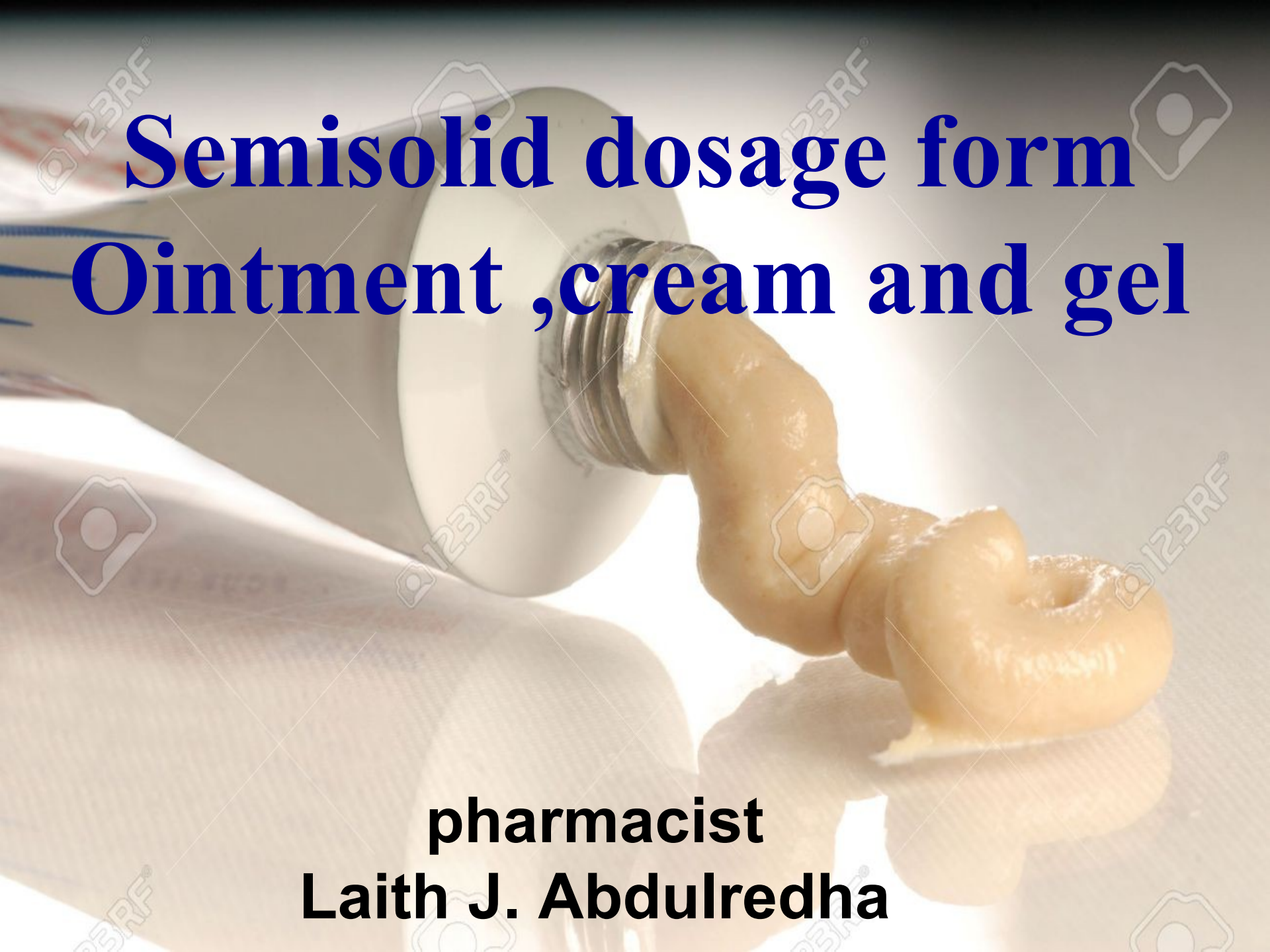

Semisolid dosage form Ointment ,cream and gel

pharmacist
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Semisolid dosage form

- **INTRODUCTION**
- **Pharmaceutical semisolid dosage preparations include :ointments, pastes, cream, plasters, gels and rigid foams.**
- 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..

