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A REVIEW: PHARMACEUTICAL SUSPENSION AND ITS ADVANCEMENT

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ABSTRACT

Additionally, pharmaceutical suspension is classified based on the nature of drug particles, particle size, and method of preparation. Various factors such as viscosity, sedimentation rate, and redispersibility affect the stability of the suspension. The formulation of the suspension involves selection of appropriate excipients, surfactants, and stabilizers to enhance the solubility and stability of the drug particles. Packaging of suspension is also crucial to prevent physical and chemical instabilities during storage. Furthermore, the review emphasizes the importance of regulatory requirements for pharmaceutical suspension. Good manufacturing practices (GMP) and quality control procedures are necessary to ensure the safety, efficacy, and quality of these formulations. The regulatory authorities also provide guidelines for the characterization, testing, and labeling of pharmaceutical suspension. In conclusion, pharmaceutical suspension is a widely used dosage form due to its high bioavailability and ease of administration. The properties, formulation, stability, and regulatory requirements of suspension are crucial to ensure the safety and efficacy of the medication.

KEYWORDS: Pharmaceutical suspension, Formulation of suspension, Preservation of suspension, Nanosuspension.

INTRODUCTION

Solutions, suspensions, and emulsions are just a few of the several forms of oral liquids. These liquids depend on the solubility, stability, and composition of the medical ingredient.

Solvents, stabilizers, viscosity modifiers, preservatives, sweeteners, colouring agents, and aromatizers are among the additional ingredients. [1]

An internal phase that is evenly distributed throughout the external phase makes up a pharmaceutical suspension, which is a coarse dispersion. The interior phase, which is made up of insoluble solid particles suspended by one or more suspending agents, For non-oral use, the external phase (suspending media), which is often aqueous, may also be an organic or oily liquid.[2] They typically consist of a finely split solid suspended in a liquid or semi-solid medium that makes up the continuous phase, with individual particles ranging in size from 0.5 to 5.0.[3] When used as a dosage form, suspension is created by dispersing solid particles in an oily or aqueous liquid where the particles are either fully insoluble or only marginally soluble.[4]

Particle-particle interactions cause pharmaceutical suspensions to be thermodynamically unstable. Povidone, microcrystalline cellulose, sodium carboxymethylcellulose, acacia, tragacanth, and okra gum are examples of suspending agents that should be used in order to improve the viscosity of the disperse medium and prevent sedimentation of the suspended medication particles. Suspending agents make it simple to redisperse the settling drug particles, keeping them uniformly suspended for precise dosing.[5] Because of their intrinsic structural instability, issues with manufacturing and packing. Suspensions may be intended for parenteral usage, external application, or oral delivery.[6] Particle sizes in suspensions used for ophthalmic purposes must not exceed 10 m; if they do, the patient will experience discomfort and agony while receiving the medication. The suspension used for the parenteral method must have smaller particles that can readily flow through the syringe's needle.[7] Oral suspension has a substance or substances that are active, suspended in an appropriate carrier. While kept, suspended solids may gradually separate but can be easily redispersed. Wide mouth bottles should be used for packaging.[8]

Fig. 1: Example of suspension - Sucralfate & Oxetacaine Suspension.[3]

Advantages of suspension[1,7,1]

1. It masks the bitter taste of drugs like chloramphenicol.
2. The chemical stability of some drugs can be improved by making suspensions, such as: Penicillin G.
3. Effective intramuscular long-acting therapy.
4. The use of co-solvents can be avoided.
5. The elderly are easy to swallow.
6. Drugs that are unstable in aqueous solution can be made into suspension.
7. Suspension is the dosage form of water-insoluble drugs, and non-aqueous carriers are not accepted.
8. The suspension, acting as a reservoir, is absorbed in the systemic circulation over a longer period of time.
9. The suspension improves the bioavailability of the drug.
10. Pharmaceutical suspensions have higher bioavailability than other dosage forms. Bioavailability is given in the following order

Solutions > Suspensions > Capsules > Compressed Tablets > Coated Tablets

11. The duration and onset of action can be controlled. For example protamine zinc insulin suspension.

Disadvantages of Suspension[2,7]

1. It is difficult to formulate.
2. Sufficient care is required during handling and transportation.
3. Physical stability, settlement and compaction can cause problems.
4. Potential for uneven and inaccurate dosage.
5. Consistent and accurate dosing can only be achieved when the suspension is packaged in unit-dose form.

