BI- PHASIC LIQUID DOSAGE FORM (SUSPENSION)



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BIPHASIC LIQUID DOSAGE FORM

- Biphasic liquid Dosage Form contain 2 Phases. This includes undissolved drug and the solvent system(Vehicle).
- Undissolved phase is distributed throughout a vehicle and intended for oral administration.
- In this preparation this phase Is called 'Dispersed phase' and the vehicle is called 'Dispersed Medium'.
- It's also called internal phase or external phase respectively
- The need of biphasic liquid dosage forms arise when the medicaments are poorly soluble in the solvent medium.
- When solid medicament is distributed in the dispersion medium , the system formed is called SUSPENSION.
- When liquid medicament is distributed in the dispersion medium , the system formed is called EMULSION





SUSPENSION Ex: muddy water, mixture of dust particles and air EMULSION Ex: egg yolk, butter, mayonnaise

INTRODUCTION TO SUSPENSION

Definition:-

• A Pharmaceutical suspension is a heterogeneous system consisting of two phases in which internal phase is dispersed uniformly throughout the external phase.

• The internal phase consists of particulate matter that is essentially insoluble (having a range of size 0.5 to 5 microns) but dispersed uniformly throughout the continuous phase/ dispersion medium with aid of single or combination of suspending agent.

• The external phase (dispersion medium) is generally aqueous in some instance, may be an organic or oily liquid for non-oral use.

The Difference Between Solution & Suspensions:

• When the 2 substances totally mix it is called a solution.

E.g. Solute + Solvent = Solution

• (sugar) + (water) = Solution



• We then say sugar is soluble in water, it has dissolved.

- The particles in a suspension are insoluble
- Sometimes when we mix substances they stay in clusters. We therefore say it is insoluble in water.
- E.g. Chalk + Water = Suspension



• Eventually the particles sink to the bottom to form sediment.

TYPES OF INSOLUBLE SOLIDS

- There are two types of insoluble solids which constitute the internal or dispersed phase. These are
- 1. Diffusible solids these sediment sufficiently slowly to enable satisfactory dose removal after redispersion. e.g. Light kaoline, magnesium trisilicate
- 2. In diffusible solids- e.g. sulphadimidine and chalk.

These sediment too rapidly and require the addition of other materials to reduce sedimentation rate to an acceptable level.

SEDIMENTATION

•This is a phenomenon which occurs in dispersed system where the dispersed particles settle to the bottom of the container. This occurs because the particles are too large to remain permanently suspended in the vehicle.

 Therefore suitable suspending agents are added to retard this process

SUSPENDING AGENTS

- Suspending agents are substances that are used to keep finely divided insoluble materials suspended in a liquid media by preventing there agglomeration (coming together) and by imparting viscosity to the dispersion media so that the particles settle more slowly. Care must be taken when selecting a suspending agent for oral preparations as the acid environment of the stomach may alter the physical characteristics of the suspension and therefore the rate of release of the drug from suspension.
- They are various types of suspending agents

TYPES OF SUSPENDING AGENTS

1.NATURAL AGENTS :-

This class consists from

a. Animal source e.g. Gelatin

b. Plant source e.g.. Acacia, Tragacanth, Starch, sea weed (Alginates)

c. Mineral sources e.g. Bentonite, Kaoline

2.SEMI-SYNTHETIC AGENTS :-

These consist of substituted cellulose (minerals)

e.g.. Hydroxyethylcellulose , Sodium Carboxy methylcellulose , methylcellulose, Microcrystalline cellulose

3.SYNTHETIC AGENTS:-

They are synthetic polymers

e.g. carboxypolymethylene (carbopol), Polyvinyl Alcohol, Polyvinyl Pyrolidone iodine complex (PVC)

• Most suspending agents perform two functions

i.e. besides acting as a suspending agent they also imparts viscosity to the solution.

- Suspending agents form film around particle and decrease interparticle attraction.
- A good suspension should have well developed thixotropy.
- At rest the solution is sufficient viscous to prevent sedimentation and thus aggregation or caking of the particles.
- When agitation is applied the viscosity is reduced and provide good flow characteristic from the mouth of bottle.

ADVANTAGES OF SUSPENSION

• Suspension can improve chemical stability of certain drug. E.g. Procaine penicillin G

• Drug in suspension exhibits higher rate of bioavailability than other dosage forms.

