IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON PHARMACEUTICAL SUSPENSION

Hawale Pratisha Bibhishan*[1], Ms. S. A Ghadage [1], Santosh Jain[1].

[1] Aditya Institute of Pharmaceutical Nalwandi Road, Beed - 431 122.

ABSTRACT:

A pharmaceutical suspension is a coarse dispersion of insoluble solid particles in a liquid 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, packaging of suspensions, evaluation of suspensions, stability of suspensions and recent research work that is being carried on suspensions.

KEYWORDS: Suspensions, Suspending agents, Evaluation, Stability.

INTRODUCTION

Definition: A Pharmaceutical suspension is a coarse dispersion in which internal phase is dispersed uniformly throughout the external phase. The internal phase consisting of insoluble solid particles having a specific range of size 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.

Classification

1. Based on General Classes

- Oral suspension
- Externally applied suspension
- Parenteral suspension

2. Based on Proportion of Solid Particles

- Dilute suspension (2 to10%w/v solid)
- Concentrated suspension (50%w/v solid)

3. Based on Electro Kinetic Nature of Solid

- Particles
- Flocculated suspension
- Deflocculated suspension

4. Based on Size of Solid Particles

- Colloidal suspension (< 1 micron)
- Coarse suspension (>1 micron)
- Nano suspension (10 ng)

Advantages

- Pharmaceutical Suspension can improve chemical stability of certain drug. E.g.Procainepenicillin 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
- Duration and onset of action can be controlled. E.g.Protamine Zinc-Insulin suspension.
- Suspension can mask the unpleasant bitter taste of drug. E.g. Chloramphenicol.

Disadvantages

- Physical stability, sedimentation and compaction can causes problems.
- It is bulky sufficient care must be taken during handling and transport.
- It is difficult to formulate.
- Uniform and accurate dose cannot be achieved unless suspension are packed in unitdosage form.

Features Desired in Pharmaceutical

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

Applications

- 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 of unpleasant drug.
  E.g. Chloramphenicol palmitate suspension.
- Suspension of drug can be formulated for topical application e.g. Calamine lotion.
- Suspension can be formulated for parentral application in order to control rate of drugabsorption.
- 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.

THEORY OF PHARMACEUTICAL SUSPENSIONS:

1. Sedimentation BehaviourIntroduction

Sedimentation means settling of particle or floccules occur under gravitational force in liquiddosage form.

2. Theory of Sedimentation

Velocity of sedimentation expressed by Stoke's equation:

$$2r^2 (\rho_s-\rho_o)g / 9\eta_o$$

Where,

v = sedimentation velocity in cm / secd = Diameter of particle

r = radius of particle

ρ s =density of disperse phase ρ o = density of disperse mediag = acceleration due to gravity

η o= viscosity of disperse medium in poiseStoke's Equation Written In Other Form

$$V' = V_{sed.}\ \varepsilon^{n}$$

V '= the rate of fall at the interface in cm/sec.

V = velocity of sedimentation according to Stoke's low

ε = represent the initial porosity of the system that is the initial volume fraction of theuniformly mixed suspension which varied to unity.

n = measure of the "hindering" of the system & constant for each system.

Limitation of Stoke's Equation

Stoke's equation applies only to:

- ❖ Spherical particles in a very dilute suspension (0.5 to 2 gm per 100 ml).
- ❖ Particles which freely settle without interference with one another (without collision).
- ❖ Particles with no physical or chemical attraction or affinity with the dispersion medium.
- ❖ But most of pharmaceutical suspension formulation has conc. 5%, 10%, or higherpercentage, so there occurs hindrance in particle settling.

Factors Affecting Sedimentation

1. Particle size diameter (d)
2. Density difference between dispersed phase and dispersion media(ρ s- ρ o)
3. Viscosity of dispersion medium(η)

3. Sedimentation Parameters

Three important parameters are considered:

Volume (F) or height (H) for flocculated suspensions:

$F = V_u / V_o$ ---------- (A)

Where, V_u = final or ultimate volume of sediment V_o = original volume of suspension before settling. Sedimentation volume is a ratio of the final or ultimate volume of sediment (Vu) to the original volume of sediment (V) before settling. Some time 'F' is represented as 'Vs' and as expressed as percentage. Similarly when a measuring cylinder is used to measure the volume

$$F= H_u / H_o$$

Where, H_u = final or ultimate height of sediment

H_o = original height of suspension before settling Sedimentation volume can have values ranging from less than 1 to greater than1; F is normally less than 1. F=1, such product is said to be in flocculation equilibrium. And show no clear Supernatant on standing Sedimentation volume (F) for deflocculated suspension

$F_¥ = V_¥ / V_o$

Where,$F_¥$ =sedimentation volume of deflocculated suspension $V_¥$ = sediment volume of completely deflocculated suspension.(Sediment volume ultimate relatively small)

V_o=Original volume of suspension

3. Sedimentation Velocity[3]

The velocity dx / dt of a particle in a unit centrifugal force can be expressed in terms of the Svedberg co-efficient 'S' Under centrifugal force, particle passes from position x at time t to position x at time t.

