

CHAPTER 3

ELEMENTS OF CHEMICAL CHANGE

19. CHEMICAL REACTIONS

As a provider of health care you will not be required, in most cases, to write and balance chemical equations. You will, however, be using and/or seeing the effects of chemical reactions on a daily basis. Chemical reactions are frequently used to explain various concepts of pharmacology and physiology. Consider drugs. All drugs are chemicals and any pharmacological reference you consult will refer to the chemical changes drugs undergo in the body. Consequently it is essential that you have a basic knowledge of what a chemical reaction involves and how that chemical reaction can be expressed as a chemical equation.

a. **Definite Composition.** When atoms combine, they do so in definite ratios of intact atoms to produce compounds with definite composition. Note that this combination is by number of atoms, not by weights of atoms. What the individual atoms happen to weigh is not material. Atoms do not know what they weigh. When they do interact and combine, it is always as whole particles, and the particle-to-particle or atom-to-atom ratio can always be expressed in simple, whole numbers. Chemical changes do not split atoms into fractional pieces. This is the reason we are able to write a formula such as HCl for the compound hydrochloric acid. Hydrochloric acid is always formed from one atom of hydrogen and one atom of chlorine. Since a chemical reaction is merely a change in matter, and matter consists of atoms or molecules, we can discuss chemical reactions by talking about interactions of individual molecules or atoms.

b. **Chemical Equations.** In discussing a chemical reaction, it would be very cumbersome to write it out in the same manner as we state it verbally. To get around this problem, chemists have developed chemical equations. Chemical equations are abbreviated ways of writing chemical reactions. They save much writing and effort and give at least as much information as a verbally stated reaction. Chemical equations show:

- (1) The kinds of atoms or molecules reacting.
- (2) The products formed.
- (3) The number of atoms entering the reaction.
- (4) The number of molecules formed in the product.
- (5) The proportion in which the substances react to give definite products.

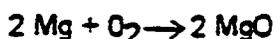
c. **Chemical Symbols.** In writing chemical equations, we use a number of symbols. The most common symbols are shown below with their meanings.

<u>SYMBOL</u>	<u>MEANING</u>
△	heat (a form of energy)
→	"yields," indicates direction of reaction
↑	given off as a gas
↓	given off as a precipitate

As we illustrate several types of reactions, the uses of these symbols will become apparent.

d. **Types of Reactions.** There are four types of chemical reactions which are possible: combination reactions, decomposition reactions, single replacement reactions, and double replacement reactions.

(1) *Combination reactions.* A combination reaction can be represented by the chemical equation $A + B \rightarrow AB$ (one atom of A plus one atom of B yield one molecule of AB). A specific example of this type of reaction is the combination of a metal with oxygen to yield a metallic oxide.



This equation tells us that two atoms of magnesium and one molecule of oxygen react to form two molecules of magnesium oxide.

(2) *Decomposition reactions.* The general equation representing decomposition reactions is $AB \rightarrow A + B$. Here is a good example:



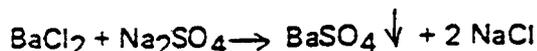
This equation tells us that calcium carbonate will yield calcium oxide and carbon dioxide. The Δ also tells us that this reaction occurs when heat is applied to calcium carbonate. The \uparrow indicates that the carbon dioxide is given off as a gas.

(3) *Single replacement reactions.* The general equation for a single replacement reaction is $A + BC \rightarrow AC + B$. An example is:



This equation tells us that one atom of zinc and one molecule of cupric sulfate yield one molecule of zinc sulfate and one atom of copper.

(4) *Double replacement reactions.* The most commonly occurring reaction is the double replacement reaction. The general equation for this reaction is $AB + CD \rightarrow AD + CB$. Double replacement reactions can be further subdivided into several classes. The most common of these classes are the precipitation reaction, the acid-base reaction, and the oxidation-reduction reaction. An example of the precipitation reaction is:



This equation tells us that one molecule of barium chloride reacts with one molecule of sodium sulfate to yield two molecules of sodium chloride and one molecule of barium sulfate as a precipitate. Acid-base and oxidation-reduction reactions will be covered later.

20. WRITING CHEMICAL EQUATIONS

At this point you have seen several examples of chemical equations and should be familiar with the symbols used in an equation. We will now examine the process of writing an equation when we are given a verbal description of the reaction. One general rule which must be kept in mind is that *there will always be the same number and kinds of atoms in the products of a reaction as in the reactants*. This is because matter can neither be created nor destroyed in a chemical reaction and, as previously stated, atoms always combine in certain proportions. When given a written verbal description of a chemical reaction, the following steps are used to write the equation for the reaction.

a. Write the symbols for all elements involved.

b. Write the correct formulas for any compounds and check for diatomic molecules. (Some elements never exist as single atoms but only as diatomic molecules. These elements can be identified from their names, which end in -gen or -ine. The common diatomic molecules are hydrogen (H_2), nitrogen (N_2), oxygen (O_2), chlorine (Cl_2), fluorine (F_2), and bromine (Br_2)).

c. Balance the equation by placing coefficients where appropriate. Remember that there must be equal numbers of atoms of each kind on both sides of the equation. In this step, the subscripts which were used in writing the correct formulas *cannot* be changed.

21. EXAMPLE

For application of these steps, consider this description of a reaction. Calcium metal and water react to yield calcium hydroxide and hydrogen gas.

a. Write the symbols for all elements involved.

Ca, O, H

b. Write the correct formulas for any compounds and check for diatomic molecules.



c. Balance the equation by placing coefficients where appropriate. Look at the number of atoms of each element in the products and reactants.

