Suspension

Its defined as a dispersion containing finely divided powder (insoluble material suspended in a liquid media or available in a dry form to be distributed in a liquid media when desired.

Also can be defined as two phase system containing finely divided solid (dispersed phase) diapered in a liquid(dispersion media)

The suspended solute may be diffusible or indiffusable.If indiffusable here the liquid contain material to help in uniform dispersion of insoluble material the product is called suspension and this substance is called as suspending agent.

In suspension the vehicle is water and sometimes may be an organic or oily liquid.

Suspensions can be used orally, parenterally, topically, rectally, ophthalmically, etc

Particle size:

- Colloidal dispersion: 1 nm – 0.5 μm.
- Fine dispersion: 0.5 μm – 10 μm.
- Coarse dispersion: 10 μm – 50 μm (Suspension).

Some suspensions are available in ready to use form (e.g. metronidazole (Flagyl®)) and others are available as dry powders intended for suspension in liquid vehicles, most often purified water (e.g. amoxicillin (Amoxil®)

Sedimentation Rate (المعادلة للفهم فقط ليست للحفظ)

With regard to actual settling rates, the well-known Stokes law describes the sedimentation velocity of a particle in suspension:

$$v = \frac{D^2(d_1 - d_2)g}{18\eta}$$

where v = velocity of the sedimentation in $cm.sec^{-1}$ and D = particle diameter in cm; d_1 and d_2 = density of the particle and the liquid, respectively, in $g.ml^{-1}$; g = gravitational constant = 980.7 $cm.sec^{-2}$; and η = the viscosity of the medium in poises, i.e., $g.cm^{-1}.sec^{-1}$

The properties of a good suspension

1-The dispersed phase must be composed of a small uniformly sized particles that do not settle slowly and should be readily redispersed upon shaking.

2- the sediment particles in the bottom of the container should not be packed in a hard cake and should be completely re dispersed with minimum amount of agitation.

3-The suspension should not be too viscous to pour freely from the orifice of the bottle ie the viscosity is should be such that the suspension pour easily

4-The product should have an agreeable odor ,color and taste and must not decomposed or support mold growth during storage.

An oral suspension must provide the patient with uniform therapeutically active dose of the drug in a preparation that is pleasant and convenient to take.

Note: Suspension must have on its container a label tell the patient shake before use

Advantages of suspension

1-Used externally and internally for a wide variety of treatment.

2- Sterile suspension are injected hypodermically and IM as well as for ophthalmic use and usually produce a more prolonged release of the medication than would the solution of the same drug.

3- Suspension for oral use have greater palatability because the taste of most drug depend on their solubility.

Disadvantages of Suspensions

- They must be well shaken prior to measuring a dose.
- The accuracy of the dose is likely to be less than with the equivalent solution.
- Conditions of storage may adversely affect the disperse system and in the case of non-diffusible solids clumping may occur, leading to potential dosing inaccuracy.

Storage of suspension

The physical stability of suspension is adversely effected by extreme variation in temperature suspension should be stored in cool place but not refrigeration . Freezing and very low temperature may cause the suspended particles to reaggregate.

Also should be stored in a wide mouth container that have a space to allow a good agitation before use.

Classification of suspension according to the suspended particles:

1- suspension containing diffusible solid

2-suspension containing indiffusible solid

3- Suspension containing ppt forming liquid.

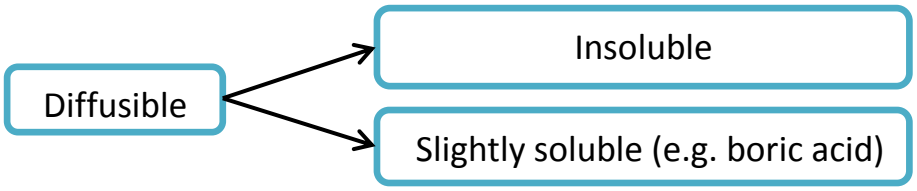
4- suspension containing poorly wetable solid.

