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A REVIEW ON SUSPENSIONS

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ABSTRACT

Particles of insoluble solid drug serve as the dispersed or internal phase of a drug formulation. Particles in the internal phase vary in size from 0.5 to 5 m. An effective dosage form's efficacy is mainly determined by how well it's formulated and how readily the active medication or medicine isavailable to patients. An oral suspension is a liquid dosage form that includes one or more active compounds suspended in an appropriate carrier. They include antacids, antibiotics, analgesics, antihelminthics, anticonvulsants, and antifungals. Particles less than 5m in size are easier to dispense via a syringe. Insoluble medication suspensions may be applied externally as well, usually as a protective agent. Lotion architecture is easier toapply with suspensions since they are less untidy. It may be used as inhalations, ear drops, and ophthalmic products as well as lotions.

KEYWORDS: Oral suspension, liquid dosage form and lotions.

INTRODUCTION

There are finely split insoluble solid drug particles that are homogeneously distributed in a liquid or semi-solid media to produce a pharmaceutical suspension that is biphasic liquid or semi-solid dose form. Particles of insoluble solid drug serve as the dispersed or internal phase of a drug formulation. Particles in the internal phase vary in size from 0.5 to 5 m.[1] In order to ensure that the dispersion is uniformly distributed throughout the medium or vehicle, appropriate suspending agents may be used alone or in combination. An effective dosage form's efficacy is mainly determined by how well it's formulated and how readily the active medication or medicine is available to patients. The factors that directly affect suspension formulation and, as a result, drug bioavailability, must thus be the focus and subject of discussion. Thereby attempting to talk about suspension dosage form formulation and bioavailability characteristics in this communication, the authors.

The following prominent characteristics of a pharmaceutical suspension dosage form make it acceptable.[2]

The medication particles in suspension should not settle out quickly.

Shaking the container will redistribute the particles that have settled to the bottom without forminga hard cake.

The suspension should be able to be poured from the container without becoming excessively viscous.

Smoothness and elegance are required for this product's look.

Chemical and physical stability are important considerations when choosing a material.It has to have a good colour, smell, and taste.

Externally applied suspensions (such as lotions) should be fluid enough to distribute readily over the skin without dripping off the top.

viii) During sterilisation, injectable suspensions should not lose their effectiveness.

ix) The particle size must be stable throughout the course of the shelf life. As compared to alternative dose forms, suspension has many benefits.[2]

It is possible to distribute suspensions of medicines that are unstable or degradable in solution.

As an example, corticosteroids suspension is the preferred dose form when non-aqueous vehiclesare not an option.

It is best for bitter-tasting medicines like chloramphenicol palmitate, which has a disagreeable tasteand odour.

As an example, consider Protamine zinc-Insulin, which acts as a reservoir to keep a medication inthe systemic circulation for a long time.

v) When compared to an equal dosage of a tablet or capsule, suspension increases a drug'sbioavailability.

Suspension classification based on method of administrationSuspension administered orally.

Liquid dosage form that includes one or more active compounds suspended in an appropriate carrieris known as an oral suspension. Standing still may cause suspended particles and/or medicines to separate, but shaking them can quickly redisperse them. 125-500 mg/5 ml of the solution are common doses for these suspensions, which may be used to deliver antibiotics. The concentration of suspended medicines may be greater in paediatric drops. Oral suspensions may be created for a wide range of medications, including antacids, antibiotics, analgesics, antihelminthics, anticonvulsants, and antifungals. Oral paediatric suspensions include medications such as azithromycin and ofloxacin.

Advantages
When compared to tablet and capsule medications, suspended insoluble powders are much easier for children and the elderly to use by just swallowing them whole.

In comparison to tablets and capsules, the suspension provides quicker dissolving required forabsorption.

Water-insoluble medicines may be able to address the palatability and stability problems.

A appropriate flavouring and sweetening ingredient may be used in the formulation to conceal the bitter taste of the medication.

Suspension injectable (ii)
The medication is disseminated in a liquid media to create injectable suspensions. They have a long shelf life and are sterile, pyrogen-free, and chemically and physically stable. They are injected intravenously and subcutaneously. To avoid vaso-occlusion, they aren't given intravenously. They typically have a drug concentration of 0.5-5.0 percent and may be injected with a hypodermic needle with no difficulty. Particles less than 5m in size are easier to dispense via a syringe. The medium's viscosity is also maintained as close to zero as possible to ensure that particles move freely. Benzathine penicillin G and Procaine benzyl penicillin G are examples of antibiotics administered intramuscularly. Procaine penicillin G was sometimes called benzathine penicillin G. Another example of an antidiabetic medication used to extend the drug's availability in the systemic circulation is Protamine Zinc-Insulin suspension, a sterile insulin solution modified by the addition of zinc chloride and protamine sulphate. Toxoids, on the other hand, are chemically modified toxins from the pathogenic microorganism that are no longer toxic but possess the antigenic property to stimulate the anti-toxin formation, for example Diphtheria, Botulism, and Tetanus toxoids. Vaccines are immunising agents that are a dispersion of killed causative microorganism (e.g. Cholera vaccine). Toxoids are produced into a suspension dosage form by adsorbing them onto a substrate such as aluminium hydroxide or phosphate.

