every pK_a stage in polyprotic acids. Protons and conjugated bases from different ionization states (s) hinder the transition zone among stages. So, the Henderson-

Hasselbalch equation fails around the equivalency of 2 pK_a stages. But calculating the equivalent pH is simple. The pH = (pK_a1 + pK_a2)/2. These values are listed in Table 6.4 (Ryan and Irwin, 2002).

The Henderson-Hasselbalch equation needs all elements to be perfect solutions. All active elements approach perfect solutions with infinite dilution. Reality cannot be perfect. The Henderson-Hasselbalch equation can only offer a rough approximation of pH. Examples and practice issues for buffers to build buffers and compute pH utilizing the Henderson-Hasselbalch equation.

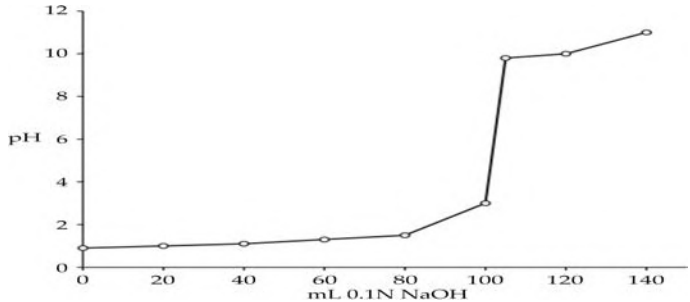

Figure 6.4. Titration A stronger acid is titrated against a stronger base. The (H^+) of the acid remaining after substantial neutralization with base determines the pH at any stage in the titration.

Source: https://chemistry.stackexchange.com/questions/9272/why-is-phenolphthalein-an-appropriate-indicator-for-titration-of-a-strong-acid-w.

Figure 6.5. Titration A weaker monoprotic acid is titrated with a stronger base. Around the pKa, a buffering area is created (4.82). The Henderson-Hasselbalch equation describes the pH at any specific spot.

Source: https://slideplayer.com/slide/16130767/.

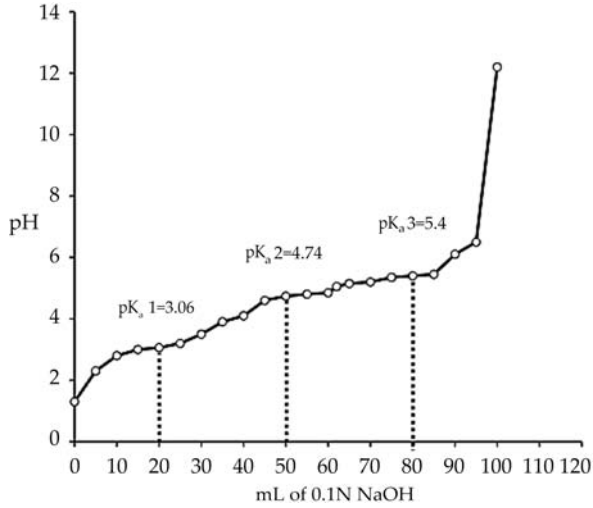

Figure 6.6. A weaker polyprotic acid is titrated with a stronger base. Every pK_a is surrounded by buffering areas. When pK_a steps are isolated by greater than three units, the Henderson-Hasselbalch equation may estimate the pH for every pK_a value. Simplified computations of transition pH values are impractical due to complicated transition mixes among pK_a stages.

Source: https://www.dlt.ncssm.edu/tiger/chem6.htm.

Table 6.4. The Values of pKa for Certain Acids Significant in the Analysis of Meal

Acid	**pK_a1**	**pK_a2**	**pK_a3**
Phosphoric	2.12	7.21	12.30
Tartaric	3.02	4.54	–
Oxalic	1.19	4.21	–
Citric	3.06	4.74	5.40
Malic	3.40	5.05	–
Ascorbic	4.10	11.79	–
Lactic	3.86	–	–
Carbonic	6.10	10.25	–
Potassium acid phthalate	5.40	–	–
Acetic	4.76	–	–

6.4.2.2. Potentiometric Titration

The quantity of acid equivalents precisely matches the number of base equivalents at the *equivalent point* in a titration, resulting in significant acid neutralization. The denominator (HA) in the Henderson-Hasselbalch equation grows inconsequentially low as the equivalence point is reached, while the quotient (A)/ (HA) rises dramatically. Consequently, the pH of the solution quickly rises, eventually approaching the titrant's pH. The precise midway point on such a sudden pH rise gradient is the comparable point (Tarakci, 2010). The *potentiometric technique* for evaluating titratable acidity uses a pH meter to determine the end. The benefit of potentiometrically identifying the equivalence point would be that the specific equivalence point is discovered. Because the conclusion of titration is signaled by a quick shift in pH (rather than a specific final pH value), proper calibration of the pH meter is unnecessary. Furthermore, a meticulous database of pH versus titrant should be maintained to obtain the equivalency point. The potentiometric technique is relatively complex due to this, as well as the physical limits of pH sensors and the delayed response of certain electrodes (Bakirci and Kavaz, 2008).

6.4.2.3. Indicators

In everyday labor, an indicator solution is frequently employed to estimate the equivalence point for simplification. That method tends to slightly exceed the equivalence point. Whenever indicators are employed, the phrase equivalence point is replaced by the *terminal or colorimetric terminus*. That underscores the fact that the results obtained are approximations and are reliant on the individual indication. The most prevalent indication for meal usage is phenolphthalein. In the pH range of 8.0–9.6, it transforms from transparent to crimson. The pH 8.2 frequently causes a significant hue shift. The phenolphthalein terminal is the pH at which the *phenolphthalein terminal* is detected (Salwa et al., 2004).

According to the pK_a values in Table 6.4, naturally produced dietary acids don't buffer at the phenolphthalein terminal zone. Phosphoric acid (utilized as an acidulant in certain beverages) and Carbonic acid (CO_2 in the solution of aqueous medium) do, although, buffer at this pH. As a result, when measuring nucleic acids, bringing the solution from the actual equivalency point to the terminal can need a substantial quantity of titrant. It's possible that this will lead to the ambiguous terminal and makes striking titration readings. Potentiometric research is normally used to titrate such acids. By

boiling the specimen and titrating the leftover acidity to a phenolphthalein terminal, Carbon dioxide interference may be eliminated (Küçüköner and Tarakçı, 2003).

Terminal signals are further hampered by darkly colored specimens. A potentiometric approach is typically utilized when colorful solutions hide the terminal. The pH versus titrant database provided in Figures 6.5 and 6.6 aren't displayed in normal work. The pH of the specimens is easily titrated to 8.2. (the phenolphthalein terminal). Although this is a potentiometric approach, the resultant number is a terminal rather than the genuine equivalence point, because it just replicates the pH value for the standard phenolphthalein terminal which significantly exceeds the equivalence point (Vahedi et al., 2008).

This might appear that a pH of Seven is a preferable objective for a potentiometric terminal than 8.2. It seems that the pH represents genuine neutral on the scale of pH. The conjugated base, on the other hand, persists after all the acid has been neutralized. Consequently, the pH at the point of equivalent is frequently marginally higher than seven. If colorful specimens were to be pH 7, and non-colored specimens were to be pH 8.2, there may be some misunderstanding.

For best titration precision, dilute acid solutions (for example, vegetable extraction) need to dilute standard base solutions. Consequently, titration from the equivalence point to pH 8.2 might need a large amount of dilute base. In low-acid settings, bromothymol blue is occasionally employed as an alternate indication. Within the pH range of 6.0 to 7.6, it transforms from yellow color to blue color. Typically, the terminal is a bright green. Terminal determination, on the other hand, is a little more subjective than the phenolphthalein terminal (Celik et al., 2006).

Indicator solutions seldom include more than a few 10ths of a percent dye (w/v) in them. All of the indicators are weaker acids or weaker bases which prefer to buffer in the color-changing zone. They may alter titration by giving their specific buffering to the specimen under examination whenever applied too generously. As a result, indicator solutions must be kept to a bare minimum to achieve efficient color. There are 2 to 3 drops of the indicator are typically attached to the titrated solution. The terminal would be stronger if the indication concentration is lesser (Farahat and El-Batawy, 2013).

6.4.3. Preparation of Reagents

6.4.3.1. Standard Alkali

The most frequent titratable acidity base is sodium hydroxide. In several aspects, it seems unsuitable for a conventional basis. Reagent grade sodium hydroxide is highly hydrophilic and includes indissolvable sodium carbonate. Because working solutions' normalcy is not accurate, each new batch of sodium hydroxide must be standardized against a recognized normal acid. Such advantages outweigh the downsides of sodium hydroxide. Working solutions are generally produced from a 50% NaOH in H_2O stocked solution. Soluble in intense base, Na_2CO_3 induces from the solution after 10 days (Johnston et al., 1933).

Sodium hydroxide reacts with dissolved and ambient carbon dioxide to form sodium carbonate. These lowers alkaline and creates a carbonate buffer that may conceal titration endpoints. As illustrated in the equations below, H_2O and carbon dioxide alone may build buffering compounds and produce H^+ ions:

$$HCO^-_3 \leftrightarrow H^+ + CO_3^{2-} \text{(carbonate)} \quad (15)$$

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \text{ (carbonic acid)} \quad (16)$$

$$H_2CO_3 \leftrightarrow H^+ + HCO_3 \text{ (bicarbonate)} \quad (17)$$

As a result, before producing the stock solution, Carbon dioxide must be eliminated from the H_2O. It may be accomplished by expelling H_2O for one day with Carbon dioxide-free gas or through boiling pure H_2O for 20 min's and then cooling it down before utilization. Air (together with Carbon dioxide) would be pulled back into the vessel while chilling and prolonged storage. A soda lime (20% Sodium Hydroxide, 65% Calcium oxide, 15% Water) or an *ascarite trap* may be used to remove CO_2 from rejoining air (NaOH-coated silica base). The air that passes through these traps may also be employed as a gas mixture, resulting in Carbon dioxide-free H_2O (Malde et al., 2001).

A 50% base solution in freshwater has a pH of around 18 normalities. Dilute the stock solution with *carbon dioxide-free H_2O* to get a working solution. For powerful base solutions, there is no perfect vessel. Both glass and plastic are utilized, although each has its own set of disadvantages. A rubber or strong plastic seal must be utilized when a glass vessel is utilized. A strong base dissolves glass over time, leading to the irreversible fusing of the contact surfaces. Glass closures must be prevented. The base's normality

is likewise reduced when it reacts with glass. Such risks apply to the long-term storage of the base in Burettes as well. The surface tension of Sodium Hydroxide is quite small. Leakage around the stopcock is more likely as a result of this. During titration, stopcock leakage would result in makes big acid levels. During lengthy periods of nonuse, gradual evaporation of titrating solution from the stopcock valve generates a limited zone of higher pH, allowing for fusion among the stopcock and burette body. Burettes must be evacuated, cleansed, and replaced with fresh working solutions after periods of silence (Reinhold and Chung, 1961).

As Carbon dioxide penetrates readily throughout most common plastics, lengthy storage of alkaline in plastic vessels necessitates extra caution. Notwithstanding this flaw, plastic vessels are commonly used to store stock alkaline solutions for lengthy periods. Working solutions must be re-standardized regularly, regardless of if they are stored in plastic or glass, to account for alkalinity losses caused by reactions with glass and Carbon dioxide (Houghton, 1980).

6.4.3.2. Standard Acid

Sodium Hydroxide is inappropriate as the main standard due to its contaminants and moisture-absorbent properties. As a result, titrating solutions containing sodium hydroxide should be standardized vs a *standard acid*. Because of this, *potassium acid phthalate* is widely utilized.

At pH 8.2, the solitary ionizable hydrogen ($pK_a = 5.4$) in potassium acid phthalate offers relatively minimal buffering. It may be made in a very pure state, is generally nonhygroscopic, and may be heated at 120°C without disintegration or evaporation. Its large molecular mass makes precise measuring possible.

Before usage, potassium acid phthalate must be dried for two hours at 120°C and then allowed to cool to room temp in a desiccator. A recognized normality basis is used to titrate a precisely calculated amount of potassium acid phthalate solution. The titrant is always the base. In acidic liquids, Carbon dioxide is practically insoluble. As a result, swirling an acid specimen to aid mix would not greatly affect the titration's precision (Schilt et al., 1956).

6.4.3.3. Sample Analysis

There are several recognized techniques for evaluating titratable acidity in different foods (Kou et al., 1993). Furthermore, measuring titratable acidity

for most specimens is very simple, and several of the stages are similar across different techniques. An amount of material (typically 10 mL) is titrated to a phenolphthalein terminal using a standardized base solution (commonly 0.1 normality Sodium Hydroxide). Whenever the usage of a color indication is problematic, potentiometric terminal point measurement is employed.