1. suspension containing diffusible solid

Some insoluble powders are light and easily wettable and therefore readily mixed with water and upon shaking they diffuse evenly through the liquid for long period enough to ensure dosing consistency. Such substances are known as diffusible or dispersible solids (e.g. kaolin, pectin, magnesium carbonate, bismuth carbonate, cpd powder of rhubarb, heavy and light magnesium, caffeine).

⦿ Some substances are soluble at low concentrations only and at high concentration, they form suspensions. These are classified as diffusible solids as well.

Example: Boric acid is soluble at concentration ≤ 4% w/v (forms clear solution). At concentrations > 4% w/v, it is not completely dissolved (suspension).



※General method to prepare suspension containing diffusible solid(s)

1. Using mortar and pestle, reduce the particle size of any ingredient having coarse particles to produce fine powders.
2. Mix insoluble powders in mortar by adding the ingredient with the smallest quantity first then diluting it with others in increasing order of bulk using amount approximately equal to the bulk already exists in the mortar. This method is called geometric dilution method.
3. After taking in consideration any liquid ingredients, measure ¾ of the vehicle and dissolve any soluble ingredients in it then use it as follows:
    - ¼ of the vehicle to prepare smooth paste.
    - ¼ of the vehicle for dilution to produce a pourable paste.
    - ¼ of the vehicle to wash the mortar.
4. The mortar's content must be homogenous before transferring it and should not be thick and rigid nor sticking to the pestle or mortar's edges.
5. Transfer the mixture from the mortar to a measuring cylinder and rinse the mortar with ¼ of the vehicle.
6. Add any liquid ingredients and complete the volume with the vehicle.
7. Label: Shake before use.

※ Notes

- Soluble solids such as sodium bicarbonate should be dissolved in the second ¼ of the vehicle (dilution part).
- Volatile substances should be added to suspension before completing the volume to avoid their loss by volatilisation (e.g. chloroform, some tinctures, flavouring spirits, etc).
- Liquids with high viscosity such as syrup, glycerine, or propylene glycol are added to the dry powder in the mortar before formation of the smooth paste.
- Dyes are added to the smooth paste before dilution to allow penetration and distribution of the colour among insoluble particles (e.g. amaranth solution).

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Boric acid		10 g	(diffusible solid)
D.W.	qs.	30 ml	(vehicle)
mitte		20 ml	

- Used as antiseptic for minor burns.
- The diluted one can be used for eye wash and as a douche (for vaginosis).
- Calculation and procedure:

¾ × final volume – (liquid ingredients)

- ¾ × 20 – (0) = 15 ml → 3 parts each part 5 ml:
- 5 ml for making smooth paste.
- 5 ml for dissolving soluble solids and dilution.
- 5 ml for washing the mortar and pestle.

❖ Grind 6.66 g boric acid using mortar and pestle.

❖ Add 5 ml of D.W. and triturate to produce smooth paste.

- ❖ Add 5 ml of D.W. to produce pourable paste.
- ❖ Transfer to measuring cylinder and wash with 5 ml of D.W.
- ❖ Complete the volume to 20 ml with D.W.
- ❖ Transfer to suitable bottle and label.

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Light magnesium carbonate		gr X	(diffusible solid)
Sodium bicarbonate		gr XV	(water soluble solid)
Chloroform water	qs.	ʒ i	(vehicle)
mitte		ʒ IV	
sig		ʒ ss q.i.d.	

- Used as antacid and has laxative effect.

Grind 2.6 g light magnesium carbonate using mortar and pestle.

Add 30 ml of chloroform water and triturate to produce smooth paste.

Dissolve 3.9 g of sodium bicarbonate in 30 ml of chloroform water and use this volume to dilute the smooth paste to pourable one.

Transfer to measuring cylinder and wash with 30 ml of chloroform water.

Complete the volume to 120 ml with chloroform water.

Transfer to suitable bottle and label.