Bioavailability is in following order,

•Solution > Suspension > Capsule > Compressed Tablet > Coated tablet

•Choice of solvent

• Suspension can mask the unpleasant/ bitter taste of drug. E.g. Chloramphenicol palmitate.

• Formulated for topical application. Ex. taclonex

DISADVANTAGES OF SUSPENSION

•Require shaking before use.

• It is bulky, therefore sufficient care must be taken during handling and transport.

- It is difficult to formulate
- Accuracy of dose is less reliable

• Storage of suspension leads to change in dispersion

IDEAL QUALITIES OF A GOOD SUSPENSION

- It should settle slowly, readily re-dispersed on gentle shaking of the container.
- It should pour readily and evenly from its container
- The suspended particles should not form a cake
- Suspended particles should be small and uniformly sized.
- Viscosity must not so high
- It should be chemically inert.

PHARMACEUTICAL APPLICATIONS OF SUSPENSIONS

Suspensions may be used pharmaceutically for a number of reasons. Some are given bellow;

- Suspension is usually applicable for drug which is insoluble or poorly soluble.
 E.g. Prednisolone
- suspension To prevent degradation of drug or to improve stability of drug.
 E.g. Oxytetracycline suspension
- To mask the taste of bitter or unpleasant drug when formulated in solution form. Drugs are formulated in as suspension which will be more palatable
 E.g. Chloramphenicol palmitate suspension
- Suspension of drug can be formulated for topical application e.g. Calamine lotion.

- Suspension can be formulated for parenteral application in order to control rate of drug absorption, E.g. penicillin procaine
- Vaccines as a immunizing agent are often formulated as suspension. e.g. Cholera vaccine
- X-ray contrast agent are also formulated as suspension.
 - E.g. Barium sulphate for examination of alimentary tract
- If the drug is unstable when in contact with the vehicle, suspensions should be prepared immediately prior to handing out to the patient in order to reduce the amount time that the drug particles are in contact with the dispersion medium. Eg Amoxicillin suspension

Classification of Suspensions

Suspensions are classified into four main classes according to its pharmaceutical use. These are:—

- (1) Oral suspensions
- (2) Parenteral suspensions
- (3) Ophthalmic suspensions
- (4) Suspension for external use

1. Oral suspensions : These suspensions are to be consumed by the patient by oral route. Oral suspensions generally contain flavouring agent and sweetening agent to mask the bitter taste of the drug. They are also made palatable by using a suitable derivatives of drugs e.g., chloramphenicol palmitate suspension is prepared to mask the bitter taste of chloramphenicol. Nowadays suspensions are available in the market in dry powder form and these are reconstituted by adding a specified quantity of freshly boiled and cooled water before use e.g., antibiotics in suspension for paediatric use.

Advantages 🕷

- (1) It is easy to swallow the suspended insoluble medicaments.
- (2) The insoluble derivatives in suspensions is more palatable than soluble derivatives in solution.
- (3) The bulky insoluble powders, such as kaolin and chalk can be administered in suspension in order to act as adsorbents of toxins or to reduce excess acidity in the gastrointestinal tract.

Disadvantages 🕷

- All suspensions are required to be shaken before measuring a dose.
- (2) The accuracy of dosage is less reliable as compared to solution.
- (3) The storage of suspension may lead to changes in disperse system, especially when there is fluctuations in temperature.

2. Parenteral suspensions : The suspensions which are administered by parenteral route are called parenteral suspensions. These suspensions are required to fulfil the following qualities:—

- (i) The particle size of the drug should be such that it can be easily pass through the needle of the syringe.
- (ii) There should not be any crystal growth in the suspension during its storage.

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- (iii) The concentration of solid particles in the suspension should be between 0.5 to 30%.
- (iv) The viscosity of the suspension should not interfere with its flow through the syringe needle.
- (v) The suspensions should be sterilised.

3. Ophthalmic suspensions : These are not commonly used as compared to eye-drops. These are prepared only in those cases, when the drug is insoluble in the desired solvent or unstable in liquid form. These suspensions must fulfil the following conditions:—

- (i) The particle size of the eye-suspensions should be fine enough so that it should be non-irritating to the eye.
- (ii) The suspensions should be sterilised.
- (iii) These suspension should be isotonic.
- (iv) These should have desired viscosity.
- (v) The suspension should be packed in a suitable container, so that it can be easily instilled into the eye.