<u>REACTANTS</u>	<u>PRODUCTS</u>
1 Ca	1 Ca
1 O	2 O
2 H	4 H

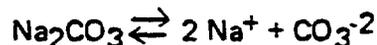
It is apparent here that there are twice as many oxygen and hydrogen atoms in the products as reactants. How can this equation be balanced to give equal numbers of atoms on both sides? Fill in the coefficients of the molecules in the equation below.



Since there are twice as many hydrogen and oxygen atoms on the right as on the left, if we could double the numbers of these atoms on the left, we would have a balanced equation. This can be done by placing a 2 in front of H₂O. All the other coefficients would be 1 (if there is no coefficient, we assume it is 1, so there is no need to write it in front of each molecule).

22. EQUILIBRIUM REACTIONS

We have implied that all reactions only go in the direction of the products, but this is not always the case. Sometimes as products are formed, they react with one another or decompose to form the reactants. Thus, the reaction is going in both directions at the same time, and if allowed to continue indefinitely, would result in a constant amount of products and reactants. Reactions that go in both directions are called equilibrium reactions, and when the rate of formation of product is the same as the rate of formation of reactant, they are said to be in equilibrium. In writing an equation, we indicate an equilibrium by drawing arrows pointing in opposite directions (\rightleftharpoons). As an example of an equilibrium reaction, consider the dissociation of a compound into ions:



Sodium carbonate in solution dissociates into sodium ions and carbonate ions. Some of the ions come back together to form sodium carbonate. Thus, an equilibrium is established.

23. EXTERNAL CONDITIONS AFFECTING CHEMICAL REACTIONS

External conditions which affect reactions are usually types of energy which are put into a reaction, such as heat or light. Chemical reactions are always accompanied by an energy change. Either energy is released or it is acquired. When the amount of energy is changed, so is the amount of matter. This is called the Law of Conservation of Matter and Energy. However, ordinary chemical reactions involve such small matter changes that they go undetected and may be ignored.

a. **Heat.** Generally, heat is the form of energy we are most concerned with. It may affect a reaction in one of two ways.

(1) *Exothermic reactions.* If a reaction gives off heat, it is called an exothermic reaction. External heat, if supplied to this type of reaction, will slow down the rate of reaction.

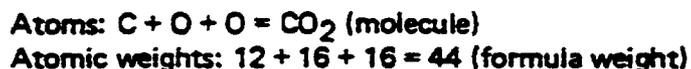
(2) *Endothermic reactions.* If a reaction takes in heat, it is an endothermic reaction. If heat is added to an endothermic reaction, the rate of reaction will increase. This may be of value in the preparation of medicinal products.

b. **Light.** Light is a form of energy which may cause many chemicals to decompose. For this reason, it is necessary to protect some drugs from contact with light by placing them in dark-colored or opaque containers. These containers prevent most or all of the outside light from coming into contact with the drug.

24. REACTING QUANTITIES

It has already been emphasized that all reactions occur on an atom-to-atom level. This presents a small problem to us, since we cannot hold an atom in our hand, or count out a specific number of atoms to put into a reaction. How then do we measure amounts of material that will react together? Chemists long ago solved this problem by learning how to count particles indirectly. They did this by measuring samples of the chemicals in particular ratios by their weights. To understand the means of doing this, we need to expand our concept of atomic weight to compounds in the form of the formula (or molecular) weight.

a. **Milligram Formula (Milligram Molecular) Weight.** When atoms combine to form compounds, the atomic nuclei are not affected. There is no net loss of weight. Regardless of whether the particle formed is a molecule or an ion group, it will have a formula and a formula weight. The formula weight of a compound is the sum of the atomic weights of all the atoms which appear in its chemical formula. Consider, for example, carbon dioxide:



While we have arrived at a formula weight which is in terms of atomic mass units, it is much more useful to express it in terms of milligrams. This is known as the milligram formula weight. For the example above, CO_2 , the milligram formula weight is 44 mg. This is a quantity that we can measure and see, and thus can easily work with. It also represents a reacting unit of the compound.

b. **Molarity.** A molar solution, or a 1 molar (1M) solution, consists of one gram molecular weight (GMW) of solute dissolved in enough water to make 1 liter of finished solution. Molarity, then, is the number of GMW's dissolved in enough water to

make a finished solution of 1000 ml. Molar solutions may have as a solute a solid, a liquid, or a gas. Later in this study guide, we will use the concept of molarity to explain the measurement of acidity, called the pH.

(1) *Calculating the gram molecular weight.* One gram molecular weight of a substance is its molecular weight expressed in grams. Thus, a GMW of NaOH would be 40 grams, where the atomic weights are as follows: Na = 23, O = 16, and H = 1. Thus, .5 GMW of NaOH would be 20 grams, and so forth. A *mole* is one gram molecular weight of a substance. Thus, a mole of NaOH is 40 grams of NaOH; a half-mole (.5 mole) is 20 grams; 2 moles of NaOH is 80 grams, and so on.

(2) *Calculating the molarity of a solution.* To find the molarity of a solution, we divide the number of gram molecular weights of solute by the number of liters of total solution. The formula may be written:

$$\text{Molarity} = \frac{\text{no. of GMW's of solute}}{\text{no. of liters of solution}}$$

Since many problems are stated in terms of the weight of solute and require you to determine the number of gram molecular weights (moles), the following formula will be of benefit:

$$\text{No. of GMW's} = \frac{\text{weight of solute}}{\text{GMW}}$$

Example: What is the molarity of a solution containing 29.25 grams of sodium chloride in 500 ml. of total solution?