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Bismuth carbonate		585 mg	(diffusible solid)
Compound powder of rhubarb		325 mg	(diffusible solid)
Compound tincture of cardamom		0.9 ml	(volatile liquid)
Syrup		1.8 ml	(thick liquid)
Peppermint water	qs.	30 ml	

- Grind 585 mg bismuth carbonate and 325 mg compound powder of rhubarb by geometrical dilution method using mortar and pestle.
- Add 6.6 ml of peppermint water and triturate to produce smooth paste.
- Add 1.8 ml of syrup to the smooth paste and triturate.
- Add 6.6 ml of peppermint water for dilution to a pourable paste.
- Transfer to measuring cylinder and wash with 6.6 ml of peppermint water.
- Add 0.9 ml of compound tincture of cardamom and stir.
- Complete the volume to 30 ml with peppermint water.
- Transfer to suitable bottle and label.

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Light kaolin		gr X	(diffusible solid)
Bismuth carbonate	gr X		(diffusible solid)
Heavy magnesium oxide		gr X	(diffusible solid)
Tincture of belladonna		℥ i	(volatile liquid)
Peppermint water	qs.	ʒ i	(vehicle)
Mitte		ʒ ii	

- Used as antidiarrheal and belladonna acts as antispasmodic.

2. Suspensions containing non-diffusible solid(s)

⦿ A solid is regarded non-diffusible when it will not remain evenly distributed in the vehicle long enough to ensure uniformity of the measured dose (e.g. aspirin, phenobarbital, phenacetin, salicylic acid, benzoic acid).

⦿ The simplest way to solve this problem is to increase the viscosity of the vehicle by adding a thickening agent (suspending agent) which will:

1. Decrease the sedimentation rate of particles.
2. Decrease the collisions of particles by each other which can lead to formation of aggregates that settle down rapidly.

⦿ Some suspending agents for general use are:

1. Acacia Gum BP: Not commonly used alone because:
    - It supports the growth of microorganisms.
    - Not used externally as it can cause shrinkage of skin cells
    - Also not used externally as it can be oxidised to give bad odour.
2. Powdered Tragacanth BP: Used in a concentration of 0.2% w/v.
3. Compound Tragacanth Powder BP: Used in a concentration of 2% w/v. Composed of powdered tragacanth 15%, acacia 20%, sucrose 45% and starch 20%. Also not to be used for suspension applied externally as it contains acacia.
4. Bentonite BP: Used in a concentration of 2-3% w/v.
5. Tragacanth mucilage: Used in a concentration of 25% v/v (¼ of the vehicle is displaced). Composed of tragacanth powder (12.5 g) + alcohol (25 ml) + chloroform water (qs. 1000 ml). It is used when the vehicle is water or chloroform water.

※ Methods of preparing suspension containing non-diffusible solid(s)

⦿ Using Powdered Tragacanth BP or Compound Tragacanth Powder BP:

1. Using mortar and pestle, reduce the particle size of any ingredient having coarse particles to produce fine powders.
2. Mix insoluble powders and suspending agent by geometrical dilution method.
3. After taking in consideration any liquid ingredients, measure ¾ of the vehicle and add part of it (≅ ¼) to the mortar and triturate until smooth paste is formed.
4. Dissolve any soluble solid ingredients in the other ¼ and add it to the mortar for diluting it to a pourable paste.
5. Transfer the content to a measuring cylinder and rinse the mortar with ¼ of the vehicle.
6. Add any liquid ingredients and complete the volume with the vehicle.
7. Label: Shake before use.

⦿ Using tragacanth mucilage:

1. Using mortar and pestle, reduce the particle size of any ingredient having coarse particles to produce fine powders.
2. Mix insoluble powders by geometrical dilution method.
3. Triturate the powder mixture above with tragacanth mucilage (25 % v/v, i.e. ¼ the final volume) to produce a smooth paste.
4. After taking in consideration any liquid ingredients, measure ½ the vehicle and add part of it (≅ ¼) for dilution to produce pourable paste (soluble solids are dissolved in this portion).
5. Transfer the content to a measuring cylinder and rinse the mortar with ¼ of the vehicle.
6. Add any liquid ingredients and complete the volume with the vehicle.