DEFINITION

- 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…

Advantage of semi-solid dosage form:

- 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

Disadvantages of semi-solid dosage form:

- There is **no dosage accuracy** in this type of dosage form
- The base which is used in the semi-solid dosage form can be **easily oxidized**.
- May cause **staining**.
- They are **bulky** to handle.
- Application with finger may cause **contamination.**
- Physico-chemically **less stable** than solid dosage form.
- May cause **irritation or allergy** to some patients

IDEAL PROPERTIES OF SEMISOLIDS

- **PHYSICAL PROPERTIES:**
- Smooth texture
- Elegant in appearance
- Non dehydrating
- Non gritty
- Non greasy and non staining
- Non hygroscopic

IDEAL PROPERTIES OF SEMISOLIDS

- **PHYSIOLOGICAL PROPERTIES**
- Non irritating
- Do not alter membrane / skin functioning
- Miscible with skin secretion
- Have low sensitization index
- **APPLICATION PROPERTIES**
- Easily applicable with efficient drug release.
- High aqueous wash ability.

PREPARATION OF SEMISOLIDS DOSAGE FORMS

INGREDIENTS USED IN PREPARATION:

- Bases
- Preservative
- Humectants
- Antioxidants
- Emulsifier
- Gelling agent
- Permeation enhancer
- Buffers

1. BASES:

- It is one of the most important ingredient used in formulation of semisolid dosage form. Ointment bases do not merely act as the carriers of the medicaments, but they also control the extent of absorption of medicaments incorporated in them.

1. BASES:

IDEAL PROPERTIES OF A BASE:

They should be:

- Inert, non-irritating and non-sensitizing.
- Compatible with skin pH and the drug.
- Good solvent and/or emulsifying agent.
- Emollient, protective, non-greasy and easily removable.
- Release medicament readily at the site of application.
- Pharmaceutically elegant and possess good stability

CLASSIFICATION OF BASES :

Ointments bases are classified by the USP into four general groups:

A- hydrocarbon bases (oleaginous bases)
(Petrolatum , Paraffin, Lanolin…..)

B- absorption bases (*cold cream, anhydrus lanolin ...)*

C- water-removable bases (oil in water)

D- water-soluble bases (polyethylene glycol)

ANTIOXIDANTS :

Oxygen is a highly reactive atom that is capable of becoming part of potentially damaging molecules commonly called **"free radicals."**

Free radicals are capable of attacking the healthy cells of the body, causing them to **lose their structure and function**. To prevent this an antioxidants are added.

E.g. **Butylated hydroxy anisole, Butylated hydroxy toluene**

PERMEATION ENHANCERS :

- Skin can act as a barrier. With the introduction of various penetration enhancers, penetration of the drug through the skin can be improved.

- **Oleic acid**

EMULSIFIER :

- An emulsifier (emulgent) is a substance that stabilizes an emulsion by increasing its kinetic stability.

- Must reduce surface tension for proper emulsification.

- Prevents coalescence.

- Ability to increase the viscosity at low concentration.

•Emulsifying agents

- Sodium lauryl sulfate :O/W emulsion

- Sodium stearate and calcium stearate.

- Glyceryl monostearate: weak W/O emulsifying agents and used as stabilization agents and emollient in the O/W emulsion.

HUMECTANT:

A humectant is a hygroscopic substance, Humectants are used to :

- increase the solubility of the active ingredient
- to elevate its skin penetration.
- elevate the hydration of the skin.

BUFFERS:

Buffers are added for various purpose such as :

- Compatibility with skin.
- Drug solubility.
- Drug stability.
- Influence ionization of drug. Skin, due to its weak acidic nature, tolerates weak acidic preparations.

