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2020

## A brief review of pharmaceuticals

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## Review Article

## A Brief Review of Pharmaceuticals

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Received: May 15, 2020; Accepted: June 04, 2020;

Published: June 11, 2020

## Background

Pharmacists and pharmaceutical scientists are often called to formulate dosage forms. To that end, the art and science of pharmaceuticals become of utmost importance. In this brief review, the essential terms that govern this science are succinctly introduced. For more information on this subject, the reader is referred to the publications listed in the Bibliography section of this review. The scientific principles that are needed to be applied during the design and execution in making the pharmaceutical dosage forms are briefly outlined in this review.

## Pharmaceuticals (Also Known as Pharmacy)

Pharmaceuticals [1-4] is an area of science that concerns itself with formulating dosage forms based on physical and chemical characteristics of ingredients and applying calculations made to ensure the proper amounts of those ingredients for the safety and therapeutic action of the drug in the formulation. Pharmaceuticals deals with physical pharmacy, compounding, pharmaceutical calculations, pharmacokinetics, and biopharmaceutics. Pharmaceuticals is considered to be the science responsible for producing pharmaceutical dosage forms for patient use. The chemical and physical characteristics of drugs, the choice of a dosage form, and the pharmacokinetic parameters of the drug are all important factors that the pharmacist should consider before formulating a medication for patient use. Pharmacists have the right and the responsibility to formulate these dosage forms extemporaneously for their patients whenever a prescription calls for such an action. On the industrial level, pharmaceutical scientists are engaged in designing dosage forms for mass production. In the United States and most of the other nations, there exists a body of professionals who took upon themselves the responsibility to monitor the quality of medicinal substances used in their country. The United States Pharmacopeia Convention, Inc. (USP) is one such organization. Since its inception, the primary goal was to develop standards to enhance the quality of patient care in the nation. The United States Pharmacopeia/National Formulary, or the USP/NF, is the publication that contains such standards.

## Concentration Units

The concentration units [1,5-7] are used in pharmacy to define the relative amounts of components in a dosage form. The label of a dosage form should provide information as to the active ingredients included and their concentrations in the formulation. There are several useful units for concentration and these are part per million

(ppm): the number of parts of a solute in one million parts of the solution. When water is the solvent (density = 1g/mL), then ppm is the number of grams of the solute in one million milliliters of the solution; percent by weight (% w/w): the amount of a solute in grams in 100g of the solution; percent by volume (% v/v): the amount of a solute in milliliters in 100mL of the solution; percent weight by volume (% w/v): the amount of a solute in grams in 100mL of the solution; milligram percent (mg%): the amount of a solute in milligrams in 100mL of the solution; mole fraction: the number of moles of a solute relative to the total number of moles in solution; molality: the number of moles of a solute in one kg of solvent; molarity: the number of moles of a solute in one liter of solution; milliequivalence: it is the equivalent weight of the solute divided by 1000. Milliequivalent is expressed in milligrams; and osmolarity/osmolality: the number of osmoles of a substance in one liter or one kilogram of solvent, respectively. Other information about the solution is usually useful to define some of the above units. For example, the density or the specific gravity of the solution is generally needed to calculate (% w/w). The molecular weight of the drug helps calculate the number of moles of the solute. Besides, knowledge of one concentration unit may lead to calculating another unit. For example, if the mole fraction of the solute is known, the molality can be calculated from the mole fraction value and the molecular weight of the solvent. In summary, the use of concentration units in pharmacy is extensive. All dosage forms' labels should contain the active ingredients and their concentrations in the dosage form.