The Sedimentation Behaviour of Flocculated and Deflocculated SuspensionsFlocculated Suspensions
In flocculated suspension, formed flocks (loose aggregates) will cause increase insedimentation rate due to increase in size of sedimenting particles. Hence, floculated suspensions sediment more rapidly.

Here, the sedimentation depends not only on the size of the flocks but also on the porosity of flocs. In flocculated suspension the loose structure of the rapidly sedimenting flocs tends to preserve in the sediment, which contains an appreciable amount of entrapped liquid. The volume of final sediment is thus relatively large and is easily redispersed by agitation.

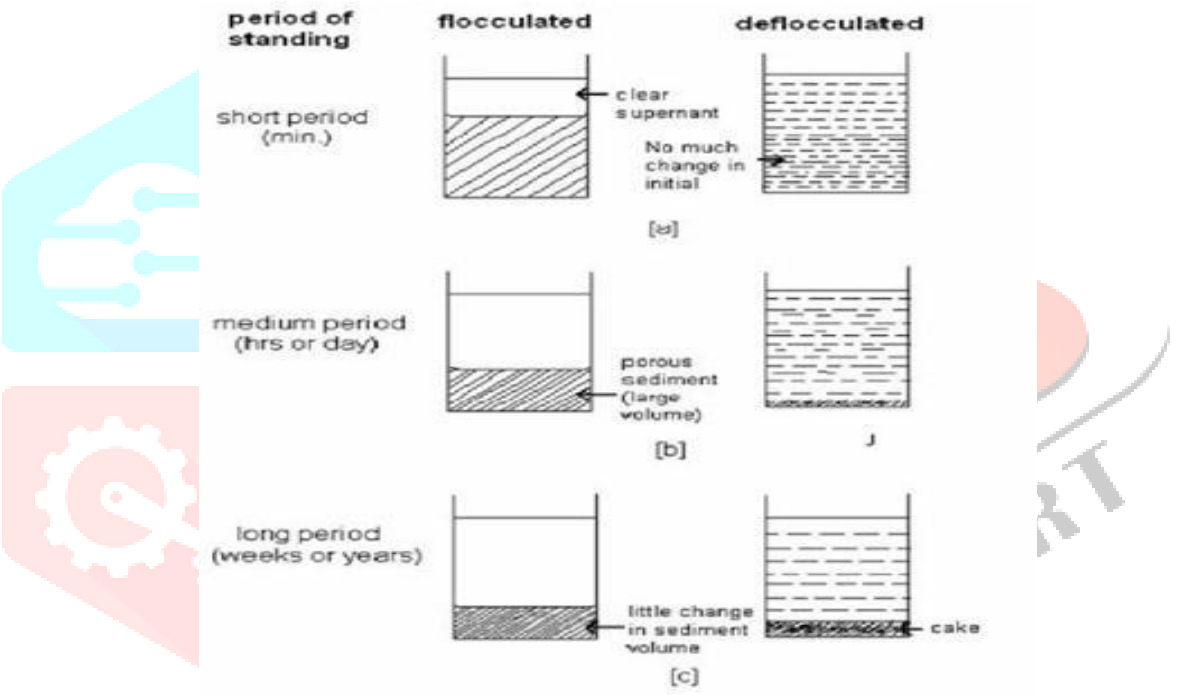

Fig 1.2: Sedimentation Behaviour of Flocculated and Deflocculated Suspensions

Deflocculated suspensions In deflocculated suspension, individual particles are settling, so rate of sedimentation is slow which prevents entrapping of liquid medium which makes it difficult to re-disperse by agitation. This phenomenon also called 'cracking' or 'claying'. In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquidso supernatant appears cloudy whereby in flocculated suspension, even the smallest particles are involved in flocs, so the supernatant does not appear cloudy.

Zeta Potential

The zeta potential is defined as the difference in potential between the surface of the tightly bound layer (shear plane) and electro-neutral region of the solution. As shown in figure 1.3, the potential drops off rapidly at first, followed by more gradual decrease as the distance fromthe surface increases. This is because the counter ions close to the surface acts as a screen thatreduce the electrostatic attraction between the charged surface and those counter ions further away from the surface.