Advantages
Drugs that are insoluble in common solvents are therapeutically used (i.e. water, water miscible andwater immiscible).

As opposed to solution dosage forms, the drug's chemical stability is improved by this method.
c) Possibility of establishing a depot.
(d) Bypassing the first-pass effect is possible.

iv) Suspension applied externally
Dermatological, cosmetic, and protective products utilise externally administered solutions that are intended to be applied topically. Such a suspension must spread readily and not be too fluid to run off the skin's surface when applied to the body's surface. Calamine lotion is a typical example of a protective suspension that also has a cosmetic aspect to it. In order to be used on damaged skin, suspension lotions often have to be microorganism-free. Lotion architecture is easier to apply with suspensions than with other semi-solid external preparations since they are less untidy. It may be used as inhalations, ear drops, and ophthalmic products as well as lotions.

Advantages
Insoluble medication suspensions may be applied externally as well, usually as a protective agent. The electro-kinetic properties of solid particles is used to classify suspensions.[4] I Suspension with flocculant Flocculation is a kind of architecture that is created when electrical repulsion between particles in suspension weakens due to the presence of a strong attraction force. When this occurs, the particles with less repulsive force begin to approach one another, forming a loosely aggregated structure known as a floc. Because a floc or floccule is made up of a high number of small particles connected together to form a larger network, sedimentation proceeds quickly. During sedimentation, the dispersion medium may pass through the floccules' loose porous structure. In addition, the floccules capture a significant quantity of liquid. This means that the ultimate sediment volume will be substantial, allowing for easy re-dispersion with just little shaking. In spite of the fact that floccules settle more quickly, flocculated particles create a lattice structure that prevents them from compacting and forming a cake.

Deflocculated suspension is another term for it.
Individual particles in a deflocculated suspension stay discretely separated and sink slowly. Particles settle slowly in suspension, thus no liquid medium can entrap them, and as a result, the suspension gets compressed, resulting in cake formation. Even with modest agitation, this cake may be tough to re-distribute. Caking is a

severe problem with physical stability that occurs whenobjects are suspended in air. This solution also has the typical property of the supernatant remaining hazy after shaking for an extended period of time. This is mainly because the suspension's tiniest particles settle at such a sluggish pace.

Creating a Suspension Formula

Whether a suspension is flocculated or deflocculated affects its formulation. A flow chart, like the one shown in fig. 3, may help visualise formulation. To create a suspension, people often use one of three methods. Structured vehicle, controlled flocculation and controlled flocculation in the structured vehicle are the three methods.

flocculation under strict supervision

Flocculation is the process of bringing particles scattered in a liquid into loose contact or adhesion. Attractive and repulsive interactions between the liquid medium's scattered particles are precisely balanced to produce this phenomena. This flocculation may be regulated by maximising the attraction force over the repulsion force, resulting in a bigger cluster or a network-like structure..... Flocculation has a bad reputation, yet managing it may often lead to a better-featured suspension than one that has been deflocculated. Contrary to popular belief, an unchecked flocculation may result in too much precipitate and a reduced gloss while simultaneously increasing viscosity. In order to create a stable and therapeutically effective dosage form, it's essential to keep the flocculation under control.

a) Electrolytes, b) Surfactants, and c) Polymers are flocculating agents that may be required[5] to produce regulated flocculation.

first, electrolytes

To change the zeta potential of the suspended particles, the electrolytes are used. ZETA potential is defined as the difference in potential between particle surface and the electro-neutral area underneath it (shear plane) in a dispersion. The electrical barrier between the scattered particles decreases as the electrolytes lower the zeta potential, and the particles become closer to one another. As a consequence, there will be flocculation in the affected area. Volatility affects an electrolyte's flocculation properties. One thousand times more powerful than the monovalent ions are divalent ions, which are 10 times more powerful. Trivalent ions are more effective, but their usage is restricted due to their toxicity. Sodium salts of chlorides, acetates, phosphates, and citrates are among the most often utilised electrolytes as flocculating agents. To accomplish flocculation, the electrolyte concentration must be at its highest possible level; otherwise, any surplus may reverse the process and lead to deflocculation. For Bismuth subnitrate flocculation and deflocculation, a monobasic potassium phosphate electrolyte concentration is indicated in fig. 4. (KH_2PO_4).