## Beer's Law

Beer's law states that there is a positive linear relationship between the concentration of the drug in the solution and absorbance. Stated in a mathematical expression [7]:

$$\text{Abs} = \text{A} \text{ C} \text{ L}$$

Where C is the concentration, L is the path length, and Abs is the absorbance. Fitting the data to the above equation requires the use of linear regression analysis. Beer's law may be used in the determination of the active principles in pharmaceutical samples [7]. Linear regression analysis is an essential mathematical manipulation of data used to define relationships between variables. Many of the relationships between variables in physical pharmacy are linear. This method is used to find the best straight line that fits the data. The equation for the straight line is given as [8,9]

$$Y = m X + b$$

Where m is the slope of the line, b is the y-intercept, X is the independent variable, and Y is the dependent variable. The correlation coefficient, r gives the strength of the relationship between the two variables. The value of r is between -1 and +1. A (+1) value indicates a perfect positive linear relationship, and a (-1) means a perfect negative linear relationship. If r equals zero, then no linear relationship exists between the two variables; however, another relationship may exist between Y and X. The slope of the line can

be either negative or positive. A zero value for the slope indicates no linear relationship exists between the variables. Note that the sign of  $r$  and  $m$  is always the same for a given equation [8,9]. The best way to find the equation for a straight line is to use a scientific calculator set at linear regression mode or use a computer program. Using calculators to solve for the best straight line may not be practical for data that contain a large number of observations. As mentioned above, many relationships in physical pharmacy are linear [2,3,7] A) Absorbance (optical density) vs. drug concentration; B)  $\log$  (drug concentration) vs. time, in the first-order reaction; C)  $\log$  (specific reaction rate) vs. (Temperature-1), in drug stability studies; D)  $\log$  (Solubility) vs. (Temperature-1), in drug solubility studies; E) The rate of shear vs. shearing stress, in Newtonian rheograms. Also, if the relationship is not linear, one can linearize it. For example, in (B) above, the relationship between drug concentrations vs. time is exponential. However, taking the  $\log$  of the concentration values produced the linear transformation. Although a high correlation coefficient value indicates a strong relationship between the variables, this should not be perceived as if X is causing Y to behave in a particular manner. Unless all external factors affecting both variables are eliminated from the experiment, one should be cautious not to imply causation [8,9]. In summary, the linear regression analysis is an essential tool to study relationships among variables.

## Bioavailability and Bioequivalence

The term bioavailability indicates the rate and extent of absorption of the drug in its pharmacologically active form [2,4]. In contrast, bioequivalence relates to a similar rate and time of absorption obtained from different drug products. Bioequivalence, therefore, refers to drug products that have similar bioavailability. When dealing with the issue related to bioavailability and bioequivalence, three parameters need to be considered. These are the maximum plasma concentration, the time for the maximum plasma concentration, and the area under the curve. The maximum plasma concentration with its time together represents a maximum point on the drug concentration-time curve. This maximum point reflects the rate of absorption. The area under the curve represents the extent of absorption. Various protocols are available to conduct bioequivalence studies. They all depend on the availability of a sensitive laboratory assay for the drug, a protocol design, and statistical analysis of the data. In addition to the three main parameters for determining bioequivalence; the variability associated with these parameters has to be considered. Statistical tests are used to compare the parameters obtained from the drug products being studied.

## Shelf-life Determination

The pharmaceutical industry uses scientific methods for the determination of shelf life of medicinal products [4,7,10]. These scientific methods are based on kinetics principles. The chemical degradation of drugs follows specific reaction orders. The simplest of these reaction orders are the zeroth, first, and second-order reactions. The rate of drug degradation depends on the concentration raised to some power  $n$ . 'When  $n$  equals to zero, one, or two, the reaction is zero, first, or second-order, respectively. The shelf life of the drug is the time necessary for the concentration of the drug to drop below a specified USP level. Usually, the shelf life is identical to  $t_{90}$ . The  $t_{90}$  is defined as the time necessary for 10% of the drug to