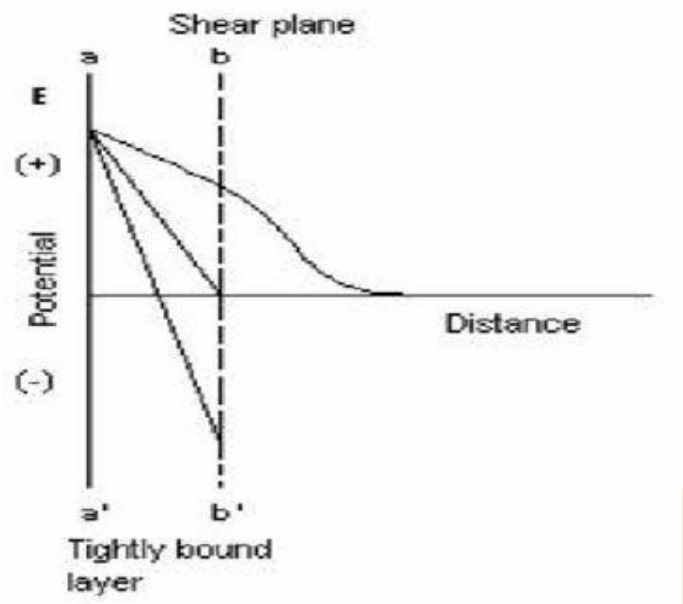

Fig 1.3: Zeta potential

Zeta potential has practical application in stability of systems containing dispersed particles since this potential, rather than the Nernst potential, governs the degree of repulsion between the adjacent, similarly charged, dispersed particles. If the zeta potential is reduced below a certain value (which depends on the particular system being used), the attractive forces exceed the repulsive forces and the particles come together. This phenomenon is known as flocculation.

The flocculated suspension is one in which zeta potential of particle is -20 to +20 mV. Thus the phenomenon of flocculation and deflocculation depends on zeta potential carried by particles. Particles carry charge may acquire it from adjuvants as well as during process like crystallization, grinding processing, adsorption of ions from solution e.g. ionic surfactants. A zeta meter is used to detect zeta potential of a system.

1. Flocculating Agents

Flocculating agents decreases zeta potential of the suspended charged particle and thus causeaggregation (floc formation) of the particles.

Examples of flocculating agents are:

- Neutral electrolytes such as KCl, NaCl.
- Calcium salts
- Alum
- Sulfate, citrates, phosphates salts

- Neutral electrolytes e.g. NaCl, KCl besides acting as flocculating agents, also decreases interfacial tension of the surfactant solution. If the particles are having less surface chargethen monovalent ions are sufficient to cause flocculation e.g. steroidal drugs. For highly charged particles e.g. insoluble polymers and poly-electrolytes species, di or trivalent flocculating agents are used.

2. Flocculated Systems

In this system, the disperse phase is in the form of large fluffy agglomerates, where individual particles are weakly bonded with each other. As the size of the sedimenting unit is increased, flocculation results in rapid rate of sedimentation. The rate of sedimentation is dependent on the size of the flocs and porosity. Floc formation of particles decreases the surface free energy between the particles and liquid medium thus acquiring thermodynamic stability.

The structure of flocs is maintained in sediment so they contain small amount of liquid entrapped within the flocs. The entrapment of liquid within the flocks increases the sedimentation volume and the sediment is easily redispersed by small amount of agitation.

Formulation of Flocculated Suspension System

There are two important steps to formulate flocculated suspension

- The wetting of particles
- Controlled flocculation

The primary step in formulation is that adequate wetting of particles is ensured. Suitable amount of wetting agents solve this problem which is described under wetting agents.

Careful control of flocculation is required to ensure that the product is easy to administer. Such control is usually is achieved by using optimum concentration of electrolytes, surface- active agents or polymers. Change in these concentrations may change suspension from flocculated to deflocculated state.

EVALUATION OF SUSPENSION:

Quality Assurance (QA) is a broad concept which takes into consideration all factors that individually or combinely affect the quality of a product. It is a system which keeps a Criticallook on what has happened yesterday, what is happening today and what is going to happen tomorrow so that it can ensure right quality of final product.

Quality Control (QC) is a small part of QA and it is concerned with sampling, testing and documentation during manufacturing and also after completion of manufacturing. Quality control is the monitoring process through which manufacturer measures actual quality performance, compares it with standards and acts on the causes of deviation from standard to ensure quality product not once but every time.

Quality control system can be divided into two parts on basis of its function: In Process Quality Control, and Final Quality control.

In Process Quality Control (IPQC) of Suspensions

In process quality control is a process of monitoring critical variables of manufacturing process to ensure a quality of the final product and to give necessary instruction if any discrepancy is found. In process manufacturing controls are established and documented by quality control and production personnel to ensure that a predictable amount of each output cycle falls within the acceptable standard range.

For proper function of In process Quality control the following must be defined.[2]Which process is to be monitored and at what phase?

Number of samples to be taken for analysis and frequency of sampling?Quantitative amounts of each sample, Allowable variability, etc.

Objectives of IPQC Tests[2]

- To minimize inter-batch and intra-batch variability.
- To ensure quality of final product.
- To ensure continuous monitoring of process variables which are going to affect thequality of product.
- To ensure implementation of GMP in manufacturing.
- To give indication of existence of a functional Quality assurance system.