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4. Suspensions for external use : These suspensions are meant for external use. e.g., lotions, inhalations, ear drops etc. These suspensions contain very small particles to avoid grittiness. Lotion containing suspended particles evaporate when applied to the skin leaving a light deposit of medicament on the surface. Lotions are easier to apply and less messy than many other semi-solid external preparations. Calamine lotion is a suspension type preparation which is applied on the skin to provide protective effect. Lotions which are meant for application on broken or inflamed skin should be free from harmful microorganisms.

PREPARATION OF SUSPENSION

Step 1:

• Suspensions are prepared by grinding the insoluble materials in the mortar To a smooth paste with a vehicle containing the wetting agent.

Step 2:

• All soluble ingredients are dissolved in same portion of the vehicle and added to the smooth paste to step1 to get slurry.

Step 3:

• The slurry is transformed to a graduated cylinder, the mortar is rinsed with successive portion of the vehicle.



Step 4:

• Decide whether the solids are suspended in a structured vehicle

• Flocculated and then suspended

Add the vehicle containing the suspending agent (or) flocculating agent

Step-5:



• Make up the dispersion to the final volume . Thus suspension is prepared.

FLOCCULATED SUSPENSION

- In flocculated system the individual particle are contact with each other to form loose aggregate & create network like structure.
- Rate of sedimentation is high.
- Sediment is loosely packed. When shaking it can be redisperse easily & reform the original suspension.
- Flocculated suspensions not be elegant because they are difficult to remove from bottles or vials & on transferring from the bottle the floccules remaining sticking to the side of the bottle.

Flocculated



DE-FLOCCULATED SUSPENSION

- In deflocculated system the individual particle are exist as separate entities.
- Rate of sedimentation is low.
- Sediment is tightly packed. When shaking it can not be redisperse easily & form the cake.
- Deflocculated suspensions be elegant. They have pleasing appearance because, the substance remain suspended for sufficient long time.







Deflocculated Suspension

- Pleasant appearance as particle are uniformly dispersed.
- 2 Supernatant is clear.
- 8 Particle experience repulsive force.
- 4 Rate of sedimentation is slow.
- h. Particle settle independently and separately.
- 6 Sediment is closely packed and form hard cake.
- 7 The re-dispersion of a sediment formed in a deflocculated suspension is difficult by agitation.
- 8. In potential energy curve it represent primary minimum.
- Bioavailability is relatively high.

Flocculated Suspension

- Unpleasant in appearance.
- Supernatant is cloudy.
- Particle experience attractive force.
- Rate of sedimentation is fast.
- 6. Particle settle as flocus.
- 6 Sediment are loosely pack net work.
- 7. The re-dispersion of a sediment formed in a flocculated suspension can easily be done by agitation
- In potential energy curve it represent secondary minimum.
- Bioavailability is comparatively less



STABILITY OF SUSPENSION

Factors that contribute to appreciable of a suspension include:

SMALL PARTICLE SIZE:-

- reduce the size of the dispersed particle increases the total surface area of the solid.
- The greater the degree of subdivision of a given solid the larger the surface area.
- The increase in surface area means also an increase in interface between the solids and liquids leading to an increase in viscosity of a system. Stability of suspension

INCREASING THE VISCOSITY :-

- Increasing the viscosity of the continuous phase can lead to the stability of suspensions.
- This is so because the rate of sedimentation can be reduced by increase in viscosity.
- Viscosity increase is brought about by addition of thickening agents to the external phase.
- It is important to note that the rate of release of a drug from a suspension is also dependent on viscosity.

TEMPERATURE.

 Another factor which negatively affects the stability and usefulness of pharmaceutical suspensions is fluctuation of temperature. Temperature fluctuations can lead to caking and claying.

ELECTROKINETIC METHOD:-

- The determination of surface electric charge or zeta potential of suspension is helpful to find out the stability of suspension.
- Certain zeta potential produce more stable suspensions because of controlled flocculation.
- Zeta potential can be calculated from the migration velocities of the particles measured by the electrophoretic method.