disappear. The  $t_{90}$  is directly proportional to the initial concentration of the drug undergoing a zero-order reaction. It is independent of the initial concentration for the first-order reaction and is inversely related to the initial concentration for the second-order reaction. In addition to the order rates mentioned above, there are two common reaction orders, the apparent zero-order, and the pseudo-first-order reactions. The apparent zero-order reaction is that of a first-order type, but because of the presence of a drug reservoir in the system (e.g., suspensions), the reaction "appears" as a zero-order. The pseudo-first-order reaction is a second-order reaction where one of the reactants' concentrations is held constant; therefore, the reaction is reduced to a first-order type. The most common chemical degradation reactions for drug products are hydrolysis and oxidation. Hydrolysis is defined as the reaction of drug molecules with water to yield byproducts. Oxidation is defined as the process where the drug undergoes dehydrogenation or the loss of electrons from drug atoms. There are several processes to overcome hydrolysis; these include the partial or complete elimination of water from the formulation and preparing the drug in a dry form. Likewise, to overcome oxidation, antioxidants may be added to the formulation and the elimination of trace metals from the formula. Two main factors affecting the degradation processes of drugs; these are the pH and temperature. The effect of pH is manifested by hydrolysis reactions, while the temperature affects all degradation reactions by increasing the rate of degradation with an increase in the temperature. Arrhenius equation is used at elevated temperatures to predict the shelf life of the drug at room temperature (or any other temperature, such as when the drug is placed under refrigeration) [2,3,7,10]. In summary, from the knowledge of the kinetics of drug degradation, the shelf-life of medicinal products is predicted with accuracy.

## Flavors and Colors

Pharmaceutical preparations may be flavored and colored to render the product more acceptable by the patient [2,3]. Several flavoring agents can be used to mask the taste of medicinal agents. The list includes cocoa, fruit, cinnamon, and licorice flavors. Coloring agents are also numerous, and they cover a wide range of shades. Coloring agents can be classified into three categories: A) Food, Drugs, And Cosmetics (FD&C), B) Drugs and Cosmetics (D&C), and C) External Drugs and Cosmetics (External D&C). Colors may be used as soluble dyes or insoluble pigments. The latter agents are also known as Lake pigments. Pigments color by dispersion. They are commonly dispersed in a vehicle such as glycerin or syrup before adding them to the formulation. Pigments are mainly used when the amount of moisture in the formulation is low (such as tablets and capsules). In summary, coloring and flavoring agents are used to improve the acceptability of the preparation by the patient.

## States of Matter

Medicinal agents exist as gases, liquids, or solids [1,4,7]. Therefore, it is crucial to study the "state" of drugs as a physical form. Gas is a phase of matter where the substance molecules are dispersed in space and are loosely bound to each other. Therefore, when the gas is confined to a closed container, its molecules move freely in space and collide with each other and the walls of the container. The effect of the collision is the production of pressure inside the container. The pressure is typically expressed in milliliters of mercury or units of

the atmosphere. Many important pharmaceutical substances exist as liquids. These substances serve as solvents (water, alcohol, propylene glycol), preservatives (glycerin), surface-active agents (Span 80, Tween 20), flavors (lemon oil, peppermint oil), or medicinal agents (pine tar, coal tar, ichthammol, nitroglycerin). The molecules in the liquid phase are free to move in three directions in space so that they are more restricted in their movement than the gas molecules. Fluid viscosity is an important parameter to be considered in the formulation. Very viscous liquids may not flow as easily so that pouring these liquids from containers can be problematic. By far, the solid phase is the most common one for drugs. Solid drugs can be crystalline (cocoa butter) or amorphous (vasopressin tannate). Polymorphic crystalline drugs exist in more than one crystal form. Polymorphs differ in their dissolution rate, density, melting point, and other physical characteristics; however, they share similar chemical characteristics. The molecules in the solid phase are immobile, and they attract each other with strong bonds.

A phase that is intermediate between the solid and the liquid phase is known as the liquid crystal, also exists in nature. Despite its widespread in nature, the applications of liquid crystals in pharmacy are limited. In summary, drugs can exist as a gas, liquid, or solid form. Knowledge of the drug state of matter is important in understanding how the drug is going to behave therapeutically.