Figure 6.7 shows the normal titration settings for colorimetric and potentiometric goals. Whenever the terminal point indicators are utilized, Erlenmeyer flasks are frequently recommended. Although a magnetic stirring bar can be employed, hand whirling is generally sufficient for combining the material. The specimen flask is spun using the right hand for hand combining. On the right-hand side, there is a stopcock. The left-hand side's four fingers are put behind the stopcock valve, while the thumb is positioned beside it. The titrant is poured at a moderate, consistent rate till the terminal point is reached, and afterwards injected dropwise till the terminal point doesn't fade after a set amount of time, generally 5 to 10 seconds (Rukunudin et al., 1998).

Whenever specimens are evaluated potentiometrically, the chunkiness of the pH electrode necessitates the usage of beakers rather than Erlenmeyer flasks. Magnetic agitation is nearly usually used to blend the samples, and splashing is more common with glass beakers as compared to Erlenmeyer flasks. However, titration procedures are the same as those described earlier for colorimetric terminal point titrations.

Issues might emerge while titrating gels, specimens, or concentrates with particles. Such matrices slow acid diffusion from a tightly compacted specimen. Steady diffusion has a diminishing ending. Dissolve concentrates in carbon dioxide-free H_2O. The initial acid composition is estimated using dilution information. Starch and other weak gels may be titrated like concentrates by adding carbon dioxide-free H_2O and stirring briskly. Certain pectin and meal gum gels required blending to sufficiently disturb the gel structure. Blending can produce dense foams. For breaking foams, utilize suction or antifoam (O'Hare et al., 1974).

Immediately after treatment, pH levels of particle specimens may fluctuate between pieces. Acid equilibration of the bulk can take several times. Meal s consisting of particles must be blended while titrating. Comminuting might include a lot of air. Volumetric calculations are inaccurate due to air entrapment. While incorporating air, aliquots are generally quantified.

6.4.3.4. Calculation of Titratable Acidity

The strength of the acid is commonly expressed in normality (equivalents per liter) in general chemistry and may be determined utilizing Eqn. (1). Meal acids, on the other hand, are normally expressed as a percentage of the overall weight of the specimen. As a result, the titratable acidity equation is given (Kok et al., 1993):

$$\%\ \text{acid}\ (\text{wt}/\text{wt}) = \frac{N \times V \times \text{Eq wt}}{W \times 1000} \times 100 \qquad (18)$$

where:

N = normality of titrant, usually NaOH (mEq/mL)
V = volume of titrant (mL)
Eq. wt. = equivalent weight of predominant acid (mg/mEq)
W = mass of sample (g)
1,000 = factor relating mg to grams (mg/g) (1/10 = 100/1,000)

The titrant's normalcy is reported in milliequivalents (mEq) / milliliter, which is a common technique of measuring normality for tiny amounts. That amount is like equivalents per liter in terms of math. It's also worth noting it's simpler to express specimen mass in grams rather than milligrams, therefore the product of specimen mass by 1,000 milligrams per gram cancels units.

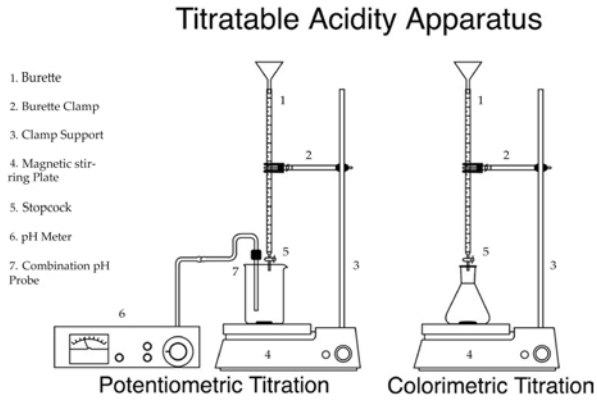

Figure 6.7. Computation equipment of titratable acidity.

Source: https://currentprotocols.onlinelibrary.wiley.com/doi/10.1002/0471142913.fag0201s00.

6.4.3.5. Acid Composition in Meal

The molecular complexity of most meals rivals that of life itself. Thus, they comprise all of the Krebs cycle acids (and derivatives), as well as amino acids and fatty acids. All of them, in theory, lead to titratable acidity. Specific acids can't be distinguished by routine titration. As a result, the major acid is frequently used to express titratable acidity. For the most part, this is unmistakable. Both acids can exist in high amounts in certain circumstances, and the dominating acid can vary with age. Before maturation, malic acid dominates in grapes, but tartaric acid prevails in fruit. Citric acids and malic in pears exhibit similar behavior. Thankfully, the corresponding weights of typical dietary acids are pretty comparable. As a result, dual dominance or wrong choice of the dominant acid has little effect on percent titratable acidity (Teerachaichayut and Ho, 2017).

Meals include a wide variety of acid contents. Acids may be present in the meal at amounts that are below the limit of detection or it might be the most prominent component contained. Acid concentration alone does not tell the story of how acids contribute to meal flavor and quality. Sugars help to attenuate the acidity of acids. As a result, the ratio of acid (commonly referred to as ratio) is the best predictor of an acid's flavor impact as compared to Brix (for example, percent sugar (w/w) in a medium; or acid alone. Fruit acidity decreases as the fruit matures, whereas sugar content rises. As a result, the Brix/acid ratio is frequently utilized as a measure of the maturity of the fruit. Variety, c Climate and horticultural methods may all influence this ratio in ripe fruit. Several economically significant fruits have characteristic acid compositions and sugar levels at maturity, as shown in Table 6.5. The most frequent acids found in fruits and most vegetables are malic and citric acids; although, leafy vegetables can also consist of considerable amounts of oxalic acid. Lactic acid is the most essential acid in dairy meals, and titratable acidity is frequently utilized in cheese and yogurt production to track the performance of lactic acid fermentation (Wehr et al., 2004).

The refractometer value of dissolvable solids is influenced by organic acids. Brix values are occasionally modified for acid content while goods are sold in pound solids. For every percent titratable acidity, 0.20° Brix is injected into citric acid.

Table 6.5. Certain Economically Significant Fruits' Acid Content and °Brix

Fruit	Principal Acid	Typical °Brix	Typical percent Acid
Bananas	Malic/citric (3:1)	16.5–19.5	0.25
Apples	Malic	9.12–13.5	0.27–1.02
Cranberries	Citric	12.9–14.2	0.9–1.36
–	Malic	–	0.70–0.98
Cherries	Malic	13.4–18.0	0.47–1.86
Grapes	Tartaric/malic (3:2)	13.3–14.4	0.84–1.16
Grapefruit	Citric	7–10	0.64–2.10
Limes	Citric	8.3–14.1	4.9–8.3
Lemons	Citric	7.1–11.9	4.2–8.33
Peaches	Citric	11.8–12.3	1–2
Oranges	Citric	9–14	0.68–1.20
Pineapples	Citric	12.3–16.8	0.78–0.84
Pears	Malic/citric	11–12.3	0.34–0.45
Strawberries	Citric	8–10.1	0.95–1.18
Tomatoes	Citric	4	0.2–0.6
Raspberries	Citric	9–11.1	1.57–2.23

6.4.3.6. Volatile Acidity

It's occasionally useful to know how much acidity originates from the CH_3COOH and how much originates from other acids in the result spontaneously in CH_3COOH fermentations. This may be accomplished by 1st doing an early titration to determine titratable acidity, which serves as a proxy for total acidity. After boiling off the CH_3COOH, allowing the solution to settle, a 2nd titration is done to measure the constant acidity. The dynamic acidity is the discrepancy between constant and overall acidity in the brewery sector, the same method is occasionally utilized to distinguish acidity owing to soluble carbon Dioxide from constant acids. After Carbon dioxide is eliminated using moderate flame (40°C) and moderate stirring, the constant acids are titrated (Benjakul and Chuenarrom, 2011).

6.4.3.7. Other Techniques

Acids in meal specimen have been measured using electrochemistry and high-performance liquid chromatography (HPLC). Both approaches can be used to identify particular acids. For certain acids, HPLC utilizes an index of refraction, UV, or electrochemical monitoring. The electrochemical sign of ascorbic acid is robust, and its absorption at 265 nanometers is substantial. Several notable acids don't absorb substantial amounts of light till they reach 200 nanometers or below.

Polarography and voltammetry are two electrochemical methods that may be used to test a variety of acids. Electrochemical techniques have remarkable selectivity and sensitivity in optimal circumstances. Obstructive substances, on the other hand, frequently make electrochemical techniques impractical (Berezin et al., 1995).

Electrochemical and chromatographic procedures, unlike titration, don't distinguish between acid and its conjugate base. As a result of the natural meal-buffer setup, these species will unavoidably coexist. Thus, acid values measured by instrumental techniques can be 50% higher than titration readings. As a result, only titrated acid measurements may be used to calculate Brix/acid fractions.

To monitor (H^+), novel pH probing designs employ an ion-sensitive field-effect transistor (ISFET). Standard calomel or Silver/ Silver Chloride reference electrodes can be used. The creation of a silicon-based reference electrode, on the other hand, has been a great achievement. Traditional electrodes have slower reaction times as compared to ISFET electrodes. Miniaturized investigations are also conceivable because of small chip technology. Because ISFET probes don't need a fluid carrier, they can assess the pH of gels, meats, cheeses, and other thick foods directly. The increased expenses of an ISFET probe, as well as the potential for reference electrode drift, prevent it from being used in the regular analysis of pH (Lang and Meier, 2007).

6.5. SUMMARY

Organic acids have a significant influence on the flavor and quality of the meal. Meal acids are only partly ionized, while strong acids are entirely ionized. Certain dietary qualities are influenced only by the ionization portion of acid molecules, whereas others are influenced by the overall acid concentration. Titration cannot be used to measure just unbound HO_3^+ ions

in solution. Others emerge from formerly un-ionized molecules as the freed ions are eliminated via a chemical process. Although indicator pigments that vary color based on the presence of HO_3^+ ion occur, these only serve to determine if a certain pH limit has been reached and don't' stoichiometrically measure free HO_3^+ ion. The best solution is to determine the secondary influence of the HO_3^+ ion atmosphere on a setup characteristic like the hue of the indicator dyes or the medium's electrochemical potential. The HO_3^+ ion establishes an electrochemical potential around a partially permeable membrane of the glass on an indicator electrode, which is measured by the pH meter. The change in the potential of the indicator electrode is compared to the potential of a reference electrode. The Nernst equation may be used to translate the discrepancy in millivolt readings between two electrodes into pH. While pH meters may be utilized in crucial work and whenever specimen color makes indicators difficult, indicator dyes are typically employed to indicate the conclusion of acidity titrations.

Utilizing the concept of pH as the –ve log of (H^+), the (HO_3^+) may be determined backwards from pH. The Henderson-Hasselbalch equation may be used to make buffer solutions of every pH. Furthermore, except if the action of acids and conjugated bases are considered, each of these equations' estimations is just approximations.

Titratable acidity is a straightforward way to assess a food's overall acid composition. Most of the time, it's only an approximation because meals typically include a variety of acids that can't be distinguished by titration. Because pH is a mixed-function of titratable acid and conjugated base, titratable acidity is not a reliable forecaster of pH. Instrumental techniques, like HPLC and electrochemical procedures, quantify acids and their conjugated bases like a single substance and, as a result, are likely to provide larger acid concentrations as compared to titration. Surprisingly, titratable acidity predicts acidity greater than the quantity of unbound HO_3^+ ions as measured via pH. The existence of sugars has a significant impact on the insight of tartness.

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CHAPTER 7

THE APPLICATION OF ACIDITY AND BASICITY IN DRUG DISCOVERY

CONTENTS

7.1. INTRODUCTION

While drug research experts adhere to several principles pertaining to drug-like character, the significance of acid/base characteristics is sometimes overlooked. Ionization constants are critical to the variability of biopharmaceutical features of medications, as well as to the underlying factors such as logD and solubility, which are both affected by pH. In addition to affecting physical and chemical qualities such as water solubility, pKa values can also have an impact on drug formulation procedures. More crucially, the distribution, absorption, excretion, metabolism, and toxicity (ADMET) of chemicals under changing pH settings are all significantly influenced by the charge state of the substances. The importance of considering pKa values in conjunction with other molecular features cannot be overstated, and it has the potential to be utilized to further increase the efficacy of drug development procedures. This chapter will serve as a suitable reminder of an essential molecular attribute that determines medical success, which is particularly relevant given the current low yearly output of new medications from medical firms.

Even though pharmaceutical firms have increased their investment in research and development, it has become plainly evident that they are experiencing financial difficulties. To their credit, thorough pre-clinical profiling has assisted in lowering the number of medication failures caused by weak human pharmacokinetics. Today, nevertheless, the reasons for medications being pulled from clinical development have been based on financial considerations, along with toxicity and formulation issues that have been identified. Several other problems, including increased regulatory scrutiny and a scarcity of simple targets, have also impacted the industry's decreased productivity (Meanwell, 2011). In other cases, the pharmaceutical industry's long-term survival has even been called into doubt by observers.

