1. (iii) POSOLOGY

Posology is derived from the Greek word posos meaning how much and logos meaning science. So posology is the branch of medicine dealing with doses.

The optimum dose of a drug varies from patient to patient. The following are some of the factors that influence the dose of a drug.

1. Age: Human beings can be categorized into the following age groups:

1. Neonate: From birth up to 30days.
2. Infant: Up to 1 year age
3. Child in between 1 to 4 years
4. Child in between 5 to 12 years.
5. Adult
6. Geriatric (elderly) patients

In children the enzyme systems in the liver and renal excretion remain less developed. So all the dose should be less than that of an adult. In elderly patients the renal functions decline. Metabolism rate in the liver also decreases. Drug absorption from the intestine becomes slower in elderly patients. So in geriatric patients the dose is less and should be judiciously administered.

2. Sex: Special care should be taken while administering any drug to a women during menstruation, pregnancy and lactation. Strong purgatives should not be given in menstruation and pregnancy. Antimalarials, ergot alkaloids should not be taken during pregnancy to avoid deformation of foetus. Antihistaminic and sedative drugs are not taken during breast feeding because these drugs are secreted in the milk and the child may consume them.

3. Body size: It influences the concentration of drug in the body. The average adult dose is calculated for a person with 70kg body weight (BW). For exceptionally obese (fat) or lean (thin) patient the dose may be calculated on body weight basis.

Another method of dose calculation is according to the body surface area (BSA). This method is more accurate than the body weight method.

The body surface area (BSA) of an individual can be obtained from the following formula:

$BSA\ (m^2) = BW(kg)^{0.425} \times Height\ (cm)^{0.725} \times 0.007184$

4. Route of administration

In case of intravenous injection the total drugs reaches immediately to the systemic circulation hence the dose is less in i.v. injection than through oral route or any other route.

5. Time of administration

The drugs are most quickly absorbed from empty stomach. The presence of food in the stomach delays the absorption of drugs. Hence a potent drug is given before meal. An irritant drug is given after meal so that the drug is diluted with food and thus produce less irritation.

6. Environmental factors

Stimulant types of drug are taken at day time and sedative types of drugs are taken at night. So the dose of a sedative required in day time will be much higher than at night.

Alcohol is better tolerated in winter than in summer.

7. Psychological state

Psychological state of mind can affect the response of a drug, e.g. a nervous and anxious patient requires more general anaesthetics. Placebo is an inert substance that does not contain any drug. Commonly used placebos are lactose tablets and distilled water injections. Some time patients often get some psychological effects from this placebo. Placebos are more often used in clinical trials of drugs.

8. Pathological states (i.e. Presence of disease)

Several diseases may affect the dose of drugs:

In gastrointestinal disease like achlorhydria (reduced secretion of HCl acid in the stomach) the absorption of aspirin decreases.

In liver disease (like liver cirrhosis) metabolism of some drugs (like morphine, pentobarbitone etc.) decreases.

In kidney diseases excretion of drugs (like aminoglycosides, digoxin, phenobarbitone) are reduced, so less dose of the drugs should be administered.

9. Accumulation

Any drug will accumulate in the body if the rate of absorption is more than the rate of elimination. Slowly eliminated drugs are often accumulated in the body and often causes toxicity e.g. prolonged use of chloroquin causes damage to retina.

10. Drug interactions

Simultaneous administration of two drugs may result in same or increased or decrease effects.

Drug administration with dose	Pharmacological effect
Drug A	Effect A

Drug B	Effect B		
Drug A + Drug B	Effect AB		
Relationship	Name of the effect		Examples
Effect AB = Effect A + Effect B	Additive effect		Aspirin + Paracetamol
Effect AB > Effect A + Effect B	Synergistic potentiation)	(or	Sulfamethaxazole + Trimethoprim
Effect AB < Effect A + Effect B	Antagonism		Histamine + Adrenaline

11. Idiosyncrasy

This an exceptional response to a drug in few individual patients. For example, in some patients, aspirin may cause asthma, penicillin causes irritating rashes on the skin etc.

12. Genetic diseases

Some patients may have genetic defects. They lack some enzymes. In those cases some drugs are contraindicated.

e.g. Patients lacking Glucose-6-phosphate dehydrogenase enzyme should not be given primaquin (an antimalarial drug) because it will cause hemolysis.