## Thermodynamics

Thermodynamics [4,7,11] is the science that deals with the transformation between heat and energy and between the various forms of energy. Energy can exist in multiple forms, and according to the relativistic theory of Dr. Albert Einstein, the matter is also another form of energy. There are four laws of thermodynamics. The Zeroth Law describes the thermal equilibrium of systems in contact with each other. Systems that are in thermal equilibrium must have the same temperature. The First Law states that the energy of a system and its surrounding remains the same during any change. The Second Law is concerned with the direction with which the reaction proceeds; a natural process proceeds in such a manner so that a state of equilibrium is achieved in the system. At equilibrium, no further change occurs in the system. A thermodynamic parameter that stems from the Second Law is called the entropy. The entropy of a system undergoing changes and its surroundings is low and increases as the system approaches equilibrium. The change of entropy for the universe (i.e., the system and its surroundings) for any change is equal to zero or is positive. For processes that occur spontaneously in nature, the net change of entropy for the universe is always positive. However, for reversible processes, the change of entropy for the universe is equal to zero. The Third Law of thermodynamics is a special case of the Second Law and states that the entropy of a perfectly crystalline solid is zero at zero Kelvin. The transfer of drugs from the site of administration to the circulation is governed mainly by a passive transport mechanism. This transport occurs from an area of high concentration of the drug to an area of low concentration. In theory, this transport should terminate once the concentration on both sides becomes the same (the system reaches a state of equilibrium according to the Second Law of thermodynamics). In summary, four laws of thermodynamics govern the transformation of the different forms of energy.

## Acids and Bases

The acidity of a solution depends on the molar concentration of hydronium ions  $[H_3O^+]$  in solution [4,7]. A high hydronium concentration indicates that the solution is acidic, and a low hydronium concentration indicates a basic solution. The acidity of a solution is given as a pH value ( $-\log [H_3O^+]$ ). The smaller the pH value, the more acidic is the solution. The pH of the solution is a function of its temperature (i.e., it changes with a change in temperature). Therefore, a solution with a pH equals 7.0 is only called neutral at 25°C. At any other temperatures, this solution cannot be labeled as neutral. The presence of drugs, weak acids, and weak bases, influence the hydronium ions concentration. The addition of a weak acid to water increases  $[H_3O^+]$  and the addition of a weak base to water decrease it. Salts of a weak acid and a strong base behave as if a weak base were added to water, and salts of a weak base and a strong acid behave as if a weak acid were added to water. Solutions containing a weak acid and its conjugate base or solutions containing a weak base and its conjugate acid are called buffers.

A buffer solution resists the change in pH upon the addition of substances that can alter the concentration of hydronium ions in the solution. The degree of the resistance to change in the pH is expressed as the buffer capacity (also known as the buffer index or value). The buffer capacity is a function of the hydronium ions in solution, the dissociation constant of the weak acid, and the total molar concentration of the buffer. The pH is one of the two main factors that affect the solubility of electrolytes in solutions; the other factor is the temperature. A weak acid begins to precipitate out in solutions if the pH of the solution goes below a specific value called the pHP (the pH of precipitation). Similarly, a weak base starts to precipitate out in solution if the pH of the solution exceeds the pHP value. The pHP depends on several factors: a) the initial concentration of the substance added to the solution, b) the intrinsic solubility of the weak acid or weak base, and c) the  $pK_a$ .

The total solubility of electrolytes depends on the pH of the solution, whereas the intrinsic solubility is independent of the pH. The total and intrinsic solubility depend on the temperature of the solution. In general, as the temperature of the solution increases, it results in an increase in the solubility of the drug in the solution. There exists a linear relationship between the log (solubility) and the inverse of temperature in Kelvin. If the slope of the straight line is negative, this indicates that the solubility increases with increasing temperature (an endothermic process). On the other hand, if the slope of the line is positive, the solubility of the substance decreases with increasing temperature (an exothermic process).

