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Review on: an Ointment



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Shelke Usha Y. *, Mahajan Ashish A.

*Amrutvahini College of Pharmacy, Sangamner, MVP
Samaja's college of Pharmacy Nasik, India.*

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ABSTRACT

Ointments are semisolid systems which usually behave as viscoelastic materials when shear stress is applied. They generally contain medicaments and are intended to be applied externally to the body or to the mucous membrane. Many medicaments meant for topical application to intact or broken skin or to mucous membranes, have been presented in the form of semisolid consistency variously designated as ointments, creams, salves, pastes etc used mainly as protective or emollient for the skin. The first step towards this goal is the screening of plants used in popular medicine. Along with other dosage forms, herbal drugs are also formulated in the form of ointment.



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INTRODUCTION

Ointments are semisolid systems which usually behave as viscoelastic materials when shear stress is applied. They generally contain medicaments and are intended to be applied externally to the body or to the mucous membrane. Non-medicated ointments commonly referred to as ointment bases meant for the preparation of medicated ointments or used as such for emollient or lubricating effects. In prescription practice, various other terms are also used as such for emollient used to designate several variation i.e. creams, pastes, cerates^{[1],[2]}.

Many medicaments meant for topical application to intact or broken skin or to mucous membranes, have been presented in the form of semisolid consistency variously designated as ointment, creams, salves, pastes etc and used mainly as protective or emollient for the skin. Modern day ointments too serve the purpose but they also carry the medicaments to the blood stream. Accordingly they are known as

- a) Epidermatic-Meant for action on epidermis.
- b) Endodermatic-meant for action on deeper layers of cutaneous tissues.
- c) Diadermic-Meant to penetrate deep and release medicaments in body fluids (systemic circulation)^[20].

All ointments consist of a base which chiefly acts as a carrier for the medicaments. The nature of the base also controls its performance. Hence selection of ointment base is very important aspect of their formulation. For scientific understanding of percutaneous absorption of ointment bases it is essential to get familiar with skin structure in relation to drug absorption^[14].

Herbal drugs are also formulated in the form of ointment. The ointment base is prepared and the ointment is formulated by incorporating the active ingredients in the base at most effective ratio by trituration. After the completion of formulation, quality of the ointment is assessed in terms of irritancy, spreadability, diffusion and stability. Traditional medicine is an important source of potentially useful new compounds for the development of chemotherapeutic agents. The first step towards this goal is the screening of plants used in popular medicine. Along with other dosage forms, herbal drugs are also formulated in the form of ointment. An ointment is a viscous semisolid preparation used topically on a variety of body surfaces. These include the skin and the

mucus membranes of eye, vagina, anus, and nose. An ointment may or may not be medicated. Medicated ointments contain a medicament dissolved, suspended or emulsified in the base. Ointments are used topically for several purposes, e.g. as protectants, antiseptics, emollients, antipruritic, keratolytics and astringents^{[4],[7]}.

Characteristics of an ideal ointment

1. It should be physically and chemically stable.
2. The base of ointment should possess no therapeutic action.
3. In ointment base, finely divided active ingredient should be uniformly distributed.
4. The ointment should be sooth and free from grittiness^[10].

Advantages of ointment

1. They provide means of site specific application of drug on affected area, which avoids unnecessary non target exposure of drug thereby avoiding side effects.
2. They avoid first pass metabolism of drug.
3. Convenient for unconscious patients having difficulty in oral administration.
4. Comparatively they are chemically more stable and easy to handle than liquid dosage forms.
5. They are suitable dosage forms for bitter taste drugs^[6].

Disadvantages of ointments

1. These oily semisolid preparations are staining and cosmetically less aesthetic.
2. Application with finger tip may contaminate the formulation or cause irritation when applied.
3. As compared to solid dosage forms, semisolid preparations are bulky to handle.
4. Though semisolids allow more flexibility in dose, dose accuracy is determined by uniformity in the quantity to be applied.
5. Physico-chemically less stable than solid dosage forms^[6].

Ointment bases

Ointment bases are anhydrous and generally contain one or more medicaments in suspension or solution or dispersion^{[3],[5]}.

On the basis of their level of action, they are classified as: epidermatic, endodermatic and diadermatic (Carter, 1987). An antiseptic ointment is aimed to destroy or inhibit the growth of

bacteria. Several antimicrobial herbal ointments have been formulated using medicinal plants. There is typically little variability between brands of generics and name brand drugs. They are often disliked by patients due to greasiness. The vehicle of an ointment is known as the ointment base^[3].