13. Tolerance

Some time higher dose of a drug is required to produce a given response (previously less dose was required).

Natural Tolerance: Some races are inherently less sensitive to some drugs, e.g. rabbits and black race (Africans) are more tolerant to atropine.

Acquired Tolerance: By repeated use of a drug in an individual for a long time require larger dose to produce the same effect that was obtained with normal dose previously.

Cross tolerance: It is the development of tolerance to pharmacologically related drugs e.g. alcoholics are relatively more tolerant to sedative drugs.

Tachyphylaxis: (Tachy = fast, phylaxis = protection) is rapid development of tolerance. When doses of a drug are repeated in quick succession a reduction in response occurs – this is called tachyphylaxis. This is usually seen in ephedrine, nicotine.

Drug resistance: It refers to tolerance of microorganisms to inhibitory action of antimicrobials e.g. Staphylococci to penicillin.

2. (i). POWDERS

Powders Pharmaceutical Powders are intimate mixtures of dry, finely divided drugs and/ or chemicals that may be intended for internal (oral powders) or external (topical or dusting powder) use.

Powders represent one of the oldest dosage forms. It is a preparation in which drug is blended with other powdered substances and used for internal or external purpose. Powder as a dosage form permits drugs to be reduced to a very fine state of division, which often enhances their therapeutic activity or efficacy by an increase of dissolution rate and/ or absorption. Divided powders are also found to be convenient for administering drugs that are excessively bitter, nauseous, or otherwise to the taste

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Although powders are not used now-a-days extensively as a dosage form, they are widely used in preparation of various dosage forms. Powdered drugs can be blended with other powdered materials prior to fabrication into other solid dosage forms such as tablet and capsule. Powdered drugs are frequently added to other ingredient to make ointments, pastes, suppositories, and others.

A good powder formulation has a uniform particle size distribution. If the particle size distribution is not uniform particle size. If the particle size distribution is not uniform, the powder can segregate as per to particle size which may result in inaccurate dosing or inconsistent performance. A uniform particle size distribution ensures a uniform dissolution rate if the powder is to dissolve, a uniform sedimentation rate if the powder is used to remain in a suspension and minimizes stratification when powders are stored or transported.

ADVANTAGES

- Powders being the solid preparation are more stable than liquid and semi-solid preparations.
- Convenient forms, to dispense large dose of drugs. They can be best administered in powder form by mixing them with food or drinks
- Since powders are in the form of small particles they offer a large surface area and are rapidly dissolved in the gastrointestinal tract minimizing the problems of local irritation.
- More convenient to swallow, faster dissolution and absorption than tablets or capsules.
- Powders offer a lot of flexibility in compounding or incompatible solids and possess good chemical stability.
- They are easy to apply
- They absorb skin moisture, which leads to reduced friction between skin surfaces, discourages bacterial growth and has a cooling effect.
- Can be applied to many body cavities such as ears, nose, tooth socket and throat.
- Can be made into many different dosage formulations eg capsules, tablets, powders for reconstitution, dusting powders, bulk powders, powders for inhalation etc.
- Highly compatible compared to liquid dosage forms.
- Manufacturing of powder is economic hence product cost is quite low as compared to other dosage forms.

DISADVANTAGES

- Less convenient to carry especially for bulk powders are not suitable for administering potent drugs with a low dose.
- Difficult to mask the unpleasant taste of the drugs.
- Light fluffy powders may be inhaled by infants leading to breathing difficulties.
- Variable dose accuracy.
- Not suitable form for drug inactivated in the stomach or cause damage to stomach these should be presented as enteric-coated tablets.
- Not suitable for bitter, nauseating and corrosive drugs, if are meant for oral administration.
- Difficulty of protecting hygroscopic , deliquescent or aromatic materials and not suitable for drugs which are unstable in normal atmospheric conditions.
- Inconvenient to carry.
- They are susceptible to physical instability.

CLASSIFICATIONS OF POWDERS

They are broadly classified in three classes

1. Bulk powders for external use: (a) Dusting powders (b) Snuffs (c) Dental powder (d) Insufflations
2. Bulk powders for internal use.
3. Simple and compound powders for internal use.
4. Effervescent granules
5. Eutectic mixtures
6. Cachets

1. Bulk powders for external use:

External bulk powders contain non-potent substances for external applications. These powders are dispensed in glass, plastic wide mouth bottles and also in cardboard with specific method of application. Bulk powders for external used are of four types.

