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Research Article

Topical formulations and Hydro-gel: An overview

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ABSTRACT

Topical drug delivery is an attractive route for local and systemic treatment. The delivery of drugs on the skin is recognized as an effective means of therapy for local dermatologic diseases. It can penetrate deeper into skin and hence give better absorption. Semi-Solids dosage forms usually are intended for localized drug delivery in the past few years. Semi-solids constitute a significant proportion of Pharmaceutical dosage forms. They can apply topically to the skin, cornea, rectal, vaginal, nasal mucosa, buccal tissue, urethral membrane and external ear lining. They should be non-greasy, non-staining and non-hygroscopic in nature, non-irritating, non-hygroscopic and miscible with skin secretion. Hydro-gels are prepared by using a dispersion method. Hydro-gels are analyzed by using a parameters Homogeneity, Grittiness, Skin irritation study, Drug content, In-vitro drug permeation study, Viscosity.

Keywords: Absorption, Semi-solids, Dermatology, Pharmaceutical dosage forms, Hydro-gel.

INTRODUCTION

Human skin is considered to be the largest organ of the body. The surface area of the skin on an average is 1.8 m^2 , and represents 16% of the total body weight¹. The skin protects us from microbes and the elements, helps regulate body temperature, and permits the sensations of touch, heat, and cold. The skin of an average adult body covers a surface area approximately 2 m^2 and receives about one third of the blood circulating through the body. An average human skin surface is known to contain, on the average 40-70 hair follicles and 200-300 sweat ducts on every square centimeter of the skin².

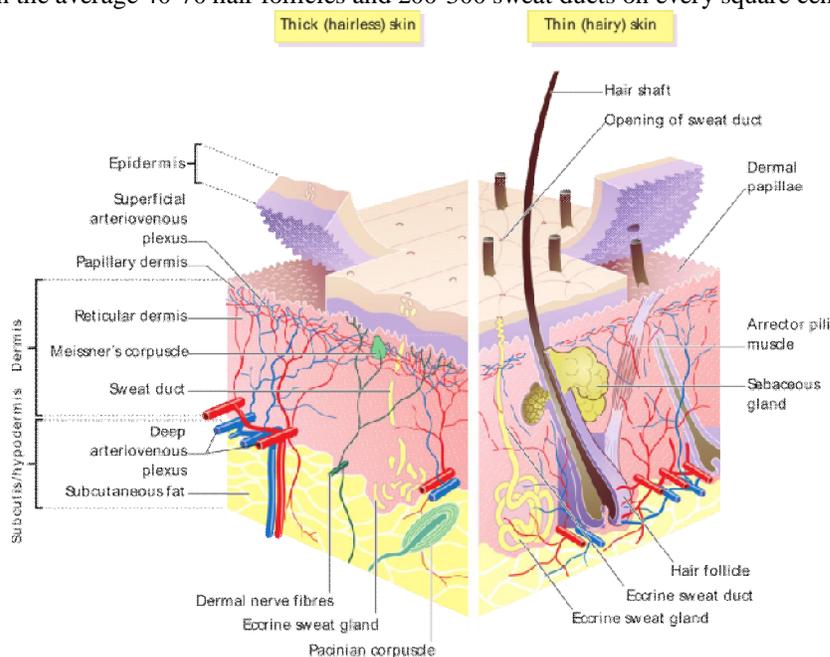


Fig. 1: Structure of Skin

Semi-Solids dosage forms usually are intended for localized drug delivery in the past few years. Semi-solids constitute a significant proportion of Pharmaceutical dosage forms. They can apply topically to the skin, cornea, rectal, vaginal, nasal mucosa, buccal tissue, urethral membrane and external ear lining. Semi-Solids dosage forms are dermatology of semi-solid consistency and applied to skin for therapeutic or protective action or cosmetic function.

Ideal Properties of Semi-Solids dosage forms

- Semi-solids should be smooth texture, Elegant in appearance, non-dehydrating.
- They should be non-greasy, non-staining and non-hygroscopic in nature.
- They should be non-irritating, non-hygroscopic and miscible with skin secretion.
- They don't alter membrane/ skin functioning.
- Easily applicable with efficient drug release.
- They should be high aqueous wash-ability.

Types of Conventional semi-solid dosage forms and their properties

Semi-solid includes ointments, Creams, pastes, gels, and many more.

1. Gels

Gels are Semi-Solids systems in which a liquid phase is contained within a 3-D polymer Matrix (consisting of natural or synthetic gum) having a high degree of physical or chemical cross-linking.

- Gels are aqueous colloidal suspensions of the hydrated forms of in soluble medicament.
- Gels are richer in liquid than magma.
- Jellies are transparent or translucent non-greasy semi-solid gels.
- Some are as transparent as well it-self an aesthetically pleasing state other are turbid, as the polymer is present in colloidal aggregates that disperse light.

Gels or jellies are characterized by a comparatively high degree of elasticity. They undergo rather large elastic deformation at shear stress below the yield value, from which they recover their shape when the stresses are removed. Recoverable deformation of 10 to 30% is not unusual, especially for polymer gel clay gels are less elastic and more like pastes.