Advantages of ointment bases

- Washable and non-greasy if oil-in-water (o/w)
- Wide range of compatibility
- Do not become rancid or support microbial growth;
- Nonirritating (to the same degree as lanolin, petrolatum, etc)
- Adhere well to skin
- Easily washed off
- Low incidence of sensitization
- Have a low index of irritation on storage
- Easy to compound and remain stable on storage
- Economic and easy to transport.
- Possess good keeping qualities.
- Pharmaceutically elegant.

Disadvantages of ointment bases:

- Subject to water loss if o/w,
- Greasy and un-washable if water-in-oil (w/o),
- Unless, a preservative is added, the Emulsion bases are subject to mold growth, sometimes undergo gradual discoloration with certain drugs.
- Unless acetyl alcohol is added, an aqueous solution can be added only to the extent of 5 percent^[6].

Ointment bases are almost always anhydrous and generally contain one or more medicaments in suspension or solution or dispersion^{[3],[5]}.

Characteristics

- a. Insoluble in water

- b. Not water washable
- c. Contains water (limited)
- d. Emollient
- e. Occlusive
- f. Greasy

Examples: Lanolin and Cold cream; water soluble drugs: Gentamycin Sulfate

Characteristics

- a. Not easily removed from skin with water washing
- b. May possess some power of penetration into the deepest layers of the skin
- c. Used for “endodermic” ointment

Uses:

As emollient but do not provide the degree of occlusion

Incorporates aqueous solutions into oleaginous bases

Examples of absorption bases:

- a. **Hydrophilic Petrolatum**, USP- composed of cholesterol, stearyl alcohol, white wax and white petrolatum

Example: Aquaphor

- b. **Anhydrous Lanolin**, USP- may contain NMT 0.25% water.

Characteristics: It is insoluble in water but mixes without separation with about 2x its weight in water. The incorporation of water results in the formation of a W/O emulsion

- c. **Lanolin**, USP- is a semisolid fat like substance obtained from the wool of sheep

Characteristics:

It is a W/O Emulsion that contains between 25 to 30% water. Additional water may be incorporated into lanolin by mixing

Synonym: Hydrous Wool Fat

- d. **Cold Cream**, USP - is a semi solid white W/O emulsion prepared with cetyl esters wax, white wax, mineral oil, sodium borate, and purified water

Examples: Eucerin cream - is a W/O emulsion of petrolatum, mineral oil, mineral wax, wool wax, alcohol and bronopol. Cold cream - emollient and base.

3. Water removable base

These are oil-in-water emulsions that are capable of being washed from skin or clothing with water. For this reason, they are frequently referred to as “water-washable” ointment bases.

Characteristics

- a. Resemble creams in their appearance
- b. May be diluted with water or with aqueous solution
- c. From therapeutic viewpoint, no ability to absorb serous discharge in dermatologic conditions
- d. Certain medicinal agents may be better absorbed in the skin
- e. Insoluble in water
- f. Water washable
- g. Contains water
- h. Can absorb water
- i. Non-occlusive
- j. Non-greasy

Example:

Hydrophilic Ointment, USP - Does “water love”. It contains sodium lauryl sulfate as the emulsifying agent, with stearyl alcohol and white petrolatum representing the oleaginous phase of emulsion, while propylene glycol and water representing the aqueous phase. Methyl and Propyl parabens are used as preservatives

Other examples include:

- a. Hydrophilic Ointment
- b. Vanishing Cream
- c. Derma base
- d. Velvachol
- e. Unibase

Use: employed as water removable vehicle for medicinal substances^[19]

4. Water soluble base

Unlike water-removable bases, which contains both water soluble and water insoluble components. Like water-removable bases, however, water soluble bases are water washable and are commonly referred to as “greaseless” because of the absence of any oleaginous materials

Characteristics

- a. Because they soften greatly with the addition of water, aqueous solutions are not effectively incorporated into these bases. Rather, they are better used for the incorporation of non-aqueous or solid substance.
- b. These penetrated the skin and better used for absorption of medicament and therefore used for “diadermic ointment”.
- c. Water soluble
- d. Water washable
- e. May contain water
- f. Can absorb water (limited)
- g. Non-occlusive
- h. Non-greasy
- i. Lipid-free

Example: polyethylene glycol ointment

Selection of the appropriate base depends on:

