Unit-V

☆ Semisolid dosage forms:-

#Defination:- Semi-solid dosage forms are dermatological preparation intended to apply externally on the skin to produce local or systemic effect e.g. ointment, creams, gels and pastes.

→ They contain one or more active ingredients dissolved or uniformaly dispersed in a suitable base and any suitable excipients such as emulsifiers, viscosity increasing agent, antimicrobial agents, antioxident etc.

#Classification:-

Type of semi-solid dosage form:-

1. ointments
2. creams
3. pastes
4. Gel
5. poultices
6. plasters.

① ointments:- ointments are semisolid preparations meant for external application to the skin or mucous membrane. They usually contain a medicaments dissolves, suspended or emulsified in the base.

② Creams:- Cream are viscous emulsions of semisolids consisteney intended for application to the skin or mucous membrain and o/w type and w/o type.

③ pastes:- pastes are the preparations which contains a large amount of finaly powdered solid such as starch

and zinc oxide. These are generally very thick and stiff.

④ Gel :- These are ~~also known~~ jelly-like semisolid dispersion of drug ment to be applied on the skin.

⑤ poultices :- These are ~~meant for insertion~~ also known as Cataplasms. They are Soft viscous wet masses of solid substances.

⑥ plasters :- These are semi-solid masses applied to the skin to enable prolonged Contact of drug with the skin or substances intendend for external use.

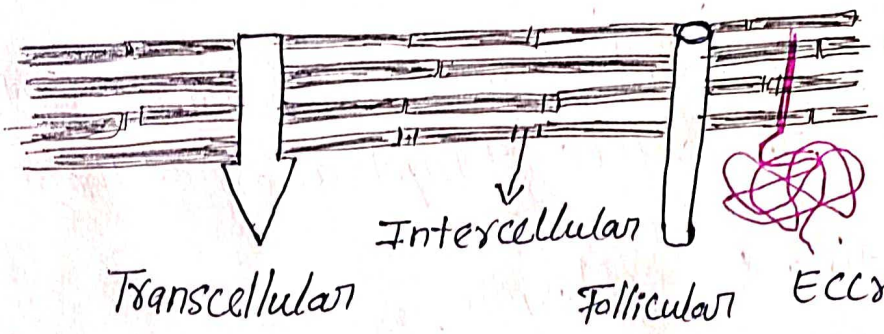
☆ Mechnism of skin permeation :-

- The skin itself has two main Layers, the epidermis, which is the outermost layer of the skin, covering the dermis that is the active part of the skin, holding the hair Muscles, blood Supply, sebaceous-gland and nerve receptor.

→ The skin is very heterogeneous membrane and has a variety of cell types, but the layer that Control the penetration of drugs is Called the Stratum Corneum and its thikness of only 15-20 μm.

→ It provides a very effective barrier to penetration.

→ The permeation of the drug through the skin has Several routes: transcellular, intercellular, and appendageal (through eccrine (sweat) gland or hair follicles)



-: Schematic representation of the different possible routes of Penetration through the skin.

✱ Factor influencing Dermal penetration of drug :-

① Physiological and pathological Condition of skin :-

(a) Skin Condition :- The permeability of the skin is affected by age disease, climate and injury.

(b) Skin age :- The young skin is more permeable than older. Childrens are more senstive for skin absorption of foxins.

(c) Blood flow :- Change in peripheral Circulation Can affect transdermal absorptim.

② Physico-chemical properties of active Substance :-

(a) Molecular Characteristic of drug :- Molecular weight upto 400 dalton Can easily penetrate through the skin Surface.

(b) Drug Concentration :- The flux is proportional to the Concentratio gradient across the barrier and concentration gradient will be higher if the Concentration of drug will be more across the barrier.

③ Effects of Vehicles :-

The Vehicles May enhance the penetration of a drug In one or More of the following Ways.

→ By ensuring good Contact with the Surface of the body.
→ By increasing the degree of hydration of the stratum Corneum.
- By penetrating the epidermis.
- By directly altering the permeability of the skin.

✱ Preparation of Ointments :-

→ "Ointment are Semi-Solid preparation for application to the skin".

→ Ointments are prepared by two general methods -

- Incorporation
- Fusion.