(a) Dusting powders (b) Snuffs (c) Douche powders (d) Dental powder (e) Insufflation

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(a) Dusting powders.

These are used externally for local application not intended for systemic action. The desired characteristics of powders include- (a) homogeneity, (b) non-irritability, (c) free flow, (d) good spread ability and covering capability, (e) adsorption and absorption capacity, (f) very fine state of subdivision, and (g) capacity to protect the skin against irritation caused by friction, moisture or chemical irritants.

Dusting powders usually contain substances such as zinc oxide, starch and boric acid or natural mineral substances such as kaolin or talc.

Talc may be contaminated with pathogenic microorganisms such as - Clostridium tetani etc., and hence it should be sterilized by dry heat. Dusting powders should not be applied to broken skin. If desired, powders should be micronised or passed through a sieve # 80 or 100. Dusting powders should preferably be dispensed in sifter-top containers. Such containers provide the protection from air,

moisture and contamination as well as convenience of application. Currently some foot powders and talcum powders have been marketed as pressure aerosols.

Dusting powders are employed chiefly as lubricants, protectives, absorbents, antiseptics, antipruritics, astringents and antiperspirants.

Zinc oxide 20 parts Salicylic acid 2 parts Starch powder 78 parts

(b) Snuffs:

These are finely divided solid dosage forms of medicaments dispensed in flat metal boxes with hinged lid. These powders are inhaled into nostrils for decongestion, antiseptic, and bronchodilator action.

(c) Douche powder:

These powders are intended to be used as antiseptics or cleansing agents for a body cavity; most commonly for vaginal use although they may be formulated for nasal, otic or ophthalmic use also. As douche powder formulation often include aromatic oils, it becomes necessary to pass them through a # 40 or 60 sieve to eliminate agglomeration and to ensure complete mixing. They can be dispensed either in wide mouth glass bottles or in powder boxes but the former are preferred because of protection afforded against air and moisture.

Zinc sulphate
Magnesium sulphate
Boric acid
Oil of lemon
Water

(d) Dental powders:

Dental powders are rarely prescribed. However this class of powders is interesting from the compounding angle. This preparation is a type of dentifrice meant for cleaning the teeth.

As such, dental powders contain detergents, abrasives, antiseptics and colouring and flavouring agents incorporated in a suitable base. Generally the base is calcium carbonate. The detergent is in the form of soap and the abrasive action is provided by finely powdered pumice stone.

Essential oils are added to provide flavour and freshness to the mouth as well as antiseptic action. Essential oils, if present in smaller quantity, are easily absorbed by calcium carbonate and pumice. This makes the uniform distribution of the oil difficult. Best results are obtained if the oil is triturated in the solids taking considerable care to distribute it uniformly.

(e) Insufflation:

Insufflations are a class of powders meant for application to the body cavities e.g., ear, nose, vagina etc. The powder has to be extremely fine and must find an entry to the cavity deep enough to bring about its action at the site. It is delivered to the affected part in a stream with the help of a device called an insufflator, which blows the powder to the site.

Some of the insufflations contain volatile liquid ingredients which may require uniform distribution in the powder. If these liquid ingredients are present in large quantity, the liquid portion may have to be evaporated. Generally evaporation is brought about slowly in a china dish which is heated on a water bath. The resultant product is re-powdered and sifted through a sieve of a suitable size.

However, active volatile liquids present in small portions should not be removed by evaporation but only incorporated by trituration in the powder.

The pharmaceutical industry packages the insufflations in pressurized form i.e., aerosols. Aerosols contain the medication in a stout container with a suitable valve, the delivery of the powder being accomplished by a liquefied or compressed gas propellant of very low boiling point. On pressing the actuator of the valve the propellant delivers the medication in a stream.

2. Bulk powders for internal use

Bulk powders contain many doses in a wide-mouth container that is suitable to remove the powder by a teaspoon. The non-potent substances are used in bulk powder form such as antacid, laxative, purgative, etc.

Rhubarb powder
Light magnesium carbonate
Heavy magnesium carbonate
Ginger powder
Make a powder.