IPQC Tests of Suspensions

The tests are carried out during the manufacturing of suspension to ensure a stable, safe and quality product. These include:

Appearance of Phases

This test is done for the dispersed phase and dispersion medium. For preparation of dispersion phase for suspension usually purified water and syrup are used. The particle size distribution, clarity of syrup, the viscosity of gum dispersion, quality control of water is monitored to keep an eye on the product quality.

Viscosity of Phases

Stability of a suspension is solely dependent on the sedimentation rate of dispersed phase, which is dependent on the viscosity of the dispersion medium. So this test is carried out to ensure optimum viscosity of the medium so a stable, redispersible suspension can be formed. The viscosity of the dispersion medium is measured before mixing with dispersed phase and also viscosity after mixing is determined using Brooke field viscometer. The calculated values are compared with the standard values and if any difference is found necessary corrective action are taken to get optimized viscosity.

Particle Size of Dispersed Phase

Optimum size of drug particle in the dispersed phase plays a vital role in stability of final suspension. So this test is carried out to microscopically analyze and find out particle size range of drug then it is compared with optimum particle size required. If any difference is found, stricter monitoring of micronisation step is ensured.

pH Test

pH of the phases of suspension also contribute to stability and characteristics of formulations.So pH of the different vehicles, phases of suspension, before mixing and after mixing are monitored and recorded time to time to ensure optimum pH environment being maintained.

Pourability

This test is carried out on the phases of suspension after mixing to ensure that the final preparation is pourable and will not cause any problem during filling and during handling by patient.

Final Product Assay

For proper dosing of the dosage form it is necessary that the active ingredient is uniformly distributed throughout the dosage form. So samples are withdrawn from the dispersed phase after micronisation and after mixing with dispersion medium, assayed to find out degree of homogeneity. if any discrepancy is found out it is suitably corrected by monitoring the mixing step to ensure a reliable dosage formulation.

Zeta Potential Measurement

Value of Zeta potential reflects the future stability of suspensions so it monitored time to timeto ensure optimum zeta potential. Zeta potential is measured by either Zeta meter or micro- electrophoresis.

Centrifugation Test

This test tells us about the physical stability of suspension. The product is checked for uniform distribution of color, absence of air globules before packing.

Final Quality Control of Suspensions

The following tests are carried out in the final quality control of suspension:

- ✓ **Appearance**
- ✓ **Color, odor and taste**
- ✓ **Physical characteristics such as particle size determination and microscopic photographyfor crystal growth**
- ✓ **Sedimentation rate and Zeta Potential measurement**
- ✓ **Sedimentation volume**
- ✓ **Redispersibility and Centrifugation tests**
- ✓ **Rheological measurement**
- ✓ **Stress test**
- ✓ **pH**
- ✓ **Freeze-Thaw temperature cycling**
- ✓ **Compatibility with container and cap liner**
- ✓ **Torque test**

Stability of Suspensions

Pharmaceutical suspensions are thermodynamically unstable system, so they always tend towards the ultimate loss of stability. What one examines at a time is only the apparent stability of the product.

Stability of suspension can be considered in two ways:

- ✓ Physical
- ✓ Chemical

1. Physical Stability

The definition of physical stability in context of suspensions is that the particles do not sediment for a specific time period and if they sediment, do not form a hard cake. To achieve this desired target, one must consider the three main factors affecting the physical stability.

A. Particle-Particle Interaction and its Behaviour

Derjaguin, Landau, Verwey & Overbeek explained a theory of attractive & repulsive forces in context of lyophobic colloids viz., DLVO theory. This theory allows us to develop insight into the factors responsible for controlling the rate at which the particles in the suspensionwill come together to produce aggregate to form duplets or triplets. The process of aggregation will accelerate the sedimentation and affect the redispersibility.

For this, the potential energy curves may be used to explain the sedimentation behaviour which generally is indicative of the interaction of the two charged surfaces which gives rise to two types pf suspension systems i.e. deflocculated and flocculated.

In deflocculated suspension systems, the particle dispersed carry a finite charge on their surface. When the particles approach one another, they experience repulsive forces. These forces create a high potential barrier, which prevent the aggregation of the particles. But when the sedimentation is complete, the particles form a closed pack arrangement with the smaller particles filling the voids between the larger ones. And further the lower portion of the sediment gets pressed by the weight of the sediment above. And this force is sufficient to overcome the high energy barrier. Once this energy barrier is crossed, the particles come in close contact with each other and establish strong attractive forces. This leads to the formation of hard cake in a deflocculated system. The re-dispersion of this type of system is difficult as enough work is to be done in order to separate the particle and create a high energy barrier between them.

B. Interfacial Properties of Solids

A good pharmaceutical suspension should not exhibit the settling of suspended particles. Thiscan be achieved by reducing the particle size to a level of 5m to exhibit the Brownian motion. As for the size reduction, work (W) is to be done which is represented as

$W = \Delta G = \gamma SL.\Delta A.$

Where, ΔG= increase in surface free energy

ɣ SL = interfacial tension between liquid medium & solid particles.