Step 1. Find the number of GMW's.

$$\text{GMW of NaCl} = 58.4 \text{ grams}$$

$$\text{No. of GMW's} = \frac{\text{weight of solute}}{\text{GMW}}$$

$$\text{No. of GMW's} = \frac{29.25}{58.4} = .5$$

Step 2. Find the molarity.

$$\text{Molarity} = \frac{\text{no. of GMW's of solute}}{\text{no. of liters of solution}}$$

$$500 \text{ ml} = .5 \text{ liter}$$

$$\text{Molarity} = \frac{.5}{.5} = 1 \text{ molar or } 1\text{M}$$

c. **Milligram Equivalent Weight (Milliequivalent Weight).** Sometimes we are interested in more than just the weight ratios of reacting compounds. Since the valence of an element is a measure of that element's combining power, the valences in a compound should be indicative of their reactivity. Therefore, chemists have modified the milligram formula weight to include the positive or negative valence of a compound. This value is called the milligram equivalent weight and is defined as the milligram molecular weight divided by the total positive or negative valence. Consider, for example, sodium hydroxide:

$$\begin{aligned} \text{Milligram molecular weight} &= 40 \text{ mg} \\ \text{Total positive valence} &= 1 \\ \text{Milligram equivalent weight} &= \frac{40 \text{ mg}}{1} = 40 \text{ mg} \end{aligned}$$

Another example is potassium phosphate (K_3PO_4):

$$\begin{aligned} \text{Milligram molecular weight} &= 212 \text{ mg} \\ \text{Total positive valence} &= 3 \\ \text{Milligram equivalent weight} &= \frac{212 \text{ mg}}{3} = 70.7 \text{ mg} \end{aligned}$$

In a reaction, one milliequivalent (meq) weight of one compound will react with one milliequivalent weight of another. If we are reacting two compounds, then, we can determine how much of each compound should be used to obtain a desired amount of product.

25. OXIDATION-REDUCTION REACTIONS

Previously, we have examined the processes involved in writing, balancing, and interpreting reactions and looked at examples of several types of reactions. One type of reaction we did not examine closely was the oxidation-reduction reaction (sometimes called redox reaction). Even though this type of reaction is very important in the chemistry of drug molecules, it is beyond the scope of our instruction to study them in detail. However, a basic understanding of this process will be valuable to you in understanding many of the incompatibilities, storage problems, and some disease states which you will encounter later.

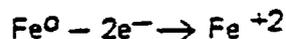
a. **Review of Valence.** Before these reactions are studied, valence should be reviewed briefly. The following two valence concepts are especially important in oxidation-reduction reactions:

(1) All elements in their free and uncombined state are considered to have a valence of zero. This holds even for those elements that are diatomic molecules in their free state.

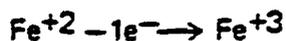
(2) All atoms can exist in a number of valence states. The common valences which you learned previously are the preferred and most stable valences under normal conditions, but other valences can and do occur.

These two concepts are important because oxidation-reduction reactions *always* involve a change in the valence numbers of some of the elements involved in the reaction.

b. **Oxidation.** Oxidation, in inorganic chemistry, is defined as the loss of electrons or an increase in the valence of an element. Consider, for example, the oxidation of elemental iron:



Iron in its free state has a valence of zero and is very reactive since its common valence state is +2 or +3. It loses two electrons to become the ferrous ion. The valence has gone from 0 to +2, thus iron has been oxidized. It can undergo further oxidation to the +3 valence state:



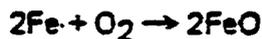
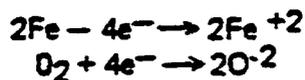
Here the ferrous ion has lost another electron to become a ferric ion.

c. **Reduction.** In inorganic chemistry, reduction is defined as the gain of electrons or a decrease in the valence of an element. Consider the reduction of elemental oxygen:



Observe that oxygen is a diatomic molecule in its free elemental form and has a valence of zero. Since the most common valence state of oxygen is -2, oxygen accepts electrons readily to become the oxygen anion. The valence of each oxygen atom has gone from 0 to -2, thus oxygen has been reduced. If the valence is made smaller (reduced), reduction has occurred.

d. **Oxidizing and Reducing Agents.** For all practical purposes, it is impossible to simply add or subtract electrons from an element except in an electrolytic cell. In actual fact, the oxidation of one element and the reduction of another always occur simultaneously. One element loses the electrons; the other element gains the electrons which are lost by the first. Consider these two reactions when they are combined:



This is an oxidation-reduction reaction which is very common in our industrialized society. The oxidation of iron by atmospheric oxygen gives us iron oxide, commonly known as rust. In this reaction, oxygen was reduced, going from a 0 to a -2 state by

receiving electrons from iron. Because it accepted the electrons from iron and allowed the iron to oxidize, oxygen is called an oxidizing agent. Iron, which gave up electrons, is called the reducing agent. General characteristics of reducing and oxidizing are shown in the table below.

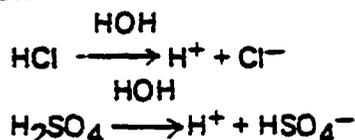
<u>REDUCING AGENT</u>	<u>OXIDIZING AGENT</u>
(1) Gives up electrons	(1) Gains electrons
(2) Oxidized during reaction	(2) Reduced during reaction
(3) Unusually low valence state compared to most common state	(3) Unusually high valence state compared to most common state

26. ACIDS AND BASES

The two most important classifications of compounds in inorganic chemistry are acids and bases. The following discussion forms the groundwork for understanding some of the most important chemical changes which you will encounter.