Water disperses the positive surface charge of bismuth subnitrate particles, creating a strong force of attraction between neighbouring particles. This results in a deflocculated texture for the bismuth subnitrate suspension. The apparent zeta potential correlates strongly with sedimentation volume, caking, and flocculation when a series of bismuth subnitrate suspensions is produced with increasing concentrations of monobasic potassium phosphate. Because monobasic potassium phosphate provides a negatively charged phosphate anion for adsorption, the positive zeta potential of the solution diminishes as the electrolyte concentration increases. Bismuth subnitrate suspension that has been previously deflocculated gets flocculated when a certain concentration range of monobasic potassium phosphate is reached. The lack of caking and an increase in sedimentation volume are both signs of this change. As more electrolyte is added, the suspension's zeta potential decreases until it is zero, at which point it rises in the opposite direction. All of the bismuth subnitrate particles act like a negatively charged species when the zeta potential is sufficiently negative, reintroducing the repulsive force as the dominant property. The sedimentation volume decreases as the suspension gets deflocculated. Finally, there is evidence of caking, which indicates that the suspension has a deflocculated texture.

b) Substances that function as surfactants

In terms of flocculation, both ionic and non-ionic surfactants are effective. As the surfactant concentration increases, it lowers the interfacial tension between the liquid medium and the solid drug particles, decreasing surface free energy. If this happens, dense agglomerates may develop. Van der Waal's force attracts particles with less surface free energy together, and this results in the formation of a loose agglomeration at a certain surfactant concentration. A flocculated suspension isthe product of ionic surfactants, which work by neutralising the charge on individual particles.

Liquids may displace an adsorbed layer of air from a solid drug particle's surface and facilitate wetting when surfactants lower interfacial tension. As a result, the surfactant concentration must be carefully regulated to produce dispersion while simultaneously facilitating wetting and acting as a deflocculating agent. There are many surfactants that may be employed to regulate flocculation, as shown in Table 2.

Polymers (c)

A polymer is a substance with a large molecular weight and a lengthy chain of bonds. Their primaryfunction is as a flocculant. As with inorganic electrolytes, the mechanism of polymer-induced flocculation is not well known. When a polymer is present, its function is determined by the polymer's affinity for the particle surface, as well as its charge, size, and orientation in the ongoing medium. The hydrocarbon backbone of many polymers contains polar functional groups. Polymer

molecules may thus attach to particle surfaces and remain in contact with a liquid continuous media as a consequence of that. In the presence of polymers, suspensions may be either flocculated or deflocculated. The zeta potential of a particle may be affected by an ionic polymer in a way that inorganic electrolytes cannot. Polymers have a flocculating function because they bridge the surfaces of distinct particles. When the concentration is raised, more particle binding sites become accessible, allowing for more inter-particle interactions to be formed. The optimal flocculation and sedimentation volume occurs when the concentration is somewhere in the middle. The particle surface is completely covered with polymer at high concentrations, and there are insufficient binding sites left to allow interparticle bridging, resulting in poor flocculation. This high polymer concentration also inhibits the tight interaction of individual particles via a process known as steric stabilisation. As a result of energetically unfavourable circumstances, adsorbed polymers have the capacity to inhibit particles from approaching too closely and adhering together. A suspension with a high polymer content that deflocculates with a tiny sedimentation volume would be an example of this (fig. 5). The degree of flocculation may also be influenced by the polymer's conformation in the continuous phase. The polymers with a linear phase conformation are more efficient flocculants than the coiled polymers at concentrations where flocculation takes place. To produce flocculation, polymer and inorganic electrolyte mixtures are often employed. Electrolytes, when employed in conjunction with polymers, increase the flocculation sensitivity of dispersed solid particles.

a vehicle with a defined structure

Natural and synthetic gums are dispersed in water to form aqueous structured carriers. The viscosity of the aqueous media rises when the gums are distributed uniformly. Because of this, thickening agents are another name for them. Particle settling is slowed down by the continuous medium's thickness because of this. As a result, suspending agents are another name for structured vehicles. Note that excessive viscosity may make pouring and administering the medication difficult. Drug absorption may be affected as well, since polymeric analogues may adsorb to the particle's surface and slow down disintegration.

