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Review about semisolid dosage form

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Abstract

Topical drug delivery system is defined as the application of pharmaceutical dosage form to the skin for direct treatment of cutaneous disorder. The skin present a first line of defence against a wide range of bacterial invaders. Topical route offer several advantages including the avoidance of systemic toxicity and side effect. Topical dosage form have been generally classified as liquid, semisolid, etc.

The main purpose of the study is document the requirements are involved in manufacturing of semisolid dosage form. The guidelines are also include classification, API, instrumentation and evaluation of semisolid dosage form. The studies about the effet of manufacturing process and formulation excipients of semisolid have contributed significantly toward their characterization. The semisolid dosage form are contain one or more active ingredients dissolved or uniformly dispersed in a suitable excipients such as emulsifier, antioxidant, preservative, penetration enhancer, gelling agent, chelating agent, emulgent, humectant, stabilizer. Semisolid can adhere to application surface for long term before washed off. So, this property help prolong drug delivery at application site. The semisolid are greasy in nature are made up of oleagenous bases. The another one is non greasy in natureare made up of water washable bases. The most conventional and probably well-known semisolid dosage form are cream, ointment, paste, gels, etc. The review is concern with all detail infomation regrading approaches to formulation and evaluation of semisolid dosage form.

Keywords: excipients, process, manufacturing tools, quality control test

Introduction

Semisolid constitute a significant proportion of pharmaceutical dosage forms. They serve as carrier for drug that topically delivered by the way of skin, cornea, rectal tissue, nasal mucosal, vagina, buccal tissue, uretharal membrane and external ear lining. A semisolid dosage form is advantageous in terms of its easy application of rapid formulation, and ability to topically delier a wide variety of drug molecules. They contain one or more actie ingredient dissolved or uniformly dispersed in a suitable base and any suitable excipients such as emulsifiers, viscosity increasing agent, antimicrobial agent, and stabilizing agent. [1]

Definition

Semisolid dosage form are the topical dosage form used for the therapeutic, protective functions. It may be applied to the skin, nasal, vaginal, or rectal cavity. Semisolid pharmaceutical system comprises a body of product, which when applied to skin or accessible mucous membrane tend to alleviate or treat a pathological condition or other protection against harmful environment. The semisolid dosage form are dermatological product of semisolid consistency. These product of semisolid consistency are applied to skin or mucous membrane for therapeutics or protective action. [2]

Examples of semisolid dosage form

Ointments, Pastes, Cream, Gels.

Ointments

Ointment is a viscous semisolid preparation used topically on a variety of body surfaces. These include the skin and the mucous membrane of the eye, vagina, anus, and nose. The ointment should be of such consistency that then easily rubbed on the skin. An ointment act as a emollient in nature to make a skin more pliable. Medicated ointment primarily consist of a drug and a vehicle is called as a base. The vehicle is used as a skin protective and emollient. The ointment in earlier time were semisolid preparation with medicament dispersed uniformly in a fatty base; while the ointment being prepared at the present time do not contain any oleaginous substance. [3]

Fig 1

Creams

Pharmaceutical cream contain one or more medicament either dissolved or dispersed in w/o or o/w emulsion or in other water washable base. Hence, creams are semisolid in nature. Vanishing cream are example of o/w emulsion containing water and stearic acid or other oleaginous component in a large amount. When applied over the skin

the water gets evaporated and a thin residue film of stearic oleaginous component remain behind. Topical skin product and rectal and vaginal product come in the form of cream. Cream are preferred over ointment due to their ease of spreading and removal. They used as a vehicle for drug substance such as local anaesthetic, anti inflammatories, anti-fungal etc. [4]

Fig 2

Pastes

Pastes are semi solid preparation intended to be used externally on the surface of the skin, in order to provide a protective covering. They contain high powder content which provides a stiff and thick consistency to the formulation and also make them porous, thus allowing perspiration through it.

Paste are usually prepared by incorporating solid directly into a congealed system by levigation with a proportion of bases to form paste like mass. Contain high percentage of insoluble solid which are finely dispersed into a suitable vehicle.

The major difference between a paste and an ointment is that the former are stiffer and less greasy. They are generally prepared by dissolving the active medicament in different base [3].

Fig 3

GELS

Gels are semi rigid structure of three dimensional network of particle or macro molecules of the dispersed phase.This 3D structure blocks the movement of the dispersing medium.

The gel are semisolid system containing either suspension of small inorganic particle or large organic molecule interpenetrated by a liquid.The gel mass has a network of small separate particle, thus is considered a two phase system.

