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Topical Gels as Drug Delivery System- A Comprehensive Review

Amol Amrutkar[1], Smita Aher[2], Rishikesh Bachhav[3]

[1]Department of Pharmaceutical Quality Assurance,
[2]Department of Pharmaceutical Chemistry,
[3]Department of Pharmacology,
[1, 2, 3]R. G, Sapkal College of Pharmacy, Anjaneri, Nashik, Maharashtra, India

ABSTRACT

The clinical proof shows that skin gel is a safe for use and best treatment for use in the administration of skin related illness types and furthermore utilized for neighbourhood activity to diminish the results which are related with the other traditional dose structure. Skin drug conveyance frameworks includes an enormous assortment of drug measurements structure like as semisolids, fluid planning, splashes and strong powders. Most generally utilized semisolid groundwork for skin drug conveyance incorporates gels, creams and balms. A gel sort of measurement structure is a cross-connected polymer network swollen in a fluid stage medium. Their properties rely unequivocally upon the cooperation between the two strong state polymer and the fluid segment. Gels decides no consistent state stream. The getting over among polymer and the fluid scattering medium structure an intertwining 3-D organization of particles of scattered stage. The expanding thickness brought about by the intertwining and important interior grinding is needed for the semisolid state. Skin gel prescription gives an appropriate conveyance framework for the medications since they are less oily and can be effectively taken out from the upper bit of skin. Gel definition gives us a superior application property and soundness in contrast with cream and different salves.

KEYWORDS: *Topical, drug delivery, gels, skin. Percutaneous penetration, drug delivery, organogels, Hydrogel*

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INTRODUCTION

Skin drug conveyance can be called as use of medication through the skin to straightforwardly treat or fix the skin issues. These various kinds of skin drug conveyance frameworks are for the most part utilized for nearby skin contamination like contagious disease or where other course of organization are no suitable.1 It can enter further into skin and henceforth give better retention. Effective application has no significantly more of the focal points over the traditional dose structures. In the above given plan of skin sort of measurements structures, targets has been made to use the medication transporters that guarantee satisfactory confinement or entrance of the medication inside or through the infiltration of skin to improve the neighborhood and limit the fundamental impacts, or to guarantee sufficient Percutaneous absorption.2 These kinds of medication forestalls the GI-aggravation, forestall the digestion of medication in the depression of liver so as increment their bioavailability of the medication. These kinds of arrangements give its activity straightforwardly to at the site of activity. A gel is having two unique sorts of segment, cross connected three-dimensional organization comprised of underlying materials. The materials that structure the gel organization can be comprised of inorganic particles or natural macromolecules, primarilypolymers.3 U.S.P. has some uncommon kinds of definition for gels which is as a semisolid medication conveyance framework comprising of the scattering comprised of either little inorganic molecule or enormous natural particle encasing and interpenetrated by fluid. Gels are comprised of bilayer stage framework in which inorganic particles are not disintegrated however only scattered all through the ceaseless stage and huge no

of natural particles are broken down in the nonstop stage, haphazardly curled in the adaptable chains.

1. Topical Drug Delivery System

A skin conveyance framework we can characterized as the substance which conveys a particular kind of medication into contact with and through the skin. The test to skin drug conveyance is the vehicle across the skin boundary.

Effective conveyance incorporates two essential sorts of item:
External sort of effective that are spread, splashed, or in any case scattered on to cutaneous tissues to cover the influenced zone. Internal kind of effective that are applied to the mucous layer orally, vaginally or on anorectal tissues for nearby action.

For the different part the skin arrangements are utilized for the limited impacts at the site of their application by the utilization of medication infiltration into the basic layers of skin or mucous layers. On the off chance that a portion of the unintended medication, are get consumed it is sub therapeutics amounts and for the most part of minor concern.

1.1. Advantages of topical drug delivery systems[1,4]

Avoidance of the first pass metabolism.

Convenient and easy to apply.

Deliver drug more selectively to a specific site.

Avoidance of the gastro-intestinal incompatibility.

After the providation of the utilization of drugs which are havinf the short biological half life, narrow therapeutic window. Improved patient compliance.

Provide suitability for self-medication.

1.2. Disadvantages of topical drug delivery systems:

Poor permeability of few drugs through skin.