Classification[1]

1. Based on the proportion of solid particles

a. Diluted suspensions (2 to 10% w/v solids)
b. Concentrated suspension (50% w/v solids)

2. Based on generic classes

a. Oral suspension
b. Suspensions for topical use

c. Parenteral suspension

3. According to the size of solid particles

a. Colloidal suspensions.

b. Coarse suspension.

c. Nanosuspensions.

4. Electrokinetic properties based on solid particles

a. Flocculation of suspensions

b. Deflocculated suspensions

a. Oral suspension

Oral suspensions are liquid preparations. It consists of one or more active ingredients suspended in a sweetened, flavored, sometimes colored and viscous carrier for oral administration. Some active ingredients may be in solution. The solids content of oral suspensions can vary widely. For example, antibiotic preparations, antacids and suspensions contain relatively large amounts of suspended material for oral administration. (2) Pictures or photographs of oral suspensions are liquid formulations for oral administration containing more active ingredients contained in a preferred, occasionally colored, usually viscous medium. For example, 5 ml of Macron solution contains 750 mg of the active ingredient (atovaquone) distributed. Some active ingredients in multi-ingredient oral solution may dissolve.

b. Suspensions/Topical Suspensions

Topical suspensions are preparations made for dermatological, cosmetic, and protective uses. These suspensions are usually colored and may contain some flavor, but lack the sweetness and pungent taste typical of oral administration. The dispersed phase concentration can be greater than 20%. Topical suspensions can be liquid solutions, such as calamine lotion, that are designed to evaporate quickly from the skin, leaving behind a small amount of active ingredient. A paste is a semisolid suspension containing concentrated particles, usually dispersed in a paraffin primer. Powdered drugs can also be suspended in an emulsion base, such as B. in zinc cream.[9]

c. Parenteral Suspension/Injection Suspension

A system in which insoluble drug particles are suspended or discarded in an aqueous or vegetable oil vehicle prior to administration to the patient. Most parenteral solutions are intended for intramuscular or subcutaneous administration. For example, injectable triamcinolone actinide suspension and insulin-zinc suspension are injected subcutaneously and intramuscularly, respectively. Solid particles in parenteral suspensions range from 0.5% to 30% by weight.[9]

Properties of a Good Pharmaceutical Suspension[3,6]

1. Sediment formed during storage is easily redispersed.
2. After gentle shaking, the drug will remain in suspension long enough for accurate dosing
3. The suspension can be poured.
4. The suspended particles are small and uniform in size, so the product does not feel grainy.

Types of suspensions

1. According to the route of administration

Oral suspensions should be consumed orally, thus they need to have the right flavouring and sweetening ingredients.

Topical suspensions should not contain any grit since they are intended for external use.

Parenteral suspensions must be sterile and have the ability to be syringed.

Ophthalmic suspensions need to have very small particles and be sterile.

2. Based on the makeup of the dispersion phase and the techniques of preparation

According to whether they contain diffusible solids, indiffusible solids, poorly wettable solids, precipitate-forming liquids, or results of chemical reactions, the suspensions are categorised.