Single phase gels have organic macro molecules distributed uniformly in a liquids so that no apparent boundaries are Formed between the dispersed macro molecules and the liquid [3].

Fig 4

Advantages of semi-solid dosage form

- It is used external.
- Suitable dosage form for bitter drugs.
- More stable than a liquid dosage form
- First pass metabolism is avoided.
- Local action and site specific action of the drug on the affected area.
- Convenient for unconsisous patient. [5]

Disadvantages of semi-solid dosage form

1. May cause staining
2. The accuracy cannot be measured for the semisolid dosage form.
3. Application with a finger may cause contamination.
4. May cause irritation or allergy to some patients.
5. Physico-chemical is less stable than a solid dosage form.
6. Drug of large particle size not easy to absorb through the skin. [5]

Ideal properties of semisolid dosage form

- Physical properties
- Physiological properties
- Application properties

Physical Properties

a. Smooth texture.
b. Elegant in appearance.
c. Non-dehydrating
d. Non-greasy and non-staining.
e. Non-hygroscopic. [5]

Physiological Properties

a. Non-irritating.
b. Do not alter membrane function.
c. Miscible with skin secretion. [5]

Application Properties

a. Easy applicable with efficient drug release
b. High aqueous washability. [5]

Development of Semisolid Dosage Forms

Methods of preparation of semisolid dosage form

1. Trituration method
2. Fusion method
3. Lavigation method
4. Thermal changes
5. Emulsification method

Trituration method

Fig 5

Fusion Method

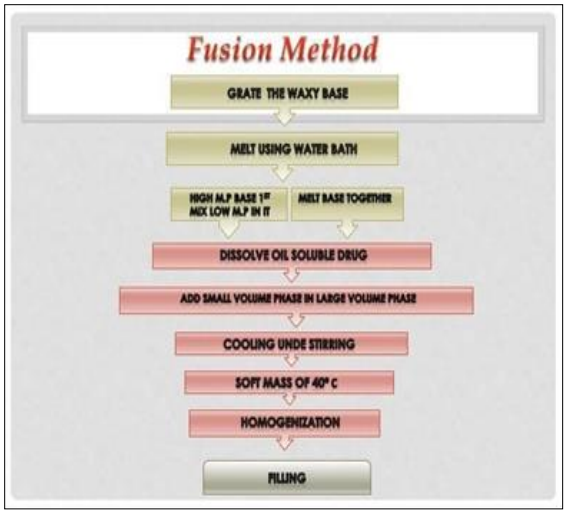

Fig 6

Lavigation Method

Through the use of water, levigation process grinds an insoluble substance into a crushed, fine powder. Thus, it is also known as 'wet grinding'. This powder stays on the water, flowing through the apparatus as it serves as a murky liquid or paste. Then, the material is brought in to join the blend [3].

Thermal changes

Solvated polymers (lipophilic colloids) are subjected to thermal changes Causes gelatin. Many hydrogen former are more soluble in hot than cold water. If the temperature is reducing, the degree of hydration is reduced and gelatin occur. Cooling of a concentrated hot solution will produce a gel. Raising the temperature of the solution will disrupt the hydrogen bonding and reduced solubility, which will cause gelation. [6]

Excipients Used In Semisolid Dosage Forms

The common excipients

a. Semisolid Base
b. Preservative
c. Humectant
d. Antioxidants
e. Emulsifier
f. Gelling agent
g. Permeation enhancer
h. Buffers
i. Surfactant
j. Chelating agent
k. Vehicle

A. Semisolid Bases

It is a one off the most important ingredient used in the formulation of semisolid dosage form. Ointment bases donot merely act as the carrier of the medicament, but they also control the extent of absorbtion of medicament incorporated with them. The properties of bases are inert, non-irritating, non-sensitizing, emollient, protective, non-greasy, and easily removable.

Classification of bases

Oleaginous Bases
Absorption Bases
Emulsifying Bases
Water soluble Bases

Oleaginous Bases

The consists of combination of more than one oleaginous material such as a water insoluble hydrophobic oils and fats. This bases are anhydrous and hydrophobic in nature. They are anhydrous, do not absorb water, readily insoluble in water, non-washable. They are highly compatible, occlusive, good emollient. Their application is avoided on infected skin. They can remain on skin for longer periods without drying. E.g.Hard paraffin, Liquid paraffin, White ointment, White petrolatum.

Absorption Bases

These are anhydrous bases which maintain their ointment like consistency even after absorbing a huge amount of water. They have capacity to absorb considerable quantities of water or aqueous solution and to water in oil with out marked changes in consistency. Their application include their use as emollients and vehicle for aqueous solution and solid drugs.