3. Simple and compound powders for internal use

These are unit dose powders normally packed in properly folded papers and dispensed in envelopes, metal foil, small heat-sealed plastic bags or other containers.

Usually for the preparation of simple powders, the ingredients are weighed correctly and blended by geometrical mixing in ascending order of weights. The mixture is then either divided into blocks of equal size, numbers of blocks representing the number of powders to be dispensed or each dose is weighed separately and placed on a powder paper. The paper is then folded according to the pharmaceutical art and placed in either an envelope or a powder box.

4. Effervescent granules

This class of preparations can be supplied either by compounding the ingredients as granules or dispensed in the form of salts. The ingredients whether in granular form or present as salts, react in presence of water evolving carbon dioxide gas.

For evolution of the gas two constituents are essential, a soluble carbonate such as sodium bicarbonate and an organic acid such as citric or tartaric acid. The preparation can be supplied either as a bulk powder or distributed in individual powders.

There are three alternative methods of dispensing depending upon the nature of prescription.

(i) If the effervescent salts are prescribed to be the dispensed in bulk form, no granulation is necessary. The ingredients are mixed uniformly and directions stated on the label to add the prescribed quantity to water, before use.

(ii) If the effervescent salt is prescribed in divided doses, the ingredients which cause effervescence on mixing with water are enclosed separately in papers of different colour. The patient is advised to take one powder of each color and add to water, before use. Quantities of the sodium bicarbonate and the organic acid, citric or tartaric, are equimolecular in proportion.

(iii) In the third case the product contains all the ingredients mixed together in a granular form. Preparation of granular products requires pharmaceutical technique. If sodium bicarbonate and citric acid are taken in equimolecular proportion and mixed to make granules, the quantity of water of crystallization liberated from the citric acid is large enough to make the mass wet and carbon dioxide may be liberated during the preparation itself. If one tries to substitute citric acid by tartaric acid, which contains no water of crystallization; it may not be possible to form a mass necessary for granulation.

Therefore both citric and tartaric acids are taken in suitable proportions leaving a little acid in surplus than the quantity required to neutralize sodium bicarbonate. This surplus is necessary to give the final preparation an acidic taste that is more palatable. There is a certain loss in weight of such a preparation due to the loss of water in drying the granules and partial loss of carbon dioxide due to its release during preparation.

Heating is done on a water bath keeping all the ingredients thoroughly mixed in a porcelain dish. Gentle application of heat liberates the water of crystallization from citric acid and the mass tends to be coherent.

Prolonged heating may result in complete evaporation of the released water leaving the product in the form of a dry lump which cannot be rendered into granules. The coherent mass is transferred from the porcelain dish to an inverted sieve of suitable aperture size kept over a glazed paper.

The mass is pressed through the sieve taking care to change the position of the sieve over the paper to prevent the formation of a lump of the sieved granules. The granules are dried in an oven taking care to regulate the temperature which should be generally kept below 80°C.

The operation requires considerable skill and experience to obtain granules of uniform size and an elegant product. If necessary, the dry granules are passed through a sieve of appropriate size to break larger granules which result due to sticking of the sieved wet granules.

The water of crystallization of the citric acid and the water from the reactions make the material coherent. Loss of weight occurs during granulation due to (a) evaporation from the damp mixture, and (b) loss of carbon dioxide. The losses constitute approximately one-seventh of the weight of powder used and must be allowed for when calculating the amount to be prepared.

Chemical reaction:

3 NaHC03 + C6H807.H20 = C6H5Na307 + 3 C02 + 3 H20 (Sodium bicarbonate) (Citric acid)

2 NaHC03 + C4H606 - C4H4Na206 + 2 C02 + 2 H20 (Sodium bicarbonate) (Tartaric acid)

5. Eutectic mixtures

They are defined as mixture of low melting point ingredients which on mixing together turn to liquid form due to depression in melting point of the mixture below room temperature. They are mixtures of substances that liquefy when mixed rubbed or triturated together. The melting points of many eutectic mixtures are below room temperature. Examples of the substances which tend to liquefy on mixing are camphor, thymol, menthol, salol. Any two of these drugs turn to liquid when mixed. This problem during formulation of powders of such material can be solved by using inert adsorbent such as

starch, talc, lactose to prevent dampness of the powder and dispensing the components of the eutectic mixture separately.