- E.g. **sodium acetate, sodium citrate, potassium**

- **Antimicrobial preservatives**

-To inhibit the growth of contaminating microorganisms,

So require the addition of chemical antimicrobial preservatives to the formulation

-E.G. **para-hydroxybenzoates (parabens), phenols, benzoic acid, sorbic acid, quaternary ammonium salts and other compounds.**

1- Ointments

- Ointments are homogenous, translucent, viscous semi-solid preparations, most commonly a greasy, thick oil (oil 80% - water 20%) intended for external application to the skin or mucous membrane. They are used as:

- **Emollients**
- **Protective**
- **Therapeutic**
- **Prophylactic purpose**

Classification of ointments

A- Epidermic ointments

- These ointments are intended to produce their action **on the surface of the skin** and produce local effect,they are not absorbed.
- They acts as protectives, antiseptics and parasiticides.

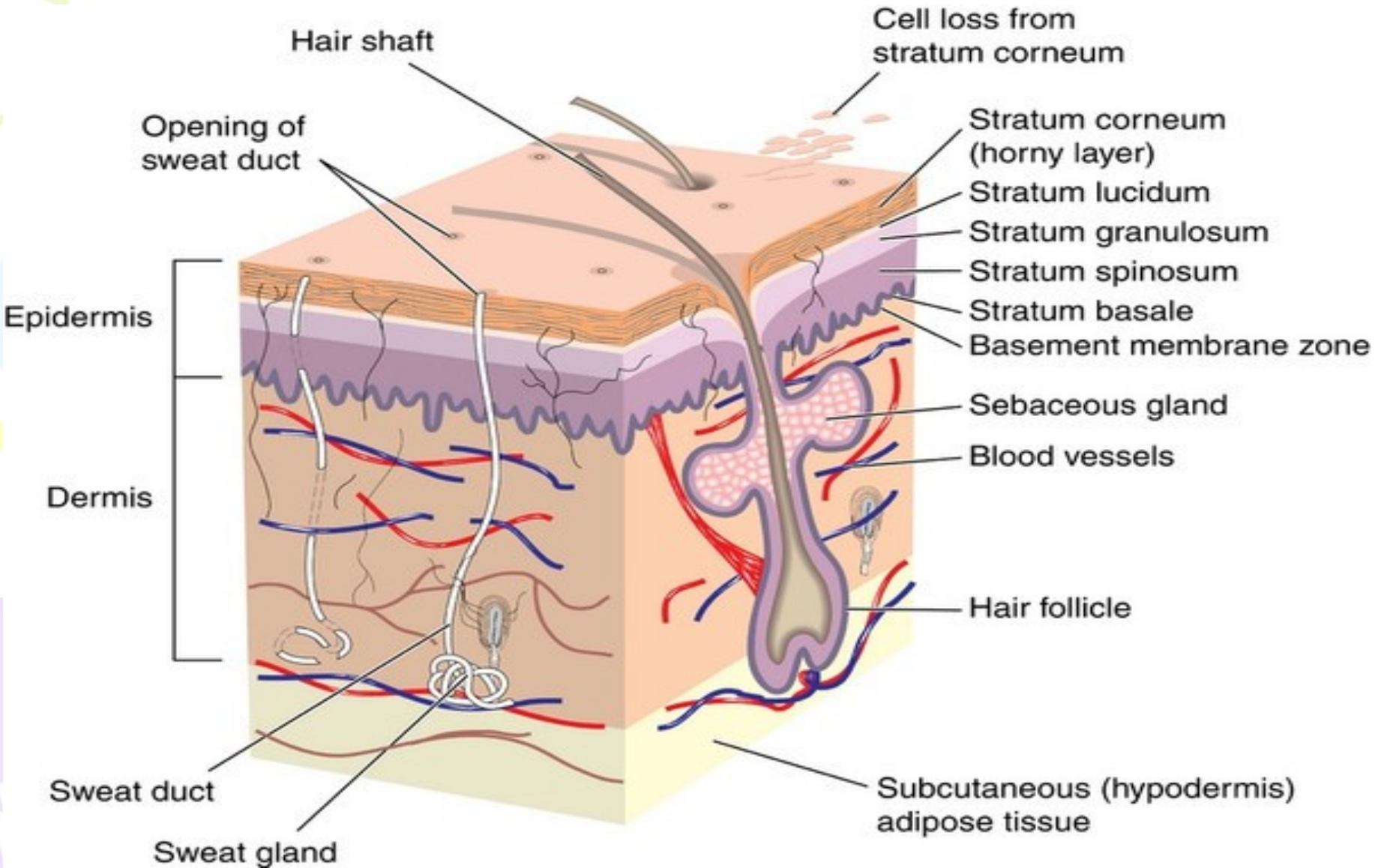
B- Endodermic ointments

- These ointments are intended to release the medicaments that **penetrate into the skin**. They are partially absorbed and acts as emollients, stimulants and local irritants.