Drugs who is having the larger particle size can't be get easily absorbed through the layer of skin.

Possibility of allergic reactions.[5]

They can be use only for those drugs who requires the need of very small plasma concentration for action.

The path of that drugs are not suitable for those drugs that irritate or sensitize the skin[1,4, 5]

2. Anatomy of Skin

Human skin is mainly based on the three but mutually dependent tissues:

The stratified, cellular, vascular called as "epidermis"

Underlying dermis of connective tissues. Hypodermis.[6] (fig.1)7

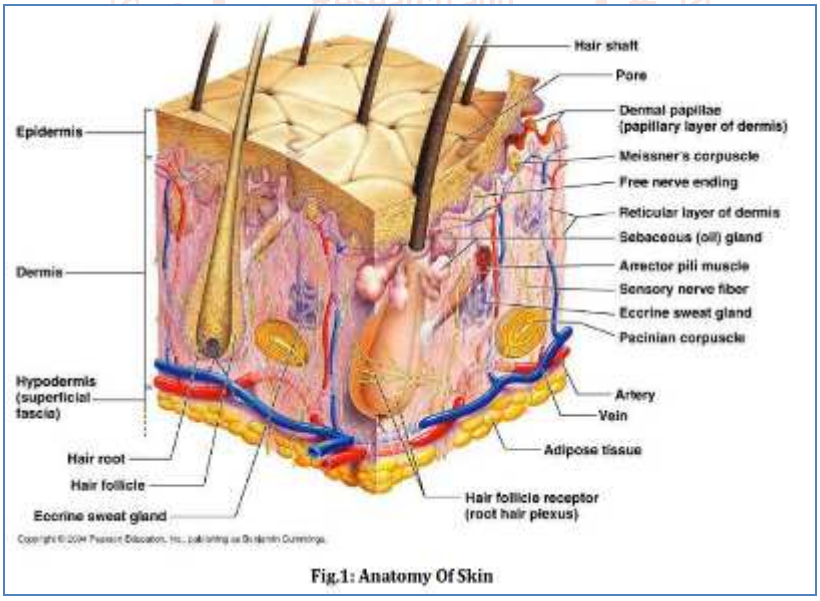

Fig.1: Anatomy Of Skin

2.1. Epidermis

Epithelium tissues is made up of 5 layers: [7, 8]

1. Stratum corneum.To (fig.2)[9]
2. Stratumlucidum
3. Stratum granulosum
4. Stratum spinosum and
5. Stratum germinativum

Very useful feature of epidermis layer is that, it does not have blood vessels. The epidermis is the topmost layer of skin. Above 90% are the keratinocytes, which is accountable for the barrier characteristics of the skin.[10] (see Figure 2)