3. According to nature of sediment

Flocculated Suspensions

This kind of solid dispersion results in a network-like structure of solid particles in the dispersion medium. No firm cake is formed by the aggregates. Due to the high rate of sedimentation and the loose, easily redispersible material that is generated, these aggregates sink quickly. Because the dispersed phase frequently separates from the dispersion medium, the suspension is not graceful. Because of this, it is preferred that flocculation be done under controlled conditions to maintain a balance between the pace of sedimentation, the type of sediment that forms, and the pourability of the suspension.[6]

Non flocculated Suspension

The solid particles are present in a distinct way in the dispersion medium of non-flocculating suspensions.[7] In this type, the solid particles reside in the dispersion medium as distinct entities. The sediments create a dense cake. The sedimentation rate of the solid medication particles is modest, and once sediments have developed, it is difficult to redisperse them. Because the dispersed phase is sustained for such a long time and seems uniform appearance.[6]

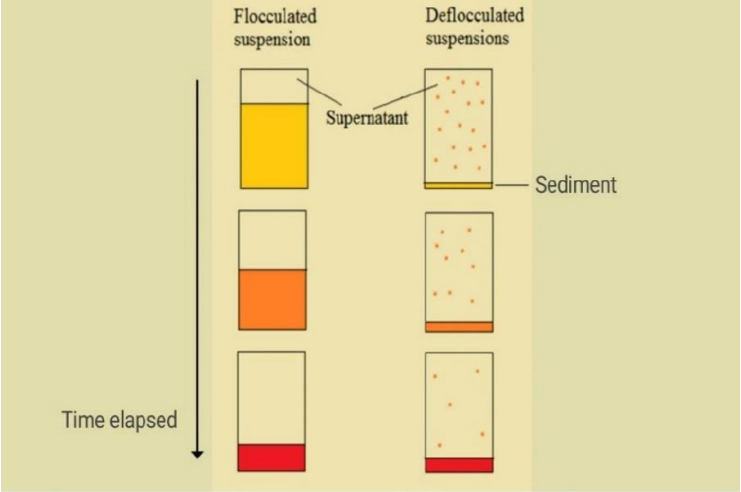

Fig. 2: Flocculated & Deflocculated Suspension.[1]

Formulation of Suspensions

The following three actions can be followed to guarantee the formation of a classy pharmaceutical suspension:

1. Regulate the particle size. To prepare this on a smaller scale, crush the components to a fine powder using a mortar and pestle.
2. Use a thickening agent to make the vehicle viscous by utilising viscosity-suspending agents.
3. Use a wetting agent.[3]

Excipients Used in Pharmaceutical Suspension

The following excipient categories could be employed in the creation of medicinal suspensions:

1. **Solvents/Vehicles:** Solvents (or vehicles) are important substances that serve as a base for the dissolution or dispersion of pharmaceuticals and other excipients. Purified water is the most often utilized ingredient in the manufacture of medicinal solutions.

2. **Buffering Agents:** In order to prevent potential pH shifts in formulations, buffering agents, also known as pH modifiers, are added to suspensions.
3. **Preservatives:** To shield aqueous solutions from microbiological contamination, preservatives are frequently added. Preservatives such parabens, alcohol, glycerine, propylene glycol, and sorbates are frequently employed in medicinal solutions.
4. **Antioxidants:** In some pharmacological solutions, antioxidants are necessary to improve the chemical stability of the therapeutic agent, which can be change by oxidation.
5. **Wetting Agents/Surfactants:** Wetting agents are employed to increase the liquid's flow across the surface of the particle, which in turn increases the uniformity of the drug particles' dispersion throughout the formulation. Polysorbates and sorbitan esters are a few examples.
6. **Antifoaming Agents:** These excipients stop foam from forming while suspensions are being made or when powder is being reconstituted for suspension. Simethicone, organic phosphates, alcohols, paraffin oils, stearates, and glycols are a few examples.
7. **Flocculation Modifiers:** These are neutral electrolytes that can stop suspended particles from clumping together. Sodium or potassium chloride, aluminium chloride, calcium salts, citrates, etc.
8. **Suspending agents and viscosity modifiers:** These are hydrophilic colloids that are added to a suspension to increase viscosity, limit agglomeration, and reduce sedimentation. Examples include cellulose derivatives, acacia, and xanthan gum.
9. **Flavouring Agents:** To conceal the taste of medicinal solutions, flavouring agents such as peppermint, lemon oils, butterscotch, "tutti-frutti" flavour, etc. are added.
10. **Sweeteners:** To increase overall palatability and to mask any unfavourable tastes of the medicine that has only partially dissolved, sweeteners are frequently added to suspensions. Sorbitol, corn syrup, sugar, saccharin, acesulfame and aspartame are a few examples.
11. **Colourants:** These are included to give the finished product a more appealing appearance.
12. **Chelating Agents:** To prevent medicinal components from being damaged by catalysts that quicken oxidative reactions, chelating agents are added to pharmaceutical solutions. Production of pharmaceutical suspensions.[3]