The use of a structured vehicle allows for the creation of a suspension that is both dimensionally and physically stable. To keep the particles defloculated, the vehicle was built specifically for this purpose. Individual particles are captured by the vehicles, which then translate them into a deflocculated suspension with the goal of preventing any settling. However, in reality, there is some sedimentation. Shear-thinning property is present in structured vehicles due to their pseudoplastic rheological nature, which makes it easier to reconstruct the suspension into a uniform dispersion. When shear is given to the suspension, it flows out of the container easily, ensuring a consistent distribution of particles in each dosage. However, owing to their high viscosity and lack of syringe ability, structured vehicles cannot be used in the formulation of suspensions for the parenteral route. Methylcellulose, carboxymethylcellulose, sodium carboxymethylcellulose, acacia, gelatin, and tragacanth are among the most frequently utilised polymers in pharmacological solutions as structured vehicles. Non-toxic, pharmacologically inert, and compatible with a broad range of active chemicals, these polymers are ideal for a variety of pharmaceutical applications.

Fluctuation in well-built automobiles

Suspensions with distinct solid particles may be considered stable from the perspective of stability. However, because of its size, sedimentation of solid particles happens over time. The more surface free energy there is, the smaller the particle has to be. The energy associated with these smaller, but very energetic, particles is released. So, the particles are getting closer together and forming a densely packed structure as a consequence. As a result of colloidal particles, the structure is dense and heavy, with sediment at the bottom and smaller particles filling in the gaps left by the bigger particles. The electric repulsive barrier is broken by the weight of the particles above it pressing down on the particles at the bottom. As a result, a firm cake forms, and shaking it is difficult to disperse.

Because of the way a structured vehicle is built, it has a deflocculated suspension by design. As a result of this development, if the flocculation principle is used, it may result in floccules that settle quickly yet disperse readily. We require a flocculating agent or flocculent with the right charge and a hydrocolloid as a protective colloid for effective flocculation in the structured vehicle. To begin with, flocks are formed when negatively charged flocculants are used to create a stable solution that contains positively charged medication particles. After that, a hydrocolloid suspending agent with a negative charge, such as Carboxymethylcellulose, Carbopol 934, Veegum, Tragacanth, or Bentonite, is used. A stable suspension was created since the flocculent and suspending agent are both negatively charged and therefore compatible. It is necessary to use a positively charged flocculent to create flocks if the medication particles are negatively charged. Using a negatively charged suspending agent will result in an incompatible product if this scenario is not handled properly. The flocculent's flocculating and protecting properties will be weakened over time as a result of the suspension agent's degradation. Use of positively charged suspending agents such as gelatin, fatty acid amine, and others is necessary to prevent this scenario. Because the flocculant and suspending agent are positively charged, a stable suspension will result if they are combined. Another method that may result in a stable suspension is possible. This method coats the drug particles initially with a positively charged protective colloid, regardless of whether the drug particles are positive, negative, or

neutrally charged. All charged particles covered with a positive colloid will be transformed as a result of this procedure. A stable suspension may currently be made using a negatively charged flocculant.

Agent has been suspended indefinitely.
The sedimentation rate of a stable suspension should be acceptable. A appropriate suspending agent is needed to regulate the sedimentation rate. High viscosity at low shear rate, and low viscosity at high shear rate are desirable in a suspending agent. The agents should display pseudoplastic flow behaviour and thixotropy from a rheological standpoint. In a 50:50 mixture, carboxymethyl cellulose and micronized bentonite exhibit the aforementioned rheological characteristics. Pseudoplastic flow behaviour may be seen in hydrocolloids such as methyl cellulose, sodium carboxymethyl cellulose, gelatin, tragacanth, and alginates. They enhance the suspension's viscosity, which delays settling. While improper usage of such a polymer may increase the in vivo diffusion rate, solubility, and ultimately absorption of the medication, it may also decrease thedrug's absorption rate. It is necessary to add thixotropic ingredients like sodium bentonite magma and colloidal silicon dioxide to increase the apparent viscosity and therefore the yield value of the solution. Because there is no flow below the yield value, the high viscosity slows sedimentation while it is at rest. A shear force greater than the yield value, on the other hand, causes the thixotropic structure to disintegrate and the apparent viscosity to decrease. When the container is placed on a shelf, thixotropy takes over, and the suspension goes from having a sol-like consistency to having a gel-like one.

CONCLUSION

Pharmaceutical suspensions now account for a significant portion of all dosages. It may be administered orally, externally, or intravenously. It is thus a difficult job to optimise the formulationparameters for this dosage form. Bioavailability problems must be addressed if optimised formulation is to be successful in achieving its therapeutic goal.

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