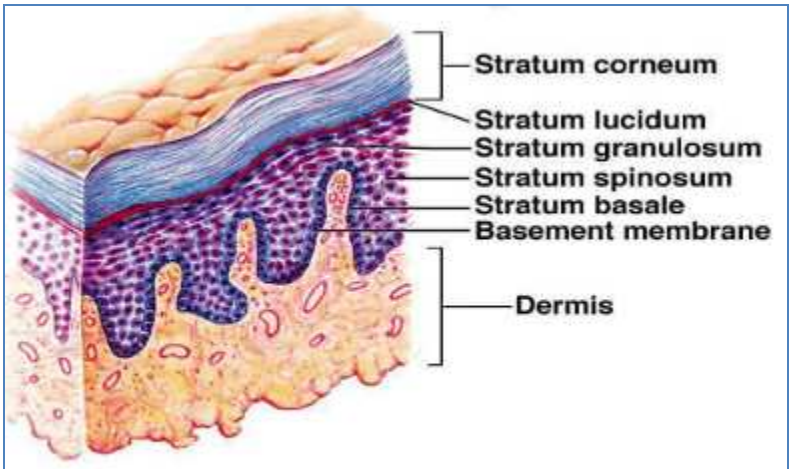

Figure 2: Epidermal Layer

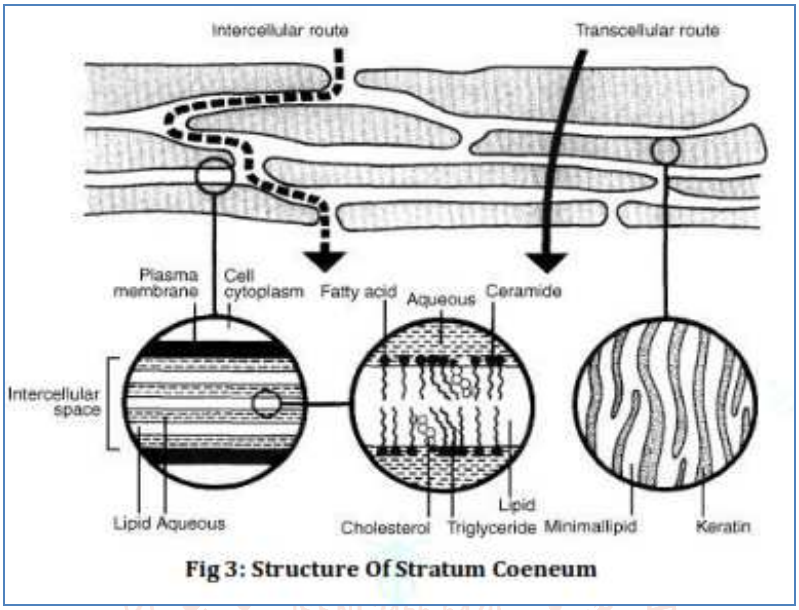

Fig 3: Structure Of Stratum Coeneum

2.2. Dermis:

The dermis is a thick layer comprised of sinewy and flexible tissue. the dermis is comprised of the sensitive spot, sweat organ, oil organ, hair follicles and last part is blood vessels9. The dermis is a vascularized collagen-rich connective tissue comprised of mucopolysaccharides aggregately known as the ground substance.11

2.3. Hypodermis:

Inward layer of skin. This layer is called as contact layer which interfaces among skin and the fundamental tissues in body, for example, muscles and bone. Sweat organs tosses a weaken salt arrangement into the outside of skin layer. The dissipation of the given weakened salt arrangement makes the external part of skin cool and this is significant for temperature guideline of both body and skin. Sweat organs are available everywhere on the body.

3. Factors that affecting absorption of drug through skin[13, 14]

Factors that affecting on the topical absorption of drug are as follows

3.1. Physiological factors.

Skin thickness.
Lipid content.
Density of the hair follicles.
Density of the sweat glands.
Skin pH.
Blood flow.
Hydration of skin.
Inflammation of skin.

3.2. Physiochemical factors.

Molecular weight
Partition coefficient.

4. Classification of Gels[15, 16]

Gels are mainly classified by two methods which are as follows:

1. Nature of the colloid phase
A. Inorganic gels (Two phase system)
B. Organic gels (single phase system)

2. Based on the nature of solvent
A. Hydrogel (Aqueous gels)
B. Xerogel[15]
C. Organicgel (Non aqueous gels)

3. Based on rheological properties

Usually gels exhibit non-Newtonian flow properties. They are classified as,

A. Plastic gels
B. Pseudo plastic gels
C. Thixotropic gels

4. Based upon physical nature

A. Elastic gel
B. rigid gel[16]

5. Hydrogel[17]

Gels that are comprise of a fluid scattering medium which is gelled with the reasonable hydrophilic gelling specialist are known as the hydrogels. Definition that permits, hydrogels are polymeric organizations inside the three-dimensional arrangement equipped for soaking up the high scope of water or natural substance. That is the reason fondness to assimilate water is then ascribed to the presence of the hydrophilic gatherings, for example, as – OH, – CONH–, - CONH2–and – SO3H in polymers framing the hydrogel structures. Due to this to the expansion of these gatherings and areas in the commitment of, the polymer is hence hydrated to different degrees, in light of the idea of the watery climate and polymer composition.17

5.1. Type of Hydrogels:

pH – Sensitive Hydrogel
Temperature Sensitive Hydrogel
Nanohydrogels
Glucose Sensitive Hydrogel

6. Organogels[19]

Organogels may likewise be alluded as oleaginous gels. They are comprised of both polar and nonpolar gatherings yet the proportion of the non-polar part is extremely high. Involment of many contain 35% water as the gels keep an eye on the swell in water. Organogelators are generally low sub-atomic weight little particles that can thicken in natural solvents in physical organogels has developed quickly with the disclosure and union of an enormous number of different atoms, which can gel natural solvents at low concentrations.19

7. Desirable Properties of Gels[4, 20]

At first, the gelling specialist should be of dormant, and safe and can't respond with other detailing segments.