It has become necessary to conduct an analysis of the complete drug development process to assist organizations to compete in the present environment in order to fix the issue of elevated attrition rates and in accordance with sound supervision practice. The study and definition of the physicochemical features of substances that predict good results have also been important in the understanding of therapeutic failures, which has been done by medicinal chemists as well (Meanwell, 2011). Despite the fact that the goal of these studies is to enhance the quality of compounds entering medical trials, there are few disagreements over whether or not these criteria are being followed (Saganuwan, 2019). Property-based optimization is

extremely important to the pharmaceutical industry because there is strong evidence that working with large and solubilized molecules is associated with problems relating to bioavailability, metabolism, promiscuity, efflux, plasma protein binding, and solubility, among other things (Gleeson, 2008; Hann, 2011).

The acid/base composition of medications has a significant impact on their biological characteristics and how they are manufactured. Many physicochemical features are widely examined in drug development, and ionization patterns have rekindled attention. The features linked with medical effectiveness and their relation to base /acid character will be outlined in this review. We'll look at how pharmacokinetic characteristics, drug-receptor interactions, and biopharmaceutical features of drug candidates are affected by charge state (Figure 7.1) (Gleeson, 2008; Leeson et al., 2011).

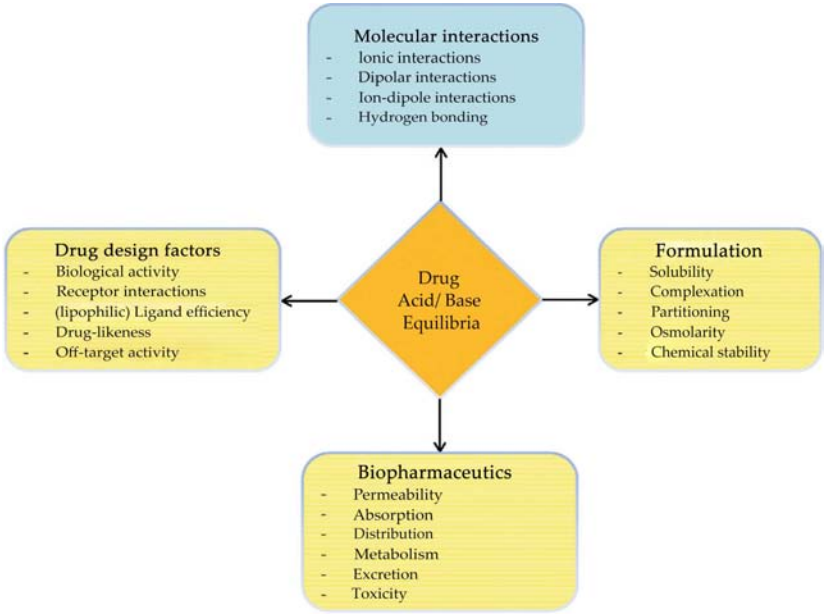

Figure 7.1. The major features of medications that are impacted by their acid/base nature in a schematic diagram. Each node focuses on a different aspect of drug discovery and development that is significant.

Source: https://www.semanticscholar.org/paper/The-significance-of-acid%2Fbase-properties-in-drug-Manallack-Prankerd/d181db-f7e79a66ce13915136b5c079ba8ad77de9/figure/2.

7.2. DRUG DISCOVERY

The drug development process usually begins with the discovery and confirmation of a particular macromolecular target with a specific disease condition in mind. Screening permits compounds to be evaluated to find hits and leads that fulfill a set of predetermined criteria for features, including physicochemical, functional activity, and potency properties. Testing at this point can assist assess the quality of these ligands if oral bioavailability is necessary. The process of turning a lead molecule into a medicine entails optimizing potency, selectivity, and biopharmaceutical aspects such as absorption, distribution, metabolism, excretion, and toxicity (ADMET) on a multifactorial basis (Figure 7.2) (Gleeson, 2008; Meanwell, 2011).

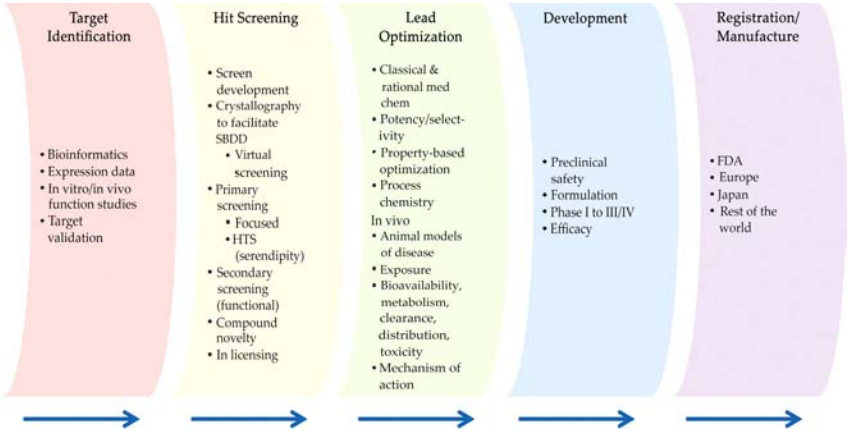

Figure 7.2. The process of drug discovery.

Source: https://www.nature.com/articles/s41573-019-0024-5.

Furthermore, it is important to note that the acid/base outline of a molecule has a direct impact on the lipophilicity of a drug, which is determined through the ionization constants of essential functional groups. Furthermore, if we want to constantly monitor lipophilicity, we must conduct an additional study and become more aware of the acid/base profiles of research compounds, clinical prospects, and pharmaceuticals in general. Four critical aspects of drug development are depicted in Figure 7.1 that are impacted by the acid/base equilibria of the drugs. As a result, the acid/base character of medicine has a significant influence on its potency and selectivity, as well as on its pharmacokinetic and biopharmaceutical characteristics (Johnson and Springthorpe, 2007).

7.3. BIOPHARMACEUTICAL PROPERTIES

Extensive efforts have been made to check the physicochemical properties of compounds that are associated with long-term feasibility, in conjunction with the collection of biological data on characteristics like efflux liability, cell toxicity, metabolic inhibition or stability, cell permeability, bioavailability, CNS permeability, brain tissue binding, protein binding, promiscuity, and volumes of distribution. With this information, researchers have attempted to establish correlations with a variety of simple physicochemical features. Most of this focus has been on metrics that are simple to compute, such as polar surface area (PSA), ClogP, molecular weight (MW), the number of hydrogen bond donors and acceptors, number of rotatable bonds, and the aromatic character (Figure 7.3) (Wager, 2010).

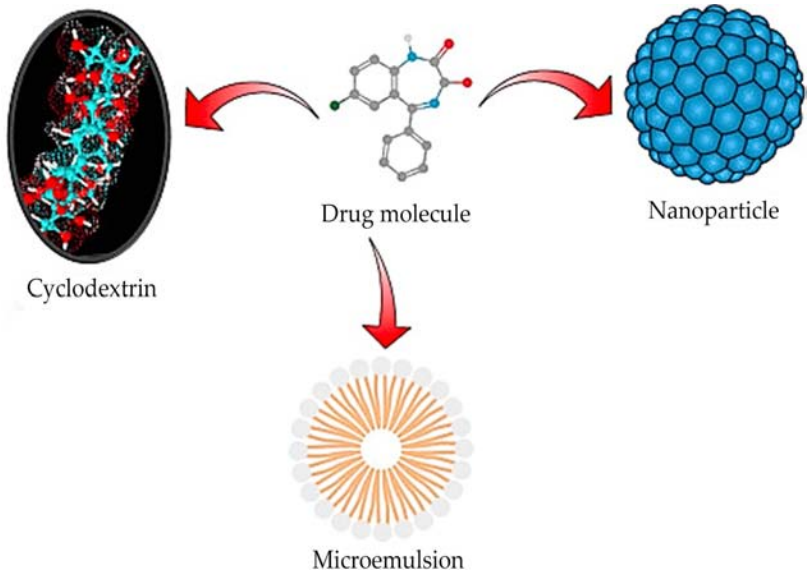

Figure 7.3. Various approaches are being used to increase the biopharmaceutical characteristics of pharmaceuticals.

Source: https://www.sciencedirect.com/science/article/pii/B9780128136294000073.

It is widely recognized that issues with oral absorption are likely to occur if a chemical fit two or more of the subsequent conditions: MW greater than 500, ClogP greater than 5, H-bond donors greater than 5, and H-bond acceptors greater than ten. The most current research was capable of

enhancing these principles, and this chapter will just cover a portion of the most recent findings. We direct the reader to Meanwell's evaluation of this issue for a more in-depth examination of the subject (Lipinski et al., 1997).

Simple ClogP estimates can be made more accurate by considering charge state in order at physiologically appropriate pH levels. At physiological pH (7.4), this is often expressed as an assessment of the water partition coefficient, which is denoted by the symbol ClogD7.4. Examples include Pfizer, which made use of a substantial corpus of in vitro clearance and internal data on cell permeability to make valuable correlations between physicochemical qualities and pharmaceuticals (Johnson et al., 2009). This required plotting the biological data on a logD versus MW plot to illustrate that molecules with appropriate values were into a region known as the 'golden triangle' of chemical properties. A significant finding was that, as a function of increasing MW, the lipophilicity range that could fulfill the criteria of acceptable clearance and permeability became substantially smaller.

Wager (2010) conducted more research on CNS medications and developed a scoring mechanism that considered the following properties: ClogD (7.4), ClogP, MW, PSA, several hydrogen bond donors, and the highly basic pKa. CNS Multiparameter Optimization (CNS MPO) rating provided an indicator of the possibility of a chemical being accepted into the clinic after being evaluated in the laboratory. Even though this was primarily intended towards CNS medications, there was a common association among the score and important in vitro qualities like metabolic stability, efflux, toxicity, and membrane permeability. Particular attention was paid in the investigation to the basicity of the complexes, and substances with a basic pKa value greater than 8.4 did not impact the total CNSMPO rating. Crucially, estimations of pKa values for each chemical were necessary to obtain ClogD (7.4) values for every substance. It has been demonstrated that basic compounds with high pKa values have two major downsides when used as CNS medicines. Cationic medications that are charged demonstrate lower penetration via the blood-brain barrier (BBB), for starters. Additionally, these basic chemicals have a larger likelihood of inhibiting hERG channels than other substances. In this investigation by Wager (2010), ClogD (7.4) values were assigned an ideal range within 2.0 and 4.0 for CNS drug-likeness, with the best range being between 2.0 and 4.0.

As previously stated, the criteria and observations encompass a broad range of drug-like features, and most pharmaceutical firms employ versions of these principles in the evaluation of their compounds. Working in low-risk regions and identifying possible issue compounds early on are the goals of this technique, which is intended to increase the likelihood of success. The danger of establishing rules is that they might be blindly obeyed without a thorough grasp of how they should be implemented or their limits, as is the case with most rules. Ionization constants have undoubtedly been studied in drug development; however, it appears that they have received less attention in comparison to the acid/base properties of compounds. The information where acid/base characteristics have been proven to impact various features of complex behavior is examined in detail in further sections.

7.4. CHARGE STATE

To properly analyze pKa values and charge state, it is necessary to define what acidic, basic, and neutral are. Most of the research that looked at the charge state features of medications in this study classified them as bases, acids, zwitterionic, or neutral. To general about the function of compounds in respect to their physicochemical qualities, this is generally adequate (Martin et al., 1993). While prior research employed pKa values to categorize each chemical at physiological pH, the focus in this study was on the structure of compounds (Schanker et al., 1958). Still, if the molecule includes a basic or acidic functional group, a chemical might have charge-neutral at its isoelectric point, according to the word "neutral." If a substance does not have a (physiologically) significant ionizable group, it is regarded as neutral (acidic or basic). The existence of basic and acidic groups inside a molecule, as well as the pH under consideration, are so emphasized. An acid is simply defined as a species HA that dissociates into the anionic A-form and a proton at a pH above the pKa. Likewise, a basic material may be represented as species B, which will receive a proton that is less than the pKa value to produce cationic species (Boisset et al., 2000).

Acid dissociation. $HA+H_2O \rightleftarrows A+H_3O^+$

Base dissociation. $B+H_2O \rightleftarrows BH^+ +OH$

We used pKa values to construct several ionization categories for our own research into charge states and pKa distributions (Manallack et al., 2005). Our definitions were designed to be more inclusive, encompassing charge states over a wide range of pH values, both physiologically and in medication formulation. We categorized certain chemicals as 'always ionized' in addition to the categories above, such as bases with pKa values over 12.0 or quaternary acids and bases with pKa values less than 0.0. The amount of basic and acidic groups in ampholytes was also characterized. Simple ampholytes are made up of one base and one acid, whereas compound ampholytes are made up of several acids and base combinations.