In addition, the degree of ionization of weak acids and weak bases is affected by the pH of the solution. As the pH of the solution increases, the degree of ionization of a weak acid increases, and that for a weak base decreases. The mole percent (mole %) of a non-dissociated acid or base is equivalent to the percent unionized of the respective electrolyte. Besides the pH, the degree of ionization is a function of the  $pK_a$ . In summary, the pH of the solution reflects  $[H_3O^+]$  ions present, and it depends on the temperature.

## Isotonic Solutions

Parenteral products, ophthalmic solutions, and irrigation

solutions are examples of pharmaceutical preparations that are intended to be administered as isotonic solutions [2,3,7]. An isotonic solution is a preparation that does not cause any significant change in the surrounding tissues. All isotonic solutions have the same osmotic pressure as the tissues they come in contact with (i.e., they are iso-osmotic). The solutes available in these solutions do not diffuse freely through the biological membrane. On the other hand, iso-osmotic solutions may not necessarily be isotonic. Only when the solutes cannot diffuse through the biological membrane, then the solution is also called isotonic. Solutions that are termed hypotonic can cause significant swelling to the surrounding tissues, and a hypertonic solution can cause significant shrinkage to these tissues. In all cases, irritation, discomfort, and damage to the tissues occur. To produce an isotonic solution, a hypertonic solution may be diluted with the solvent to the desired strength, and to the hypotonic solution, an inert substance may be added. There are several methods to render hypotonic solutions isotonic with body fluids. Among these methods are i) The freezing point depression method, ii) the sodium chloride equivalent method, iii) White-Vincent method, and iv) Sprowls' method. All of these methods are based on comparing the prepared solution to saline solution (0.9% NaCl). In summary, isotonic solutions are prepared so that no discomfort or damage to tissues occurs when the solution comes in contact with the tissues.

## Oral Solutions, Syrups and Elixirs

Oral solutions are widely used preparations by most patients, especially the young and elderly [1-3,7]. Pharmaceutical oral solutions are defined as liquid preparations of molecular dispersion type containing soluble ingredients in water. They are intended to be administered orally. In addition to the drug, one finds coloring, flavoring, and stabilizing agents in these preparations. Oral solutions can be prepared by simple methods, by chemical reactions, or by extraction. Syrups are solutions made by dissolving sugar in water or other aqueous liquids. They are considered to be concentrated solutions. Two types of syrups exist, medicated and flavored. Syrups can be prepared by heat, by agitation without heat, by percolation, and by the addition of other medicinal liquids to them. Syrups must contain preservatives when the concentration of sugar is relatively low (below 65% w/w or 85% w/v). Elixirs are liquid preparations intended for oral administration. They are clear liquids with a pleasant and sweet flavor. Elixirs are prepared using two main ingredients, water, and alcohol. Thus, elixirs are hydro-alcoholic preparations. Other ingredients are also added to elixirs for flavoring and solubilizing actions. In summary, oral liquid dosage forms are widely used in preparations containing soluble medicinal components.

## Interfacial Phenomena

Molecules at or near the interface between two immiscible phases are the subject of the interfacial phenomena [1,4,7]. Surface tension and interfacial tension are both defined as the force per unit length that exists at the interface. Interfacial tension helps us understand issues related to mixing immiscible phases. In pharmacy, the applications of such studies involve emulsions and suspensions, among others. The spreading coefficient is used to determine the degree of spread ability of one liquid phase on the surface of another immiscible liquid. The contact angle between a liquid phase and a solid phase determines whether or not the liquid wets the solid surface. In summary, the

applications of the interfacial phenomena in pharmacy are mainly for emulsions and suspensions.