C- Diadermic ointments

- These ointments are intended to release the medicaments that pass through the skin and produce **systemic effects**.

Anatomy of skin



Preparation of Ointments

- Both on a large and a small scale, ointments are prepared by three general methods:

(1) incorporation method

(2) fusion method

(3) emulsification method

❖ The method for a particular preparation depends primarily upon the nature of the ingredients

(1) incorporation

-The components of the ointment are mixed together by various means until a **uniform preparation has been attained.**

- On a small scale, the pharmacist may mix the components of an ointment in **a mortar with a pestle**, or a **spatula and an ointment slab** may be used to rub the ingredients together.

TRITURATION METHOD

(2) fusion

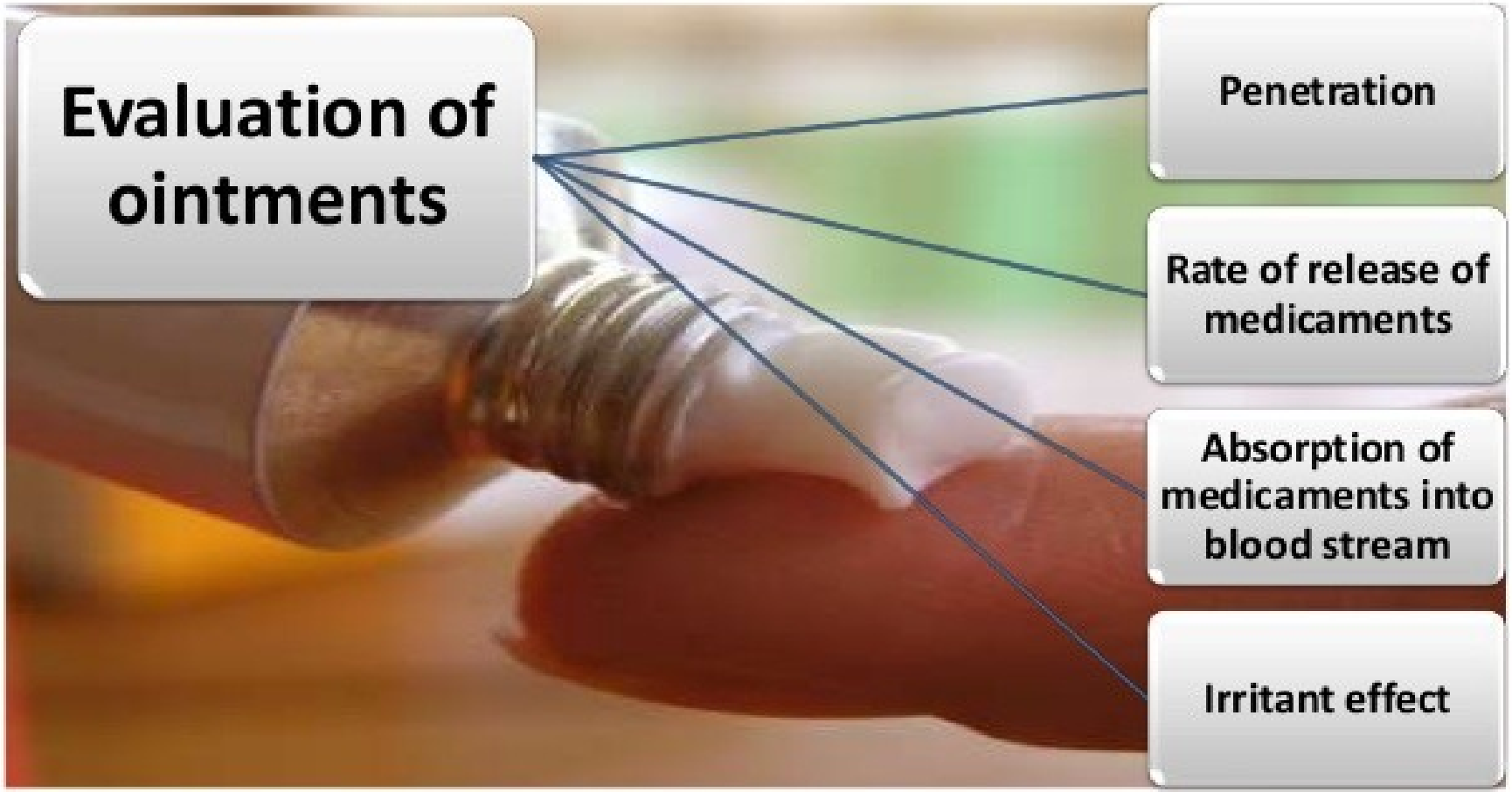
- By the fusion method, **all or some** of the components of an ointment are combined by being **melted together** and cooled with constant stirring until congealed.
- Those components not melted are generally added to the congealing mixture as it is being cooled and stirred.
- Naturally, heat-labile substances and any volatile components are added last when the temperature of the mixture is low enough not to cause decomposition of volatilization of the components.