Sulfonamides, phenols, carboxylates, hydroxamates, heterocyclic nitrogen atoms, and, less commonly, tetrazoles, phosphates, carbon acids, acidic amides, alcohols, thiols, hydrazides, carbamates, acidic anilines, sulfates, and imides are all examples of acidic groups. Aliphatic amines, heterocyclic nitrogen atoms, anilines, guanidine's, amidines, and basic amides are examples of bases. Box 1 contains more information, including a definition of pKa (Pagliara et al., 1999).

7.5. ABSORPTION, PERMEABILITY, AND BIOAVAILABILITY

A significant amount of study has been conducted to better understand the mechanisms that influence the absorption of medicines across intestinal membranes. In their early researchers, described their 'pH partition theory,' which proved that ionization state had a significant influence on the rate of absorption of medicines from the small intestine (Schanker et al., 1958). They discovered that acids with pKa values less than three and bases with pKa values greater than eight were inadequately absorbed in this groundbreaking research. Since the completion of this study, more research has been conducted in which the pKa and ADME behavior have been discussed. Examples include the work of Palm et al. (1999), who built on the previous findings to demonstrate that the transfer of molecules through coverings is more than fast for the uncharged species (Figure 7.4).

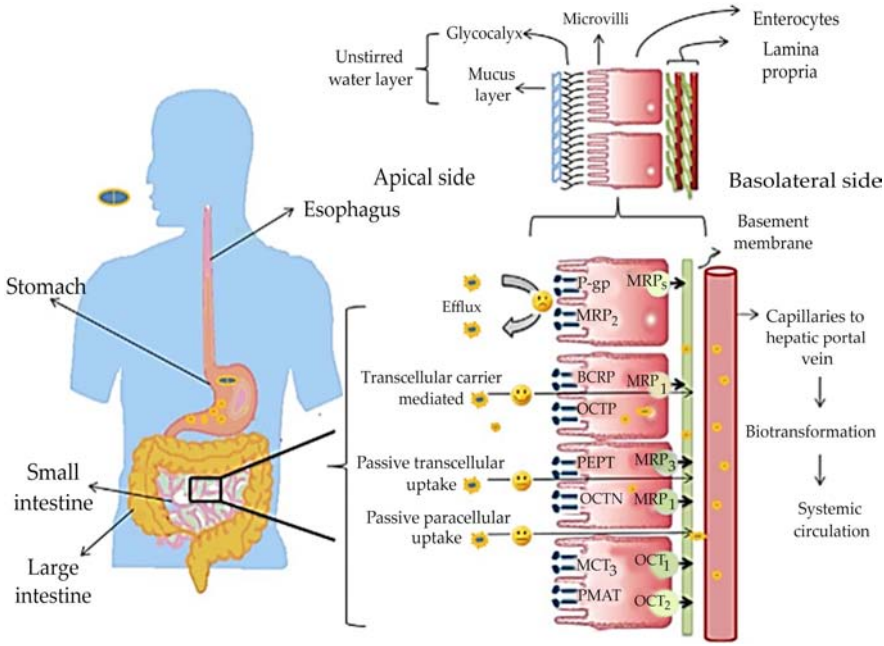

Figure 7.4. Journey of the drug in the gastrointestinal tract.

Source: https://www.sciencedirect.com/science/article/pii/S2211383516300090#f0015.

As an illustration of this theory, a sequence of three structurally comparable AT1 receptor antagonists with slight changes in their ionization state at pH 7.4 and 6.0 were used to demonstrate the concept (Boisset et al., 2000).

In model systems using perfused jejunum loops, Using chambers, or Caco-2 transport investigations, all molecules were ionized at a pH of 7.4, resulting in low permeability in all cases. However, at pH 6.0, just one molecule was substantially uncharged, and this complex was responsible for a significant amount of absorption. This work not only brought attention to the need for prudence when working with these model systems but also highlighted that the ionization profiles of research chemicals should be carefully considered (Boisset et al., 2000).

Castro et al. (1998) developed a sequence of complexes to solve an issue of poor oral absorption in a lead compound as an illustration of their approach. Even though the lead had a favorable in vitro profile, < 5% of it was absorbed by the oral route. The issue was assumed to be a basic amine

group with a pKa value near 9.7, which was suspected to be the culprit. Fluorinated analogs of the amine were synthesized, and the pKa values of the amine were decreased to between 8.0 and 8.8. Subsequent tests revealed that the fluorinated derivatives had a significant increase in oral absorption when compared to the baseline. The increased absorption was related to a larger number of neutral species in the stomach, which was found to be true.

Martin also mentioned charge state as a significant element in determining bioavailability in rats (Martin et al., 1993). Gleeson (2008) used an artificial membrane test (PAMPA) to look at both bioavailability and permeability for a wide range of GSK drugs in a broader investigation. The following is the permeability ranking: acids < zwitterions <bases <neutrals. This was justified in terms of the anionic nature of the membranes utilized, and hence electrostatic grounds were used to justify it. Bioavailability is more difficult to understand than permeability, according to Gleeson's research, because bioavailability includes both clearance and absorption components. Even though ionization state had only a tiny effect on bioavailability, on average, acids were shown to be more bioavailable, contrary to acid permeability evidence generally. His findings were consistent with a prior study that showed acids had increased oral bioavailability, which was likely due to improved solubility and reduced clearance (Gleeson, 2008). Because bases are protonated in the gastrointestinal system, they have a stronger polarity and lower lipophilicity, which restricts passive absorption across biomembranes.

The amount of ionization, which has been examined by earlier investigators using pKa values, is not taken into consideration by the simple categorization of substances into acids and bases.

"Medical chemists, who previously were unconcerned by the pKa values of their bases or acids, are now well aware of the issues that might arise when those values are too far away from 7, the pH value that is considered neutral" —Kubinyi (1997) summarized this notion.

The generalizations above about non-ionized states and permeability are clearly comprehensible when considering the nature of membranes along with their lipophilic properties. In contrast to charged substances, neutral molecules are more easily capable of cross non-polar lipidic membrane settings, where this procedure is energetically disfavorable.

Even with these findings and the prevalent belief that neutral species have a significant advantage in passive transfer through membranes, proof exists that charged molecules can be absorbed in some cases. Monolayers of Caco-2 cells were employed in one investigation to demonstrate that ionic species may have a role in whole drug transport (Pagliara et al., 1999). However, Palm et al. (1999) found substantial improvements in permeability coefficients as the proportion of un-ionized (f(u)) drugs increased. They also noted that the contribution of the ionized form was considerable when the f(u) was less than 0.1. 15 Absorption is plainly complicated by a variety of mechanisms, which makes it difficult to generalize about drug qualities. Although pKa values and acid/base character are essential factors for permeation and absorption, additional parameters such as metabolic lability, size, lipophilicity, hydrophilicity, and efflux mechanisms must also be considered, as previously discussed (Vieth et al., 2004).

7.6. THE VOLUME OF DISTRIBUTION (VD), PLASMA PROTEIN BINDING

Although medication may be effectively absorbed, further characteristics might cause it to be inadequately distributed or removed from the body, making it incapable of eliciting an acceptable pharmacological response. Large values of the parameter volume of distribution (Vd) show that medicine is broadly dispersed, whereas modest values indicate that the molecule is concentrated largely in the systemic flow. The Vd of a medication is a critical factor of its pharmacokinetic features, and when combined with clearance information, the biological half-life of a drug may be calculated. Chemical compounds with higher lipophilicity have a greater value of Vd than chemical compounds with lower lipophilicity and vice versa. More significantly, binding to blood plasma proteins has a major impact on the amount of drug that is released into the circulation. Human plasma comprises more than 60 proteins, but just three of these are responsible for most drug binding: albumen, 1-acid glycoprotein, and lipoproteins (Figure 7.5) (Zhang et al., 2012).

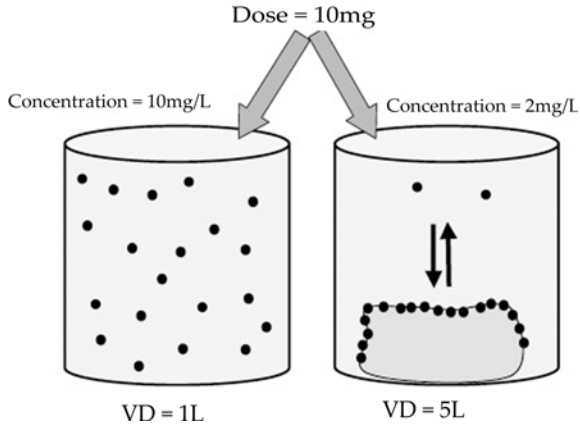

Figure 7.5. The volume of distribution of the center compartment and the compartmental model. The diagram depicts the relationship between a tricompartmental model (on the right) and physiological and anatomical reality (left).

Source: https://www.researchgate.net/figure/Compartmental-model-and-the-volume-of-distribution-of-the-central-compartment-The-figure_fig1_8129382.

At physiological pH, most of the computer research that examines the relationship between acid/base properties and plasma protein binding has been restricted to developing the complexes using one of the four main categories of basic, acidic, zwitterionic, or neutral. Numbers (Gleeson et al., 2006) are the same as in the previous sentence. The values of Vd for basic chemicals are often big, whereas the values for acidic compounds are less in general. Consequently, the quantity of medication exposed to the liver and kidneys differs significantly between acids and bases in humans. The acidic head groups of lipids prefer to create connections with tissue-bound substances such as bases, while acids easily bind to lysine remains found in blood plasma proteins. Current research conducted by GlaxoSmithKline confirmed these long-held conclusions, indicating that basic chemicals are more broadly dispersed throughout the body than previously thought (Gleeson et al., 2006). This analysis also revealed that acids had lower levels of Vd than either zwitterionic or neutral substances, which was surprising. Once again, additional parameters, notably lipophilicity, have a role in the amount to which medicines bind to proteins, and when combined with acid/base characteristics, they have a significant impact on elimination and target organ exposure.

7.7. BRAIN TISSUE BINDING, BLOOD-BRAIN BARRIER PERMEABILITY

Corporations engaged in new medicine research are concerned with the permeability of their research substances to the central nervous system (CNS) and the extent to which they attach to brain tissue. Organizations engaged in the development of medications for CNS objectives are well informed that the pharmacological reaction of a chemical is completely tied to its availability to binding to the appropriate macromolecule in that organ (Cory and Maurer, 2002). If a molecule is substantially protein-bound, it must have adequate effectiveness to account for the tiny proportion of the medicine that is present in the free state of the body. Interestingly, there were only small changes in the binding of acids and bases to brain tissue as opposed to the binding of zwitterionic and neutral substances, although a unique pattern was detected for the binding of plasma proteins. Instead, it was shown that non-specific characteristics, such as lipophilicity, were the most important determinants of brain tissue binding (Figure 7.6) (Gleeson, 2008).

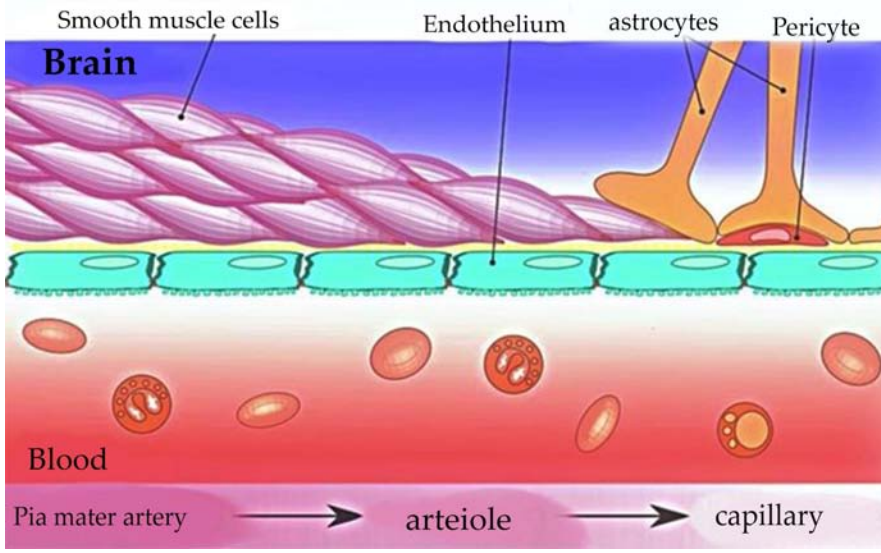

Figure 7.6. A microvessel in the brain protected by the blood-brain barrier.

Source: https://asm.org/Articles/2020/April/How-Pathogens-Penetrate-the-Blood-Brain-Barrier.