## Rheology

Rheology is the study of flow. Materials undergo flowing if subjected to enough pressure [1,4,7,12]. The flow of a material is related to its viscosity. The higher the viscosity, the more difficult the flow is systems can be divided into two classes, the Newtonian and the non-Newtonian. The non-Newtonian systems are plastic, pseudoplastic, and dilatant. One important property of plastic and pseudoplastic material is thixotropy. Its applications are essential in formulating dosage forms such as suspensions. Viscosity can be measured using devices such as the capillary viscometer for Newtonian fluids and cone and plate viscometer for both the Newtonian and non-Newtonian materials. In summary, rheological data allows the pharmacist to determine the behavior of a material when incorporated in a dosage form.

## Suspensions

Among the important pharmaceutical coarse dispersions are the suspensions [1-3,7]. A suspension is a two-phase system in which a solid phase is distributed throughout a liquid phase. Suspensions are common pharmaceutical liquid preparations due to their ease of administration. Suspensions provide a sustained-release action as compared to simple solution. State of the art in compounding suspensions is to prepare a flocculated suspension. In this preparation, the pharmacist relies on the presence of zeta potential in the system to produce flocculation. Flocculated particles in suspensions, though they settle rapidly, form sediment which can be readily re-dispersed. There are two main parameters to define the physical characteristics of suspensions. These are the sedimentation volume (F) and the degree of flocculation ( $\beta$ ). As stated above, the current technology is to prepare flocculated suspensions. Flocculation can be induced by a change in the zeta potential, by the addition of surfactants, or the inclusion of polymers in the formula. All suspensions should have a "shake well" label on their container. In summary, suspensions are pharmaceutical preparations that are widely used as liquid dosage forms containing the solid drug suspended in a liquid medium.

## Emulsions

Emulsions are another important pharmaceutical coarse system [1-3,7]. Unlike suspensions, the dispersed phase in an emulsion is a liquid. Emulsions contain oil, and an aqueous phase kept mixed in a stable physical state by a stabilizer (known as an emulsifying agent). Active medicinal ingredients may be added to either or both phases of the emulsion. Depending on the relative locations of the two phases, an emulsion can be oil in water (o/w) or water in oil (w/o) preparation. Several stabilizers or emulsifying agents are used in the preparation of emulsions. These are classified into five categories, carbohydrate materials, protein substances, high molecular weight alcohols, surfactants, and finely divided solids. The Hydrophile-Lipophile Balance system (HLB) is often used in the preparation of emulsions. The HLB system gives information on the type of emulsifying agents that are needed in the formulation. It does not, however, provide information on how much or the amount of emulsifier(s) is needed. Several methods can be used in the preparation of pharmaceutical emulsions. These include the continental or dry gum method, the

English or wet gum method, the bottle of Forbes' bottle method, and the fusion method. Once an emulsion is prepared, it is subjected to environmental stresses such as temperature and gravity. Its physical stability, therefore, is manifested by several outcomes. An emulsion can cream (reversible), flocculate (reversible), or coalesce (irreversible). All emulsions should have a "shake well" label on their container. In summary, emulsions are pharmaceutical preparations containing two immiscible liquid phases held together in a stable physical form by an emulsifier. Emulsions can be prepared by several methods to yield o/w or w/o formulations.

## Colloidal Dispersions, Magma and Gels

Colloidal dispersions are one of the three classes of the dispersed systems [1-3,7]. The particles of the dispersed phase in those systems range in size between 1.0nm to 0.5 $\mu$ m. Colloidal dispersions are classified into lyophilic, lyophobic, or association colloids. The lyophilic systems are easy to make as compared to the lyophobic dispersions. Association colloids consist of amphiphiles dispersed in a liquid medium. Magmas and Gels are thick preparations that are made of organic or inorganic materials. They do not require suspending agents added to them. However, a "shake well" label must be attached to all magma preparations. Another name for magma is milk.