The gelling specialist should create a reasonable strong like nature at the hour of capacity which is handily broken when presented to shear.

It ought to have reasonable enemy of microbial specialist.

It ought to be no tacky.

The ophthalmic gel should be sterile.

The evident thickness or gel strength increments with an increment in the viable crosslink thickness of the gel. Morever, the increment in temperature may get increment or get decline the evident consistency, in light of the sub-atomic communications between the two diffierent polymer and dissolvable.

They display the mechanical qualities of the strong state. Every segment is nonstop all through the system.4, 20

8. Characteristics of Gels [21, 22]

Swelling: At the point when a fluid is left in contact with a gelling specialist that solvates it, after that extensive measure of fluid is consumed by the specialist and the volume increments. This is called as expanding. This proces happens because of dissolvable ingestion into the framework.

Syneresis: Contraction of many gels spontaneously on standing and exude some fluid medium. This process is known as syneresis. The degree to which Syneresis happens, gets increases as the concentration of gelling agent decreases.

Ageing: Slow accumulation is normally appeared by colloidal framework. This cycle is known as maturing. In gels, maturing causes gradually development of a denser organization of the gelling specialist**.**

Rheology: Solutions of the gelling specialists and scattering of flocculated strong are available in pseudo plastic in nature, for example permits the Non-Newtonian stream conduct, described by decline in thickness with increment in shear rate.

9. Formulation Design[22]

Topical gel may involve the following components:

9.1. Gel forming agent or polymer
9.2. Drug Substance
9.3. Penetration Enhancers

9.1. Gel forming agent or Polymer[23]

For structural network polymers are used, which is important for the preparation of gels. Gel producing Polymers are classified as follows:

Natural Polymers:[23, 24]

Proteins – Collagen, Gelatin Polysaccharides – Agar, Alginate acid,Xanthan, Sodium or Potassium carageenan,Pectin, Tragacanth, Guar Gum, Cassia tora, Gellum Gum

Semisynthetic polymers cellulose derivatives:

Carboxymethyl cellulose, Methylcellulose, Hydroxy propyl (methyl cellulose), Hydroxyethyl cellulose Hydroxypropyl cellulose.

Synthetic polymers:
Carbomer – Carbopol 934, Carbopol 940
Polyacrylamide
Poloxamer
Polyvinyl alcohol
Polyethylene and its copolymers

Inorganic substances: [25]
Bentonite
Aluminium hydroxide

Surfactants:
Cebrostearyl alcohol
Brij – 96

The given below criteria should be satisfied for a polymer to be used in a topical system.

- Molecular weight

Chemical functionality of polymer must allow diffierentation and release of the special type of drugThe polymer should allow the incorporation of a huge amount of drug.

Polymers and its degradation products must avoid toxicity.

9.2. Drug Substance [8, 26]
Drug Substance is having a very important role in the successful development and research of a topical product. The main drug properties that effect its diffusion through gels as well as through skin are as following.

- Physicochemical properties

Drug have a molecular weigh of 500 Daltons.

A solution of the drug should have a pH value ranges between 5 and 98

- Biological properties

They are free from skin irritation.

Avoidance to the drug must not develop under the near zero order release profile of topical delivery.

The drug should not get stimulated an immune reaction in the skin.[26]

9.3. Penetration Enhancer[26, 27]
An ideal penetration have the following properties:

It should have chemically inert, and chemically stable.

It should be non-toxic, non-irritant, noncomedogenic and non-allergenic.

It should not have any odour, no taste ,colorless, and inexpensive.

It should have pharmaceutically and cosmetically acceptable.

It should be non-toxic, non-irritating, and non-allergenic.

It should have a solubility parameter similar to that of skin[26]

It should have no pharmacological impact within the body, i.e., should not conjugate to receptor sites.