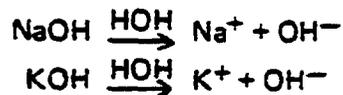
a. **Classical Acid-Base Theory.** Svante Arrhenius, in 1887, published the first satisfactory explanation of the acid-base phenomena that had been observed by chemists.

(1) *Acids.* Arrhenius defined an acid as a compound which donates protons (H^+) in solution. Examples would be any of the compounds you learned to name as acids earlier in this study guide.



Note the HOH (H_2O) which indicates that water is the solvent in these reactions. Both HCl and H_2SO_4 contribute protons in solution.

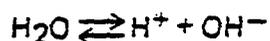
(2) *Bases.* Arrhenius defined a base as any compound that donates hydroxyl (OH^-) ions in solution. Again, you should be familiar with several examples from your nomenclature studies.



(3) *Discussion.* These classical definitions are based on the dissociation of the compounds into ions in solution. This implies that all acids and bases must contain exchangeable hydrogen and hydroxyl ions, respectively, in their formulas. This theory did explain the majority of the compounds known at the time, but there were some exceptions. Chemists knew, for example, that metal oxides (MgO , CaO , etc.) dissolved in water exhibited base-like properties. Also, ammonia (NH_3) in solution exhibited the properties of a base. The attempts to explain these exceptions led to new definitions of acids and bases.

b. **Modern Acid-Base Theory.** In 1923, Bronsted and Lowry, two chemists in different countries, independently derived new definitions of acids and bases to explain the exceptions to the classical theory. The new theory they developed was named, appropriately, the Bronsted-Lowry theory. This theory differs from the classical theory in that the dissociation of water is considered as well as the dissociation of the compound.

(1) *Dissociation of water.* Even though we often think of water as merely being an inert solvent, it does dissociate into ions.

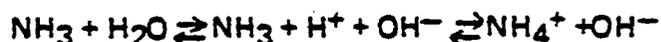


Note that this is an equilibrium type reaction as indicated by the double arrow. Actually, very few ions exist at any time since they rapidly recombine to form molecular water. If we put numbers in this reaction, there are 500 million molecules of water for each hydrogen or hydroxyl ion.

(2) *Bronsted-Lowry acid.* By the Bronsted-Lowry theory, an acid is any compound (charged or uncharged) capable of donating a proton. This is essentially the same as the classical definition.

(3) *Bronsted-Lowry base.* The real value of the Bronsted-Lowry theory is in the definition of a base. A base is defined as a charged or uncharged substance capable of accepting a proton. Generally, the proton a base accepts comes from the dissociation of water.

(a) Consider, for example, ammonia dissolved in water:



By accepting a proton from water, ammonia has effectively increased the concentration of hydroxyl ions in the solution. This would account for the properties like those of a classical base.

(b) A second example would be magnesium oxide dissolved in water.



By accepting a proton from water, magnesium oxide has likewise increased the concentration of hydroxyl ions in the solution.

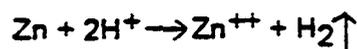
NOTE: The two theories explain all the properties of acids and bases which will be utilized in medicine. It deserves mention that there are other theories of acids and bases that explain more complex phenomena. If these are of interest to you, a college chemistry text should have a discussion of some of them.

c. **Properties of Acids.** We have defined all acids on the basis of one common property, the ability to donate hydrogen ions in solution. Therefore, you should expect them all to exhibit a set of common properties, which they do. The properties we are concerned with are as follows:

(1) Acids change blue litmus paper to red. Litmus paper, which contains dyes sensitive to hydrogen ion concentration, turns red when there is a high concentration, blue when there is a low concentration.

(2) Acids have a sour taste. This property is familiar to you if you have ever tasted a lemon. Lemons contain citric acid, which gives them their sour taste.

(3) Acids react with metals to release hydrogen gas. For example:

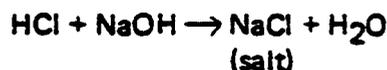


You will notice that this reaction is an oxidation-reduction reaction. For practice, pick out the oxidizing and reducing agents.

(4) Acids react with carbonates and bicarbonates to form carbon dioxide. For example:



(5) Acids react with bases to form salts and water (neutralization reaction). For example:



d. **Properties of Bases.** In the same manner that all acids had certain properties in common, all bases have related properties. The ones which are important to the pharmacy specialist are as follows:

(1) Bases change red litmus paper to blue. This is just the opposite of the change which acids cause in litmus paper.

(2) Bases possess a bitter taste and feel soapy when in contact with the skin.

(3) Bases react with acids to form salts and water (neutralization reaction). This is the same type reaction as previously discussed under acids.

e. **Classification of Acids and Bases.** Even though all acids possess certain properties in common, as do bases, not all possess them to the same degree. Some acids, for example, will completely neutralize sodium hydroxide with equal concentrations while others will only partially neutralize this base. As you might

suspect, the differences in the strengths of acids results from differing abilities to donate hydrogen ions and the differences in bases from differing abilities to donate hydroxyl ions or accept hydrogen ions.

(1) We can more clearly identify these abilities by considering the dissociation of the substances. Some acids or bases dissociate into ions completely when placed in solution. Hydrochloric acid, for example, dissociates into hydrogen and chloride ions; at any time, 100% of the HCl will exist as ions. Carbonic acid (H_2CO_3), on the other hand, does not dissociate completely into ions in solution. A good fraction of the carbonic acid will exist in molecular form.