① Incorporation :-

By the incorporation method, the Components are mixed until a uniform preparation is attained.

② Fusion Method :-

→ Fusion is the act or procedure of liquefying or melting by the application of heat.

→ By the fusion method, all or some of the Components of an ointments are Combined by melted together and Cooled with Constant Stirring until Congealed.

- Heat labile Substances added last, When the temperature of the mixture is low enough not to Cause decomposition of the ingredients.

✱ Preparation of paste :-

- pastes generally Contains a Large amount (50-1.) of finely powdered Solid, so they are often Stiffer then ointments.

Procedure :-

Method - I :-

- Emulsifying wax is melted in a tarred dish (70°C)
- The Coal tar is weight in the dish. Stirred to mix.
- Soft paraffin is melted in a Separate dish (70°C) and about half is added to the tar-wax mixture; stirred well.
- Remainder is added : stirred again until homogeneous.
- Allowed to Cool at about (30°C) and zinc oxide and starch, in Small amount with Constant-stirring. stirred untill Cold.

✱ Preparation of Cream :-

- Method - I :-

① Trituration :-

- Used for finely divided insoluble powder particles or liquids insoluble powder are added by geometric dilution liquid are added by making well in centre.
- Air pot pocket formation avoided. Involved the use of glass Slab when small quantities are used mortar and Pestle used when we have large quantities.

(2) Fusion Method :-

- The fusion method is followed when the drugs are and other solid are soluble in the ointment bases.
- The base is liquefied and the soluble components are dissolved in the molten base.
- The congeal mixture is then speculated or triturated to obtain a smooth texture.
- Care is taken to avoid thermal degradation of the base or other components during the fusion process.

☆ preparation of Gels :-

- Gels are semi-solid preparation that contain small inorganic particles or large organic molecules interpenetrated by a liquid.
- Method - II :-

Step-I :- Required quantity of polymer was weight and it was sprinkled slowly on surface of purified water for 2hr. After which it was continuously stirred by mechnical stirrer, till the polymer soaked in the water.

Step-II :- With continuous stirring, triethanolamine was added to neutralize the gel and it maintain the pH 7 of the gel. Now the appropriate quantity of Econazole nitrate was dissolved first in Dmso (Dimethyl Sulfoxide) which was added to the gel, which behaves as the penetration enhancer.

Step-3 :- Finally methyl paraben was added to the gel with continuous stirring till it get dispersed in gel completely.

☆Excipients used in semi-solid dosage forms:-

① API :- Active pharmaceutical ingredient is any part of drug which produces any effect.

② preservatives :- To stop microbial growth preservative are added. preservatives for ~~a given per~~ ointment includes: p-hydroxy benzoates, phenol, benzoic acid, sorbic acid, Methyl peraben, etc.

③ Humectant :- Such as glycerine, polylene glycol and Sorbitol may be added to prevent the loss of moisture from the preparation.

④ Emulsifying agent :- like polysorbate, anionic emulsifying agent etc. are added if required.

⑤ Antioxidant :- Some ingredients like wool fat and wool alcohols are susceptible to oxidation, therefore a suitable antioxidant may be incorporated to protect the active ingredients from oxidation.

⑥ Organoleptic Agent :- Suitable Colouring agent - (amaranth, brilliant blue etc) flavouring agent (vanilla, strawberry, raspberry) are added.

Evaluation of semi-solid dosage forms :-

① **Content Uniformity of drug :-** A known weight of ointment is taken and assayed for amount of the drug.

② **Penetration :-** A weighed quantity of ointment is rubbed over skin for a given period of time and unabsorbed ointment is collected and weighed. The differences in weights represent the amount absorbed.

③ **Rate of release of medicament :-**

To assess rate of release of medicament, small amount of the ointment can be placed on the surface of nutrient agar contained in a petri dish.

- If the medicament is bactericidal the agar plate is previously seeded with a suitable organism like S. aureus.
- After a suitable period of incubation, the zone of inhibition is measured and correlated with the rate of release.

④ **Absorption of medicament in blood stream :-**

- ointment should evaluated for the rate of absorption of drug into the blood stream.
- This test can be run in-vivo only. Definite amount of ointment should be rubbed through the skin.
- Under standard conditions and medicaments are estimated in the blood plasma or urine.