Syllabus

- Semisolid dosage forms – Definitions
- Classification
- Mechanisms and factors influencing dermal penetration of drugs.
- Preparation of ointments, pastes, creams and gels
- Excipients used in semi solid dosage forms
- Evaluation of semi solid dosages forms

SEMI-SOLID

BP103P - PHARMACEUTICS UNIT 5

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Definitions

- Semi solids are the topical dosage form used for the therapeutic, protective or cosmetic function.
- They may be applied to the skin, or used nasally, vaginally, or rectally.
- Pharmaceutical semisolid dosage preparations include ointments, cream, pastes, gels etc.
- They contain one or more active ingredients dissolved or uniformly dispersed in a suitable base and any suitable excipients such as emulsifiers, viscosity increasing agents, anti microbial agents, antioxidants, or stabilizing agents etc.

Advantage –

- It is used externally.
- Probability of side effect can be reduce.
- First pass gut and hepatic metabolism is avoided.
- local action and Site specific action of drug on affected area.
- Convenient for unconscious patient or patient having difficulty on oral administration.
- Suitable dosage form for bitter drugs.
- More stable than liquid dosage form.

Classification

semisolids

- ointments
- poultices
- Pastes
- Gels & jelles
- creams
- suppositories

Mechanism & factors Influencing Dermal Penetration of drug

Absorption of substances through the skin depends on a number of factors:

- ❖ Concentration
- ❖ Molecular Weight of the molecule
- ❖ Duration of contact
- ❖ Solubility of medication
- ❖ Physical condition of the skin

- Part of the body exposed including the amount of hair on the skin
- small amounts of chemicals may enter the body rapidly through the glands or hair follicles, they are primarily absorbed through the epidermis.
- The stratum corneum is the outermost layer of the epidermis and the rate limiting barrier in absorption of an agent.
- Once a substance passes through stratum corneum, then its no significant further hindrance to penetration of the remaining epidermal layer & corium.
- The stratum corneum is primarily composed of lipophilic cholesterol, cholesterol esters and ceramides (fatty acids).
- Thus lipid-soluble chemicals it through the layer and into the circulation faster, however nearly all molecules penetrate it to some minimal degree.
- Also, penetration depending upon effective blood flow, interstitial fluid movement.

Ointments - Ointment are homogenous, translucent, viscous semisolid preparation intended for external application to skin of mucous membrane.

Preparation of Ointments -

(1) Trituration Method –

- Most commonly used method
- for small scale manufacturing of Ointment.
- used when base is soft and medicament is insoluble in base.

Trituration method

Simple ointment

Wool fat 5g

Hard paraffin 5g

Cetostearyl alcohol 5g

White soft paraffin 85g

Procedure :-

finely powder the solid medicament (in pestle and mortar or Ointment slab)

↓

Weigh required quantity of an ointment base.

↓

Triturate solid medicaments with small amount of base (on ointment slab with S.S. spatula) Until homogenous product is formed.

↓

Add remaining base and mix uniformly (Add any Liquid ingredient if present’)

↓

Ointment so prepared pass through roller mill to ensure uniform drug dispersion, removal of any aggregates.

↓

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(2) Fusion Method :-

This method is suitable when base is solid.
Small Scale porcelain dish is placed on water bath.
Large Scale → Carried out in large steam-jacket kettles.

Fusion method
Wool alcohol ointment
Wool alcohol 6g
Hard paraffin 24g
White soft paraffin 10g
Liquid paraffin 60g

Procedure: The ingredients and base are melted and properly mixed to obtain a uniform product.

↓

Initially the ingredient of highest melting point is melted then remaining are added in decreasing order ↓ M.P.

↓

Mixture is removed from water bath and stirr to cool it.

- Insoluble drugs in base • added in powdered form
- Liquids or semisolids → added at a temp. of 40°C
- Volatile or heat-labile ingredients added at last

(3) Chemical Reaction Method – This method is based on the chemical reaction b/w result in elegant and stable product (like non staining iodine ointment).

Formula of Non-staining Iodine Ointment Iodine Arachis Oil

Procedure:- Iodine is powdered in mortar-pestle

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arachis oil is added

↓

mixture is heated to 50°C (stirr occasionally till -black colour appears)

↓

green - yellow soft paraffin added at 40°c mixed and cooled

Gels

Definition- Gels are defined as semisolid dispersion systems which may contains suspension of small molecules dispersed in a suitable vehicle using gelling agent.