1. Desired release rate of the particular drug substance from the ointment base.
2. Desirability for enhancement by the base of the percutaneous absorption of the drug.
3. Advisability of occlusion of moisture from the skin by the base.
4. Short term and long term stability of the drug in the ointment base
5. Influence, if any, of the drug on the consistency or other features of the ointment base.^[9]

Other additives in ointments

Besides base and medicaments, the ointments may contain one or other of following groups of additives:

A. Preservatives: The microbial compounds and their quantities should be carefully decided upon if the same are being used to prevent contamination, deterioration or spoilage of ointment bases by bacteria and fungi. The first consideration in selection is the irritancy or toxicity of compound to the tissue to which the ointment is to be applied. For, instance methyl and propyl parabens are irritants to nasal passages. Boric acid may be toxic. Quaternary ammonium compounds or phenyl mercuric nitrates are better tolerated by nasal tissues. On occasions the plastic containers or rubber closures may 'take up' some amount of preservatives thus reducing their availability for antimicrobial action. Sometimes the preservatives get complexed by other ingredients and are thus not available in sufficient concentration for microbial action. In the presence of tween 80, methyl paraben, benzalkonium chloride, benzoic acid, etc get inactivated to appreciable extents. The bacterial activity also depends upon the partition coefficient of antimicrobial compound between aqueous and oily phase. If both phases are to be protected additional amount may be needed.

B. Antioxidants:

Antioxidants should be included whenever there is possibility of oxidative degradation of base. It may be more desirable to select two antioxidants instead of one. The concentration of antioxidants depends upon their partition coefficients between the aqueous and oil phase of both the phases are present in a base.

Examples-butylated hydroxyl anisole, propyl gallate are used in ointment bases.

C. Chelating agents:

Whenever it is anticipated that traces of metallic ions are likely to catalyze oxidative degradations small amount of substances such as citric acid, maleic acid, phosphoric acid etc. may be added to chelate the metallic ions.

D. Perfumes:

Most ointment bases these days have a pleasant smell Imparted by incorporation of select blends. The selection of perfume blend is a very tricky business and every manufacturer would like to give a distinctive odorific quality to this product.

Preparation of ointments

Ointments can be prepared either by mechanical incorporation or by fusion methods. Irrespective of the method employed for preparation, ointments should be smooth and free from granular or gritty particles. In compounding of ointments, the following general aspects should be considered.

- (i) If insoluble substances are to be incorporated in the ointment base then they should be in impalpable powder form.
- (ii) For efficient incorporation of insoluble substances they should first be levigated with a little quantity of base to form a smooth cream and then incorporated into the remainder of the base.
- (iii) Water-soluble salts are best incorporated by dissolving them in a small quantity of water and then incorporating in the base.
- (iv) Drugs soluble in ointment bases may also be incorporated by fusion (melting the highest melting point ingredient of the base and mixing the medicament into it). Remaining ingredients are then added and mixed by stirring.

Preparation of Ointments by Mechanical Incorporation

This can be achieved by the use of

- (I) Mortar and pestle,
- (ii) Ointment slab and spatula, and
- (iii) An ointment mill.

Mechanical method of incorporation is particularly advantageous when the substance to be incorporated into ointment base is in a fine state of subdivision.

(a) Mortar and pestle:



Fig. 1: Mortar and pestle ^[30]

This method is used to a limited extent in compounding practice particularly when large quantities of liquids are to be incorporated in a base or when exceptionally large quantities of the ointments are to be prepared. Compounding a homogeneous ointment in a mortar and pestle is not as simple as compounding of a powder^[17].

(b) Ointment slab:



Fig. 2: Ointment slab^[30]

In this case both mixing and size reduction of insoluble medicaments are better than the previous method. The powder is first rubbed with a small quantity of the base to form a concentrated ointment base containing a finely divided powder uniformly distributed in it.

The concentrated ointment is then gradually diluted with remaining quantity of the base by rubbing with a spatula. A small quantity (approximately 5%) of oil or oil-soluble substances can be used as a levitating agent. Large amounts of levitating agents may cause undue softening of the finished preparation^[17].

The spatula should be of stainless steel with a long, broad flexible blade. When steel spatula cannot be used for reasons of reacting with certain drugs like iodine, salicylic acid, and mercury salts etc., a hard rubber spatula or a wooden tongue depressor may be used.