Another element of CNS drug research that has received a great deal of attention is the capacity of medications to pass across the blood-brain barrier. In terms of physiology, the BBB shows itself as a considerable barrier to the entry of medicines into the CNS. It is possible to form tight connections among the epithelial cells of the BBB, and there are large populations of effluence pumps that can prevent drug passage into the body. Easy models that predict the degree of drug infiltration into the CNS are restricted by the quality of the data, and as previously stated, highly studies partition substances into different charge states for the purpose of study (Fan et al., 2010). While the MW, hydrogen bond donor ability, and lipophilicity are all important elements in BBB penetration, the ionization state also performs an important impact. Fischer et al. (1998) highlighted the absence of CNS medicines with acidic pKa values less than four and basic pKa values more than 10. According to Fan et al. (2010), acidic medications were the minimum penetrant, whereas basic and neutral substances had mean log B values that were around the same as –0.5. In accordance with our findings, Broccatelli et al. (2012) discovered that acidic compounds with pKa values less than 5.5 were less likely to be CNS penetrant than other acidic compounds.

7.8. EFFLUX MECHANISMS

To protect the skin from hazardous compounds, it has several efflux mechanisms. P-glycoprotein, a membrane-bound protein found on the anterior membrane of the colonic epithelium and the astrocyte membranes of the BBB, is a good example. The pharmaceutical industry is very interested in transporters like P-gp because this efflux pump may strictly limit the oral absorption of drugs or prevent entrance to the CNS. Molecule interaction fields have been used to create a helpful prediction model for P-GP inhibitor affinity, and there are obvious connections among affinity for molecular size and P-GP and the amount of hydrogen bond donors (Seelig, 1998). P-gp, like many other metabolic enzymes, is undiscerning when it comes to substrates. Both metabolism enzymes and P-GP are generally co-located in the gut, where they fulfill the identical role of avoiding undesirable and potentially hazardous chemicals (Benet, 2009).

Acids have lower efflux ratios than basic and neutral substances, but zwitterions have larger efflux ratios. Ionization states also have a role.

A ‘rule of four’ was devised to broadly explain P-GP substrate specificity to simplify compound categorization (33). The characteristics of pKa values, MW, and the sum of the number of oxygen and nitrogen atoms (N+O)

are used in this rule. In summary, it was discovered that compounds with parameters (N+O) 8, MW > 400, and acid pKa > 4 were more likely to be P-GP substrates than those with parameters (N+O) 4, MW > 400, and base pKa 8 (Didziapetris et al., 2003). These criteria are helpful since they allow researchers to track certain physicochemical parameters and charge states to determine P-GP susceptibility. Though these discoveries are significant, P-GP affinity for every structural class will differ, necessitating laboratory testing at an initial stage to determine any potential risks.

7.9. HERG BINDING

The necessity to avoid chemicals that disrupt the hERG potassium channel is critical for the pharmaceutical industry throughout therapeutic development. Inhibiting hERG channels can have serious negative effects, such as QT prolongation, which can take to death and heart arrhythmias in severe cases. Advanced hERG channel models have recently been constructed, allowing for more accurate estimates of channel affinity (Raschi et al., 2009). Many of the models for predicting hERG affinity explain a link between the existence of a channel blockage and a basic group (Raschi et al., 2009). Similarly, the existence of basic aliphatic nitrogen prompts medicinal chemists to do early hERG affinity tests (Table 7.1) (Vaz et al., 2005).

Table 7.1. Relationship between Lipophilicity, Charge State, and hERG Inhibition

	Target upper limits of $logD_{7.4}$ and ClogP to estimate >70% of compounds achieve a hERG IC_{50} of greater than 10 μM			
	Acids	**Bases**	**Neutrals**	**Zwitterions**
$logD_{7.4}$	>4	1.4	3.3	2.3
ClogP	>9	1.9	4.0	4.4
From Ref. (Pelletier et al., 2007) $logD_{7.4}$ and ClogP upper limits to avoid hERG inhibition for various charge states.				

7.10. PHOSPHOLIPIDOSIS

Phospholipidosis is defined by an accumulation of phospholipids in cells, which gives the cells a foamy appearance. It has been shown to be generated by some substances that are cationic amphiphiles in the past. However, this is a minor side effect of certain medications; it can be problematic through drug development since further trials are required to demonstrate that the

effects are reversible. The model established by Tomizawa et al. (2006) predicts whether cationic chemicals would produce phospholipidosis in each environment. In subsequent years, this model was refined to include the following straightforward computation that considers both the pKa and lipophilicity of the basic group if (ClogP)2 + (calculated basic pKa)2, a chemical may have the potential to cause phospholipidosis if the ClogP is more than two and the pKa is greater than 6 (Figure 7.7) (Pelletier et al., 2007).

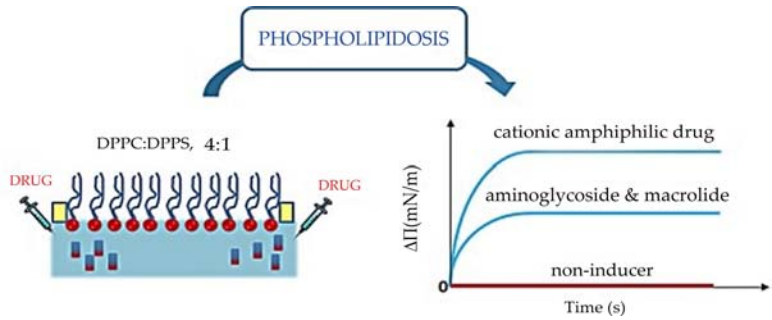

Figure 7.7. Drug phospholipids caused by adsorption onto lipid monolayers.

Source: https://www.sciencedirect.com/science/article/abs/pii/S0927776515301727.

Other researchers have also looked for simple methods to forecast the development of phospholipidosis. Tomizawa et al. (2006) demonstrated, using an in vitro model, that there is a link between ClogP, pKa, and phospholipidosis for basic chemicals (Horii and Yamada, 2007). At pH 4.0, they plotted NC (net charge) versus ClogP and established a prediction system for phospholipidosis because of this. They then extended this to additional chemical classes (Table 7.2).

Table 7.2. Possibility of Phospholipidosis

ClogP	**Net Charge**		
	<1	**1**	**1 < NC ≤ 2**
< 1.61	None	Low	High
1.61 ≤ ClogP < 2.75	None	Medium	High
≥ 2.75	None	High	High

The model developed by Hanumegowda and colleagues is improved to using ClogP and pKa values alone in cases where data on the Vd is available. This model was developed for more sophisticated cases of drug development in which data on the Vd is presented. When a very basic ClogP × Vd × pKa value was greater than 180, inducers of phospholipidosis could be predicted with an 82% degree of accuracy. These straightforward models, which make use of pKa values to predict chemical toxicity, may be implemented quickly and effectively in a drug development scenario (Hanumegowda et al., 2010).

7.11. MITOCHONDRIAL DYSFUNCTION

The disruption of mitochondrial methods has lately been recognized as a source of off-target medication toxicities, which has resulted in the removal from the clinic of various drugs. Specifically, the effects of troglitazone and cerivastatin on mitochondrial oxidative phosphorylation resulted in their removal from the list of approved pharmaceuticals (Dykens and Will, 2007). ATP (adenosine triphosphate) is produced by mitochondria, which serves as the principal source of energy for the cell (ATP). The usage of complexes that cause a temporary decrease in ATP generation can affect a variety of symptoms, including lactic acidosis, which manifests clinically as vomiting, nausea, and stomach discomfort, among others. Pre-clinical screening approaches have been established to detect chemicals that impair mitochondrial function to avoid these compounds from being tested on animals or humans in the future (Nadanaciva et al., 2007). Acidic medications are the most problematic, according to research conducted by Naven et al. (2013) on over 2,000 substances. They also discovered that enhanced lipophilicity was associated with a greater proclivity for uncoupling activity than previously thought. Several acidic functional groups were identified as being mainly troublesome, including anthranilic acids, thiazolidinediones (including thiazolidinedione-based compounds), fluoromethylsulfonanilides (including salicylates), salicylates (including salicylates), and acyclindolones (including acyclindolone-based compounds).

7.12. CLEARANCE, METABOLISM, AND CYTOCHROME P450 ENZYMES

When considering medication clearance, it is necessary to consider both the hepatic and renal routes. There is also a requirement to consist of biliary systems, as these systems together impact pharmacokinetic characteristics

like removal half-life, among other things. Lipophilicity is the most important element in drug clearance since it influences the permeability of a drug's membrane, which is particularly important in renal systems. When the kidneys filter out water from the blood, the reabsorption of substances is proportional to their logD (logarithmic distribution). Positive $logD_{7.4}$ values indicate that a complex will be reabsorbed, whilst negative logD7.4 values indicate that a compound will be removed more quickly. The ionization state performs a role in clearance, and it is notably influenced by the presence of a protein. Because the anionic form of acids can be heavily attached to plasma proteins, they have a lower likelihood of being eliminated, whereas bases have a higher likelihood of being cleared, as previously stated (Dykens and Will, 2007).

It is also necessary to examine secondary metabolism since initial metabolism can frequently result in the formation of ionizable functional groups. For instance, carboxylic acid-containing composites are susceptible to acyl-glucuronidation, which has an impact on their chemical reactivity as well as their side effect profile (Skonberg et al., 2008). Despite this, carboxylates are found in around 19% of all medications (unpublished findings of FDA-approved pharmaceuticals), and for medicinal chemists, they continue to be a significant functional group.

Because in the kidneys, the lipophilic chemicals are reabsorbed, metabolism is necessary to make them more water-soluble in the bloodstream. It is common for cytochrome P450 enzymes to metabolize pharmaceuticals and other foreign substances. The cytochrome P450 isoforms 1A2, 2C9, 2C19, 2D6, and 3A4 are responsible for the bulk of drug metabolism (Skonberg et al., 2005). Many attempts are made in the drug discovery sector to minimize the metabolism of pharmaceuticals by P450 enzymes, which are known to be toxic. The causes for this are to reduce the development of potentially hazardous metabolites as well as to prevent meddling with the metabolism of other medications, which might result in drug interactions if they are taken together. Reduced metabolism of medicine allows for longer half-lives and less frequent dosage regimens, which are both beneficial. The

P450 isoforms 2C9 and 2D6 were shown to be the most strongly impacted by the charge state, whereas the ionization state was found to be a minor influence on the remaining isoforms. Other constraints, like the MW and logP of the organic substance, influence the predilection of cytochrome P450 isoforms for organic compounds. Bioactivation is the process by which cytochrome P450 enzymes and other drug-metabolizing enzymes convert inactive drugs into physiologically active metabolites. Luckily, 3D protein structure information is beginning to be used to better understand substrate preferences, even though these enzymes are famously promiscuous in their substrate selection. This is understandable when one considers their extensive involvement in the metabolism of equally endogenous and foreign substances (Williams et al., 2003).

7.13. ACID/BASE OUTLINE OF ORAL DRUGS

To categorize each chemical, we looked at the pKa of every functional group in the acid/base profile of tiny organic compounds. Our initial study appeared at a collection of previously reported pKa values for several older medicines. Even though this was useful, a larger collection of chemicals was examined later, including those currently in clinical use (Manallack et al., 2005). The percentage of charge state forms to the pKa distributions of bases and acids was examined at different levels in this work. Furthermore, the compounds were divided into two groups: oral medications and CNS drugs, allowing for comparisons between the two. These kinds of surveys provide information on pharmaceuticals in general, and the findings have the potential to be used in early-stage drug development.

Ionizable compounds are primarily composed of molecules that include a single basic or acidic group, along with simple ampholytes that contain one acid and one base. The high proportion of ionizable compounds is an intriguing statistic that reflects the optimization process that results in features that are suited for binding site interactions and biopharmaceutical properties (Figure 7.8).

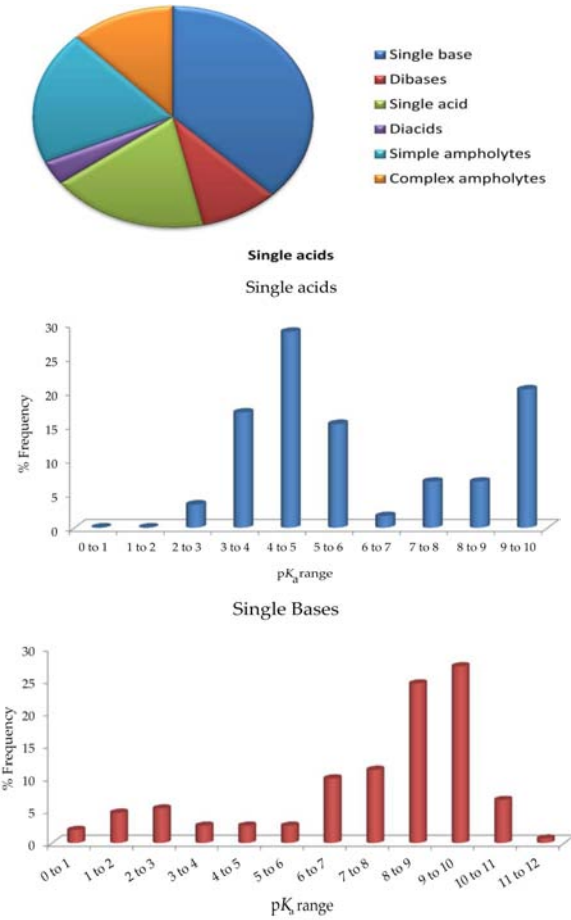

Figure 7.8. (A) Compound category proportion for ionizable oral medicines; (B) pKa distributions of oral medicines with a single acidic functional group; or (C) a single basic functional group.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3641858/.