Stability of suspensions

The state in which particles do not agglomerate and stay evenly dispersed from dispersions is known as the physical stability of suspension. The suspension should have additives added to it to make resuspension easier in order to obtain this perfect state. An illustration would be

the flocculation of positively charged particle dispersion when an anionic electrolyte, such as monobasic potassium phosphate, is added. By adding carboxymethylcellulose, Carbopol 934, veegum, tragacanth, or bentonite either alone or in combination, the system's physical stability is improved. Since the bulk of hydrophilic colloids are negatively charged, there is no physical incompatibility that has been observed. These work well with flocculating agents that are anionic.[1]

Preservation of Suspension

The most frequent cause of microbial contamination is water. As a result, microorganisms can grow on any pharmacological formulation that contains water. Additionally, naturally occurring additions like acacia and tragacanth may contain spores and microorganisms. Preservative action may be reduced as a result of contact with suspending agents or preservative adsorption onto solid medication particles. Chloroform water, benzoic acid, and hydroxybenzoates are all helpful preservatives.[3]

Quality control tests for suspensions[1,6]

1. Sedimentation volume

The primary factor in determining whether a suspension is acceptable is redistribubility. Two of the most used fundamental evaluation techniques are the measurement of the sedimentation volume and the ease of redispersion. The simple ratio of the height of the sediment to the height of the starting suspension is the sedimentation volume. The better the value, the more suspendable it is.

2. Distribution of particle sizes and sizes

The increase in particle growth caused by the freeze-thaw cycle method used to evaluate suspension for stress testing for stability testing may be a sign of what would happen during prolonged storage. Studying the changes in absolute particle size and distribution is crucial. Using the sedimentation method; you may measure the size of a particle in relation to how quickly it settles through a suspending medium.

3. Research on rheology

Rheologic techniques are utilised to identify the suspension's settling behaviour. To measure the viscosity of suspensions, a Brookefield viscometer is employed. It is composed of a spindle for a T-bar that is lowered into the suspension. The dial reading, which measures the resistance the spindle encounters at varying suspension levels, is taken note of. Additionally,

this method identifies the level of the suspension where the structure is stronger due to particle aggregates.

Nanosuspension

The form of suspension known as a nanosuspension is made up of pure medication particles dispersed in water. These are colloidal dispersions of surfactant-stabilized nanoscale drug particles.[1] In aqueous or non-aqueous vehicles, bottom-up (such as precipitation) or top-down (such as wet milling) methods can be used to create nanosuspensions. High pressure homogenizers, such the piston gap homogenizer, have proven to be a very effective technology for the creation of nanosuspension. This method is based on the cavitation forces created when an emulsion or dispersion is driven through a tiny opening. Pressure, the number of cycles, and in the case of suspension, the hardness of the drug particles all affects the nanosuspension's particle size.[10]

Increased dissolving rate and subsequent bioavailability afterrelease should be the result of the submicron size of nanosuspension particles and, consequently, the larger surface area of the drug particles. However, stratum corneum penetration by nanosuspensions is not possible.[11] Nanosuspensions are colloidal dispersions containing medication particles that are nanoscale in size and are stabilised by surfactants.In nanosuspensions, the poorly water-soluble medication is suspended in a dispersion without any matrix components. These can be used to improve a drug's solubility if it is poorly soluble in lipid or water-based systems.[12]