(2) This means one mole (gram molecular weight) of HCl will produce more hydrogen ion in solution than will one mole of H_2CO_3 and will consequently exhibit acidic properties to a greater degree than will carbonic acid. A simpler way to say this is that HCl is a stronger acid than H_2CO_3 .

(3) The same rationale holds for bases as well as acids. Therefore, we can divide or classify acids or bases into groups based on their dissociation—strong acids or bases (those that dissociate completely) and weak acids or bases (those that dissociate to a small degree).

f. **Acids and Bases of Medicinal Importance.** There are a number of important acids and bases which you may come in contact with as a medical specialist. You must be able to identify them as acids or bases and know their relative strengths. Table 4 shows these acids and bases. There is not an easy way to differentiate between strong and weak acids, but strong and weak bases can be differentiated on the basis of valence. Strong bases have a positive valence of 1; weak bases have a positive valence greater than 1.

g. **Safety and Antidotes.** Acids and bases should be handled with care to avoid spilling on skin. They should not be taken internally unless intended for that purpose. If these compounds should come in contact with the skin or be ingested, the following are recommended antidotes for first aid treatment.

(1) **Acids.**

(a) **External.** Wash acids off the skin with large amounts of water. Exception: if phenol (an organic acid) is spilled on the skin, wash off with alcohol.

(b) **Internal.** Give an antacid, other than a carbonate or bicarbonate, such as milk of magnesia or magnesium oxide. DO NOT give an emetic or induce vomiting.

(2) **Bases.**

(a) **External.** Wash the area with large amounts of water.

<u>Relative strength of common acids and bases</u>	
<u>STRONG ACIDS</u>	<u>WEAK ACIDS</u>
HCl - Hydrochloric acid	HC ₂ H ₃ O ₂ (HAc) - Acetic acid
H ₂ SO ₄ - Sulfuric acid	H ₂ CO ₃ - Carbonic acid
H ₃ PO ₄ - Phosphoric acid	H ₃ BO ₃ - Boric acid
HNO ₃ - Nitric acid	
<u>STRONG BASES</u>	<u>WEAK BASES</u>
KOH - Potassium hydroxide	Fe(OH) ₂ - Ferrous hydroxide
NaOH - Sodium hydroxide	Al(OH) ₃ - Aluminum hydroxide
Ca(OH) ₂ - Calcium hydroxide	NH ₃ - Ammonia
Mg(OH) ₂ - Magnesium hydroxide	
MgO - Magnesium oxide	

*Notice that Ca(OH)₂, Mg(OH)₂, and MgO (which forms Mg(OH)₂ in water) are chemically classified as strong bases because of their high degree of dissociation. Because they are only slightly soluble in water, they produce low concentrations of the hydroxide (OH⁻) ion in solution. Since calcium hydroxide and magnesium hydroxide do not produce tissue damage, they can be safely used as therapeutic agents (i.e., antacids).

Table 4. Relative strength of common acids and bases.

(b) *Internal*. Give a *weak* acid such as vinegar or fruit juice. Weak acids (or weak bases) are only effective if administered within 10-15 minutes of ingestion of strong base (or strong acid). DO NOT give an emetic or induce vomiting.

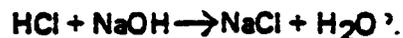
27. SALTS

Previously it has been stated that one of the properties associated with acids and bases is the neutralization reaction. This reaction involves the production of a salt and water from the reaction of an acid and a base. We will now examine various types of salts produced in neutralization reactions. Salts are the third major classification of inorganic compounds (acids and bases being the first two). They are important in the physiology of the body and are often used as therapeutic agents.

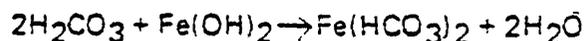
a. **Definition.** We have already given one definition of a salt in our discussion, that is, the product of a reaction between an acid and a base. A more specific definition, however, would be an ionic compound formed by the replacement of part or all of the acid hydrogen of an acid by a metal or a radical acting like a metal. It is an ionic compound that contains a positive ion other than hydrogen and a negative ion other than hydroxyl (OH⁻) or "O⁻²", as in MgO.

b. **Types of Salts.** There are four types of reactions possible between acids and bases as we classified them (strong or weak) earlier. These are as follows:

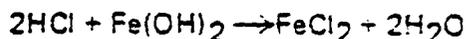
(1) *Strong acid and strong base.*



(2) *Weak acid and weak base.*



(3) *Strong acid and weak base.*



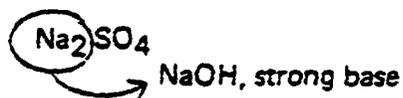
(4) *Weak acid and strong base.*



These four reactions result in three types of salts. Reactions (1) and (2) result in neutral salts, which means a solution of the salt in water will be a neutral solution. Reactions such as (3) result in acidic salts, which produce acidic solutions. Reaction (4) results in basic salts, which produce basic solutions.

c. **Determination of Salt Type.** To determine the type of salt from a chemical formula, we employ the following steps:

(1) The first element comes from a base. Determine which base and whether it is weak or strong.



(2) The remainder of the formula comes from the acid. Determine which acid and whether it is weak or strong.



(3) By knowing the strengths of the acid and base that formed the salt, the salt type can be assigned. Table 5 is a summary of salt types resulting from various acid-base combinations.

d. **Example— $\text{Al}_2(\text{SO}_4)_3$.**

(1) The first element, aluminum, comes from the base $\text{Al}(\text{OH})_3$. Since it has a valence of +3, it is a weak base.