ΔA = increase in surface area of interface due to size-reduction.

`The Size reduction tends to increase the surface-free energy of the particles, a state in whichthe system is thermodynamically unstable.

In order to approach the stable state, the system tends to reduce the surface free energy andequilibrium is reached when ΔG = 0, which is not desirable.

Thus, the following two approaches are used to retain the stability.

1) By reducing the ΔA. Provided that they are loosely attached (flocculated system) and are easily redispersible.

2) By reducing the interfacial tension, the system can be stabilized, but cannot be made equal to zero, as dispersion particles have certain positive interfacial tension. Thus, the manufacturemust add certain surface-active agents to reduce g to a minimum value, so that the system canbe stabilized.

C. Chemical Stability of the Suspensions

Most of the drug materials although insoluble, when suspended in a liquid medium has some intrinsic solubility, which triggers the chemical reactions such as hydrolysis, to occur leading to degradation. So, the particles that are completely insoluble in a liquid vehicle are unlikely to undergo chemical degradation. The Chemical stability of the suspensions is governed by the following facts:

It is assumed that the decomposition of the suspension is solely due to the amount of the drugdissolved in aqueous phase. This solution will be responsible for drug decomposition and more drug will be released from insoluble suspended particles within the range of solubility.It behaves like a reservoir depot. So, the amount of the drug in the solution remains constant inspite of the decomposition with time, Thus, primarily suspensions behave as a zero order. But once all the suspended particles have been converted into the drug in the solution, the entire system changes from zero order to first order, as now the degradation depends upon theconcentration in the solution. Thus, it can be said that suspension follows apparent zeroorder kinetics.

PACKAGING OF SUSPENSIONS

Due to the world wide emergence of the drug regulations and increasing sophistication in variety of dosage forms and development of new packaging materials, today pharmacist mustaware of wide range of packaging material that relates directly to the stability and acceptability of dosage forms. For example, to optimize shelf life industrial pharmacist must understand inter-relationship of material properties, while the retail pharmacist must not compromise with the storage of the dosage forms. So because of that labeling and storage requirements are important for both patient as well as pharmacist.

Pharmaceutical suspensions for oral use are generally packed in wide mouth container havingadequate space above the liquid to ensure proper mixing. Parenteral suspensions are packedin either glass ampoules or vials.

Ideal Requirements of Packaging Material

- ❖ It should be inert.
- ❖ It should effectively preserve the product from light, air, and other contamination throughshelf life.
- ❖ It should be cheap. It should effectively deliver the product without any difficulty.

Materials Used for Packaging

Generally glass and various grades of plastics are used in packaging of suspension.

1. Glass

Generally soda lime and borosilicate glass are used in preparation of non sterile suspensions. Some times it is advisable to use amber colored glass where light is the cause of degradation of the product. Amber glass doesn't allow U.V light to pass through. Amber characteristics can be developed in the glass by addition of various types of additives.

Table 1.5: Type of Glasses and Additives Giving Amber Colour

Type of Glass	Additive Giving Amber Colour
Soda lime	FeO+ sulfur(in presence of reducing agent)
Borosilicate	FeO+TiO2

Disadvantages of Glass Materials

- ✓ They are fragile. difficult.
- ✓ They are very heavy as compared to plastic so handling and transport is difficult.
- ✓
- ✓ Most important disadvantage of glass is that glass constituents get extracted in to the product.
- ✓ So for sterile dosage forms powder glass test as well as water attack test has to be carried out to ensure the amount of alkali material leached out in the product. Also typical test forextractable material is some time carried out.

Table: Typical Characteristics of Borosilicate Glass For Example

Assay of Borosilicate Glass	Value
Initial pH	6
Final pH	8
pH change	±0.24
SiO2ppm	21.0
Na ppm K ppm	301 0.74
Al ppm	1.3
Ba ppm	0.7

Plastic

Due to the negative aspects of glass, coupled with the many positive attributes of the plastic material significantly inroads for the use of plastic as packaging material for sterile as well as non-sterile pharmaceutical suspensions.

Advantages Of Plastic Material:

- ✓ Non breakability.
- ✓ Light weight.
- ✓ Flexibility.

Materials used: - Polyethylene, PVC, polystyrene, polycarbonate etc.

Drug Plastic Consideration

There are mainly five factors which is to be considered during selection of plastic as apackaging material for suspension.

- ✓ Permeation
- ✓ Leaching
- ✓ Sorption
- ✓ Chemical reaction
- ✓ Alteration of the physical properties of plastic.

E.g. Deformation of polyethylene containers is often caused by permeation of gas andvapours from the environment. Also sometimes solvent effect is also found to be the factor for altering the physical properties of plastic viz., oils has softening effect on polyethyleneand PVC.