(c) Ointment mill:

Ointment mills are particularly suitable for large scale manufacture of ointments although small mills are available for laboratory scale ointment preparation.



Fig. 3: Triple roller mill machine (G.M.P.MODEL)^[29]

Ointments containing gritty particles are also passed through the ointment mill to ensure further uniformity and smoothness.

The problems of stability of ointments are mostly concerned with the initial and during use microbial contamination.. Many ophthalmic ointments are found to be heavily contaminated with pathogenic micro-organisms. The main source of microbial contamination in ointments is water which supports the growth of micro-organisms.

To safeguard the stability of the packaged product the following points should be borne in mind.

- (i) In general, the pharmacist or the manufacturer should follow Good Manufacturing Practice (GMP).
- (ii) Use of preservatives protect against the contamination, deterioration or spoilage of ointment bases by bacteria and fungi.
- (iii) Use of antioxidants is advisable when there is possibility of oxidative degradation of the base.
- (iv) Use of chelating agents is advisable where the presence of traces of metallic ions is anticipated. The traces of metallic ions, if present, may catalyse oxidative degradation. If the metallic ions are chelated their catalytic effect is nullified.
- (v) The immediate container should not permit evaporation of water from the packaged ointments otherwise an emulsion base may lose aqueous phase and others may become dry and hard.
- (vi) The containers should ensure not only the sterility of ophthalmic ointments initially but also up to a time till whole of the preparation is consumed.

(viii) Due to wide variations in the climatic conditions in different regions in tropical countries, maintenance of desirable consistency of an ointment is also an important consideration.

(ix) Most of the problems related to the stability of packaged ointments can be solved by dispensing them as single application capsules although it works out to be more expensive. This is particularly recommended in case of ophthalmic ointments where sterility and absence of particles are the prime considerate.

1. Incorporation method

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

In small scale or in extemporaneous compounding of the Rx, the pharmacist may use two means:

- i. Mixing ingredients in a mortar with pestle until smooth ointment produced
- ii. Use a spatula and an ointment slab (a large glass or porcelain plate) to rub the ingredients together (spatulation)

a. Incorporation of solid

In preparing ointment by spatulation, the pharmacist uses **stainless steel spatula** but if the components react with metal (such as iodine, tannins, mercuric salts), the hard rubber is used.

1. The ointment base is placed on one side of the working surface.
2. The powdered components (previously reduced into fine powders) are placed on the other side.
3. Then a portion of the powder is mixed with a portion of the base until homogeneity is attained.
4. Repeat until all portions of the product and based are combined.
5. The portions of prepared ointment are then combined and thoroughly blended by continuous movement of the spatula^[17].

Formulations: some important formulation on ointments

1) Simple ointment I.P, 1966

Ingredients (100)

Wool fat.....5.0 g
Hard paraffin.....5.0 g

Cetostearyl Alcohol.....5.0 g
White soft paraffin or yellow soft paraffin.....85.0 g

Method of preparation

All components are melted together and stirred it until cold.

Comments

1. Unless otherwise directed, simple ointment prepared with white soft paraffin should be used white ointments. Simple ointment prepared with yellow soft paraffin should be used in colored ointments.

Uses

It is employed chiefly as a pharmaceutical aid and forms basis of ointments.

Wool-fat provides emollient action. By itself it is not readily absorbed but when mixed with soft paraffin or suitable vegetable oil it forms the cream which penetrate the skin and facilitates the absorption of therapeutically active ingredient .

Hard paraffin works as stiffening agent.

Cetosteryl alcohol improves the emollient properties of simple ointment.

White or yellow soft paraffin form protective ointment basis for surface action. They are also useful as an emollient ^{[19] [25]}.

2) Ammoniated Mercury Ointment I.P.1966 (i.e. White Precipitate Ointment)

Ingredient (for 100 gm)

Ammoniated Mercury,
Finely powdered.....2.5 gm
Simple ointment.....97.5 gm

Methods of preparation

Ammoniated Mercury is triturated with a proportion of simple ointment until smooth. Then rest of the simple ointment is added gradually and mixed thoroughly.

Comments

1. It is externally used as anti-infective. It is generally applied to the perineal region to destroy threadworms and prevents reinfestation.

Precaution:

It should be cautiously applied to infants and children as it may cause ocerodinia (pink disease).It should also not be applied to extensively excoriated areas for prolonged periods.