6. Cachets

Cachet as a unit dosage form was very popular sometime back. Presently cachets are seldom used and have been replaced by capsules. Cachets, like capsules, can be easily filled and sealed at the dispensing counter.

This dosage form holds larger quantity of the medication as compared to capsules. Since the cachets are made of flour and water they are easily damaged in handling. Further this dosage form offers little protection against light and moisture.

Due to its size and shape a cachet is difficult to swallow. The process of filling is similar to that of capsules. The drug is placed in one of the two halves of the cachet, the upper half is then placed over it and pressed with the help of a suitable device.

The flange of the upper plate is moistened carefully taking care not to wet it, with the help of a dampener. The sealing takes place due to the moisture between the flanges of the upper and the lower half and the pressure over the flanges. About 15 minutes are allowed for drying of the seal.

After this time the middle portion of the cachet is slightly pressed to ensure complete sealing. In absence of a machine a pharmacist can improvise and use two bottles the mouths of which are broad enough so that flanges of the plates - upper and lower, when kept over the mouths of the bottles, just rest over them. The drug is transferred to one of the plates resting over the mouth of the bottle kept vertically on the working bench. The flange of the empty half resting over the mouth of another bottle is moistened with the help of a damp camel hair brush.

The empty half of the cachet is then placed over the other half in which the medication is kept so that the flanges of the two halves are perfectly superimposed. The second bottle is then inverted and brought over the superimposed cachet and carefully put over the flange and pressed in position without disturbing the resting place of the cachet.

This provides a good seal. Cachets can be dry-sealed also. These cachets however are of a different shape where the cap is pressed over the body of the cachet. A protruded stud is also provided to hold the upper and lower halves together.

Like capsules, cachets are also expected to remain untouched by hand and one should use gloves while handling them. Since there are inherent losses of the drug in this operation also like that of powders and capsules, the quantities of each ingredient should be weighed for an extra powder over the number to be dispensed. The cachets are dispensed in wide-mouthed bottles of glass or plastic with a perfectly fitting cap. The patient should be instructed to keep the bottle securely closed.

Cachets are of two types:

(a) Wet seal Cachets and

(b) Dry seal Cachets

(a) Wet seal Cachets:

They are made up of two similar covex halves having flat edges The weighed amount of powder is placed in one half; the edges of the other are moistened with water and placed exactly over the first

half containing the powder. The edges of both the halve are pressed together so as to make a perfect seal.

(b) Dry seal Cachets:

They consist or two halves, the upper half and the lower half. The former one is little larger in diameter than the lower half. The powder is filled in a lower half and upper half is fitted over it like a lid on a box.

Cachets are dispensed in a box. If necessary the empty spaces are filled by cotton wool so as to fix them properly in the boxes. The boxes are labeled with direction of use " Immerse in water for few seconds and then swallow with draught of water".

Tablet trituates:

They are prepared by moulding powder into tablets. They are flat and circular disk shaped. Usually they are prepared for potent medicaments and highly toxic drugs by diluting the with diluents like lactose, dextrose sucrose etc. the drug and the diluents are mixed and the moistened with suitable dilution of alcohol (usually 50-60% alcohol is used) and mixed and then as to get a damp mass. This damp mass is filled in the perforations of the mould with a spatula. The excess amount damp mass is squeezed with the edge of the spatula. The filled perforated plate is superimposed on another plate having the same number of projecting pegs as that perforation. A little pressure is put over the upper plate which will allow the plate to go downward leaving the moulded tablets on the top of the pegs. These moulded tablets are carefully spread on the clean surface and dried either in open air or in oven at a controlled temperature.

Official preparations

Simple powders:

Simple powders only one ingredient either in crystalline or amorphous form. These powders should preferable be reduced to fine powder, weighed properly and supplied in a single dose packet separately. The wrapping of powders may be single wrapped or double wrapped (lined with waxed paper) according to the properties of the drugs. If the drug is resistant to atmospheric conditions, it can be wrapped singly and if sensitive to those conditions, must be double wrapped

For example:

Rx

Paracetamol …500mg

Method:

Weigh accurately the required amount of paracetamol powder which is already in its fine state. If not, then first reduce to fine powder and weigh. Wrap each dose in a white demy paper Compound powders.