Figures 7.8(B) and 7.8(C) show plots of the pKa distributions of a single base and single acid comprising compounds. Surprisingly, there is a biphasic dispersal for acids, indicating a scarcity of acids with pKa values among 6 and 7. The preponderance of carboxylate and phenolic compounds in this collection, as well as the range of pKa values often observed for these groups, can explain this (Hopkins et al., 2004). Instead, the bases exhibit a distribution that shows that most of these compounds have pKa values greater than 6.0. This may be explained, once again, by the huge number of aliphatic

amines in this collection, which primarily target GPCRs. Numerous variables impact the overall composition of pKa distributions and compound classes (Manallack et al., 2005). Given that these are well-established medications, ADMET characteristics, with the necessity to fulfill the required binding site interfaces, are important considerations. This research was valuable since it provided information beyond typical physicochemical parameters that might impact the screening collections used and the variety of ionizable functional groups found in these compounds. This study on pharmaceuticals is supplemented by our analysis of screening chemicals and chemogenomic datasets, and a publication on the subject is in the works.

Other organizations have considered the charge states of medications as part of their overall physicochemical property studies (Böcker et al., 2010).

Bocker et al. (2010) concentrated on carboxylates, but they also compared typical physicochemical features, categorizing the medications as zwitterions, bases, neutrals, and acids (Böcker et al., 2010). There were minor changes across the groups, but neutral medications had fewer basic drugs, and rotatable bonds had a much smaller amount of hydrogen bond acceptors. Their research yielded a set of findings that may be used to calculate whether a carboxylic acid-containing drug would have acceptable ADME qualities. The subsequent list contains the required attributes, and no more than one cut-off value should be exceeded in this situation:

- MW < 400;
- # H-bond donors < 3;
- # H-bond acceptors ≤ 6;
- # rotatable bonds ≤ 9;
- ClogP < 3;
- $-1.5 < \text{ClogD}_{7.4} < 1.5$;
- 60 < PSA < 140;
- pK_a (COOH) > 3.

Leeson et al. (2011) looked at molecular characteristics and charge states in greater detail, as well as changes in these characteristics over the last few decades. Complexes were divided into zwitterions, bases, neutrals, and acids once more, but quaternary amines were given their own class of 'cations.' A broad range of attributes were evaluated to see if there were any trends that may indicate whether certain traits have come to an agreement over time. Lipophilicity has been demonstrated to increase over time for neutral and acidic oral medications, whereas basic pharmaceuticals have

already attained a lipophilicity range that is comparable to the other groups. According to another research (Leeson et al., 2011):

- MW is increasing in all classes over time;
- # H-bond donors is stable;
- # H-bond acceptors is increasing with time;
- Aromatic atom count – sp^3 atom count (Ar-sp^3) is constant with time.

This type of analysis is extremely valuable for identifying trends in the way medicinal chemistry and drug development are carried out, and it can also be used to compare trends between organizations to detect patterns. It has been hypothesized that in the case of neutral and acid medicines, there is the ability to tolerate more lipophilicity.

7.14. DRUG-RECEPTOR INTERACTIONS

There are two types of drug binding spots in macromolecular targets: hydrophilic and hydrophobic regions. The hydrophilic may be implicated in binding to ligands beyond electrostatic interactions such as hydrogen bonding, ionic bonding, ion-dipole interactions, dipole-dipole interactions, and ion-cation interactions, among others. Drug designers will benefit from an increased understanding of the shape and strength of these connections that have been gained by surveys of these interactions. 48 Connections between ionizable groups in medicines and complementary groups in macromolecules can result in strong contacts; however, the strength of these interactions can be lowered by competing effects such as hydration and entropy. To increase the efficacy of lead, medicinal chemists can manipulate the thermodynamic components known as entropic or enthalpic thermodynamic components. The quickest and most straightforward solution is to enhance lipophilicity or the number of groups that interact (Andrews et al., 1984). Molecular obesity is the phrase used to describe this technique, which sends the researcher down a path that is expected to result in future solubility or ADMET issues. To achieve more precise interactions, such as those achieved by H-bonding, it is necessary to optimize the positioning of the functional group in the binding spot, although keeping in mind that desolation might result in an entropic cost. When measured in terms of energy, dissolving a non-polar group needs 10 times less energy, which is why medicinal chemists discover themselves adding hydrophobic groups to their compounds to increase potency. Attempting to obtain maximum influence in these circumstances implies that the chemist is frequently led down the incorrect road.

Several metrics have been created to help prevent molecular overweightness issues and to particularly check the quality of lead compounds. These factors include When optimizing lead compounds, for example, monitoring ligand efficiency can be used to determine the potential to produce a new molecule (LE) (Hopkins et al., 2004). This parameter accounts for both the effectiveness and the MW of a molecule to calculate the binding free energy per heavy atom. In the field of medicinal chemistry, several ligand efficiency metrics have been established, and these are now popular among researchers in the field. According to Andrews et al. (1984), ligand efficiency in extremely tiny MW molecules is impacted by charged groups, which can result in significant increases in LE when present in high concentrations. It is also possible to trade off ligand efficiency in exchange for the incorporation of a charged functional group, which may be necessary to increase the solubility of the ligand or biopharmaceutical properties (Perola, 2010).

7.15. OFF-TARGET ACTIVITY

Selectivity for the chosen target is a crucial challenge for scientists researching novel drugs. While interaction with more than one macromolecule may be desired in some cases, off-target activity might result in toxicity and adverse effects. Several research has delved into this issue, aiming to establish connections between simple physicochemical parameters (Leeson and Springthorpe, 2007). Basic chemicals frequently interact with several targets, whereas zwitterions, neutrals, and acids have a lower proclivity for off-target action (Peters et al., 2009). While some of these researchers have found connections between MW, ClogP, and promiscuity, the statistics must be interpreted with caution. With a larger ClogP and MW, a compound's complexity increases, implying that it has a greater chance of intermingling with additional targets (Leeson and Springthorpe, 2007). Off-target activity is another cause to consider size and lipophilicity, as well as logD7 when ionizable groups are present. There are four values that must be kept track of.

7.16. FORMULATION

Drugs that must be delivered in solution may have their pKa value(s) determined, which can have a significant impact on several elements of their composition. For example, the pKa values of medicine have a significant impact on its aqueous solubility, and generally, the ionized form of a

drug is far more water-soluble than the unionized form. It is an incredibly essential physicochemical parameter in the pharmaceutical business, and it is frequently researched in this sector of the industry. As a result of its impact on solute-solvent interfaces, polarity is one of the two most important factors to aqueous drug solubility, the further being water. Other factors to consider include the energetic nature of the solid-state, namely the crystal lattice energy, which changes from one drug structure to the next and across polymorphic versions of the same structure, among other factors. The ability of a medicine to reach the site of action, which begins with absorption from the gastrointestinal system, and to bind with the proper receptor are both dependent on the degree of lipophilicity it possesses. As a result, the required lipophilicity frequently causes a decrease in water solubility to some amount. The acid/base character of medicine is vital in determining its solubility; however, the pH of a solution formulation has a significant impact on this, resulting in varying polarity in aqueous solution in many cases. Drug solubility is discussed extensively, and the reader is directed to two significant works on the subject (Grant et al., 1984).

Since the beginning of time, it has been widely acknowledged that the pH of injectable solutions should not exceed the range, mostly for reasons relating to discomfort or tissue damage during the injection process (Manallack et al., 2005; Leeson and Springthorpe, 2007). To get acceptable solubility in the design of an ionizable weakly water-soluble medication, it may be necessary to use an extremely high pH value. A careful selection of the ionizable group or groups can make a significant difference in the solution of this solubility problem. A considerable ionization of the inserted group in the preparation vehicle, and preferably also under physiological circumstances, is required for the successful delivery of the compound. In general, effective pKa values for solubility development should be in the range of (Manallack et al., 2005; Leeson and Springthorpe, 2007) to guarantee that there is a sufficient proportion of ionized medication to produce appropriate solubility in water. However, this is difficult to generalize. Acids should have pKa values that are closer to the top end of this range, whereas

bases should have values that are closer to the lower end. Of course, it will be easier to develop a medicine that is considerably water-soluble than it will be to formulate a drug that is marginally water-soluble. Besides osmotic action, another consideration for injectable and ophthalmic medications is pH regulation, which is regulated by the solution pH and the drug material pKa, among other things. This is particularly important in situations where the drug intensity is elevated, and the drug itself is the primary osmotic determining factor.

Yet another factor that might have an impact on preparation is the possible impact of drug stability on the ionization state of a compound. As an example, when the pH is greater than 6, morphine reduces by two oxidation routes: one using the free base form of the alicyclic 3° nitrogen and another involving the anionically bound anionic form of the 3-OH phenolic group. It is observed that, in both circumstances, the oxidation rate rises when the deprotonation of every functional group is increased. If drug design factors result in oxidizable groups with pKa values in the physiologically related range for either kind of degradation route, then oxidative degradation may be enhanced for both types of degradation pathways (Connors et al., 1986).

7.17. PKA PREDICTION METHODS

Note that the major focus of research on acid/base equilibria of pharmaceuticals has been on aqueous biological systems, which is crucial to remember. The changes in aqueous solution drug characteristics that occur because of the altered ionization (protonation deprotonation processes) of one or more functional groups are the mechanism through which acid/base behavior has an influence on these systems. The ability to properly estimate or reliably measure pKa values is another significant consideration when evaluating acid/base character. This also has an impact on the calculation of logD values. Software tools are available that may be used to estimate the pH of water-soluble compounds. These programs differ in terms of accuracy as well as the technique used to calculate the pKa value (Figure 7.9).

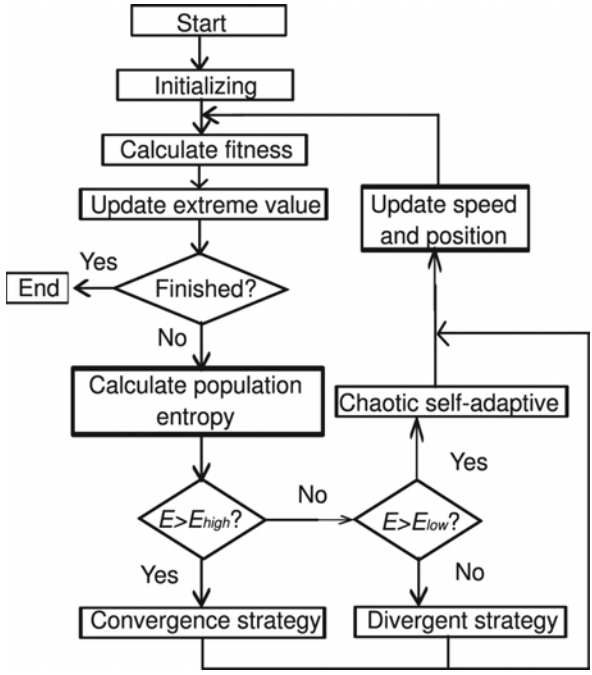

Figure 7.9. Flow diagram of CSAPSO-EDCD algorithm.

Source: https://www.nature.com/articles/s41598-018-22332-7.

Because of the scope of this topic, we recommend that the reader consult Lee and Crippen (2009), who explain the numerous approaches and software packages accessible.

