Available online on 15.03.2021 at ijmspr.com

International Journal of Medical Sciences and Pharma Research

Open Access to Medical and Pharma Research

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Open Access **Review Article**

An Overview on Recent Advances in Pharmaceutical Suspensions

Yogesh Sahu[1], Arvind Singh Jadon[2], Prateek Jain[1], Bhupendra Singh Thakur[1], Basant Khare[1], Anushree Jain[1]*

[1] *Adina College of Pharmacy, Sagar, Madhya Pradesh, India-470001*
[2] *Amity Institute of Pharmacy, Amity University, Gwalior, Madhya Pradesh, India-474001*

Article Info:

Article History:

Received 02 Jan 2021
Reviewed 13 Feb 2021
Accepted 27 Feb 2021
Published 15 March 2021

Cite this article as:

Sahu Y, Jadon AS, Jain P, Thakur PS, Khare B, Jain A, An Overview on Recent Advances in Pharmaceutical Suspensions, International Journal of Medical Sciences & Pharma Research, 2021; 7(1):1-3

DOI: http://dx.doi.org/10.22270/ijmspr.v7i1.54

*Address for Correspondence:

Anushree Jain, Adina College of Pharmacy, Sagar, Madhya Pradesh, India-470001.

Mail ID: anushree1595@gmail.com

Abstract

The suspension is a biphasic liquid or semi-solid dosage form where the finely divided insoluble solid drug particles are homogeneously dispersed in a liquid or semi-solid medium. The solid drug particles act here as the dispersed phase and the liquid or the semi-solid as the dispersion medium. The particle diameter in a suspension is usually greater than 0.5 µm. However, it is difficult and also impractical to impose a sharp boundary between the suspensions and the dispersions having finer particles. Suspensions are an important class of pharmaceutical dosage forms. The advantages of suspension dosage forms include effective dispensing of hydrophobic drugs; avoidance of the use of cosolvents; masking of unpleasant taste of certain ingredients; offering resistance to degradation of drugs due to hydrolysis, oxidation or microbial activity; easy swallowing for young or elderly patients; and efficient intramuscular depot therapy. In addition, when compared to solution dosage forms, relatively higher concentration of drugs can be incorporated into suspension products. The present review provides an overview of various aspects of suspensions such as classification of suspensions, theories of suspensions, various suspending agents, formulations aspects of suspensions, stability of suspensions and recent research work that is being carried on suspensions.

Keywords: Suspensions, suspending agents, flocculated, Stability.

Introduction

The pharmaceutical suspension is a biphasic liquid or semi-solid dosage form where the finely divided insoluble solid drug particles are homogeneously dispersed in particles act as the dispersed phase or internal phase. The internal phase consisting of insoluble solid particles having a range of size(0.5 to 5 microns) which is maintained uniformly throughout the suspending vehicle with aid of single or combination of suspending agent. The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non-oral use. A pharmaceutical suspension defined as a coarse dispersion containingfinely divided insoluble material suspended in a liquid medium. The physical chemist defines the word "suspension" as two-phase system consisting of an un dissolved or immisciblematerial dispersed in a vehicle (solid, liquid, or gas).[1]

Examples of Pharmaceutical Suspensions

Antacid oral suspensions Antibacterial oral suspension
Dry powders for oral suspension (antibiotic)
Analgesic oral suspension
Anthelmintic oral suspension
Anticonvulsant oral suspension
Antifungal oral suspension

Features Desired in Pharmaceutical Suspensions[2]

- The suspended particles should not settle rapidly and sediment produced, must be easily re-suspended by the use of moderate amount of shaking
- It should be easy to pour yet not watery and no grittiness.
- It should have pleased odour, colour and palatability.
- 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 physically, chemically and microbiologically stable.
- Parenteral/Ophthalmic suspension should be sterilizable.

Advantages and Disadvantages of Suspension[3-4]

Advantages

Suspension can improve chemical stabilityof certain drug. For example, Procaine penicillin G. Drug in suspension exhibits higher rate of bioavailability than other dosageforms. Solution > Suspension > Capsule > Compressed Tablet > Coated tablet

Duration and onset of action can be Controlled. For example, ProtamineZinc-Insulin suspension. Suspension can mask the unpleasant/bitter taste of drug. For example,Chloramphenicol.