FUSION METHOD

(3) emulsification

- In the preparation of ointments having an emulsion type of formula, the general method of manufacture involves a melting process as well as an emulsification process.

Evaluation Of Topical Dosage Form



Evaluation of ointments

A- Penetration

- Weighed quantities of the ointments are rubbed over definite areas of the skin for a given length of time. Thereafter the unabsorbed ointment is collected from the skin and weighed. **The difference between the two weights roughly represents the amount absorbed.**

Evaluation of ointments

B- 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 asuitable period of incubation, the zone of inhibition is measured and correlated with the rate of release.

RATE OF RELEASE OF MEDICAMENT

- smear internal surface of test tubes with thin layers of ointment, fill the tubes with saline/serum and after a gap of time estimating the amount of drug present in the serum/saline.

Evaluation of ointments

C- ABSORPTION OF MEDICAMENT INTO BLOOD STREAM:

- Definite amount of ointments should be rubbed through the skin. Under standard conditions and medicaments are estimated in the blood plasma or urine

Evaluation of ointments

D- IRRITANT EFFECT:

- The irritant effect can also be judged to a certain extent by injecting the ointment into thigh muscles and under the abdominal skin of rats. Reaction are noted at intervals of 24,48,72 and 96 hours. Presence of patches on the skin within 2 weeks indicate irritancy to pressing skin

2- creams:

Creams are homogeneous, semi-solid preparations consisting of **opaque emulsion** ,contains lipophilic emulsifying agent . Their consistency depend on the type of emulsion, either water-in-oil (w/o) or oil-in – water (o/w), and on the nature of the solids in the internal phase. Creams are intended for the application to the skin or certain mucous membranes for:

- **Protective**
- **Therapeutic**
- **prophylactic purposes**

Classification of creams

- **Creams containing microspheres**

(VIT. A CREAM … 200-250 micron)

- **Lamellar faced creams**

(liquid paraffin in water emulsion)

- **Cream containing liquid nanoparticles**

(a w/o cream , more occlusive)

Preparation of creams

Steps

- **Preparation of oil phase** :flack/powder ingredient are dispersed in mineral oil or silicone oil) heating may required for melting
- **Hydration of aqueous phase:** emulsifiers, stabilizer, thickener are dispersed in water heating may required for hydrating
- **Forming the emulsion:** two phases are blended under vigorous agitation
- **Dispersion of active ingredient**

Evaluation of creams

A- Rheology:

- . The rheology or viscosity should remain constant. Rheologic measurements are utilized to characterize the ease of pouring from a bottle, squeezing from a tube or container

  - maintaining product shape in ajar or after extrusion, rubbing the product onto the skin

- The viscosity can be measured using **viscometers** used for such liquids.

Evaluation of creams

B- Sensitivity:

As various types of ingredients are used with occasional use of antiseptic, hormones. etc., there is a possibility of sensitization or photosensitization of the skin. This should be tested before hand. This test is normally done by patch test on skin and 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.