(2) The sulfate radical comes from H_2SO_4 , sulfuric acid, which is a strong acid.

(3) This compound is an acidic salt since it is the product of a reaction between a strong acid and a weak base.

e. Example— FeBO_3 .

(1) The first element, iron, comes from the base $\text{Fe}(\text{OH})_3$, and since its valence is +3, it is a weak base.

(2) The borate radical comes from boric acid, which is a weak acid.

(3) Thus, this is a neutral salt, since it is the product of a reaction between a weak acid and a weak base.

Importance of Type of Salt. The type of salt is very important when a salt is used medicinally since the body maintains a specific acidity in the tissues and fluids. The type of salt is also important in the prediction and understanding of incompatibilities. At the present time, it is important for you to identify the type of salt from its formula. The importance and use of the type will become clear to you as you progress through the course.

REACTANTS	WEAK ACID	STRONG ACID
WEAK BASE	Neutral Salt	Acidic Salt
STRONG BASE	Basic Salt	Neutral Salt

Table 5. Salt types resulting from various acid-base combinations.

28. pH AND ACIDITY

In discussing acids, bases, and salts, we often made references to a solution or compound being acidic, neutral, or basic in a qualitative manner. This concept is useful to us in a general sense, but would be of much greater value if we could speak in quantitative terms. It would be valuable if we could answer the question of how acidic one solution is in relation to another solution.

a. pH. The solution to this problem is not as difficult as it may seem. Acids donate protons (hydrogen ions, H^+) in solution. Thus, the acidity of a solution must be related to this property.

(1) In fact, the acidity of a solution is the concentration of hydrogen ions in that solution. Since we can calculate the hydrogen ion concentration, as you will learn later, we can now have a numerical value of the acidity of a solution. The concentrations of hydrogen ions in both acidic and basic solutions are generally very

small. A strong solution of HCl, for example, may contain only 0.01 mole of hydrogen ions per liter of solution. A solution of NaOH may have as little as 0.0000000001 mole of hydrogen ion per liter of solution.

(2) To simplify the expression of such terms, chemists have transformed the concentration values into numbers, called pH numbers, which are easier to utilize. This is done according to the following equation:

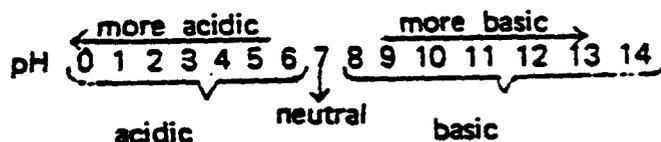
$$\text{pH} = -\log[\text{H}^+]$$

The abbreviation log stands for logarithm. (For example, $\log 1 = 0$, $\log 0.1 = -1$, $\log 0.01 = -2$, $\log 0.001 = -3$, $\log 0.0001 = -4$.) The expression $[\text{H}^+]$ here is the concentration of hydrogen ions in moles per liter. If we consider the two previous examples, you can see how this transformation aids us. The pH of the HCl solution would be $-(-2.0) = 2.0$; the pH of the NaOH solution would be $-(-11.0) = 11.0$. These numbers, 2 and 11, are certainly easier to work with than 0.01 and 0.0000000001.

b. **pH Scale.** This transformation results in a range of pH numbers from 0 to 14 which is called the pH scale.

(1) The limits of the scale are related to the dissociation; how they are arrived at is beyond our scope. Further information on this relationship can be found in an inorganic chemistry textbook.

(2) While you will not need to calculate a pH value, you will need to interpret what a pH value means at times. To learn this function, examine the following pH scale:



(3) A pH value less than 7.0 means the solution is acidic; the lower the number, the more acidic. A solution with a pH of 2.0 is more acidic than one with a pH of 4.0. Any pH value greater than 7.0 means the solution is basic, with larger numbers indicating more basic solutions. The only value on the scale which indicates a neutral solution is 7.0. The pH values for some common pharmaceutical products are given below.

<u>PRODUCT</u>	<u>pH</u>
Cherry Syrup	3.5 - 4
Benylin ^R Expectorant	5.0 - 5.5
Glycyrrhiza ^R Syrup	6.0 - 6.5
Iso-Alcoholic Elixir	5.0
Orange Syrup	2.5 - 3.0
Terpin Hydrate Elixir with Codeine	8.0

c. **Measurement of pH.** There are three common methods for measuring pH which you may encounter in medicine.

(1) *Litmus paper.* Litmus paper is a paper coated with a dye which is red in an acid pH or blue in a basic pH. It will only indicate whether a solution is acidic or basic; it will not give an actual pH value.

(2) *pH paper.* pH paper works on the same principle as litmus but uses several different dyes. By comparing paper color with a chart, the pH of a solution can be determined within 1 pH unit. If a closer measurement is needed, special narrow-range papers can be used to determine the pH within 0.1 pH unit.

(3) *pH meter.* The most accurate tool for pH measurement is the pH meter. This makes use of an electrode dipped into solution and is accurate to about 0.01 pH unit, depending on the particular machine.