These bases are further divided into two types.

- **Non-emulsified bases:** These bases produces w/o emulsion by absorbing water and aqueous solutions.
  E.g. Wool fat, Wool Alcohol, Beeswax, and cholesterol.

- **Water in oil Emulsion Bases:** These bases are similar to non-emulsified bases with respect to their Properties. However they absorb comparatively large amount of water.
  E.g. hydrous wool fat.

Emulsifying Bases

- **Oil in Water Bases:** The basic properties of these bases include their hydrous, water soluble, water absorbable, water washable in nature.
  Example of this bases acting as drug carrier or vehicle includes PEG ointment, Poly bases etc.

- **Water in oil Emulsion Bases:** These bases are hydrous, hydrophilic in nature, absorb Water, and

cannot washed. Their thermal conductivity and occlusive property is low. Some of their properties are similar to that absorption bases.
E.g. cold cream type, hydrous lanolin, rose water ointment, and hydro cream.

Water Soluble Bases
As the name "Grease less" these bases are oil free. They show complete solubility in water. They are hydrous as well as anhydrous in nature.
E. g. PEG, Polysorbates and Macrogols (mixture of water and condensation products of ethylene oxide) [7].

B. Preservatives
Certain semisolid base are capable of tolerating microbial attack. Since these bases have high water content, an anti-microbial preservative is added in the semisolid formulation to maintain their potency and integrity.
The resist the microbial attack but because of their water content, it require an anti-microbial preservative.
Example are, Methyl paraben, Ethyl paraben, Propyl paraben, Benzoic acid, Methyl hydroxy benzoate. [7]

C. Humectant
The Humectant is a hygroscopic substance.It is often a molecule with several hydrophilic group, most often hydroxl group. Humectant are used to increase the solubility of active ingredients, to elevate the its skin preparation and elevate the hydration of the skin. The humectant are added in the semisolid preparation Preparation for prevent the dryness and also prevent the formation of crust in the container. Examples are, Glycerine, Propylene Glycol and Low molecular weight PEG [7].

D. Antioxidant
The Humectant is a hygroscopic substance. It is often a molecule with several hydrophilic group, most often hydroxl group. Humectant are used to increase the solubility of active ingredients, to elevate the its skin preparation and elevate the hydration of the skin. The humectant are added in the preparation of cream for prevent the dryness and also prevent the formation of crust in the container. Examples are, Glycerine, Propylene Glycol and Low molecular weight PEG. [7]

E. Emulsifiers
Emulsifiers are important for process of emulsifiation. In o/w emulsion ionic surfactant are used, whereas nonionic surfactant used in both o/w and w/o formulation Examples are, Polysorbate 20, Polaxmer, SLS, Sorbitan monostearate [8]

F. Gelling Agent
Gelling agent form a gel dissolve in a liquid phase as a colloid mixture that forms a weakly cohesive internal structure. These are hydro colloids or hydrophilic inorganic substances. Examples are, Tragacanth, Sodium alginate, Pectin, Gelatin, Cellulose derivatives. [7]

G. Permeation Enhancer
Skin act as a barrier with the introduction of various panetration enhancer, pantration of the drug through the skin can be improved. Examples are, Limeone, Oleic acid, Methanol, Nerolidol. [7]

H. Buffers
The buffers added in the preparation of semisolid dosage form for various purpose such as compatibility with skin, drug stabiity, drug solubility, Influence on ionization of drug. Examples are, Sodium acetate, Sodium citrate, Potassium Meta phosphate. [7]

I. Surfactant
Surfactant are added to form micelles in aqueous media. Due to hydrophilic functional groups, micelles can enhance the solubility of poor water soluble drug .In topical formulation 2-10% surfactant help in the formation of micro structure and improves the transmuccosal absorption.
Examples are, Tween 60, Tween 80, Potassiumoleate. [7]

J. Vehicle
Water is usually consider as a universal solvent. Solvent instead of water is given to stabilize the drugs. The using these solvents along with water, catalyses the oxidation effect.
Example are, Ethanol, Cetyl alcohol, Phenol etc. [7]

Equipment used in semisolid dosage form
1. Triple Roller mill
2. Colloid Mill
3. Planetary mixer
4. Sigma Blade Mixer
5. Double Cone\Blender mixer.