Formulation of gels:-

1) Gelling agents :- these are organic hydrocolloids same times hydrophilic inorganic substance are used.

Example:- gum tragacanth , starch , pectin , gelatin , clays , sodium alginate, carbomers, polyvinyl alcohol Cellulose derivatives (SCMC, HPMC)

2) Preservatives:- Gels Are Most Susceptible To Microbial Growth Due To High Water Content

(3) Other Ingredients :-

(a) Hygroscopic Substances :- Quick evaporation of water from gel lead to formation of flakes on skin. To prevent this hygroscopic substances are added.

Examples: Glycerin, propylene glycol and sorbitol

(b) Chelating Agents :- Chelating agents inactive the heavy metals prevent degradation of medicament sensitive to heavy metals.

Example: Ethylene Diamine tetraacetic acid (EDTA)

Preparation of Gels –

Drug is dissolved in aqueous vehicle and thickening agent is added by triturating in a mortar.

Trituration is carried out untill a is formed homogenous preparation is formed.

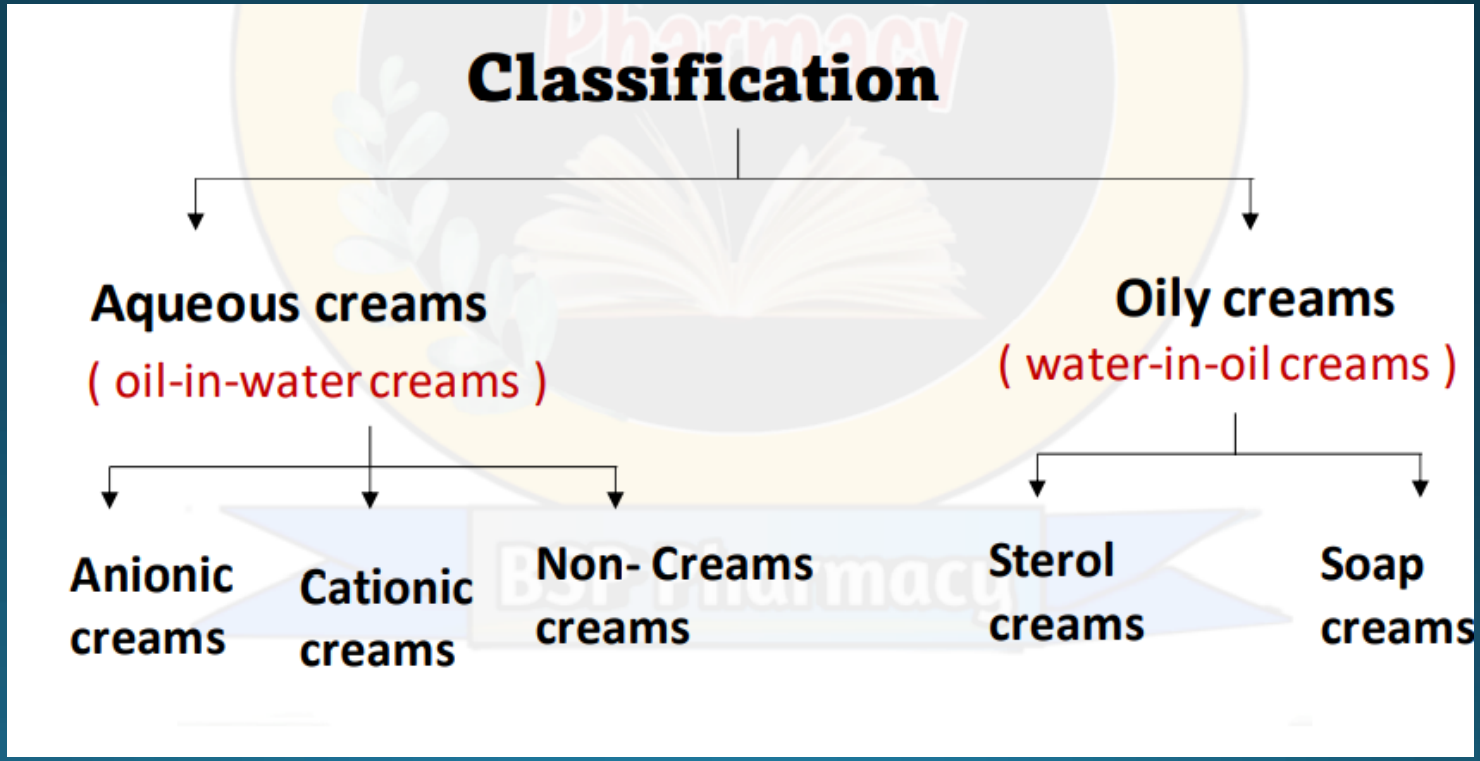
Packing - Packed in Packed in plastic or Aluminium squeeze tubes. Jars (Plastic or glass). Some times prefilled syringes and pump dispensers are also used.