Advantages of nano suspension

1. Make medications more soluble and bioavailable
2. Appropriate for hydrophilic medicines
3. More medication can be loaded
4. It is possible to lower the dosage.
5. Make medications more physically and chemically stable
6. Gives a medication targeting that is passive.[12]

Packaging of Suspension

The stability and acceptability of the suspension are specifically impacted by the packaging materials. Today's chemists must be knowledgeable with a wide range of packaging materials due to the development of drug regulations on a global scale and the intricacy of dosage forms. To maximise the suspension's shelf life, the industrial chemist needs to be aware of

how different material qualities interact with one another. Pharmaceutical suspensions are frequently stored in wide-mouth bottles with spaces between the walls to allow for optimal mixing while shaking. Parenteral suspensions are packaged in glass ampoules or vials. The ideal kind of packaging material is inert. The product should be effectively protected from light, air, and other elements. To distribute the product with ease, the transportation method must be affordable and efficient.[7]

Materials Used for Packaging

Most suspension packaging is composed of different types of glass and plastic.

Plastic

Nowadays, plastic is frequently used for packaging due to its many benefits over glass. Plastic is flexible, lightweight, and unbreakable. Materials including polyethylene, PVC, polysorbate, and others are used to make plastic packaging. When selecting plastic as a suspension packing medium, the following factors are taken into account: Leaching, penetration, chemical processes, sorption, and modifications to the physical properties of plastic.

Glass

Non-parenteral suspensions are typically created using borosilicate glass and soda lime. Amber-colored glass containers are used to pack compositions that are susceptible to light degradation. Amber glass blocks the flow of UV light through the composition.

Disadvantage of glass

- They are difficult to transport and handle, and they are easily broken.
- The following types of glasses and additives are used to provide amber colour
- Soda lime: FeO+ sulphur
- Borosilicate: FeO+ TiO2

Closure

All containers, with the exception of ampoules, must have an elastomeric closure. Closures must work with the formulation. Processing shouldn't compromise the integrity of the seal or closure. Rubber and plastic can be used to make a closure.[7]

Applications of pharmaceutical suspensions[1,2,3,6,7]

Uses for medicinal suspensions include:

1. To cover up a bitter or unpleasant drug's taste. e.g. chloramphenicol palmitate.
2. Insoluble derivatives or non-aqueous carriers can be utilised to create suspensions for medications that are unstable in aqueous solutions.
3. Suspension dosage forms are the greatest option for giving insoluble medications to patients who are younger or older.
4. It can be administered via a variety of methods, including oral, parental, and tropical.
5. Those medications that are not stable in a dispersion medium for an extended period of time are reconstituted as suspensions to shorten the time the drug particles are in contact with the dispersion medium
6. Drugs with extremely low solubility can be made into suspensions.
7. The medication needs to be dissolved into a liquid form if some persons have trouble swallowing solid dosage forms.
8. Drugs in insoluble forms can delay the onset of their effects by delaying the drug's rapid deterioration in the presence of water.
9. The absorption rate of drug from gastrointestinal tract is quicker in suspension because drug is delivered in finely divided form.
10. Contrast media use for the diagnosis purpose is also given in the form of suspension. barium sulphate for examination of alimentary canal.
11. Suspension is typically used for drugs that are poorly soluble.
    e.g. Prednisolone suspension.
12. To stop drug deterioration or to increase drug stability. e.g. oxytetracycline suspension.
13. Drug suspensions can be designed for topical application, such as in calamine lotion.
14. To regulate the rate of drug absorption, suspension can be created for parenteral administration.
15. Vaccines are frequently prepared as suspensions for use as immunisation agents.
    e.g. Vaccine against cholera.
16. X-ray contrast agents are also made by suspensions,
    e.g. Barium sulphate, is used to examine the digestive system.

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