Evaluation of creams

C- Effect of thermal stresses:

It is usual to evaluate the stability of an emulsion by subjecting it too high and low temperatures in alternating cycles. The samples are first exposed to 60º C for a few hours and then to o to 40ºC. Such exposures are repeated a number of times and emulsion stability assessed after each cycle.

Evaluation of creams

D- phase separation:

The rate and degree of phase separation in an emulsion can be easily determined by keeping a certain amount in a graduated cylinder and measuring the volume of separated phase after definite time intervals. The phase separation may result from creaming or coalescence of globules. The phase separation test can be accelerated by centrifugation at low/moderate speeds.

3- Gels:

- *Gels* are homogeneous, clear, semisolid systems consisting of dispersions of small or large molecules in an aqueous liquid vehicle rendered jellylike by the addition of a *gelling agent*.

Gels are aqueous **colloidal suspensions** of the hydrated forms of insoluble medicament, used for medication and lubrication.

gelling agents

- Among the gelling agents used

- Synthetic macromolecules, such as **carbomer 934**

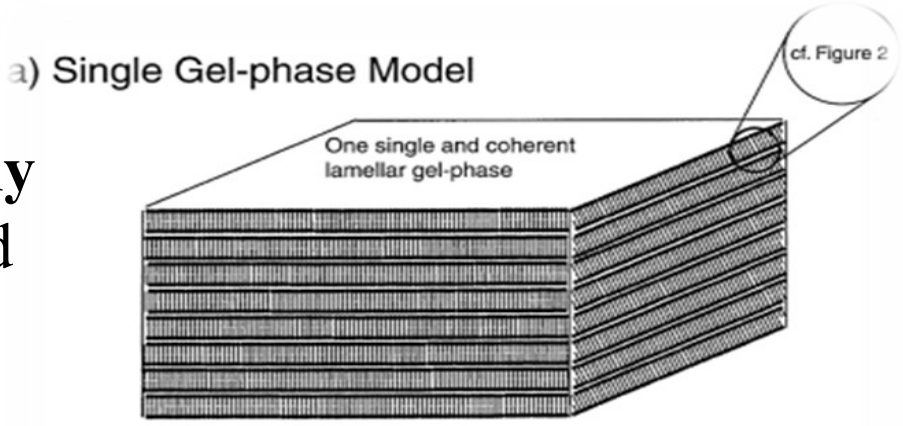
- Cellulose derivatives, such as **carboxymethylcellulose or hydroxypropyl methylcellulose**

- Natural gums, such as **tragacanth**

TYPES OF GEL-PHASE

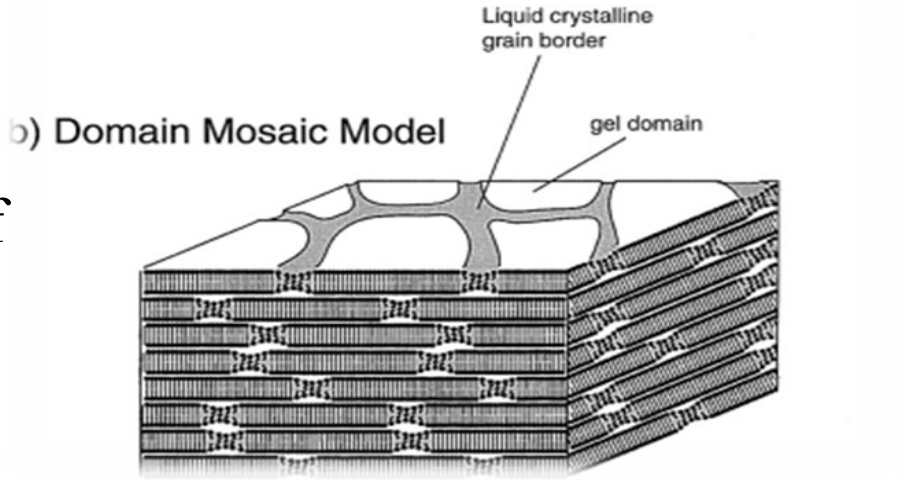
Single Phase

Gels in which the macromolecules are **uniformly** distributed throughout a liquid with no apparent boundaries between the dispersed macromolecules and the liquid
Usually involve **organics**