Storage:- Should be stored at room temperature without exposing to direct sun light and moisture.

Creams

In pharmaceutical practice creams are viscous, semi – solid emulsions meant for external application or use.

Usually contain water soluble base due to which they can be easily removed from skin.



1) Aqueous creams (o/w cream):- Composed of small droplets of oil dispersed in continuous aqueous phase.

A. Anionic Creams - These creams prepared by fusion method

oily ingredients are melted together (60°C)aqueous solution is warmed at 60°C

↓

aqueous solution added in molten mixture with constant stirring to cool its temp

Example- Phenoxyethanol Aqueous Cream BP

(b) Cationic Creams: These creams are prepared by fusion method Example - Cetrimide Cream BP

(C) Non-ionic Creams : These are prepared by fusion method. The creams are prepared by using non-ionic emulsifying agents fatty alcohols, macrogol ester polysorbates, polyvinyl alcohol etc

Oily Creams (w/o Creams) :- These creams are composed of small droplets of water dispersed in a continuous oily phase.

(a) Sterol Creams - In sterol creams, wool fat or wool alcohol used as emulsifying agent.

Example: Proflavine Cream BPC.

(b) Soap Creams: In soap creams, Calcium soap, triethanolamine soap etc. used as emulsifying agent.

Example :- Cold cream (Borax (ream) Barrier cream (Triethanolamine cream)

Pastes

Definition:- Pastes are defined as the semi-solid preparations meant for external application on skin form a protective coating over it

They are used as antiseptic protective or soothing dressings often spread on lint before being applied.

Bases used for Pastes

(1) Hydrocarbon Bases - It includes lanolin, soft paraffin, liquid paraffin

(2) Water miscible Bases - Emulsifying Ointment is used as a water miscible bases for preparation of pastes. Glycerine is also used as water miscible base

(3) Wate Soluble Bases:- Extra Pharmacopoeia preparation like Water soluble dental Paste containing neomycin Sulphate is prepared with macrogol base. Sodium Carboxymethyl Cellulose, pectin and gelatin used as bases in paste.

Types of Pastes –

Based on types of base used pastes can be classified. As

(1) fatty Pastes :- These paste contain fatty or Oleaginous base

e.g. Lassar’s Paste, Zinc Oxide Coal tar Paste and Zinc Oxide Paste.

(2) Aqueous Gel Pastes: These are prepared by Water Miscible bases.

e.g. Titanium Dioxide Paste Resorcinol & Sulphur Paste Magnesium Sulphate Paste.

(3) Hydrocolloid Pastes: These are prepared by Hydrocarbon bases.

e.g. Tooth Paste, Zinc Oxide Paste Unna's Paste.

Procedure:- The ingredients and base are melted and properly mixed to obtain a uniform product.

↓

Initially the ingredient of highest melting point is melted then remaining are added in decreasing order of M . P.

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Mixture is removed from water bath and Stirr to cool it.

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Insoluble drugs in base added in powdered form.

Liquids or semisolids added at a temp. of 40°C.

Volatile or heat-labile ingredients added at last

Excipients used in semi solid dosage forms

The are & common excipients used in liquid formulation are :

(1) Vehicles

(2) Solubilizers

(3) Stabilizers

(4) Preservatives

(5) Organoleptic agents

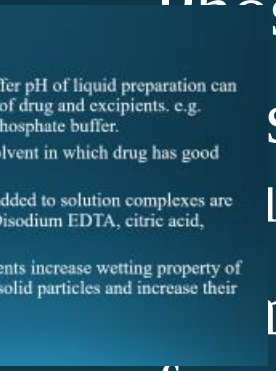
(1)Vehicles →

(a) Solvents: Solvents are vehicles → used as base in which drug and other excipients are dissolved or dispersed. e.g. Water, hydro-alcoholic liquid, polyhydric alcohol acetic acid, and buffers. the oily vehicles includes vehicles oils, mineral oils etc.

(b) Co-solvents: Defined as water miscible organic solvents that are used increase solubility of poorly water soluble substances .* The most commonly used co-solvent is ethanol other co-solvents are sorbitol, glycol, propylene glycol.