Compound powders:

contain two or more ingredients supplied in the form of fine state of powder in divided dose, i.e. each dose is supplied in a single packet.

For example:

Rx

Aspirin 250mg

Paracetamol 150mg

Caffeine 50mg

Method: Powder each ingredient and weigh required quantities. Mix them in geometrical proportional and supply in divided doses. Wrap each dose in a doublewrapped paper.

Preparation of powders.

Step (1) Particle size reduction:

For the preparation of powder, each ingredient should be needed in finely ground form; hence manufacture must use a number of procedures and equipment to reduce the particle size of powder ingredients, this process is called as comminution. The most common method used for particle size reduction is powder formulation is trituration, which involves placing the solid in a mortar and continually grinding the chemical between the mortar and the pestle using a firm, downward pressure. The powder must be frequently scraped from the sides of the mortar to ensure that all particles are evenly reduced and mixed. A levigating agent, such as glycerin, may be added to the solid and processed by either continued trituration or by placing the mixture on an ointment slab and using spatulation to wet the solid and further reduce the particle size of a powder after it has been triturated.

In laboratory scale

Trituration, Pulverization and Levigation

In industrial scale

Bowl chopper, Hammer mill, Roller mills, Attrition mill, Colloid mill, Ball mill etc.

Advance size reduction technologies

Microfluidics particle reduction

Factors affecting size reduction of powder materials:

- Hardness or strength of the compound, the harder the material the more difficult it is reduce the size Toughness is more important than hardness; a soft but tough material may present more problems in size reduction than a hard or brittle substance.
- Toughness is encountered in many pharmaceutical materials, particularly in fibrous drugs and is often related to moisture content.
- Stickness is property that causes considerable difficulty in size reduction, for material may adhere to the grinding surfaces, or the meshes of the screen may become choked or if the material gummy or resinous may be troublesome to the size reduction process it can be overcome by addition of inert substances such as kaolin to sulphur.
- Softening temperature during the process of size reduction heat is generated which cause some substances to soften like waxy compounds stearic acids, drugs containing oils or fats. To overcome this problem by cooling the mill, either by water jacket or by passing stream of air through the equipment's
- Material substance, all substances are not homogeneous in character some show special structure like mineral substance may have lines of weakness along with material splits

to form flake-like particles, while vegetables drugs have a cellular structure often leading to long fibrous particles

- Moisture content influences a number of properties that can affect size reduction, like hardness, toughness or stickness.
- Purity required, certain types of size reduction apparatus cause the griding surfaces to wear, and such methods must be avoided if a high degree of purity of product is needed.

Step (2) Preparing a homogenous mixture:

The powders may be mixed by any one of the following methods:

Spatulation, Trituration, Geometric dilution, Sifting and Tumbling

a. Spatulation:

In this method, mixing of powders is done by the movement of a spatula throughout the powders on a sheet of a paper or on a porcelain tile. The method is very useful in mixing a small amount of powder or solid substances that liquiefy (eutectic mixtures)

b. Trituration:

It is used for both reduce particle size and mix powders. If the particle size reduction is desired along with mixing of powders, a porcelain mortar with a rough inner surface is preferred to glass mortar with a smooth working surface.

c. Geometric dilution:

The method is used when potent substances are too mixed with a large amount of diluent. The potent drug is placed upon an approximately equal volume of the dilute in a mortar and the substances are slightly mixed by trituration. A second portion of diluent equal in volume to the powder mixture in the mortar is added and trituration is repeated. The process is continued adding diluent equal in volume to the mixture in the mortar at each step until all the diluent is incorporated. For example, if 100mg of potent drug is required to be mixed with 900mg of lactose then according to geometric dilution, the following procedure should be followed:- 100mg of potent drug + 100mg of lactose = 200mg of mixture, 200mg of the mixture + 200 mg of lactose= 400 mg of mixture 400mg of the mixture + 400mg of lactose =800mg of mixture 800mg of the mixture + remaining portion = 1000mg of mixture of lactose

d. Sifting:

The powders are mixed by passing through sifters. This process results in alight fluffy product and is generally not acceptable for incorporation of potent drugs into a diluent base

e. Tumbling:

It is the process of mixing powders in a large container rotated by an electric motor. These blenders are widely employed in industry as large volume powder mixers Equipment’s used in powder

mixing are Tumbler mixing, Ribbon mixer, Screw mixer etc Factors that influence mixing quality such as mixing time, speed of mixing rotation, the type of the mixer, dry or wet mixing process and so on Step.