29. BUFFERS

Many drugs are stable in solution only at certain pH's or in narrow pH ranges. If a solution of one of these drugs is desired, the manufacturer must find a way to maintain this certain pH over a period of time. This is accomplished by the use of buffer systems. A buffer is a solution of a weak acid and the salt of that weak acid (weak bases could also be used, but usually are not practical). The function of the buffer is to resist changes in pH by reacting with any hydrogen or hydroxyl ions that are added to the solution. Two of the most common buffer systems are:

a. **Acetic Acid/Sodium Acetate.** This is a common buffer found in many drug solutions.

b. **Carbonic Acid/Sodium Bicarbonate.** This is the buffer system which is most common in the fluids and tissues of the body, and is used to keep the pH of the blood and body fluids constant.

30. WATER

Water is the most important liquid to all living organisms. It comprises about 57% of your body weight. It is the solvent for or is contained in most of the nutrients your body requires for growth or maintenance. It is also the primary vehicle for almost all liquid pharmaceutical preparations. Because of the inherent importance of water in the practice of medicine, it is essential to acquire a basic knowledge of the properties of water and aqueous (water-based) solutions.

a. **Properties of Water.** All of us are familiar with some properties of water. We know that generally water is a bland-tasting, colorless liquid. There are some other specific properties of water that are of importance in medicine.

(1) Its boiling point is 100° C (212° F).

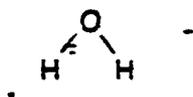
(2) Its freezing point is 0° C (32° F).

(3) It is a polar solvent (dissolves ionic compounds).

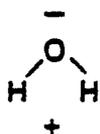
(4) Generally, it is chemically inert (unreactive) in biological or drug systems.

b. **Importance of Properties.** The properties above are the specific reasons that water is so valuable to living systems and to pharmaceutical preparations. The wide difference between the freezing point (water as ice) and the boiling point (water as steam or vapor) indicates that water will be a liquid at most of the temperatures encountered under normal conditions. An example should help emphasize the importance of these properties. If we wanted to prepare a liquid drug solution for a patient who could not swallow capsules and we used a liquid vehicle with a freezing point of 25° C (77° F) and a boiling point of 30° C (86° F), we would be giving the patient a worthless product. As the patient left home, the drug solution would boil if it was a normal summer day (temperature = 86° F), and when the patient entered his air-conditioned home, the remaining solution might become a solid which could not be poured from the bottle. We also want our vehicle to be as unreactive as possible so that only the drug is exerting a pharmacological effect.

c. **Structure of Water.** The properties of water may best be explained by examining the structure of the water molecule. The water molecule consists of two hydrogen atoms bonded covalently to one oxygen atom. The three atoms are bound together as shown below.

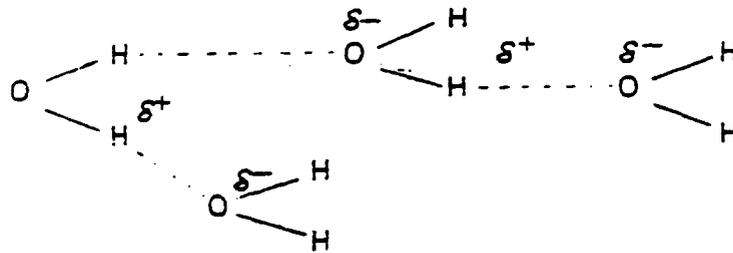


This arrangement leads to an electron-rich atom, oxygen, on one end and two electron-poor atoms, hydrogen, on the other end. This results in a molecule that resembles a bar magnet in that it has a negative pole and a positive pole, as shown below.



Actually, there are not distinct electrical charges on the molecule, only partial charges, referred to as $\delta+$ and $\delta-$ (the Greek letter delta, δ , meaning partial). While these charges are only partial, they are still strong enough for water to be referred to as a polar molecule, meaning that it has a positive and negative end.

d. **Hydrogen Bond.** The polarity of the water molecule gives rise to an unused type of bond between water molecules, the hydrogen bond. This bond is the electrical attraction between the partially negative oxygen atom of one molecule and the partially positive hydrogen atom of another molecule.



The hydrogen bond is a very weak attraction about 1/10 to 1/20 the strength of the hydrogen-oxygen covalent bond. The hydrogen bond explains why water has such a high boiling point in relation to other compounds of similar molecular weight. For example, methane (CH_4 , molecular weight = 16) boils at a temperature below 0°C , while water (molecular weight = 18) boils at 100°C . Methane does not exhibit hydrogen bonding.

e. **Water Purification.** We are all familiar with some of the ecological problems facing the world today. Water is subject to mineral and biological contamination. Since we will often be using water in the preparation of our products, we must be concerned with its purity and the methods utilized for its purification. There are two common methods of water purification used at Army medical treatment facilities, distillation and ion exchange.

(1) *Distillation.* Distillation is the process of boiling water, collecting the vapor, and then condensing the vapor back into water. Minerals and some of the bacterial contamination will remain in the boiling vessel as a residue. Very pure water may be prepared by repeating the distillation process several times. If sterile water is desired, the water must be sterilized, because the process of distillation does not necessarily sterilize water.

(2) *Ion exchange (deionization).* Less common than distillation because it is less efficient, ion exchange involves passing water through a column containing a charged resin. Ions in the water are held by electrical attraction and are thus removed from the water.