Commercial pK_a prediction software packages:

- ACD Labs/pKa (ACD Labs, http://www.acdlabs.com/home/);
- ADME Boxes (Pharma Algorithms, http://pharma-algorithms.com/);
- ADMET Predictor (Simulations Plus, http://www.simulations-plus.com/);
- CSpKa (ChemSilico, http://www.chemsilico.com/);
- Marvin (ChemAxon, http://www.chemaxon.com/);
- Moka (Molecular Discovery, http://www.moldiscovery.com/) Pipeline Pilot (Accelrys, http://accelrys.com/) pKalc (CompuDrug, http://www.compudrug.com/);

- QikProp and Epik (Schrödinger, http://www.schrodinger.com/);
- Quapaw (OpenEye, http://www.eyesopen.com/).

pKa prediction techniques developed by SPARC have also been tested for their precision in this study (Manchester et al., 2010). One issue that must be taken into consideration for these calculations is the selection of the right tautomeric state for a molecule since this would have a significant impact on pKa predictions (Martin, 2009). Furthermore, the quality of experimental data that is utilized for verifying pKa prediction models should be taken into consideration as well. This data is frequently erroneous, or else the experimental procedure necessitates a thorough examination. Another compilation that was just completed has offered several numbers in which the dependability of the experimental approach has been evaluated (Box and Comer, 2008). Finally, greater throughput apparatus for measuring pKa values have been recently developed, and the reader is directed to Comer's study for further details (Prankerd, 2007).

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CHAPTER 8

THE ALKALINE DIET AND HUMAN HEALTH

CONTENTS

8.1. INTRODUCTION

Appropriate pH levels mostly around live creatures and cells are essential for life on Earth. For the survival, humans need a strictly controlled pH level in the blood around 7.4 (the mildly base limit of 7.35 to 7.45) (MacManus et al., 2007).

In comparison, as per the industrialization has increased, the ocean's pH has declined from 8.2 to 8.1 due to increased CO_2 deposition during the last 100 years. This has a severe influence on ocean life and may cause a coral reef collapse (MacManus et al., 2007). Also, the soil's pH in which plants grow can have a significant impact on the quality of minerals of food that we consume (because minerals are utilized like buffers to sustain pH). pH in soil should be between 6 and 7 for the highest total supply of key nutrients. Acidic soils with pH levels below 6 may have lower calcium and magnesium levels, whereas soils with pH levels above 7 may have chemically inaccessible iron, manganese, copper, and zinc. When the pH in an acid soil environment falls below 6, dolomite, and manure are used to raise it (Meriño-Gergichevich et al., 2010).

From the hunter-gatherer culture to the present, there has been a significant shift in the total load of acid and the pH in the individual eating plan (Ströhle et al., 2010). The agrarian revolution (the previous thousands of years) and, currently, industrialization (the last two centuries) have resulted in a drop in the potassium (K) relative to sodium (Na) as well as a rise in chloride in comparison to bicarbonate in food (Ströhle et al., 2010). The ratio of potassium-to-sodium has been inverted; formerly, K/Na was 10 to 1, while the present food has a ratio of 1 to 3. In comparison to pre-agricultural humans, nowadays, pre-agricultural humans have a diet that is low in potassium, and magnesium and fiber, as well as high in dense fat, normal carbohydrates, salt, as well as chloride As a result, the diet may generate metabolic acidosis and is out of sync with the genetically established nutritional needs. While on the contemporary food plan, there is the steady decrease of renal acid-base regulation capacity with aging, resulting in a rise in food-generating metabolic acidosis. A high-protein, low-carbohydrate meal along an elevated acid weight has minimal effect on blood chemistry and pH, but has a large impact on urine chemistry. Urine magnesium, citrate, and pH levels are lowered, while phosphate, un-ionized uric acid, and urinary calcium levels are increased. These all factors contribute to a higher risk of kidney stones (Ströhle et al., 2010).

A lot of data has been published in an unprofessional works and on several websites elaborating on the advantages of the alkaline diet. This report attempts to maintain the proof given in the literature of research (Table 8.1).

Table 8.1. Ph of Selected Fluids, Organs, and Membranes

Organ, Fluid, or Membrane	pH	Function of pH
Pancreatic fluid	8.8	Counterbalance acid of stomach, aid in ingestion
Gastric	1.35 to 3.5	crumble protein
Intracellular fluid	6.0–7.2 (19)	Because of acid production in cells
Serum arterial	7.4	Strongly controlled
Vaginal fluid	<4.7 (13)	Bound extra growth of unhealthy microbes
Urine	4.6 to 8.0 (18)	bound extra growth of bacteria
Skin	Natural pH is between 4 and 6.5 (17)	Block defense from microbes
Serum venous	7.35	Strongly controlled
Cerebrospinal fluid	7.3	Cleans the outside of the brain
Bile	7.6 to 8.8	Counterbalance stomach acid, help in digestion

8.2. THE ROLE OF PH IN VARIOUS CELLS, ORGANS, AND MEMBRANES

The pH of our bodies varies significantly from one region to another with the stomach having the greatest acidity (pH from 1.35 to 3.5) to support in ingestion and defend from opportunistic bacterial classes. However, also in a stomach, layer immediately exterior to the epithelium plays a critical role in preventing mucosal damage. It has been reported that reduced stomach lining bicarbonate production and reduced alkaline/acid secretion might perform an important role in duodenal ulcer for patients. The skin has a large amount of acid (around pH 4–6.5) to generate an acid layer that plays a role as a defensive block against bacterial growth in the environment. The exterior horny layer (of pH 4) is more acidic as compared to alkaline layer

(pH 6.9). It is as well observed in the vagina, at where the pH below 4.7 inhibits bacterial growth (Remer and Manz, 1994).

The pH of urine can range from acid to base, based on the necessity for inner environment balance. Acid excretion in urine might be calculated using Remer's formula (sulfate + organic acids + chloride + 1.8x phosphate) minus (sodium + 2x magnesium+ potassium + 2x calcium) Eq. Foods may be classified according to their potential renal acid loads (PRALs), as presented in Table 8.2. Fruit juices, fruits, potatoes, veggies, as well as drinks that are high in alkali and low in phosphorus (white and mineral soda waters, red wine,) all have a low acid load. Whole grains, dairy items, meats, alkali-deficient, and fish, and less-phosphorus liquids (e.g., chocolate, pale beers,) have comparatively more acid loading (Remer, 2001). The urine's pH was not predictive of fractures in bones or injury of mineral density of bone over a five-year period (as evaluated in a current study using 2 pre-lunch specimens taken over a period of five years) (Fenton et al., 2010). This, however, might not be indicative of an acidic or alkaline diet at the time of this period.

8.3. PH OF DIFFERENT BODY FLUIDS

A blood's pH limits around 7.35–7.45, but some physiologic substances have a different pH. The amount of Hydrogen ion is evaluated by pH, with the low pH suggesting that there are so many hydrogen ions as well as a large pH value indicating that there are so many hydroxyl ions. If the pH level goes less than 6.9, coma may develop. Other liquids, on either hand, have a certain pH. Salivary pH ranges from 6.5 and 7.5. The food enters the stomach after swallowing, in which the levels of pH in the lower and upper portions of the stomach vary. The top portion does have a pH around 46.5, whereas the lower half does have the pH around 1.54.0, indicating that it is very acidic. It then enters the gut, that does have the pH around 78.5 and is somewhat basic. Certain locations' pH levels must be maintained consistent for them to operate effectively (Figure 8.1) (Ströhle et al., 2010).

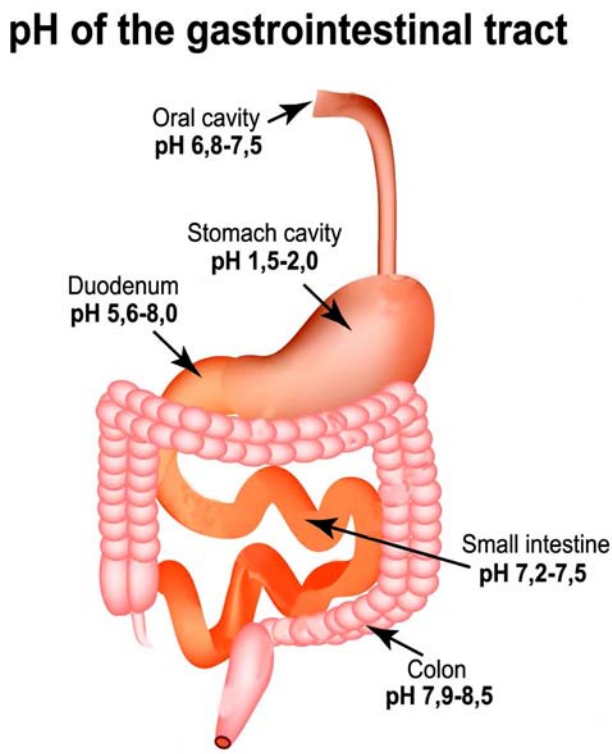

Figure 8.1. The gastrointestinal tract's pH. The esophagus, duodenum, stomach, colon, and small intestine.

Source: https://www.news-medical.net/health/pH-in-the-Human-Body.aspx.

8.3.1. Impact of Altering the pH Balance

Various parts of the bodywork optimally at the limit of their own ideal pH level. For instance, the enzyme pepsin functions best in a low pH environment, but the enzymes in the gut operate best in an alkaline or high pH environment. Likewise, any change inside the blood pH might result in a variety of illnesses.

8.3.2. Maintaining the Body pH

The three fundamental mechanisms that maintain the body's pH in balance are respiratory control, buffer systems, and renal regulation.

8.4. CHRONIC ACIDOSIS AND BONE DISEASE

Calcium in the kind of carbonates as well as phosphate is the significant source of alkaline in the individuals. Those salts are secreted into complete circulation in response to a load of acid, like the contemporary eating plan, in order to restore pH equilibrium. Calcium loss in the urine as a result of a contemporary diet has been estimated to be as greater as over 480 gm during a period of two decades, or approximately partial of calcium skeletal mass (Fenton et al., 2008). Though, urinary calcium loss are indirect indicator of osteoporosis. Numerous regulatory mechanisms may substitute the calcium loss in the urine. When arterial pH is normal, a little decrease in plasma bicarbonate causes a reduced calcium balance that may benefit from bicarbonate supplementation in a kind of potassium bicarbonate. Bicarbonate, which raises the alkalis of a meal but not the potassium amount, has been shown to reduce bone loss in strong elderly people (Dawson-Hughes et al., 2009). The minerals of bone lost in the urine might not be completely compensated for by intestinal absorption, resulting in osteoporosis. Appropriate vitamin D absorption having a 25(OH)D level >80 nmol/L, on the other hand, may permit for optimal calcium intestinal absorption magnesium, and phosphate as required. Regrettably, the majority of populations are vitamin D deficient, particularly those living in northern climates (Schwalfenberg et al., 2010). Restoration of metabolic alkalosis with bicarbonate considerably increases parathyroid hormone values as well as the live component of vitamin D, $1,25(OH)_2D_3$ in severe renal failure (Lu et al., 1995). Recent research demonstrated the critical role of phosphate in Remer's PRAL formula. Increases in phosphate should result in a rise in loss of urinary calcium and a deleterious calcium balance in bone, must be caused by an increase in phosphate, as predicted by the formula. This should be noted that phosphate supplementation decreased urine calcium flow but did not stop bone loss in individuals on bed rest (Hulley et al., 1971). Recently, an organized analysis and meta-analysis demonstrated that phosphate maintains and improves calcium homeostasis, which contradicts the acid-ash theory (Fenton et al., 2009). Additionally, current research examined the relationship between soda consumption (which contains a substantial quantity of phosphate) and osteoporosis in postmenopausal American first nations women. It is also likely that the large content of acid indicated by Remer's categorization should reconsider in view of compensating phosphate consumption. There is internet material and a lot of publications recommending an alkaline eating plan for bone health. However, a current comprehensive assessment of a literature in search of data supporting dietary

acid load that has no preventive impact against osteoporosis, according to an alkaline eating plan for bone health (Fenton et al., 2011).

Table 8.2. Selected Foods having Potential Renal Acid Loads (PRALs) (Remer and Manz, 1995)

Food or Food Group	**PRAL mEq of: Cl + $P0_4$ + SO_4 – Na – K – Ca – Mg**
Dairy: Parmesan cheese	34.2
Processed cheese plain	28.7
Cheddar reduced fat	26.4
Hard cheese (average)	19.2
Fresh cheese (quark)	11.3
Cottage cheese plain	8.7
Yogurt whole milk	1.5
Ice cream	0.8
Whole milk	0.7
Buttermilk	0.5
Eggs yolk	23.4
Eggs white	1.1
Eggs chicken whole	8.2
Meats: Corned beef	13.2
Luncheon meat canned	10.2
Turkey	9.9
Veal	9.0
Lean beef	7.8
Frankfurters	6.7
Sugars sugar white	–0.1
Honey	–0.3
Vegetables: Cucumber	–0.8
Broccoli	–1.2
Tomato	–3.1
Eggplant	–3.4
Celery	–5.2
Spinach	–14.0
Fats and oils: Butter	0.6
Margarine	–0.5
Olive oil	0.0

Fruits and nuts and fruit juices: Peanuts	8.3
Walnuts	6.8
Grape juice unsweetened	–1.0
Orange juice unsweetened	–2.9
Apples or apple juice unsweetened	–2.2
Apricots	–4.8
Banana	–5.5
Black currents	–6.5
Raisins	–21.0
Grains and grain products: Brown rice	12.5
Rolled oats	10.7
Spaghetti wholemeal	7.3
Spaghetti white	6.5
Cornflakes	6.0
Rice white	4.6
Bread rye flower	4.1
Bread whole wheat	1.8
Legumes: Lentils green and brown	3.5
Green beans	–3.1
Fish: Trout brown	10.8
Cod filets	7.1
Beverages: Beer pale	0.9
Coca-Cola	0.4
Beer draft	–0.2
Wine white	–1.2
Coffee infusion	–1.4
Wine red	2.4

Another feature of the contemporary diet is an abundance of salt. There is proof that increasing salt in food could estimate an amount of hyperchloremic metabolic acidosis in healthy adults at the time of ingesting a total acid generating food. Furthermore, it is an indication that sodium chloride has negative impacts on the aging people. A huge salt diet would increase disuse-induced bone and muscle losses while immobilized by enhancing bone regeneration as well as wasting of protein (Frings-Meuthen et al., 2011). Excess sodium in the diet has been linked to osteoporosis and hypertension in females (Devine et al., 1995). Furthermore, dietetic potassium, that is deficient in an advance meal plan, will modify the pressor

and hypercalciuric influences of sodium chloride surplus (Figure 8.2) (Morris et al., 2006).