Closure and Liners

With an exception of ampoules all containers required elastomeric closure. Factors affecting in selecting closure:

- ✓ Compatibility with product.
- ✓ Effect of processing should not affect the integrity of the closure.
- ✓ Seal integrity.
- ✓ It should be stable throughout the shelf life.
- ✓ Lot to lot variability has to be considered.

Factors Affecting in Selecting Liner

- ✓ Chemical resistance.
- ✓ Appearance
- ✓ Gas and vapour transmission.
- ✓ Removal torque.
- ✓ Heat resistance.
- ✓ Shelf life.

- ✓ Economical factors.

FDA Regulations for Packaging

When FDA evaluates drug, the agency must be firmly convinced that package for a specific drug will preserve the drug's efficacy as well as its purity, identity, strength and quality for the entire shelf life.

The FDA does not approve the container as such, but only the material used in container. A list of substance "Generally recognized as safe" (GRAS) have been published by FDA. Underthe opinion of qualified experts they are safe in normal conditions. The material does not fall in this category (GRAS) must be evaluated by manufacturer and data has to be submitted to FDA. The specific FDA regulation for the drug states that "container, closure and other components of the packaging must not be reactive, additive or absorptive to the extent that identity, strength, quality, or purity of the drug will be affected".

3.

Storage Requirements (Labelling)

- ➢ Shake well before use
- ➢ Do not freeze
- ➢ Protect from direct light (For light sensitive drugs).

4. Innovations in Suspensions

1. Taste Masked Pharmaceutical Suspensions

Un-palatability due to bad taste is a major concern in most of the dosage forms containing bitter drugs. In case of suspensions also taste masking is being applied to mask bitterness of drugs formulated. The taste masking approaches for suspensions can be summarized.

Polymer Coating of Drugs

The polymer coat allows the time for all of the particles to be swallowed before the threshold concentration is reached in the mouth and the taste is perceived. The polymers used for coating are

- ➢ Ethyl cellulose
- ➢ Eudragit RS 100
- ➢ Eudragit RL 100
- ➢ Eudragit RS 30 D
- ➢ Eudragit RL 30 D

Polymer coated drug powders are also used for preparation of reconstitutable powders that means dry powder drug products that are reconstituted as suspension in a liquid vehicle such as water before usage. These reconstitutable polymer coated powders are long shelf-life and once reconstituted have adequate taste masking.

Encapsulation with a Basic Substance

Here a basic substance is mixed with a bitter tasting drug which is insoluble at high pH. The mixer is then encapsulated with a polymer (cellulose derivative, vinyl derivative or an acid soluble polymer for example

copolymer of dimethyl ammonium methyl methacrylate). The drug after encapsulation are suspended, dispersed or emulsified in suspending medium togive the final dosage form.

Polymer Coated Drug with a Basic Substance

This method has claimed to give stable taste masked suspensions on reconstitution (taste masked for prolonged period).

Coating and pH Control

Those drugs which are soluble at high pH are preferably be maintained in a suspension at a low pH where the drug exhibit maximum insolubility. Similarly drugs which are soluble at low pH are preferably maintained in suspension at a high pH where the drug is insoluble. Also applying polymeric coating to the drug substance avoids solubilization of drug when administered providing taste masking.

Table: Some Examples of Taste Masked Suspensions:

Nano-Suspension:

S.I No.	Name of the Drug	Taste Masking Approach
01	Risperidone	pH control and polymer coating(with Eudragit RS) The coated drug is suspended in water basedliquid constituted at an optimum pH.
02	Roxithromycin-I And ROxithromycin-II	Polymer coating with Eudragit RS 100
03	Diclofenac	Polymer coating with Eudragit RS 100
04	Levofloxacin	Polymer coating (Eudragit 100:Cellulose acetate, 60:40 or 70:30)

Nano-suspension of potent insoluble active pharmaceutical ingredient will become improved drug delivery formulations when delivered to at sizes less than 50 nm.

When delivered I.V. at sizes less than 50 nm, the suspension particles avoids the normal reticulo-endothelial system filtration mechanisms and circulates for long periods. The suspension particles may be insoluble API particles or nanoparticle polymeric carriers of soluble or insoluble drugs and may be useful in delivering genetic therapeutic materials targeted to the cells.

In transdermal delivery application, control of particulates in the 10-50 nm size range should allow the formulation of API in formats that match requirements of delivery rates and for penetration depth target. The drug particulates may involve insoluble active structures or active either soluble or insoluble in degradable polymeric structures.

For oral delivery, nanometer size particles may allow delivery of API through the intestinal wall into the blood stream, at desired rates and with minimal degradation in the GI tract. Insoluble particles at these sizes may be

designed to be transportable across this barrier. Another strategy involves encapsulation of active drugs in nano-particulate degradable polymer structures.

Preparation of Nano-Particles

The technology used should produce nanoparticles of insoluble API or of encapsulated APIs. A new reactor system has been developed known as Multiple Stream Mixer or Reactor (MMR) produces nano-particles by several methods.