It should have appropriate for formulation into diverse topical preparations, thus should be compatible with both excipients and drugs.

It should have cosmetically compliance with an acceptable skin "feel."[27]

10. Application of Gel[28]
As a drug delivery systems for drugs administered orally.

To deliver topical drug applied directly to the skin, eye or mucous membrane.

In cosmetics like shampoos, fragrance products, dentifrices, skin and hair care preparations.

11. Evaluation of gels[29, 30,31,32,33,34]
pH Measurement: The pH of different gel definitions are dictated by utilizing computerized pH meter.1 g of gel is broken down in 100 ml. newly arranged refined water and put away for two hours. The estimation of pH of every detailing is done in three-fold and normal qualities are determined.

Viscosity Measurement: Brookfield advanced viscometer can be utilized to gauge the thickness of arranged gel details. The gels are turned at 0.3, 0.6 and 1.5 revolutions every moment. At each speed, the relating dial perusing is noted. The thickness of gel is gotten by duplication of dial perusing with calculate given the Brookfield viscometer catalogues.29

Spread capacity: Spread capacity alludes to the degree of territory to which gel promptly spreads on application. It is dictated by wooden square and glass slide device. The time in sec. taken by two slides to sneak off from gel which is put in the middle of the slides under the heading of certain heap is communicated as spread ability. Lesser the time taken for the partition of two slides, better the spread capacity. Spread capacity is determined by utilizing the formula:

S = M.L / T

Where, S = Spread ability

M = Weight tide to the upper slide

L = Length of a glass slide

T = Time taken to separate the slide completely from each other.

Homogeneity: All formulated gels are tested for homogeneity by visual inspection after the gels have been pour in the container. Gels are tested for their appearance and presence of any impurities.[30]

Grittiness- All the gel formulations are checked microscopically for the presence of any particulate matter.

Extrudability-The gel plans are filled in folding cylinders, subsequent to being set in the compartments. The extrudability of gel plans are resolved regarding weight needed in grams to expel 0.5 cm. strip of gel in 10 sec.31

Stability test- Stability study is carried out by freeze-thaw cycling. The product is subjected to a temperature of 40^{C}

Drug content: 1 g gel is get dissolved in the 100 ml. of suitable solvent with appropriate weight. Absorbance is then measured after suitable dilution at λmax nm using UV spectrophotometer.[32]

In-vitro Drug Diffusion Study: In-vitro drug release studies are carried out by using the instrument which is called as Franz diffusion cell. Lets take 0.5 g of gel is taken in cellophane membrane. Diffusion studies are conducted at $37^{0C} \pm 1^{0C}$ employing 250 ml. phosphate buffer, pH 7.4 as the dissolution medium. At time interval of 1 hr, 1 ml pg sample is then collected and replaced with the new buffer solution. Collected samples are analyzed by using suitable analytical method [33]

12. **Skin irritation test:** Firstly select the volunteers and then take 100 mg gel was applied on area of 2 cm for 6 hours, on the interior surface of upper arm and covered with cotton bandage. After For 6 hrof administration the sites were cleaned with acetone and readings are prepared to the scale given by Draize. No irritation: 0 Slight irritation:1 Irritation: 2.[33]

13. **In-vivo Study:** Inhibition of carrageenan induced rat paw edema is studied in male wistar albino rats with the use of mercury plethysmometer. The volume of unilateral hind paw of experimental animals is measured, before and after administration of carrageenan. % inhibition is noted.[30, 34]

Future Perspective:

During detailing and advancement of any new detailing the most basic issues looked from hydrophobic conduct of medications which prompts helpless water dissolvability and bioavailability issues. Due to hydrophobic nature of numerous medications conveyance of these to the organic framework have be testing. Creams, salves and moisturizer are of various sorts of medication conveyance framework which has been applied topically have astounding emollient properties however hinders the arrival of medications because of essence of oleaginous bases. When contrasted with other effective frameworks gel gives faster arrival of medication since gel gives watery climate to drugs. Hydrophobic medication can be consolidated in slick base and conveyed to skin by utilizing emulgel. All such focal points of Emulgel over other skin drug conveyance frameworks make them more successful and productive. In future these properties will be used to pass on more number of effective prescriptions as Emulgel.[35]

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