## Pharmaceutical Aerosols

Pharmaceutical aerosols, or pressurized packages, contain active ingredients in vehicles forming dispersion systems [1-3,4,7]. When actuated, a fine dispersion of liquid or solid materials in a gaseous medium is produced. The components of a pharmaceutical aerosol are the propellants, the containers, and the valves. The customary propellants for pharmaceutical preparations are nitrogen, carbon dioxide, various hydrocarbons, and nitrous oxide, among others. The pressure inside the container is based on Raoult's law and Dalton's law. Containers for pharmaceutical aerosols can be made of aluminum, tin, stainless steel, or glass. Two types of valves are available, the continuous spray valves and the metering valves.

Aerosols are formulated by mixing in a container the product concentrate and the propellants. Four general groups of systems exist for pharmaceutical aerosols. The first is solutions, the second is water-based aerosols, the third are suspensions or dispersions, and the fourth is foam systems.

The filling operation starts by placing the drug concentrate in the container and then adding the propellants to it. There are three different ways of adding propellants. Cold filling (not suitable for water-containing aerosols), pressure filling, and compressed gas filling are all methods used in this operation. In summary, pharmaceutical aerosols are systems where the product concentrate containing the drug is mixed with the propellants in a pressurized container. The drug is delivered to the patient by actuating the device.

## Powders

A powder mixture is a dry form of finely divided substances [1-3,13]. The particles' shape and size vary greatly within a given batch. Thus, the term polydisperse is associated with a collection of particles in a powder mixture. Because of this polydispersity, a calculated average particle diameter is used to describe a powder mixture.

Several properties of the powder are usually recognized. Among these, porosity, density, bulkiness, and flow properties are important pharmaceutically.

The preparation of a powder dosage form requires that the drugs and other materials be pulverized. This is achieved on a small scale by using porcelain or Wedgwood mortars and pestles. Mixing powders, on a small scale, can be done by using a glass mortar and pestle. However, other methods of mixing are also available, such as mixing by spatulation.

Powder preparation can be packaged in large volume containers for bulk dispensing. Moreover, for single-use dispensing, the pharmacist uses divided powders. In summary, a powder dosage form is a dry mixture of drugs and other inert substances that can be prepared by grinding and mixing. It can be dispensed as bulk or as a divided powder form.

## Capsules

A capsule is an enclosed system of a gelatin envelope containing drugs and vehicles in dry or liquid forms [1-3,10]. Two types of capsules exist, the hard gelatin capsules and the soft gelatin capsules. Though both forms can be used to dispense solid materials, the hard gelatin capsules are primarily used for this purpose, while the soft gelatin capsules are used for liquids. Hard gelatin capsules come in different sizes and shapes. The most popular one for human use is the oblong shape of size 0 and 1. In selecting the hard gelatin capsule size, several methods can be used. The pharmacist may rely on trial and error, the rule of 7, the rule of 6's, or the bulk density method. Having selected the proper capsule size, then the pharmacist prepares the powder mixture to be encapsulated by grinding and mixing procedures. The filling operation of capsules can be done using bench-top machines or by hand. Finally, and before dispensing, capsules are polished and cleaned. Soft gelatin capsules are used primarily for encapsulating liquids. Water (above 5%), low molecular weight water-soluble and volatile organic compounds, emulsions, liquids with a pH below 2.5 or above 7.5, strong acids and bases, and their corresponding salts cannot be encapsulated. In summary, capsules are oral dosage forms that contain drugs inside a gelatin envelope. They are of two types, hard gelatin and soft gelatin capsules.

## Tablets

Tablets are solid dosage forms that contain medicinal substances in a compressed physical form [1-3,14]. In addition to the medicinal agents, other ingredients may be found in a tablet formulation. The list includes bulking agents, binders, lubricants, glidants, anti-adherents, disintegrants, coloring agents, flavoring agents, and adsorbents. Tablets may be prepared by two methods, the dry and the wet methods. They are produced on machines called presses. Many quality control tests are performed on the finished tablets. These include the hardness test, friability test, disintegration, dissolution, weight variation, and content uniformity test. The hardness test is now a USP test and was re-named as Tablet Breaking Force Test. In summary, tablets are solid dosage forms that contain medicinal substances and are produced on machines known as presses.