Triple roller mill
A three roll mill has three horizontally positioned rollers. Each roller rotates in an opposite direction from the adjacent roller with a tiny gap between them, creating tremendous shear force that can finely disperse, mix, refine or homogenize viscous materials. Three roll mill is a dispersing tool, not generally a size reduction tool. Fine particles tend to agglomerate and a three roll mill applies powerful shear force to break apart those agglomerations. As a result, the final fineness depends on the original particle size of the dry ingredients. The material is fed through the hopper into roller A and B where they are crushed or dispersed. Then they are passed to roller B and C where they are further crushed and smooth mixture is formed. Finally the mixture is removed by scrapper from the rollers. [9]

Fig 7

Colloid Mill

Colloid mill is a machine that is used to reduce the particle size of a solid in suspension in a liquid, or to reduce the droplet size in emulsions. When a liquid is suspended in another liquid, meaning they are immiscible, this machine is used to alternatively to reduce the size of this droplet. A high level of hydraulic shear stress is applied on the fluid which results in disrupting and breaking down the structure.

Mechanism

The material is placed into the mill though the inlet hopper. It is then passed through the narrow gap between the rotor having and stator and thus reduced the fine particle size. By the help of pulverization. Then it will come to the auto circular tube, until we allow it to came out from the discharge port The rotor speed is 3000 to 20000rpm and can produce particle size of 1µ [10]

Fig 8

Planetary Mixer

Planetary mixers are one of the most widely used mixers in the pharmaceutical industry. In the pharmaceutical industry, the planetary mixer is often used for basic operations of mixing, blending, and low-shear granulation. This machine is also used in other industries like cosmetics and personal care products, food, glass, cements, ceramics, metal industry etc. The Planetary Mixer have two blades which rotate on their own axes, while they orbit the mix vessel on a common axis. The blades continuously advance along the periphery of the vessel, removing material from the vessel wall and transporting it to the interior. These mixers are ideal for mixing and kneading viscous pastes or putty- like materials.

Fig 9

Sigma Blade Mixture

The two blades rotate towards each other and operate in a mixing vessel which has a double trough shape, each blade fitting into a trough. The two blades rotate at different speeds, one usually about twice the speed of the other, resulting in a lateral pulling of the material and divisions into two troughs, while the blade shape and difference in speed causes end-to-end movement [10].

Quality Control Test for Semisoid Dosage Form

Common evaluation of semisolid dosage form

- Drug content
- Release rate of medicament from base
- Penetration rate of medicament
- Irritant effect
- Consistency of preparation
- Sensitivity
- Abrasiveness
- Particle size
- Rheology
- Foaming character

Drug content

In the minimum fill test, select any 10 filled containers. Weigh the required amount of ointment and Medicament is extracted in a suitable solvent. Drug Content is determined by suitable analytical technique. Results should be with in labeled quantity. [11]

Release rate of medicament from base

The Release rate of medicament from base is determined by two in vitro techniques they are 1. Agar cup plate method 2. Diffusion method

Agar cup plate method

To asses the rate release of medicament from the small amount of ointment can e placed on the surface of nutrient agar containing in the petri dish or alternatively in a small cup cut in agar surfaces. If the medicament is bactericidal the agar plate is previously seeded with a suitable organisim like s.aureus after a suitable period of incubation, the zone of inhibition is measured and correlated with rate release of medicament.

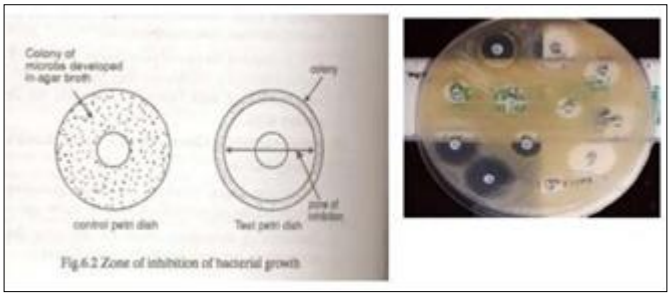

Fig 10

Diffusion Method

Diffusion method is used to find the release rate of any type of medicament from the base .A parchment membrane is tied at one end of glass tube, Ointment is filled in the tube, properly spread on the membrane. Tube is dipped in the distilled water maintained at 37±1OC, Samples are withdrawn after a specified period of time. Samples are immediately replaced with fresh distilled water and

Analyzed for the drug content. Plot a graph between drug concentration and time [11].