7. Label: Shake before use.

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Phenacetin		1 g	(non-diffusible solid)
Caffeine		0.5 g	(diffusible solid)
Syrup of orange		6 ml	(thick liquid)
P.W.	qs.	90 ml	(vehicle)
mitte		20 ml	

Phenacetin is analgesic and antipyretic. Caffeine is CNS stimulant.

- Grind 0.333 g of phenacetin, 0.166 g of caffeine and 0.6 g of compound tragacanth powder by geometrical dilution using mortar and pestle.
- Add 2 ml of syrup to the dry powder and triturate.
- Add 6.83 ml of vehicle to the mortar and triturate until smooth paste is formed.
- Add 6.83 ml of the vehicle for dilution.
- Transfer to measuring cylinder and wash with 6.83 ml of the vehicle.
- Complete the volume to 30 ml with the vehicle.
- Transfer to suitable bottle and label.

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Aspirin		500 mg	(non-diffusible solid)
Ammonium bromide		65 mg	(water soluble solid)
Syrup of orange		1 ml	(thick liquid)
Concentrated chloroform water		0.25	(volatile liquid)
Peppermint water	qs.	10 ml	(vehicle)
mitte		25 ml	

- Aspirin is analgesic and anti-inflammatory.

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Aspirin gr ii

Potassium citrate gr X

Cpd tr. Of camphor ♏ V

P.W q.s fʒ i

Note: aspirin in the presence of sodium or potassium citrate or acetate (except caffeine citrate) it will be react with these salts and form a soluble complex but the amount of salts should be double the amount of aspirin in order to form soluble complex

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Aspirin 500 mg

Syr. Of orange 1 ml

Conc. Chloroform water 0.25 ml

Water qs. 10ml

Mitt. 50 ml

3. Suspensions containing precipitate forming liquid(s)

◉ Some liquid preparations may contain resinous material that is precipitated upon addition of water.

◉ Resins are insoluble in water and form non-diffusible masses particularly when salts are present.

◉ Examples on precipitate forming liquids:

- Compound benzoin tincture.
- Myrrh tincture.
- Tolu tincture.
- Podophyllum tincture.

◉ The precipitated resinous materials may adhere to the sides of the bottle or form a clotted precipitate which will not re-suspended upon shaking. To prevent this, it is necessary to add suspending agent as Compound Tragacanth powder BP or tragacanth mucilage (in the same percentages used for suspensions containing non-diffusible solids).

※*Method of preparing suspension containing precipitate forming liquid(s) using:*

A\\ compound powder of tragacanth

This method is suitable when diffusible or non-diffusible solids are also present in the mixture and its always be used when the vehicle is medicinally active.

1. Using mortar and pestle, reduce the particle size of insoluble solids to produce fine powders.
2. Mix insoluble powders and suspending agent by geometrical dilution method (if there is no insoluble solid ingredient in the prescription, put the suspending agent alone in the mortar).
3. After taking in consideration any liquid ingredients, measure ¾ of the vehicle and add part of it (≅ ¼) to the mortar and triturate until smooth paste is formed.

4. Measure the precipitate forming liquid in a dry measuring cylinder and add it gradually and slowly in the centre of the smooth paste with rapid stirring.
5. Dissolve any soluble ingredients in the other ¼ of the vehicle and add it to the mortar for dilution to a pourable paste (stirring is continued).
6. Transfer the content to a measuring cylinder and rinse the mortar with ¼ of the vehicle.
7. Add any liquid ingredients and complete the volume with the vehicle.
    1. Label: Shake before use.

◉ The precipitate forming liquids are adsorbed on the hydrocolloid (acacia, tragacanth or starch) which offers hydrophilic properties and prevents aggregation into clots.

B\\ using tragacanth mucilage

1-mix the mucilage with equal volume of aqueous vehicle (¼+¼)

2- measure the ppt forming liquid and pour it slowly into the center of the mixture with constant stirring

3- The electrolyte added after dilution and dissolving in part of the vehicle.