## Controlled Release Dosage Forms

The term controlled-release implies that the delivery of drugs

from these dosage forms is in “a planned, predictable, and slower than usual manner [1-3,4,10].” They are classified into three types, sustained-release, repeat action, and delayed action forms. The sustained-release dosage forms are prepared by 1) microencapsulation or coated beads or granules, 2) embedding the drug in a slowly eroding matrix, 3) embedding the drug in an inert plastic matrix, 4) complex formation, 5) ion-exchange resin, 6) hydro-colloidal systems and, 7) osmotic pump. The repeat action systems have in the same dosage form multiple dosages. The delayed action forms have an enteric coat to protect the drug from being released in the stomach but allow it to be released in the intestine. Sugar-coating does not render the unit a controlled release dosage form, but used primarily for aesthetic reasons and for the purpose to protect the drug from the environment. In summary, controlled-release preparations can be of several types and may be prepared by several technological methods.

## Suppositories

Suppositories are solid dosage forms containing medicinal agents and are intended to be administered in body cavities [2,3]. Several bases are used in the preparation of suppositories. These include the fatty bases and the water-soluble/water-miscible bases. Suppositories are prepared by molding, by compression, or by hand-rolling and shaping. In summary, suppositories are intended to deliver the drug via one of the body cavities. They are solid preparation and made of either fatty or water-miscible bases.

## Ointments, Creams and Pastes

Ointments are semisolid preparations that are externally administered [1-4]. There are two different classes, medicated and non-medicated. Several bases are employed in the preparation of ointments. These are hydrocarbon, absorption, water-removable, and water-soluble bases. The hydrocarbon bases are not miscible with aqueous liquids. Absorption bases can be mixed with water to some extent to form w/o emulsions if they are not already w/o emulsions. Water-removable bases are o/w emulsions, and thus they mix with water without difficulty. Water-soluble bases are intended to carry and deliver solid materials. They are not, however, a good choice for aqueous liquids because water softens them. Ointments are prepared by incorporation using either an ointment pad or a mortar and pestle. Levigating agents are customarily employed during the mixing of powders in the ointment base. Ointments can also be prepared by the fusion technique. The fusion method is used whenever the base contains solid materials that do not lend themselves to easy mixing.

Pastes, similar to ointments, are semisolid preparation intended for external use. As compared to ointments, they contain a larger percentage of solid materials in them (a minimum of 20% of the solid material is found in pastes). Thus, pastes are thicker and much stiffer than ointments. Creams, by definition, are emulsions of the semisolid type. They are employed for their emollient action on the skin or to deliver a drug to the affected area. In summary, all three preparations are semisolid preparations intended to be used externally on the affected areas of the skin.

## Sterile Products

Sterile products are perhaps the most used preparations in institutions, such as hospitals or nursing care facilities [1-4]. These preparations are intended either be given via injection through layers of the skin, instilled in the eyes, or used during surgery. Thus, sterile preparations must be free from any microbial containments or toxic substances. They should also contain materials with a high level of purity. Vehicles used in sterile products are of two types, aqueous and non-aqueous. Sterile products are packaged in either glass or plastic containers. Glass Type NP should not be used for packaging these formulations. Sterile products are filled in areas called aseptic areas. Following the filling process, units are sterilized either by thermal or non-thermal methods (ultraviolet light, ionizing radiation, filtration, or gas sterilization). Quality control tests are done on the finished units before shipment. Tests include leaker test, clarity test, pyrogen detection, sterility, and safety. In summary, sterile products are high-quality preparations that are free from any contamination. Quality control tests are performed on sterile products to assure this high quality.

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