3) Chrysarobin ointment I.P.1966

Ingredients (for100 gm)

Chrysarobin.....6.0 gm
Chloroform.....7.0 gm
Simple ointment.....87.0 gm

Method of preparation: Firstly, the Chrysarobin is triturated with Chloroform. Then the Simple Ointment (see serial number 1) is melted and incorporated gradually into the Chrysarobin Chloroform mix. The Whole content is finally stirred until congeals.

Comments

- (a) Uses: it is chiefly used in the treatment of parasitic skin infections.
- (b) Precautions: Because of the irritant action of the Ointment due to the chrysarobin, it should not be used on the face, genitalia, and scalp and over a large of the skin.
- (c) The Ointment can stain the skin and clothing brownish violet .This colour can be removed with chlorinated lime solution.

(4) Sulphur ointment I.P.1966 Ingredients (for 100 gm)

Sublimed sulphur, finely sifted.....90 gm
Simple Ointment prepared with
White soft paraffin.....90 gm

Method of preparation: Sublimed sulphur is triturated with a portion of the simple ointment (see serial number (1) until smooth. Then the rest of the simple ointment is added gradually and mixed thoroughly.

Comments

- (a) Uses: It is mainly used as scabicide. It is applied to the affected area of the skin after washing with soft soap. The ointment is also used as a mild antiseptic.
- (b) Precautions: It should not be applied longer than three days otherwise dermatitis may be caused^[18].

(5) Zinc oxide ointment I.P. 1996 (Synonym-zinc ointment) ingredients (for 100 gm)

Zinc oxide, finely sifted.....15 gm
Simple Ointment.....85 gm

Method of preparation:

Zinc oxide is triturated with a portion of simple Ointment until smooth. Then the rest of the simple ointment is added gradually and mixed thoroughly.

Comments:

(a)Uses: It is used as an astringent (mild)for the skin and as a soothing and protective application in eczema .It is also applied as a protective to slight excoriations^[19].

(6) Wool alcohols ointment I.P 1966 Ingredients (for 100gm)

Wool alcohols.....6.0 gm
Hard paraffin.....24.0 gm
Yellow soft paraffin.....10.0 gm
Liquid paraffin.....60.0 gm

Method of preparation:

All ingredients are melted together and stirred until cold.

Comments:

(a) For preparation of wool alcohols ointment of desired consistency and properties, The proportion of hard paraffin, soft paraffin and liquid paraffin may be varied .further ,the liquid paraffin may be replaced wholly or partly by light liquid paraffin.

(b) When this ointment is used in a white ointment the same may be prepared with white soft paraffin; and when used in a colored ointment it should be prepared with yellow soft paraffin.

(c) Uses: It is mainly used as an emollient. It also forms ointment base for many therapeutically active ingredients.

Further, the wool alcohols of this ointment can also work as a good emulent for W\O type emulsions when the wool alcohols ointment is used as an ointment base. The presence of wool alcohols prevents darkening of ointments on the surface and in hot weathers ointments do not give any objectionable odour.

(d) For the reasons behind addition of hard paraffin and soft paraffin see comments, of serial number 1.

(e) Liquid paraffin, present in this ointment, works as an emollient to remove crusts^[19].

(7) Hydrous-ointment I.P. 1966 (synonym-oleic cream) ingredients (for 100 gm)

Wool alcohols ointment.....50 gm

Purified water.....50 gm

Method of preparation: Wool alcohols ointment (see serial number 6) is melted and the warmed purified water is added gradually with constant stirring. Then the whole content is mixed vigorously until a smooth cream is obtained. Mixing is continued until room temperature is attained.

Comments:

It is employed as ointment base for many therapeutically active substances. It is also used as an emollient^[19].

(8) Hydrous zinc oxide ointment I.P 1966 ingredients (for 100 gm)

Zinc oxide, finely sifted.....15.0 gm

Hydrous ointment.....85.0 gm

Method of preparation: Zinc oxide is triturated with a portion of hydrous ointment until smooth. Then rest of the hydrous ointment is added gradually and finally mixed thoroughly^[18].

(9) Hydrous wool fat I.P 1966 (synonym-lanolin) ingredient (for 100 gm)

Wool fat (Anhydrous Lanolin).....70 gm

Purified water.....30 gm

Method of preparation: Wool fat is melted and the purified water is added to it gradually with constant stirring till the mass is homogeneous.

Comments:

(a) Use: Hydrous wool fat is mainly used as a component of ointment bases.