(2) Solubilizes –

(a) pH Adjustment :- By addition of suitable buffer pH of liquid preparation can be adjusted. The selection of buffer stability of drug and excipients. e.g. Phosphate buffer, acetate buffer, citric acid phosphate buffer.



solvency :- Addition of water miscible solvent in which drug has good ıbility.

nplexation :- when complexing agent is added to solution complexes are formed. It increase solubility of drug. E.g . Disodium EDTA, citric acid, dihydroxy ethyl glycine.

(d) Wetting agents and Surfactants – Wetting agents increase wetting property of hydrophobic drug particles by adsorption at solid particles and increase their solubility. e. g. Sodium lauryl sulphate.

(3) Stabilizers -

(a) Antioxidants :- To prevent oxidation in liquid formulation. antioxidants are used . E.g. ascorbic acid, thiourea.

(b) Antifoaming agents:- Antifoaming agent discouraging the formation of stable foams during manufacturing and transportation . E.g. Simthicone, organic phosphate, alcohol, paraffin etc.

(c) Suspending and viscosity Enhancing agents :- Suspending agent and viscosity enhancing agents import viscosity, so reduce particle settling. E.g. clays, natural gums, synthetic gum.

(d) Humectants :- Humectants are hygroscopic substances prevent evaporation of aqueous vehicals from liquid dosage forms E.g. Propylene glycol, glycerol, polyethylene glycol.

(e) Flocculating agent : It prevent formation. hard cake. Addition of electrolytes reduce the magnitude of zeta potential of particles. e.g. Starch, Starch, sodium alginate.

(4) Preservatives:- The major problem with liquid dosage form is microbial contamination use of preservatives prevent growth of micro-organisms.

Preservatives must be –

- ❖ effective against broad spectrum of micro organisms
- ❖ physically and chemically stable
- ❖ non toxic, non sensitizing, soluble and compatible
- ❖ should have acceptable taste and odour.

e.g. Acidic phenol – sorbic acid, benzoic acid

Neutral preservative – chloro butanol, benzyl alcohol.

Quarternary ammonium compounds - Benzalkonium chloride

(5) Organoleptic Properties :-

(a) Sweetening agents: Sweetening agent are used to mask. unpleasant or bitter taste of drug gives pleasant texture in mouth.

e.g. Sugar- Sucrose, fructose

Sugar fee- Sorbitol, mannitol, saccharin, aspartame

(b) Colouring agents: The colour used in the liquid dosage form must be certified by FDA as per Drug & Cosmetic Act 1940.

(c) flavouring agents: Flavour refers to a mixed sensation of taste, touch, smell, sight and sound ↓ all of which together produce an infinite number of gradations.

e.g. fruity or spicy flavour for oral - use pine apple, banana, ginger, cardamom, peppermint

for external use → rose, jasmine, lavender, perfume etc

Evaluation of semi solid dosages forms

Evaluation of ointment includes following parameters –

a) Penetration
b) Rate of release of medicamente
c) Absorption of medicament into blood stream
d) irritant effect
e) content uniformity of drug

a) **Penetration -** weighed quantity of ointment is rubbed over skin for a given period of time. Then unabsorbed ointment is collected and weighed. The difference in weights represent the amount absorbed.

b) **Rate of release of medicaments –**

Small amount of the ointment is placed on the surface of nutrient agar contained in petri dish.

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Depending on the medicament content, agar plate is previously Seeded with a suitable organism.

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Example - for bactericidal drug content, S. aureus organum is seeded. After a suitable period of incubation, the zone of inhibition is measured and correlated with rate of release.

c) **Absorption of medicament into blood stream -** The test can be run-in vivo only. Definite amount of ointments should be rubbed through the skin. Under standard condition and medicaments are estimated in the blood plasma or urine.

d**) Titant effect -** Test for writancy of ointment can be carried out and eyes of rabbits the skin of human beings.

Draize test (Skin) :-

A known amount of test substance is introduced under a one square inch gauge patch. The patch is applied to skin of 12 albino rabbits (6 with intact skin) & 6 (with abraded skin). Patch is secured in place with adhesive tape and the entire trunk of the animal is wrapped with an impervious material for a 24 have period. After 24 hours the patches are removed and resulting reaction is evaluated for erythema and edema formation The reaction is again scored at the end of 72 hours and the two readings are averaged following observation decide the results.