Two Phase(Domain)

When the gel mass consists of **floccules** of small distinct particles
Usually involve **inorganics**



Kind of gels

- Controlled release gels
- Bioadhesive gels
- Organogels
- Extended release gel
- Amphiphilic gels
- Hydrophilic gel
- Complexation gels
- Thrmosensitive sol-gel resevesible hydrogel

Evaluation of gels

- **Drug content** -1gm of gel was accurately weighed in a 50ml of volumetric flask to which 20ml purified water was added with continuous shaking. Volume was adjusted with a mixture of 10% methanol in water. Absorbance of the solution with the blank was measured at 360nm using **UV-spectrophotometer**.

- **Measurement of pH** -The pH of gels were determined by **digital pH meter**. One gram of gel was dissolved in 100ml of distilled water and stored at 4°C for two hours.

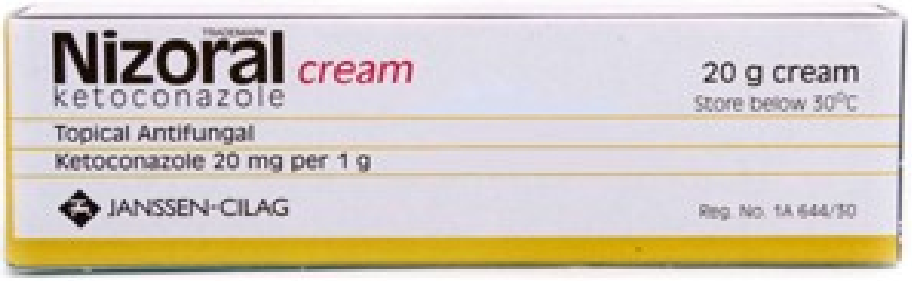
Evaluation of gels

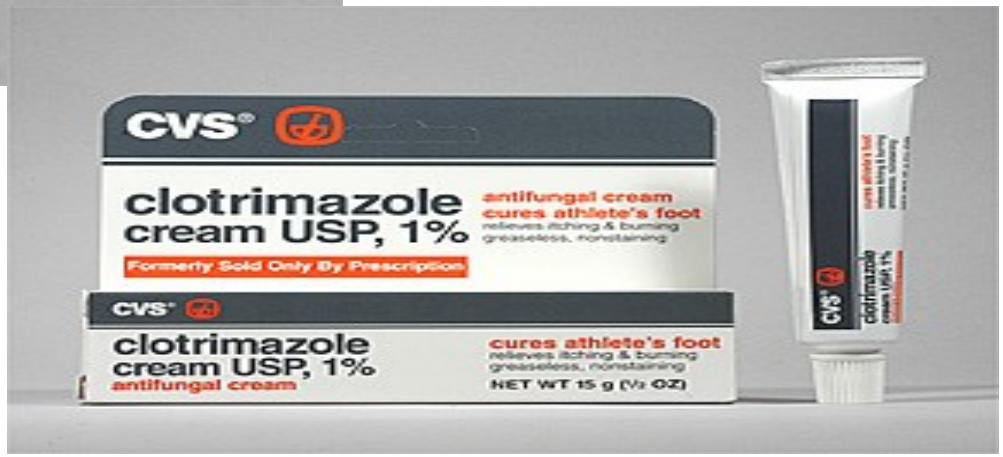
- **Viscosity** -**Brookfield viscometer** is used for determination of viscosity. Gels were filled in jar and spindle was lowered perpendicularly taking care that spindle do not touch bottom of the jar. The spindle was rotated in the gel at increasing shear rates 0.5, 1, 2.5 and 5rpm. At each speed,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