Disadvantages

Physical stability, sedimentation and Compaction can cause problems.It is bulky. Sufficient care must be taken during handling and transport.It is difficult to formulate.Uniform and

accurate dose may not be achieved.

Types of suspension on the basis of route of administration[5]

Oral suspension

eg: Paracetamol suspension, Antacids, Tetracycline HCl.

Externally applied suspension

eg: Calamine lotion.

Parenteral suspension

eg: Procaine penicillin G, Insulin Zinc suspension

(1)*Oral suspension:* Oral suspension is biphasic liquid dosage form contains one or more active ingredients suspended in a suitable vehicle.These kinds of suspensions are formulated to administer drugs like antibiotics which may contain a dose in the range of 125-500 mg/ml of the suspension.In pediatric drops, the concentration of suspended drugs may be relatively higher.

Advantages

It is easy to swallow suspended insoluble powdered drugs especially by the pediatric andgeriatric patient than the tablets and capsules.The suspension ensures faster dissolution needed for absorption compared to the tablets and capsules.

(2)*Injectable suspension*

Injectable suspensions are heterogeneous systems consisting of the drug dispersed in a liquid medium. They are sterile, pyrogen free and physically and chemically stabile over the intended shelf-life. They are administered through the subcutaneous and intramuscular routes. They are not administered intravenously as it may lead to vaso-occlusion. They may usually contain a drug concentration in between 0.5-5.0% which passes easily through the hypodermic needle. Procaine benzyl penicillin, known as Procaine penicillin G and Benzathinebenzylpenicillin were also known as benzathine penicillin G are the examples of antibiotics which are injected intramuscularly

Advantages

(a) Therapeutic use of drugs those are insoluble in conventional solvents (i.e. water, water miscible and water immiscible).

(b) Increase chemical stability when compared to solution dosageforms.

(c) Possible for depot formation.

(3) *Externally applied suspension*

Externally applied suspensions are used topically and designed for dermatological, cosmetic and protective purposes. Such kind of suspension should spread easily and must not be too fluidic to run off the skin surface.Calamine lotion is a classic example of such suspension applied for protective rationale but it also possesses a cosmetic feel.

Classifications of suspension[6]

Suspension can be classified as flocculated suspension and deflocculated suspension,

***Flocculated suspension*:**

Flocculation is an architecture which results from the lowering of the electrical forces of repulsion between the dispersed particles of suspension along with dominant attraction force. Under this condition, the particles with reduced repulsive force approach each other resulting into a loosely aggregated structure popularly known as floc. As the floc or floccule is composed of many individual particles resulting in a large network of individual particles, the rate of sedimentation is always rapid. The floccules have loose porous structure and the dispersion medium can flow through them during SedimentationThe floccules also entrap a large amount of the liquid phase. Therefore, the volume of the final sediment will still be large and facilitate re-dispersion with ease by moderate shaking.

***Deflocculated suspension*:**

In a deflocculated suspension, the individual particles remain as discrete separated units and settle slowly. The slow rate of settling of particles prevents the individual particles of this suspension to entrap any liquid medium and becomes compacted leading to cake formation. This phenomenon of caking is a very serious physical stability issue encountered in suspension. Another characteristic feature of this suspension is that the supernatant remains cloudy for sufficient time after shaking. Particles exist as separate entities and do not form floccules.The rate of sedimentation is high. The rate of sedimentation is slow.Sediment is easy to re-disperse.

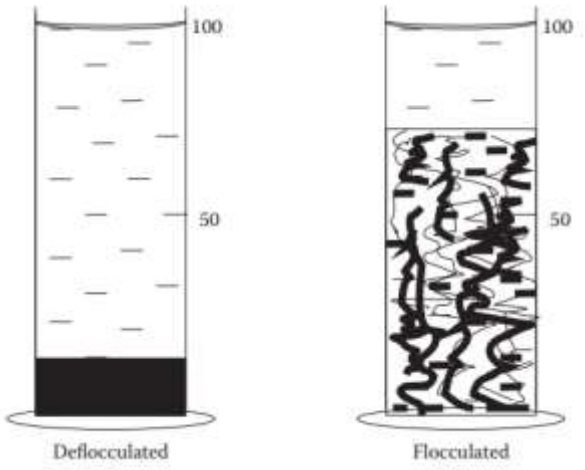

Figure 1: flocculated suspension and deflocculated suspension

Pharmaceutical applications of suspensions[7-8]