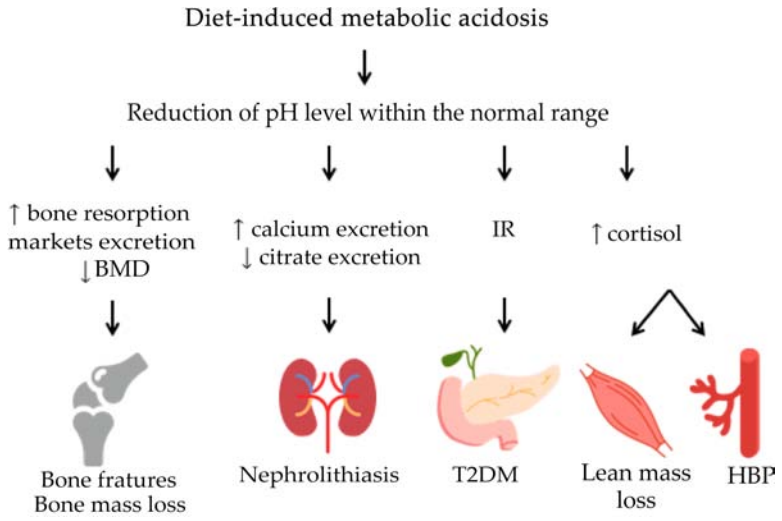

Figure 8.2. Metabolic acidosis caused by diet.

Source: https://www.mdpi.com/2072-6643/9/6/538/htm.

Excessive protein in diet combined with a large acidic renal load may result in a decrease in density of bone if not compensated for by alkali-rich supplements or meals. However, enough protein intake is necessary to avoid osteoporosis and sarcopenia; hence, raisings number of veggies as well as fruits rather than limiting protein, may be necessary (Heaney and Heaney, 2008).

8.5. ALKALINE DIETS AND MUSCLE

Muscle mass declines with aging, which may lead to injuries and fracture. Three-year research that looked at a potassium-rich diet, including fruit and veggies, and the lower acid load, results in muscle mass protection in elderly individuals (Dawson-Hughes et al., 2008). Prolonged renal failure, which results in chronic metabolic acidosis, causes skeletal muscle degradation to be accelerated. Restoration of acidosis might retain mass of muscle in situations characterized by wasting of muscle, like trauma, diabetic ketosis, sepsis, renal failure chronic, and obstructive pulmonary disease (Caso and Garlick, 2005). providing younger individuals with sodium bicarbonate

before an intense workout led to much low acidity in blood than the individuals who were not supplied with the sodium bicarbonate (Figure 8.3).

Figure 8.3. Alkaline foods for muscle growth.

Source: https://in.pinterest.com/pin/854698835517519398/.

8.6. ALKALINE SUPPLEMENTATION AND GROWTH HORMONE

A few times ago, it invented those various types of metabolic acidosis in kids, including renal tubular acidosis, are related along with the less developing hormone states and consequent less height. Acidosis correction with potassium citrate or bicarbonate dramatically enhances growing hormone as well as promotes growth. Consuming sufficient potassium bicarbonate inside a meal in order to balance the regular total acid load led to a considerable rise in growth hormone and subsequent osteocalcin in post-menopausal women (Frassetto et al., 1997). Enhancing growth hormone levels has been shown to increase total quality of life, decrease cardiovascular risk, enhance physical shape, and learning and memory (McSherry and Morris, 1978). Additionally, this leads to a decrease in urine calcium loss equal to 5% of the content of bone calcium during the period of three-year (Figure 8.4) (Frassetto et al., 1997).

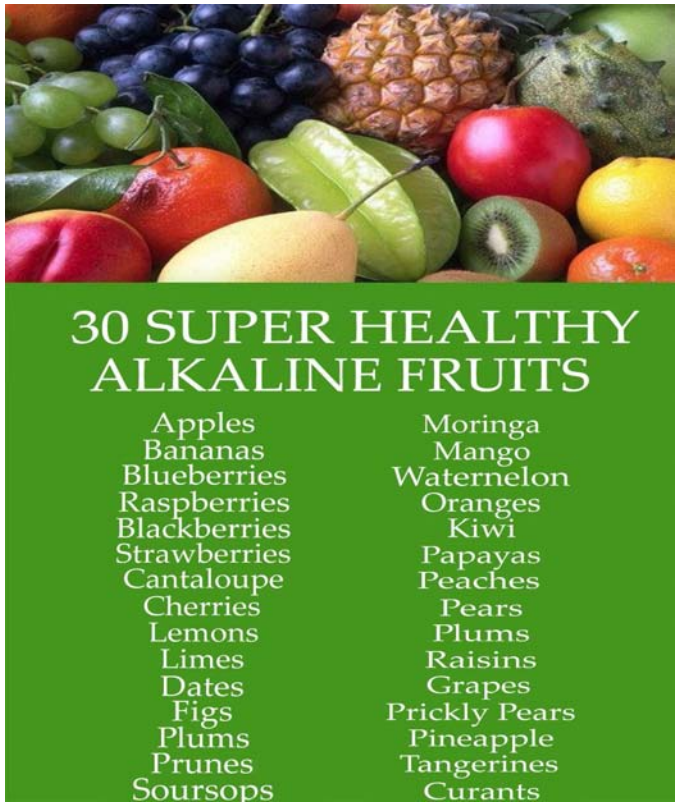

Figure 8.4. List of alkaline fruits.

Source: https://www.pinterest.com/pin/365636063489886050/.

8.7. ALKALINE DIET AND BACK PAIN

There is a few information which shows that alkaline mineral supplementation can help with persistent low back pain (Vormann et al., 2001). There was a small but substantial rise in pH of blood and intracellular magnesium after treatment. Providing that there is sufficient intracellular magnesium permits enzyme systems to operate properly and vitamin D to be activated. Back pain has been proven to improve as a result of it.

8.8. ALKALINITY AND CHEMOTHERAPY

pH has a significant effect on the efficacy of chemotherapy drugs. Numerous medicines, like Epirubicin and Adriamycin, are more effective in

an alkaline medium. Others, like cisplatin, mitomycin C, and thiotepa, are much more deadly in the acidic environment (Groos et al., 1986). Acidosis is associated with the cell death, and intracellular pH increases higher (more alkaline) during chemotherapy might represent the therapeutic reply. It has been proposed that generating metabolic alkalosis, with the use of sodium bicarbonate, carbicab, and furosemide may be beneficial in improving some therapy regimens (Gillies et al., 2002). Extracellular alkalinization with bicarbonate may increase treatment efficacy (Raghunand et al., 1999). At the moment, there is no systematic evidence showing the advantage of an alkaline eating plan for cancer prevention.

8.9. DISCUSSION

An individual's body has a remarkable capacity to sustain the constant pH in blood, along the renal and respiratory systems serving as the primary compensating mechanisms. Numerous membranes in our bodies need an acidic pH to defend us and support in food digestion. An alkaline diet has been recommended to help to avoid a variety of ailments and provide considerable health advantages. When considering the aforementioned description of bone health in isolation, several parts appear to be of dubious usefulness. It doesn't seem to be sufficient proof that cheese or milk are as harmful as Remer's formula implies, given that phosphate enhances bone health and results in the increasing calcium balance. Some other way by which an alkaline diet may promote bone health is by an enhancement in overall hormone and subsequent rise in osteocalcin. There are some various evidences that the K/Na ratio matters and that the high salt content of our food is harmful. Even a few administrations are putting pressure on the meal sector to lower the amount of salt in our diets. While high-protein diets may have an effect on bone health, a few proteins are necessary for bone health. Muscle wasting, on the other hand, appears to be decreased with an alkaline diet, and back discomfort may also improve. While an alkaline/base atmosphere might enhance the efficiency of a few chemotherapy medicines, it does not improve the efficacy of others (Raghunand et al., 1999).

8.10. SUMMARY

Alkaline diets create a higher alkaline urine pH and might even lead to less calcium in the urine; nevertheless, as some current studies have shown, it might not reflect complete calcium balance due to additional buffers like phosphate. There is not a sufficient proof which promotes bone health or

defends against osteoporosis. Alkaline diets, on the other hand, may cause a number of health advantages, as presented below:

- Increasing the amount of vegetables and fruits in a base eating plan will enhance the K/Na ratio, which would aid bone strength, minimize muscle losses, and help to prevent other chronic conditions including strokes and hypertension.
- An increment in growth hormone caused by base consuming diet might benefit a variety of outcomes ranging from cardiovascular health to cognition and memory.
- Another advantage of the alkaline diet is a rise in intracellular magnesium, that really is essential for an activity of several enzyme systems. The availability of magnesium, which is essential for vitamin D activation, will cause various additional advantages in the vitamin D apocrine/exocrine systems.
- Alkalinity may assist some chemotherapy drugs that need the higher pH.

Based on the information presented above, an alkaline diet should be investigated in order to reduce the mortality and morbidity rates linked with serious diseases that affect our elderly society. The very first issues with an alkali diet rich in fruits and veggies is determining the kind of soil in which they were grown, since this may have a significant effect on mineral content. There is presently very little scientific study in this topic, far more is required to better understand muscle function, growing hormone, and vitamin D connections.

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INDEX

Acidity and Basicity in Chemistry

The issue of acidity and basicity is enormously valuable economically and technologically, and it continues to pose great scientific problems, with the potential for considerable technological advancements in the future. Historically, industrial advances in acidity/basicity have frequently anticipated scientific comprehension of the underlying processes, most notably in the petroleum sector, a major beneficiary and user of acidity principles. However, this procedure is prohibitively expensive and inefficient in comparison to advancements based on a basic grasp of the scientific phenomenon at hand. This has been realized throughout time, which explains why university, government, and industry laboratories have spent significant effort over the last 50 years to studying acidity (and, to a lesser extent, basicity) in order to obtain a technical edge. There is a vast amount of scientific literature on the issue. There have been a number of significant essays and books published on the subject that aim to critically analyze several individual contributions. Three events over the previous few years resulted in the creation of this book which are:

- Significant advances in the theory of acids and bases;
- Significant advances in the concept of acids and bases;
- The ASI's structure represented the convergence of these three forces.

This book contains detailed information about acids, bases, different types of alkaline and acidic materials and their applications. There are eight chapters in the book. Chapter 1 introduces the readers with fundamentals of acids and bases and their classifications. Chapter 2 focusses on the acid-bases properties of the surface.

Chapter 3 contains information regarding the measurement of pH and alkalinity of water. Chapter 4 illustrates the effects of pH variation on the properties and behavior of soil. Chapter 5 describes the historical developments in acid-base characteristics of food products.

Chapter 6 further expands the information about pH of food products by providing information about titratable acidity and pH in food products. Chapter 7 focuses on the applications of acidity and basicity in drug delivery and medical sciences. Finally, Chapter 8 sheds light on alkaline diet and its effects on human health.

The text of the book assumes no prior understanding of acidity of basicity beyond what would be taught in a standard secondary school. It is aimed for chemistry students who wish to learn more about the connections between acidity and basicity, as well as the macroscopic features of acidic and basic compounds.

Dr Saeed Farrokhpay is a Chemical Engineer with several years of experience in mineral & material processing. He obtained his PhD from University of South Australia in 2005. He is currently a Technical Consultant in Australia. He has worked for more than 20 years at mineral and chemical industries, universities and research centers around the world. Dr Farrokhpay has published more than 90 papers in high ranked journals and conference proceedings. He has also edited several technical and scientific books, and served as an editorial board member of several international scientific journals.

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