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Tincture of tolu balsam		5 ml	(precipitate forming liquid)
Syrup of orange		2 ml	(thick liquid)
Peppermint water	qs.	30 ml	(vehicle)

- Used as expectorant (for cough).

4. Suspensions containing poorly wettable solid(s)

◉ Some substances as sulphur, calamine, zinc oxide, and hydrocortisone are insoluble in water and poorly wetted by it. Upon preparing simple aqueous dispersions, it is difficult to disperse clumps and the foam produced upon shaking will not rapidly subside because it is stabilised by a film of a non-wettable solid at the liquid-air interface.

◉ The interfacial energy between the solid and liquid must be reduced. This could be achieved by adding a suitable wetting agent which is adsorbed at the solid-liquid interface to increase the affinity of solid particles to the surrounding medium and reduce the interparticle forces.

◉ Examples on wetting agents: Alcohol, glycerine and propylene glycol. Polysorbate (Tween) and sorbitan ester (Span) are SAA used as wetting agent for internal preparation. While sodium lauryl sulphate (SLS) and quillia tincture are used in external preparation.

◉ However, in lotions the compound preferred for oral and parenteral suspensions are nontoxic non-ionic surface active agents known as polysorbates (spans and tweens).

◉ Lotions are liquid or semiliquid preparations containing one or more pharmaceutically active ingredient intended for external application to the unbroken skin without friction. They usually contain suspended particles or emulsified liquid droplets which may be diffusible or non-diffusible. A suspending or emulsifying agent is needed if non-diffusible material is present (suspending agent: solid–liquid, emulsifying agent: liquid–liquid).

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Calamine	150 g	(poorly wettable solid)
Zinc oxide	50 g	(poorly wettable solid)
Bentonite	30 g	(suspending agent)
Sodium citrate	5 g	(convert bentonite from gel to solution)
Liquefied phenol	5 ml	(preservative, antiseptic)
Glycerol	50 ml	(thick liquid)
P.W.	qs. 1000 ml	(vehicle)
mitte		25 ml

- Used as antipruritic (e.g. for chickenpox).

◉ Special procedure: Triturate the calamine, the zinc oxide and the bentonite with a solution of the sodium citrate in about 700 ml of the purified water and add the liquefied phenol, the glycerol and sufficient purified water to produce 1000 ml.

℞ Compound sulphur lotion

Precipitated sulphur	40 g	(poorly wettable solid)
Alcohol (95%)	60 ml	(wetting agent)
Glycerol	20 ml	(wetting agent)
Quillaia tincture	0.5 % v/v	(wetting agent – saponin)
Calcium hydroxide solution	qs. 1000 ml	(vehicle)
mitte		25 ml

- Used for scabies.

◉ Calcium hydroxide solution also known as lime water.

5. Dispersions of oil in inhalation

◉ Inhalations are liquid products that contain volatile ingredients intended to be released and brought into contact with the respiratory lining.

◉ Here, the volatile ingredient is adsorbed onto a carrier powder (a diffusible solid) and formulated as suspension.

◉ When used, an accurate dose of the suspension is added to hot (about 65 °C) but not boiling water, so that the volatile ingredient is released and inhaled by the patient.

◉ Example: A volatile oil is suspended in water after being adsorbed on light magnesium carbonate powder. If the quantity of light magnesium carbonate is not included in the formula, 1 g of it is added to each 2 ml of oil (e.g. eucalyptus and pumilio pine oil) or 2 g of volatile solid (e.g. menthol and thymol).

6. Suspensions prepared by chemical reaction

◉ Here, the insoluble active constituent of the suspension is formed by chemical reaction.

◉ Example: White lotion is prepared by mixing dilute solutions of zinc sulphate and sulphureted potash. The mixing must be slowly with continuous stirring so that a finely divided precipitate will be formed in the reaction.

$ZnSO_4 + K_2S \rightarrow K_2SO_4 + ZnS \downarrow$ (insoluble diffusible)

◉ White lotion is used in the treatment of number of dermatological diseases.