1. Suspension is usually applicable for drug which is insoluble (or) poorly soluble.

E.g. Prednisolone suspension

2. To prevent degradation of drug or to improve stability of drug.

E.g. Oxy tetracycline suspension

3. To mask the taste of bitter of unpleasant drug.

E.g. Chloramphenicol palmitate suspension

4. Suspension of drug can be formulated for topical application

e.g. Calamine lotion

5. Insoluble drug or poorly soluble drugs which required to be given orally in liquid dosage forms.

(in case of children, elderly, and patients have difficulty in swallowing solids dosage forms)

6. To overcome the instability of certain drug in aqueous solutionInsoluble derivative formulated as suspension. An example is oxytetracycline HCL (instable) calcium salt (stable)

Bio-availability influencing factors of suspension[9]

The major rate-limiting step in the absorption of drugs from suspension dosage form is drug dissolution which is generally rapid due to the large surface area of the particles. Suspensions are expected to demonstrate improved bioavailability compared to the same drug formulated as a tablet or capsule. This is because the suspension already contains discrete drug particles whereas tablet dosage from must undergo disintegration in order to maximize the necessary dissolution process. Frequently antacid suspensions are perceived as being more rapid in action and therefore more effective than an equivalent dose in the form of tablets.

Particle size and shape

The particle size of the active pharmaceutical ingredient (API) and inert excipients is a very important parameter that has the surface area increases inversely with the particles size.

When the particles are non-spherical there is an extra energy indulgence

Polymorphism

Polymorphism of pharmaceuticals is the ability of the molecule to assemble into multiple crystal structures. Different polymorphs have different arrangements of atoms within the unit cell, and this can quite often have a remarkable impact affect the pharmacokinetics and Pharmacodynamics increased rate and extent of oral absorption compared to crystalline drugs.

Wetting agent

It is a prerequisite that the hydrophobic drug particles must be wetted properly for the uniformdispersion in the continuous medium. The wetting is very important irrespective of the physical nature of the drug, diffusible or in-diffusible. The finely distributed hydrophobic drug particles are coated with a film of air preventing its dispersion in the external medium.

If the drug particles are not wetted properly, the suspension may exhibit poor physicalstability and poor dissolution properties. As a result, the drugs bioavailability and invivo performances can greatly be at stake.

Formulation of Suspension[10-11]

Formulation of suspensions may seem to be simple. After encountering numerous technical problems during pharmaceutical suspension development, the formulator (pharmacist) makes it simple. Some pharmaceutical suspensions are marketed as either prepared form or granular mixtures or dry powders called PFS (powder for suspension) intended for reconstitution.Pharmaceutical suspension may be formulated for different routes of administration for example oral, topical, ophthalmic, inhalation, otic, rectal, and injection. Examples of some pharmaceutical suspensions: Amoxicillin Oral Suspension, Mebendazole Oral Suspension, Albendazole Oral Suspension, Natamycin Ophthalmic Suspension etc.

The various components, which are used in suspension formulation, are as follows.

API: Active drug substances

Wetting agents: They are added to disperse solids in continuous liquid phase.

Flocculating agents: They are added to floc the drug particles

Thickeners: They are added to increase the viscosity of suspension.

Buffers and pH adjusting agents: They are added to stabilize the suspension to a desired pH range.

Osmotic agents: They are added to adjust osmotic pressure comparable to biological fluid.

Coloring agents: They are added to impart desired color to suspension and improve elegance.

Preservatives: They are added to prevent microbial growth.

External liquid vehicle: They are added to construct structure.

Recent advances in suspension[12]

Taste masked pharmaceutical suspensions.Sustained release suspensions.Nano suspensions are the biphasic colloidal dispersions of nanosizeddrug particles stabilized by surfactants without the matrix materials.They can also be defined as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle in which the diameter of the/suspended particle is less than 1 pm in size.They have average diameter of particle 200-600nm.

Conclusion

Today pharmaceutical suspension has occupied a vast space among the dosage forms. It can administer through different routes like oral, external and injectable. Hence, the optimization of formulation parameters of this dosage form is a very challenging task. The rationale of optimized formulation for a particular therapeutic target would only be achieved if the bio-availability issues are addressed properly.

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