(b) It is W/O type emulsion ointment base^[19].

(10) Paraffin ointment I.P. 1966 Ingredients (for 100 gm)

White Beeswax.....2 gm

Hard Paraffin.....3 gm

Cetostearyl Alcohol.....5 gm

White Soft Paraffin or
Yellow Soft Paraffin.....90 gm

Method of preparation:

All these ingredients are melted together and stirred. Then the source of heat is removed and the stirring is continued until the mass reaches room temperature.

Comments: (a) When paraffin ointment is used in a white ointment, It should be prepared with white soft paraffin and when used in colored ointment it should be prepared with yellow soft paraffin.

(b) Use: It is mainly used as an ointment base for therapeutically active substances.

(c) Cetostearyl alcohol improves the emollient properties^[18].

(11) Small myrobalan ointment I.P. 1966 Ingredients (for 100 gm)

Small myrobalan, in
Fine powder.....20 gm
Paraffin ointment.....80 gm

Method of preparation: Both the ingredients are mixed thoroughly by trituration.

Comment:

(a) It is used as an astringent^[19].

(12) Salicylic acid ointment (I.P.1966) Ingredients(for100 gm)

Salicylic acid, finely sifted.....2 gm
Wool alcohols ointment.....98 gm

Method of preparation: Wool alcohols ointment (see serial number 6) Is melted and then salicylic acid is added into it with constant stirring until cold.

Comment:

(a) Uses: This preparation is mainly used as bacteriostatic and fungicide. It is generally applied for the treatment of chronic ulcers, dandruff, eczema, psoriasis, hyperhydrosis and parasitic skin diseases.

(b) Precautions: Its application to large areas of body should be avoided. it has also been reported that the continuous application of salicylic acid ointment causes dermatitis occasionally^[18].

(13) Emulsifying wax I.P. ingredients (for 100gm)

Cetostearyl alcohol.....90.0 gm

Sodium lauryl sulphate.....10.0 gm

Purified water.....4.0 gm

Method of preparation:

Cetostearyl alcohol is melted and heated to about 95°C. Sodium lauryl sulphate is added and mixed. Then the purified water is added and heated to 115°C with vigorous stirring, the heating is continued at 115°C until frothing ceases and the product is translucent. The product is cooled quickly from the final product, 100 gm can be dispensed in a wide mouthed bottle.

Comments:

(a) As per I.P. the sodium lauryl sulphate may be replaced by similar sodium salts of sulphated higher primary aliphatic alcohols.

(b) It is mainly used as an ingredient to fatty or oleaginous bases which facilitates the preparation of O/W type emulsion bases. These types of bases protect the skin against dirt and grease^[18].

Evaluation of ointments^[7]

The different methods of evaluation of ointments are

(1) Physical methods

- Test of rate of absorption
- Test of non-irritancy
- Test of rate of penetration
- Test of rate of drug release
- Test of rheological properties
- Test of content uniformity

(2) Microbiological methods

- Test of microbial content
- Test of preservative efficacy

A. Physical methods

Test of rate of absorption

Diadermic ointments are those from which the drug moves into deeper skin tissues and finally into the systemic circulation. Such ointments should be evaluated for the rate of absorption of

drugs. The ointment should be applied over a definite area of the skin by rubbing. At regular intervals of time, serum and urine samples should be analysed for the quantity of drug absorbed. The rate of absorption i.e., the amount of drug absorbed per unit time should be more.

Test of non-irritancy

The bases used in the formulation of ointments may cause irritation or allergic reactions. Non irritancy of the preparation is evaluated by patch test. In this test 24 human volunteers are selected. Definite quantity of ointment is applied under occlusion daily on the back or volar forearm for 21 days. Daily the type of pharmacological action observed is noted. No visible reaction or erythema or intense erythema with edema and vesicular erosion should occur. A good ointment base shows no visible reaction.

Test of rate of penetration

The rate of penetration of a semisolid dosage form is crucial in the onset and duration of action of the drug. Weighed quantity of the preparation should be applied over selected area of the skin for a definite period of time. Then the preparation left over is collected and weighed. The difference between the initial and the final weights of the preparation gives the amount of preparation penetrated through the skin and this when divided by the area and time period of application gives the rate of penetration of the preparation. The test should be repeated twice or thrice. This procedure is tedious and not followed anymore.