Evaluation of gels

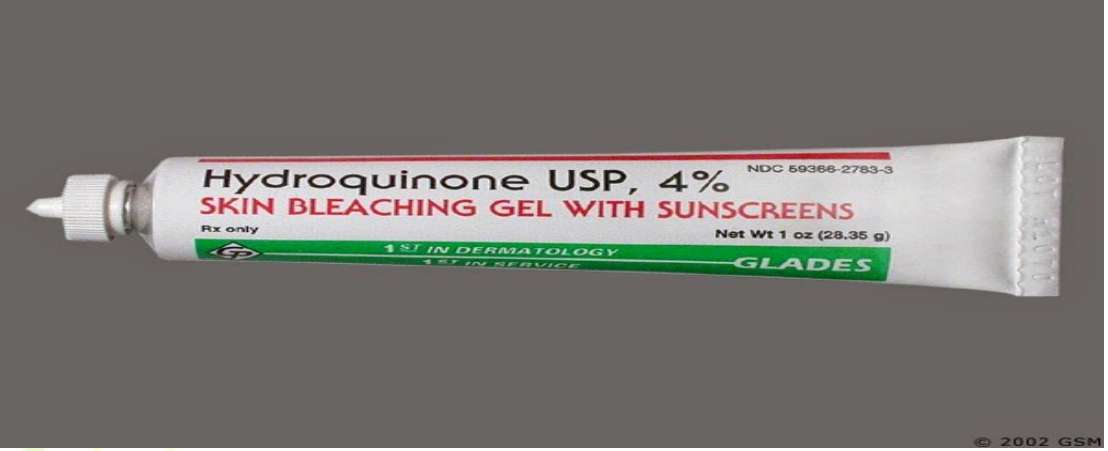
- **Spreadability-** A modified apparatus consisting of two glass slides containing gel in between with the lower slide fixed to a wooden plate and the upper one attached to a balance by a hook was used to determine spreadability.

- **Extrudability -** A simple method was adopted for determination of extrudability in terms of weight in grams required to extrude a 0.5cm ribbon of gel in 10 seconds from the collapsible tube.





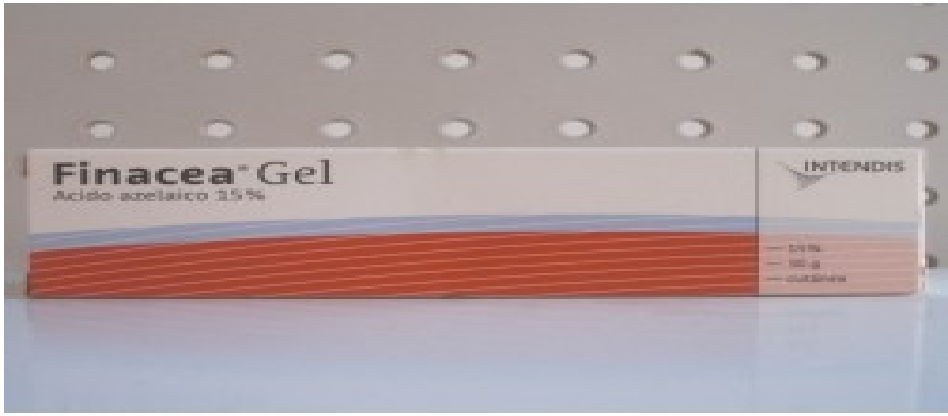
Topical Retinoids For Psoriasis


Hydroquinone USP, 4%
NDC 59366-2783-3
SKIN BLEACHING GEL WITH SUNSCREENS
Rx only
Net Wt 1 oz (28.35 g)
1 ST IN DERMATOLOGY
1 ST IN SERVICE
GLADES
© 2002 GSM


Metrogel
metronidazol
GEL
tubo con 30 g
0.75%
30 g
GALDERMA


Voltaren
Osteo Gel
For the temporary relief of local pain and inflammation associated with mild forms of osteoarthritis of the knees and fingers
Diclofenac diethylammonium gel 11.6 mg/g equivalent to diclofenac sodium 10 mg/g (1 % w/w)
AUST R 175889


IODENT
Compare to the active ingredient of Orajel
MAXIMUM STRENGTH
ORAL ANALGESIC
GEL Benzocaine 20%
MAXIMUM STRENGTH
ORAL ANALGESIC
GEL Benzocaine 20%
Provides IMMEDIATE Relief from:
• Toothache
• Denture and Gum Irritations
• Cold and Canker Sores
NET WT 0.42 OZ (11.9 g)


Finacea Gel
Acido azelaico 15%
INTENDIS

THANK YOU