2. Ointments

They are soft-hydrocarbon based semi-solid preparation, composed of fluid hydrocarbon meshed in a matrix of higher melting solid hydrocarbon petrolatum being a tasteless, odorless, unctuous material with a melting range. Since they are greasy nature so they stain cloths. Principle ingredient forming the system hydrocarbon and silicon oil are generally poor solvent for most drugs, seemingly setting a low limit on the drug delivery capabilities of the system.

3. Creams

They are viscous semi-solid emulsion with opaque appearance as contrasted with translucent ointment consistency and rheological characters depends on the cream is w/o or o/w.

- Properly designed o/w creams are elegant drug delivery system, pleasing in both appearance and feel post application.
- O/W creams are non-greasy and are rinsable.
- They are good for most Topical purpose and are considered particularly suited for application to oozing wounds.

4. Pastes

Pastes are basically ointment into which a high percentage of insoluble solid has been added. They extraordinary amount of particulate matter stiffens the system through direct interactions of the dispersed particulates and by absorbing the liquid hydrocarbon.

- Paste are less penetrating and less macerating and less heating than ointment.
- Paste make particularly good protective barrier when placed on the skin for, in addition to forming an unbroken film, the solid they contain can absorb and there by neutralize certain noxious chemicals before they ever reach the skin³.

Hydro-gels

Hydro-gels are polymeric network that absorb large quantities of water while remaining insoluble in aqueous solutions due to chemical or physical cross linking of individual polymer chains. Differing from hydrophobic polymeric networks such as poly(lactic acid)(PLA) or poly (lactide-co-glycolide)(PLGA) which have limited water-absorption capabilities, hydrophilic hydro-gels exhibit many unique physicochemical properties that make them advantageous for biomedical application including drug delivery⁴.

Gels formation usually proceeds at ambient temperature and organic solvents are rarely required. In-situ gelation with cell and drug encapsulation capabilities future distinguishes hydro-gels from the other hydrophobic polymers. Hydro-gels can be prepared from natural or synthetic polymers⁵.

Hydro-gels are water swollen three dimensional structures composed of primarily hydrophilic polymers. These are cross linked macro-molecular network that are insoluble but able to swell rapidly in water or biological fluids.

Classification of hydro-gels

The existing classification of topical dosage forms needs to be re-examined to ensure that definitions for different dosage forms are based on consistent scientific principles and dosage forms can be distinguished from one another. The purpose of this study is to obtain a scientifically based, systematic classification of dosage forms for topical drugs. Hydro-gels also called aqua gel is a network of polymer chains that are hydrophilic, sometimes found as a colloidal gel in which water is the dispersion medium.

Hydro-gels are highly absorbent natural or synthetic polymers. A variety of prescription and over-the-counter topical products currently marketed as lotions, gels, creams, and ointments are evaluated using different technique including rheology, loss on drying, specific gravity, surface tension. Hydro-gels also possess a degree of flexibility very similar to natural tissue, due to their significant water content⁵.

Based on the method of preparation hydro-gels are classified into

- Homo-polymer hydro-gels
- Co-polymer hydro-gels
- Multi polymer hydro-gels

Based on the ionic charges hydro-gels can be classified into

- Natural hydro-gel
- Anionic hydro-gels
- Cationic hydro-gels
- Ampholytic hydro-gel

Based on the structure hydro-gels can be classified into

- Amorphous hydro-gels
- Semi-crystalline hydro-gels
- Hydrogen bounded hydro-gels

Based on the mechanism controlling the drug release they are classified into

- Diffusion controlling release system
- Swelling controlling release system
- Chemically controlling release system
- Environment responsive system⁵

Topical drug delivery is an attractive route for local and systemic treatment. The delivery of drugs onto the skin is recognized as an effective means of therapy for local dermatologic diseases. It can penetrate deeper into skin and hence give better absorption⁶. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Topical formulations apply a wide spectrum of preparations, cosmetics, dermatological, analgesics to their healthy or diseased skin⁷.

Drug substances are seldom administered alone, but rather as part of a formulation, in combination with one or more nonmedical agents that serve varied and specialized pharmaceutical functions⁸. Drugs are administered topically for their action at the site of application, or for systemic effects⁹. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes presence of enzymes, gastric emptying they are other advantage of topical preparations¹⁰. The topical drug delivery system is generally used where other systems of drug administration fails or it is mainly used in fungal infection and anti – inflammatory¹¹.

Advantages

The topical administration of drug in order to achieve optimal cutaneous and percutaneous drug delivery has recently gained an importance because of various advantages.

- They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH and enzymatic activity and drug interaction with food and drinks.
- They can substitute for oral administration of medication when that route is unsuitable.