Using flow-through diffusion cell or microdialys method; the rate of penetration of the preparation can be estimated. Animal or human skin of definite area should be collected and tied to the holder present in a diffusion cell. The diffusion cell is placed in a fluid bath. Measured quantity of the preparation is applied over the skin and the amount of drug passed into the fluid is measured at regular intervals by analyzing the aliquots of fluid using a spectrophotometer.

Test of rate of drug release

A clean test tube is taken and the internal surfaces coated with the preparation as a thin layer. Saline or serum is poured into the test tube. After a certain period of time the saline is analyzed

for the quantity of the drug. The amount of drug when divided by the time period gives the rate of drug release.

Test of rheological properties

The viscosity of the preparation should be such that the product can be easily removed from the container and easily applied to the skin. Using cone and plate viscometer the viscosity of the preparation is determined.

Test of content uniformity

The net weight of contents of ten filled ointment containers is determined. The results should match each other and with the labeled quantity. This test is also called minimum fill test.

B. Microbial method

Test of microbial content

Micro-organisms like *Pseudomonas aeruginosa* and *Staphylococcus aureus* may contaminate the preparation and finally infect the skin. So ointments should be tested for the absence of such micro-organisms. Solutions of different samples of the preparation are made. Each sample is inoculated into separate volumes of 0.5 ml of rabbit's plasma under aseptic conditions and incubated at 37°C for 1-4 hours. No formation of the clot in the incubated mass indicates the absence of the micro-organisms.

Test of preservative efficacy

Using pour plate technique the number of micro-organisms initially presents in the preparation is determined. Solutions of different samples of the preparation are made and mixed with Tryptone Azolecti (TAT) broth separately. All cultures of the micro-organisms are added into each mixture; under aseptic conditions. All mixtures are incubated. Then numbers of micro-organisms in each sample are counted on 7th, 14th, 21st and 28th days of inoculation.

Microbial limits

On 14th day, the number of vegetative cells should not be more than 0.1% of initial concentration.

On 28th day, the number of organisms should be below or equal to initial concentration.

Specified tests for evaluation of ointments

The evaluation of a drug means to perform the tests for the maintenance of quality and quantity according to the specifications. After the manufacturing of drug or during the production, the specific tests are done for that particular product to evaluate it ^[14].

Following tests are specified for the evaluation of ointments:

1. Weight variation test.
2. Consistency.
3. Identification of active contents.
4. Assay of active contents.
5. Melting point.
6. Solubility.

1) Weight variation test (USP)

Select the sample of 10 filled container and remove any labeling that might alter weight during removing of the contents from the containers.

Thoroughly clean and dry the outside of the container by a suitable means and weigh individually.

Remove the contents from each container by cutting opening and washing with a suitable solvent, taking care to retain the closures and any other parts of each container. Dry and again weigh each empty container together with its corresponding parts. The difference between weights is the net weight of the contents of each container. The average net weight of contents of 10 containers is not less than the labeled amount and the net weight of contents of any single container is not less than 90% of the labeled amount, where the labeled amount is more than 60 grams but not more than 150 grams. If the requirements are not met, determine the net weight of the contents of 20 additional containers. The average weight of the contents of 30 containers is not less than the labeled amount and the net weight of contents of not more than one container of the 30 containers is not less than 90% of the labeled amount, where the labeled amount is 60

grams or less and not less than 95% of the labeled amount, where the labeled amount is more than 60 grams but not more than 150 grams.

2) Consistency

Should be smooth, no solid particles.

3) Identification of active contents

Warm a saturated solution in water with Silver Ammonium Nitrate solution in a test tube. Metallic Silver is deposited as a mirror on the sides of the tube.

4) Assay of the active contents

For example: Salicylate ointment.

Dissolve 10 grams in a mixture of 20 ml of alcohol (95%) previous neutralized to phenol red solution and 20ml of ether and titrate with 0.1N NaOH using phenol red solution as indicator.

1ml of 0.1N NaOH=0.01381 grams of salicylic acid.

5) **Melting point** Not less than 11°C.

6) Solubility

Should be soluble in 9 parts of water and 17 parts of boiling water, miscible with alcohol, with solvent such as ether, chloroform or with volatile oils.

Other standards

In additional to USP requirements manufacturer often examine semisolid preparation for viscosity and for *in-vitro* drug release to ensure within lot and lot to lot uniformity^{[3][4]}.

In vitro drug release test include diffusion cells studies to determine the drug's release profile from the semisolid product^[10].

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