31. SOLUTIONS

We are seldom concerned with just water in the hospital. We are generally more concerned with substances dissolved in water. These are solutions. When we speak of a solution, there are several terms which are important to understand.

a. **Solute.** A solute is the substance which is dissolved in a solution.

b. **Solvent.** The solvent is the substance which dissolves the solute. It is usually water in pharmaceutical solutions, but not always.

c. **Solubility.** The maximum amount of a compound which will dissolve in a given amount of solvent at a given temperature is the solubility of that compound.

d. **Dissociation. (Ionization).** In general, two things can happen to a solute in a solution. It can dissolve and exist in solution as molecules or it can dissociate and exist entirely or partially as ions. The process of splitting a molecule into ions is known as dissociation.

e. **Electrolyte.** When a substance dissociates to a fair extent in water, it will produce enough ions to support an electric current. We can use this property to differentiate between substances that are molecular and substances that are ionic in solution. An electrolyte is a substance which dissociates sufficiently in solution to carry an electric current. It is therefore ionic in nature (fig. 3).

f. **Non-Electrolyte.** A substance which does not dissociate or carry an electric current in solution is called a non-electrolyte.

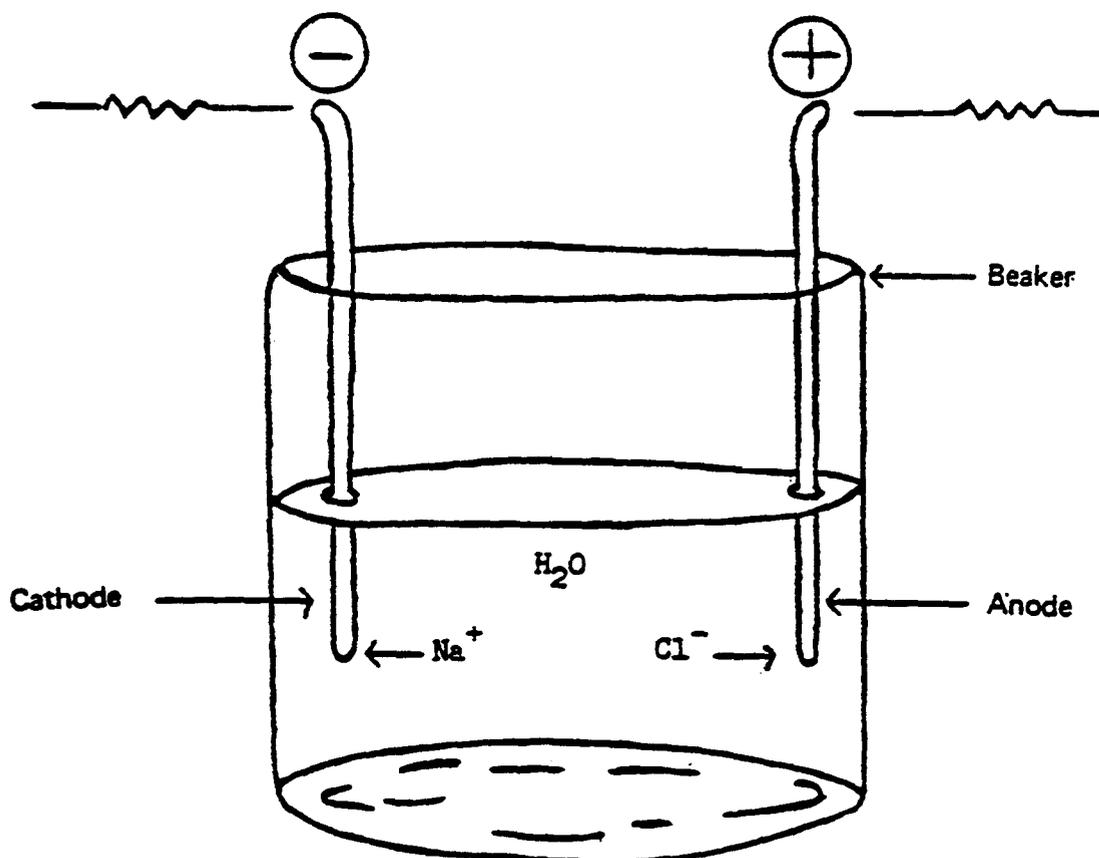
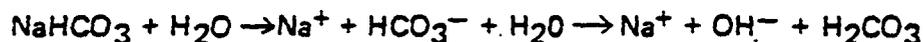


Figure 3. Flow of electric current through electrolyte solution.

g. **Hydrolysis.** Some compounds that form ions in solution do so by reacting with water. This reaction with water is called hydrolysis. Hydrolysis is the dissociation of a compound through the splitting and incorporation of water. Hydrolysis occurs when we dissolve acidic, basic, or neutral (weak acid/weak base) salts in water. Consider, for example, the basic salt, sodium bicarbonate.



The hydroxyl ion from water is associated with the sodium ion from the salt. The hydrogen ion from water is associated with the bicarbonate radical, and these two exist primarily as undissociated carbonic acid. The net result of this hydrolysis reaction is a basic solution containing sodium and hydroxyl ions and undissociated carbonic acid.

h. **Electrolyte Strength.** It should be apparent, recalling the discussion of acids and bases, that not all electrolytes will dissociate to the same extent in solution.

(1) Those that dissociate and exist entirely as ions in solution are called strong electrolytes. Strong electrolytes include strong acids, strong bases, and their neutral salts.

(2) Compounds that dissociate to a small extent and exist only partially as ions in solution are called weak electrolytes. Weak electrolytes include weak acids, weak bases, and salts of weak acids and/or weak bases.

(3) To identify whether a compound is a strong or weak electrolyte, it is first necessary to identify what type of compound it is. For example, consider NaCl. This compound is a salt formed from a strong base (NaOH) and a strong acid (HCl) and is, therefore, a neutral salt. Since it is a neutral salt of a strong acid and a strong base, it is a strong electrolyte as defined above. Other salts can be determined in a like manner.