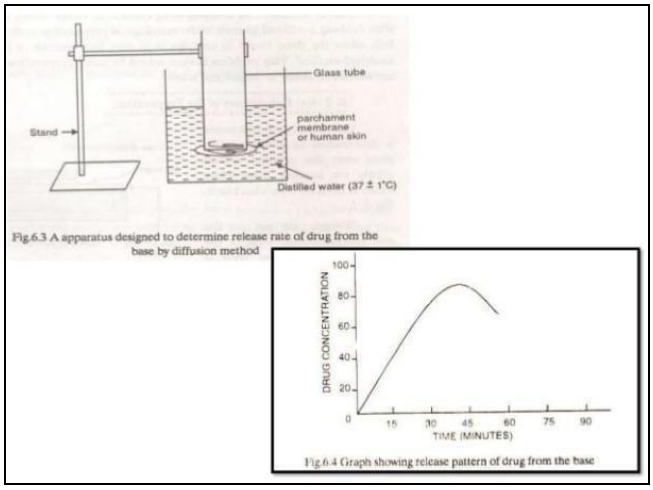

Fig 11

Penetration Rate of Medicament

A weighed quantity of medicament is rubbed over the skin for given period, after the time period the unabsorbed material is removed completely and weighed. The difference in weight represent the amount is absorbed, then the rate is calculated. [11]

Irritant Effect

Test is performed on skin and eyes of rabbit or human skin. Ointment is injected in to thigh muscles and under abdominal skin in rats. Results are observed daily for a week. Irritant effect of dermatological preparation is shown as lesions on cornea, iris and conjunctiva. [11]

Consistency of preparation

Consistency of preparation is determined by sliding a glass plate over the product by means of a pulley. Product is spread evenly on another glass plate fixed on a wooden block. Weight are added to the pan so that sliding of the movable glass plate is obtained. Ointment which require more weight to allow the plate to slide over have high consistency or vice versa. [11]

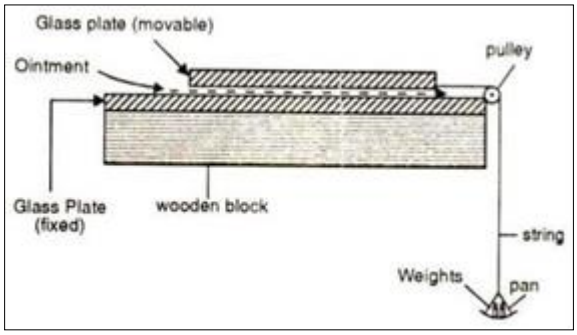

Fig 12

Sensitivity

As a various type of ingredient are used with occasional use of antiseptic hormone etc. There is a possibility of sensitization or photosensitization of skin. This test is normally done by patch test on and can be either open or occlusive. The test sample is applied along with standard market product at different place and effect is compared after time period. [11]

Abrasiveness

They measure the amount of solid medicament as per the unit of the paste. [11]

Particle size

This can be determined by microscopic study of particle.

Rheology

Rheology are viscosity should remain constant. AS there products are normally non newtanian in nature, the viscosity can be measured using viscometer are used for such liquid. [11]

Foaming character

This test is specially required for forming tooth paste or tooth paste or tooth powder. Especially amount of product can be mixed specific amount of water to be shaken. The foam thus formed is studies for its nature, stability, wash ability. [11]

Conclusion

There are different physical forms that can effectively deliver a drug topically. Pharmaceutical factors are stability, solvent properties, emulsifying property. In addition, patient acceptability is much better than other route of drug delivery due to their non-invasiveness. Various topical preparations like cream, gel, ointment, paste etc play a vital role in variety of skin infection.

Reference

1. Idson B, Lazarus J. Semisolids in the Theory and Practice of Industial Pharmacy. In: Lachman L, Lieberman HA, Kanig JL editors; Varghese Publishing House, Bombay, India, 1991, 534-563.
2. Block LH. Medicated Applications. In Gennaro AR: Remington: The Science and Practise of Pharmacy. Mack Publishing Company, Easton, Pennsylvania, 1995, 1577-1597.
3. https://images.app.goo.gl/yi9yE3iBx6YzpR948
4. Nwoko VE. Semi solid dosage forms manufacturing: tools, critical process parameters, strategies, optimization and validation. Sch Acad J Pharm,2014:3(2):153-161.
5. https://www.slideshare.net/laithalasadi/semi-solid-dosage-form-68119310.
6. Kaur LP. Topical gel: a recent approach for novel drug delivery. Asain journal of biomedical and pharmaceutical science,2013: 3(17),p.1.
7. https://www.slideshare.net/rababambreen1/semisolid-dosage-form
8. Patel H, Parmar S, Patel B. A comprehensive review on Quality by Design (QbD) in pharmaceutical. development,2013:4:5.
9. https://www.scribd.com/doc/40268318/Semi-Solid-Mixers
10. https://www.slideshare.net/docmano15/semi-solid-dosage-forms
11. https://www.slideshare.net/pkcchhajer/semi-solid-dosage-forms-44039499