Principle:- The system (MMR) conducts two or more streams of reactants to an interaction zone where the streams collid at high velocity under extreme pressure.

Designing of Nano-Particle Formulations

Using the MMR, nano-particles formulation can be designed using several approaches.

Direct Reactions

It is carried out if the API is a result of a synthesis which yields an insoluble material. The reactant streams can be fed into the MMR to yield particles of nanometer size.

pH Shift Reaction

Many APIs are soluble as a basic form and insoluble as active acid form. The synthesized material dissolve in a basic medium constitutes one feed stream, into the MMR, which an acidifying element. The result of collision reaction is a nano-particle suspension of insoluble active acid form.

Controlled Re-crystallization

This approach enables preparation of nanosuspension from API feed material made in a kilo lab or other sources of synthesized solution to the problem of producing nanoparticles from any insoluble API feed material. The API is dissolved in a solvent and the dissolved API from one input stream and other stream is either water or water solution which recrystallizes the insoluble active on contact because the recrystallization occurs in a ultra turbulent collision zone, the resultant insoluble API forms as nano-particles. After necessary clean up process the API can be dispersed into the aqueous final formulation (saline for injection) by passage through dispersion or mixing system (micro-fluidized fluid processing system).

Because the intrinsic API crystallizes where formed as nanoparticles, they can be re- dispersed as nanosuspension.

Sustained Release Suspensions

Sustained release is a method to increase only the duration of action of drug being formulated without affecting onset of action. In suspension sustained release affected by coating the drugto be formulated as suspension by insoluble polymer coating. The polymer coating provides sustained release and also masks the taste of the bitter drug. The polymer used for sustained release in suspension is enlisted as follows as Ethyl cellulose, Eudragit, Cellulose acetate, etc.The main advantage of sustained release suspension is to decrease in dosing frequency.

CONCLUSION

Oral suspension shows high level of acceptance in case of administration of dosage form and its patient compliance. Due the stability and ability of masking the unpleasant taste of drugs substances oral suspension is convenient route of drug delivery and also improves the bioavailability and potency of drug that having low solubility.

The suspension is stable till the system follows zero order, but once it enters the first order kinetics, the degradation is rapid. But, if the suspension is concentrated, the system will require more time to convert from zero order to first order. And this is the reason that a concentrated suspension is often stable enough to market, but a dilute is not. But a concentrated suspension affects the physical stability of the suspension. So, the manufacturing pharmacist should optimize both physical & chemical parameters of the dispersed particles to achieve the desired stability of the suspensions.

REFERENCES

1) Kulshreshtha, A.K., Singh, O.N. and Wall, G.M. eds., 2009. *Pharmaceutical suspensions: from formulation development to manufacturing*. Springer Science & Business Media.
2) Goins, R.A., Ascher, D., Waecker, N., Arnold, J. and Moorefield, E., 2002. Comparison of fluconazole and nystatin oral suspensions for treatment of oral candidiasis in infants. *The Pediatric infectious disease journal*, *21*(12), pp.1165-1167.
3) Nahata, M.C., 1999. Development of two stable oral suspensions for gabapentin. *Pediatric neurology*, *20*(3), pp.195-197.
4) Grießmann, K., Brietkreutz, J., Schubert-Zsilavecz, M. and Abdel-Tawab, M., 2007. Dosing accuracy of measuring devices provided with antibiotic oral suspensions. *Paediatric and Perinatal Drug Therapy*, *8*(2), p.61.
5) Dickinson, E., 2003. Hydrocolloids at interfaces and the influence on the properties of dispersed systems. *Food hydrocolloids*, *17*(1), pp.25-39.
6) Matveenko, V.N. and Kirsanov, E.A., 2011. The viscosity and structure of dispersed systems. *Moscow University Chemistry Bulletin*, *66*(4), pp.199-228.
7) Viveksarathi, K., Rajarajan, R., Kannan, K. and Manavalan, R., 2012. Dosage form design and evaluation of eperisone hydrochloride matrix film coated extended release tablets. *Int J Pharm Pharm Sci*, *4*(2), pp.575-

581.