(3) Packaging of powders:

Bulk powders for external use are often dispensed in a shaker top container to facilitate topical application. They may also be dispensed in a wide mouth jar or a plastic container with flip-top lid. The jar or plastic container can be closed tightly to provide increased stability and protection from light and moisture, especially for compounds that contain volatile ingredients. Package should contain label as "For external use only".

Bulk powders intended for internal use should be dispensed in an amber colored widemouth powder jar with a tight-fitting lid. They should be accompanied by an appropriately sized dosing spoon or cup and adequate directions for removing and administering a correct dose. Bulk powders for internal use should be labeled with the strength of the active ingredient per dose.

Powders may be wrapped in paper, weigh the required number of powders and wrap in the papers. White glazed paper is generally used for wrapping. The wrapping should be done on a clean tile or large sheet of a glazed paper to protect the product. In a wellwrapped powder, there should be no powder within the flaps or folds. When powder is opened, for administration, the powdered material should appear in the center of the paper.

Double- Wrapping:

Double-wrapping is essential for volatile or hygroscopic drugs like Menthol, thymal, citric acid, Pepsin etc. Double wrapping is also must for drugs those are sensitive to the atmospheric conditions.

For this purpose a wax paper is cut slightly smaller than the demy paper each way and fold both paper at once similar to the single wrapping method

Labelling:

Patient should be instructed that individual powder should be dispersed in a little water or placed on the back of the tongue before swallowing.

Dispensing of powders involving special problems/ problems encountered in powder formulation.

A number of problems arise while dispensing a powder containing volatile substances, hygroscopic and deliquescent powders, eutectic mixtures, efflorescent powders, liquids, explosive substance and potent drugs. So special consideration are done while dispensing such powders.

Volatile substances

Certain vegetable powders contain volatile oils. To prevent the loss of volatile oils, these vegetable drugs must be powdered lightly in a mortar. Similarly the volatilization of substances like menthol, camphor and essential oils may take place on incorporation in powders. This is prevented or at least minimized by the use of double wrapping. The inner wrapper should be of wax paper and outer wrapper may be of any thick paper.

Hygroscopic powders and deliquescent powder

The powders which absorb moisture from the atmosphere are called hygroscopic powders. But certain powders absorb moisture to such a great extent that they go into solution and are celled deliquescent powders. Examples of such substances include ammonium citrate, pepsin, phenobarbitone, sodium bromide, sodium iodide, potassium citrate, zinc chloride etc.

Such substances are usually supplied in granular from in order to expose less surface area to the atmosphere. These powders should not be finely powdered. Such powders should be double wrapped. In humid weather or when dealing with very deliquescent substances, for there wrapping in aluminium foil or plastic cover is advisable.

Efflorescent powders

Some crystalline substances liberate water of crystallization wholly or partly on exposure to humid atmosphere or during trituration and thus become wet or liquefy. Example of such substances include caffeine, citric acid, ferrous sulphate etc. the difficulty may be overcome by using corresponding anhydrous salt or an inert substance may be mixed with efflorescent substance before incorporating with other ingredients.

Problems pertaining to efflorescent powder include: water liberated when the drug or chemical is triturated may cause the powders to become damp or pasty. If water is released to the atmosphere because of low relative humidity, the drug loses its crystallinity and becomes powdery. Water of hydration is given off; a given weight of the resulting powder no longer contains the same amount of the drug. Hence strategies for handling efflorescent powders includes: storage and dispense of these powders in airtight containers. The anhydrous form of the drug may be substituted for the hydrate, but be sure to make appropriate dose corrections.

Eutectic mixtures:

These substances can be dispensed by two methods.

Dispense as separate set of powders with directions that one of each kind shall be taken as a dose

An equal amount of any of inert absorbent like magnesium carbonate, light magnesium oxide kaolin starch may be mixed with eutectic substance then blended together lightly with a spatula on a sheet of paper. When in addition to liquefying substances, other ingredients also present, the liquefiable substances should first be triturated together to form the eutectic mixture. Then the remaining ingredients of the prescription are incorporated and mixed together.