- ❖ well defined erythema & slight edema – mild
- ❖ Moderate to severe erythema and moderate edema (area raised appelmm) – moderate
- ❖ severe erythema (beet red new to Slight eschar formation & severe edema
- ❖ The irritant effect can also be judged to a certain extent by injecting the ointment into thigh muscles and under the abdominal skin rate.
- ❖ Reactions are noted at interval of 24, 48, 72 and 96 hours
- ❖ Lesions on cornea, iris, conjunctiva are used for judging the irritancy to the eyes
- ❖ Presence of patches on the skin within 2 weeks indicates irritancy to pressing skin.

Evaluation of Creams –

❖ cream are evaluated for –

(a) D Rheology - Rheology /viscosity should remain constant. These products are normally non-Newtonian in nature, so, viscosity can be measured using viscometers used for such liquids Rheologic measurements are utilized to characterize the ease of pouring from a bottle, squeezing from a tube of other deformable container, maintaining product shape in jar of after extrusion rubbing the product onto and into the skin and pumping the product from mixing and storage to filling equipment.

(b) Sensitivity - This test is done by patch test on can be either open or occlusive. The test sample is applied along with a standard market product at different places and effect is compared after a period of time.

C) pH - pH of the cream can be measured on a standard pH meter at room temperature by taking adequate amount of formulation diluted with a suitable solvent in a suitable beaker.

d) Spread ability - Adequate amount of sample is taken between two glass slides and a weight of 100gm is applied on the slides for 5 minutes.

Spread ability can be expressed as – S = m*l/ t

Where m= weight applied to upper side

L= length moved on the glass slide

T= time taken

e) Particle size - It is determined by microscopic study of the particles.

f) Rheology- viscosity is measured using viscometers.

g) pH of product - pH of the dispersion of 10% of the product in water is determined by pH meter.

h) Foaming character - This test is required for foam forming toothpastes of tooth powders. A specified amount of product is mixed with specific amount of water and then it is shaken, thus foam formed is studied for its nature, stability and washability .

Evaluation of gel - Gels are jelly-like semisolid dispersions of drug meant to be applied on the skin.

Gels are evaluated for –

1. Dye test— ❖ This helps to check whether cream is w/o or 0/w type. Scarlet dye is mixed with the cream. Then a drop of cream is placed on a slide and covered with cover slip and examined under microscope. If the disperse globule appears red and the ground colourless then it is w/o type and reverse condition for 0/w type.
2. **pH Determination:-** The pH of gel is determined by digital pH meter. Standard pH - 5 to 5.5
3. **Drug Content -** 1 gm of get is weighed in a solution of volumetric flask. Then add 20 ml of purified water with continous shaking. volume is adjusted with a mixture of 10% methanol in water. Absorbance the solution with the blank is measured of at 360mm using UV- Spectrophotometer.

4. Spreadibility :- Spreadibility is measured by spreading 60.5 g gel on a circle of 2 cm diameter a glass plate. then a second glass plate is employed 1/2 kg weight placed on upper glass plate "for" for 5 min.

diameter of circle after spreading is determined .

S = M.L/T

m = weight

L = Length of circle. (Diameter)

T = time.

5. Test for Stability:- known as shipping testIt is performed to determine stability of gel at various temperatures.

6. Homogeneity of drug content - Six tubes are taken randomly and assayed for drug Content.

7. Viscosity - ❖ Brookfield viscometer is used for determination of viscosity. Gels were filled in jar and spindle was lowered perpendicularly taking care that spindle do not touch bottom of the jar. Spindle was rotated in the gel at increasing shear rates 0.5, 1, 2.5 and 5rpm. At each speed, the corresponding dial reading was noted.

8. Test for clarity - test formulated solution is visually inspected under black and white background.

9. Sterility testing - Sterility testing is carried out as per the IP 1996. The formulation is incubated for not less than 14 days at 300-350°C in the fluid thioglycolate medium to the growth of bacteria and at 200-250°C in soyabean casein digest medium to find the growth of fungi in formulation.

Paste - Paste contains a large amount of finely powdered solids such as starch and zinc oxide. These are generally very thick and stiff.

Pastes are evaluated for –

a) Abrasiveness - Amount of solid medicament per unit of paste is determined

b) Particle size - It is determined by microscopic study of the particles.

c) Rheology - viscosity is measured using viscometers.

d) pH of product - pH of the dispersion of 10% of the product in water is determined by pH meter.

e) Foaming character - This test is required for foam forming toothpastes a toothpowders. A specified amount of product is mixed with specific amount of water and then it is shaken. foam thus formed is studied for its nature, stability and washability.

Thank You