8) Pharmacopoeia, I., 1996. Ministry of health and family welfare, Govt. of India. *controller of publications, New Delhi*, *736*, pp.A80-83.
9) Kumar, R.S. and Yagnesh, T.N.S., 2016. Pharmaceutical suspensions: patient compliance oral dosage forms. *World Journal of Pharmacy and Pharmaceutical Sciences*, *7*(12), pp.1471-1537.
10) Pons, V., Greenspan, D., Lozada-Nur, F., McPhail, L., Gallant, J.E., Tunkel, A., Johnson, C.C., McCarty, J., Panzer, H., Levenstein, M. and Barranco, A., 1997. Oropharyngeal candidiasis in patients with AIDS: randomized comparison of fluconazole versus nystatin oral suspensions. *Clinical infectious diseases*, *24*(6), pp.1204-1207.
11) ardeskar, C. and Geeverghese, R., 2014. Reconstitutable oral suspensions (dry syrups): An overview. *World Journal of Pharmaceutical Research*, *4*(3), pp.462-484.
12) Bruns, C. and Ober, M., 2018. Development and Preparation of Oral Suspensions for Paediatric Patients–a Challenge for Pharmacists. *Pharmaceutical Technology in Hospital Pharmacy*, *3*(2), pp.113-119.
13) Ribeiro, A.M., Figueiras, A. and Veiga, F., 2015. Improvements in topical ocular drug delivery systems: hydrogels and contact lenses. *Journal of Pharmacy & Pharmaceutical Sciences*, *18*(5), pp.683-695.
14) Pabst, W., 2004. Fundamental considerations on suspension rheology. *CERAMICS SILIKATY.*, *48*(1), pp.6-13.
15) Weiner, N., 1986. Strategies for formulation and evaluation of emulsions and suspensions: Some thermodynamic considerations. *Drug Development and Industrial Pharmacy*, *12*(7), pp.933-951.
16) Gallardo, V., Zurita, L., Ontiveros, A. and Durán, J.D.G., 2000. Interfacial properties of barium sulfate suspensions. Implications in their stability. *Journal of pharmaceutical sciences*, *89*(9), pp.1134-1142.
17) Garcell, L., Morales, M.P., Andres-Verges, M., Tartaj, P. and Serna, C.J., 1998. Interfacial and rheological characteristics of maghemite aqueous suspensions. *Journal of Colloid and Interface science*, *205*(2), pp.470-475.
18) Osorio, F., Valdés, G., Skurtys, O., Andrade, R., Villalobos-Carvajal, R., Silva-Weiss, A., Silva-Vera, W., Giménez, B., Zamorano, M. and Lopez, J., 2017. Surface free energy utilization to evaluate wettability of hydrocolloid suspension on different vegetable epicarps. *Coatings*, *8*(1), p.16.
19) Reiner, E.S. and Radke, C.J., 1990. Variational approach to the electrostatic free energy in charged colloidal suspensions: general theory for open systems. *Journal of the Chemical Society, Faraday Transactions*, *86*(23), pp.3901-3912.
20) Hansen, J.P. and Löwen, H., 2000. Effective interactions between electric double layers. *Annual Review of Physical Chemistry*, *51*(1), pp.209-242.
21) Hou, T., Xu, R., Tiwari, D. and Zhao, A., 2007. Interaction between electrical double layers of soil colloids and Fe/Al oxides in suspensions. *Journal of Colloid and Interface Science*, *310*(2), pp.670-674.
22) Larsson, M., Hill, A. and Duffy, J., 2012. Suspension stability; why particle size, zeta potential and rheology are important. *Annual transactions of the Nordic rheology society*, *20*(2012), p.6.
23) Júnior, J.A.A. and Baldo, J.B., 2014. The behavior of zeta potential of silica suspensions. *New Journal of Glass and Ceramics*, *4*(02), p.29.

24) Greenwood, R., 2003. Review of the measurement of zeta potentials in concentrated aqueous suspensions using electroacoustics. *Advances in Colloid and Interface Science*, *106*(1-3), pp.55-81.

25) Bossler, F. and Koos, E., 2016. Structure of particle networks in capillary suspensions with wetting and nonwetting fluids. *Langmuir*, *32*(6), pp.1489-1501.

26) Sun, Y.Q. and Gao, T., 2002. The optimum wetting angle for the stabilization of liquid-metal foams by ceramic particles: Experimental simulations. *Metallurgical and Materials Transactions A*, *33*(10), pp.3285-3292.

27) Ninham, B.W., 1999. On progress in forces since the DLVO theory. *Advances in colloid and interface science*, *83*(1-3), pp.1-17.

28) Trefalt, G. and Borkovec, M., 2014. Overview of DLVO theory.

29) Adamczyk, Z. and Weroński, P., 1999. Application of the DLVO theory for particle deposition problems. *Advances in colloid and interface science*, *83*(1-3), pp.137-226.

30) Gregory, J. and O'Melia, C.R., 1989. Fundamentals of flocculation. *Critical Reviews in Environmental Science and Technology*, *19*(3), pp.185-230.

31) Bratby, J., 1980. Coagulation and flocculation. *Uplands: Croydon, England*.

32) Landrou, G., Brumaud, C. and Habert, G., 2018. Influence of magnesium on deflocculated kaolinite suspension: Mechanism and kinetic control. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *544*, pp.196-204.

33) Sutherland, I.W., 1991. Alginates. In *Biomaterials* (pp. 307-331). Palgrave Macmillan, London.

34) Marques-Marinho, F.D. and Vianna-Soares, C.D., 2013. Cellulose and its derivatives use in the pharmaceutical compounding practice. In *Cellulose-Medical, Pharmaceutical and Electronic Applications*. IntechOpen.