- Topical gels avoid the first pass effect, that is the initial pass of drug substance through the systemic and portal circulation following gastrointestinal absorption, possibly avoiding the deactivation by digestive and liver enzyme.
- They are non-invasive and have patient compliance and they are greasy or non-greasy and can be easily removed from the skin.
- Cost effective.
- Reduction of doses as compare to oral dosage forms.
- Localized effect with minimum side effects.
- Topical gels can reduce local inflammations²

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Topical formulations apply a wide spectrum of preparation, cosmetic dermatological, to their healthy or diseased skin¹². Drugs are administered topically for their action at the site of application, or for systemic effects¹³. Drugs applied to the skin for their local action include antiseptics, analgesics, antifungal agents, skin emollients and protect-ants. The main advantage of topical delivery system is to bypass first pass metabolism, avoidance of the risks and inconveniences of intravenous therapy and of the varied condition absorption, like pH changes presence of enzymes, gastric emptying they are other advantage of topical preparations¹⁴.

Increasing the release rate of the drug from the dosage form might therefore improve percutaneous absorption. The release rates of drugs from topical preparations depend directly on the physicochemical properties of the carriers and the drug employed¹⁵. Topical deliveries also provided on increased bioavailability, Topical delivery vehicles (creams, gels) can improve patient compliance due to decreased in the dose frequency¹⁶.

Methods of preparation of hydro-gels

- Fusion method
- Cold method
- Dispersion method

Whether the scale of preparation is large or small, semisolid dosage forms are produced by one of two general methods. Either they are made at high temperature by blending the liquid or liquefied components and dispersing the solids (fusion method) or the drug is incorporation in the already semi-solid base (cold incorporation). Cold incorporation is used with heat labile drugs, when a drug is to be added to already prepared semi-solid base or when the vehicle itself is heat labile as happens with plastibase¹⁷.

The preparation of gels may involve a fusion process or may require a special procedure, depending on the gelling agent involved. Tragacanth system must be prepared at low temperature due to the extreme heat liability of this natural gum. On the other hand, it is easier to disperse methyl cellulose in hot than in cold water. The carbopol are gelled by a unique procedure. The polymer is dispersed in an acidic medium. When the dispersion is uniform, gelation is induced by neutralizing the system with an inorganic base (aqueous system) or with an amine such as tri-ethanolamine. This ionize the acidic functional groups on the polymer, drawing the polymer into colloidal solution, in which state it forms the requisite structural matrix¹⁷.

Dispersion method

Disperse the polymers in distilled water by continuous stirring. Warm the colloidal viscous dispersion to get a gel. Dissolve the drug in solvent and incorporate into gel by stirring followed by penetration enhancer. Add pH adjustifier to modify the buffering capacity of the gel, if necessary¹⁷.

Evaluation of Hydro-gels

Following parameters were used for the evaluation of gels:

- pH
- Drug content
- Viscosity
- Spreadability
- Extrudability study
- In-vitro release

Homogeneity

All developed gels tested for Homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates¹⁸.

Grittiness

The four formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation¹⁸.

Extrudability

A good gel extrude optimally from the gel with slight pressure applied. The Extrudability of formulations from aluminium collapsible tubes was determined using universal tube filling machine. Aluminium collapsible tube filled with 10 g gels were held between two clamps. A tube was compressed and Extrudability of formulation was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of gel in 10 seconds¹⁸.

pH Determination

The pH of gel formulations was determined by using digital pH meter. 1 gram of gel was dissolved in 100 ml of distilled and stored for 2 hours. The measurement of pH of each formulation was done in triplicate and average values were calculated¹⁹.

Viscosity

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gel were rotated at 20 and 30 rpm using spindle no.64 at each speed, the corresponding dial reading was noted¹⁹.

Skin irritation study

Guinea pigs (400-500g) of every sex were used for testing of skin irritation. The animals were maintained on standard animal feed and had free access to water. The animals were kept under standard conditions. Hair was shaved from back of guinea pigs and area of 4 cm² was marked on both the sides one side served as control while the other side was test. Gel was applied (500 mg/guinea pig) twice a day for 7 days and the site was observed for any sensitivity and the reaction if any²⁰.

Drug content determination

Drug content was studied by an accurately weighing a gel (about 100 mg) and was dissolved in 100 ml of Phosphate buffer 7.4 and then the solution was stirred continuously for 24 h on magnetic stirrer. Then the whole solution was sonicated. After sonication and subsequent filtration, drug in solution was estimated spectrophotometrically by appropriate dilution²⁰.

In -vivo permeation studies

The diffusion studies of the prepared gels were carried out in Keshary-Chien diffusion cell for studying the dissolution release of gels through a cellophane membrane. Gel sample (0.5g) was taken in cellophane membrane and the diffusion studies were carried out at 37±1° using 25 ml of phosphate buffer (pH 7.4) as the dissolution medium. 5 ml of each sample was withdrawn at constant interval of time 1,2,3,4,5,6,7 and 8 h and each sample was replaced with equal volume of fresh dissolution medium. Then the sample were analyzed for through content at 362 nm using phosphate buffer as blank²¹.

CONCLUSION

Topical drug delivery systems and dosage forms which are intended to be applied to the skin. In semi-solids formulations ointments, lotions, gels, and topical solutions represent the most frequently used dosage forms dermatologically; preparations are applied to the skin either for their physical effects, that is for their ability to act as skin protectants, lubricants, emollients, drying agents etc. or for the specific effect of medicinal agent present.

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