Incorporation of liquids

In some powders along with solids; liquid ingredients are necessary to add. Proper distribution of liquid in entire powder is necessary. In this case liquid is triturated with an equal weight of the powder and then remaining powder is added in several portions with trituration. Adsorbent such as light kaolin is incorporated to avoid this problem.

Liquid extracts and tinctures are evaporated to syrupy mass in a china dish. Lactose or some other suitable diluent is mixed and then continue the evaporation to dryness. Mix other ingredients. Another alternative is to substitute a liquid extract by a dry extract.

Incorporation of extracts

Some plant extracts are available as powders or as powders or as semisolid (for example, liquid extract of liquorice). In this case, powdered extracts have no problems and treated generally as powders. Semisolid extract should be mixed with an equal quantity of lactose and reduced to a dry powder by evaporation before incorporation with other ingredients. Careful heating, if present, to save potency of the extract is required.

Incompatible salts

Chemically incompatible salts when triturated together produce discoloration, chemical deterioration or loss of potency. To avoid this problem; minimum pressure is used while compounding such materials. Use a convenient method for mixing the powder like tumbling in a jar or spatulation on a sheet paper. Each substance should be powdered separately in a clean mortar and then combined with other ingredients gently. Otherwise such materials are powdered and dispensed separately.

Potent drugs

The substances having a maximum dose of less than one grain and poisonous substances are regarded as the potent drugs. Small quantities of potent drugs should not be weighed on dispensing balance. The potent drug is triturated with some diluent such as lactose in definite proportion to make a weighable quantity for each powder. Generally potent drug is reduced to fine powder and to this a equal quantity of diluent is mixed by thorough trituration in a mortar. Then the rest of diluent is incorporated in successive portions with thorough trituration each time. The whole of the diluent should never be added to the drug at one time otherwise the potent drug will not be mixed uniformly and thoroughly in the diluent.

For example: Dispense the following powder

Codiene phosphate 10mg

Make powder

The quantity of codeiene phosphate prescribed is very small and it is not possible to weigh it on dispensing balance. Minimum weighable quantity is 100mg

Finely powder and weigh 100mg of codeine phosphate and 900mg of lactose. Mix them in ascending order of their weight on a piece of paper with powder spatula. Out of 1.0 g of triturate, weigh 100 mg of each powder and pack of powder paper. Prepare five such powder, label and dispense.

Granulation powders

These are certain solid medicaments which are required to be administered orally in large dose. They cannot be prescribed in tablets and capsules because a large number of them will be required to take as a single dose, which is not possible. These medicaments are difficult to dispense as such in

powder form because of its bitter, nauseous and unpleasant taste. It is also difficult to convert it into liquid dosage form due to stability problem. The only alternative left is to convert this powdered medicament into granular form.

The solid medicaments are mixed with sweetening, flavoring and coloring agent. A suitable granulating agent is added to moisten the powders so as to make a coherent mass through sieve number 10 to make granules. Dry the granules are passed through sieve number 20 and store in a dry well closed wide mouth bottles.

Nowadays, various antibiotics like erythromycin, phenoxymethyl penicillin, ampicillin etc. which are unstable in solution are prepared in the dry granular form in which drug is mixed with suspending, sweetening, flavoring, coloring and granulating agents. The granules are prepared and packed in a special type of bottles with a specific direction on its label for the patient to add specified amount of freshly boiled and cooled water to dissolve it or shake well to form a homogenous solution. The label should also state the time limit within which the reconstituted preparation should be consumed.

Effervescent granules

Explosive mixtures:

Oxidizing agents such as potassium salts of chlorate, dichromate, permanganate and nitrate-sodium peroxide-silver nitrate and silver oxide explore violently when triturated in a mortar with a reducing agent such saturated sulfides-sulfur-tannic acid- charcoal. To avoid this problem, each salt is triturated separately or minimum pressure is used during trituration.

Evaluation of powder

Pharmaceutical powders are evaluated for following quality control parameters:

- Content uniformity
- Particle size and size distribution
- Flow property: Angle of repose, Flow rate Density: Bulk density, tapped density and true density Hausners ratio
- Moisture content
- Tensile and cohensive strength measurements
- Safety and efficacy.