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A comprehensive review on topical gel

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Abstract
Most of topical preparations are meant to be applied to the skin. The basic knowledge of skin and its physiology function and biochemistry is very important for designing topicals. It is suggested that acidity of the skin helps in limiting or preventing the growth of pathogens and other organisms. Delivery systems are designed chemical entities that carry a chosen active compound and allow its approach to its site of action. Drug delivery system serves as a strategic tool for expanding market share, extending the product life cycles and generating newer opportunities which has become increasingly important in the pharmaceutical industry. The definition of drug delivery system as we describe them is quite broad & includes the carrier formulation, (i.e., gel, emulsion, suspension etc.) as well as particulate or molecular carriers (i.e., niosomes, liposomes, transfersomes). The advanced drug delivery system extends the proprietary status of drugs facing patent expiration, thereby providing increased profitability.

Keywords: topical gel, skin, gel, niosomes, liposomes etc.

Introduction
Delivery systems are designed chemical entities that carry a chosen active compound and allow its approach to its site of action. Drug delivery system serves as a strategic tool for expanding market share, extending the product life cycles and generating newer opportunities which has become increasingly important in the pharmaceutical industry. The definition of drug delivery system as we describe them is quite broad & includes the carrier formulation, (i.e., gel, emulsion, suspension etc.) as well as particulate or molecular carriers (i.e., niosomes, liposomes, transfersomes). The advanced drug delivery system extends the proprietary status of drugs facing patent expiration, thereby providing increased profitability.

Common rationale required for the development of a DDS

1. **Improved stability:** Protection from light/air, prolongation of shelf life & sensitivity to elevated temperature.
2. **Modulation of skin penetration properties:** Controlled, sustained or delayed release of drug.
3. **Protection from component interactions:** Prevent contact of incompatible ingredients within the formulation.
4. **Change of form:** To resolve solubility/incorporation/ application limitations.
5. **Improved skin tolerance:** To expand therapeutic index, improve efficacy & safety.
6. **Improved esthetics:** Consumer appeal.
7. **Mask undesirable properties:** Change color or eliminate undesired odor.

Table 1: Differences between topical and transdermal drug delivery

Topical drug delivery systems	Transdermal drug delivery systems
Topical dermal delivery can be defined as application of a system directly at the affected area to deliver the drug in dermal and the underlying tissue at the site of application.	Transdermal delivery can be defined as application of a system to skin at a practically accessible site with an intent of treating a systemic disease, for which drug is required to achieve therapeutic levels in plasma.
The formulation commonly used to deliver drugs by this route are ointments, lotions, creams, gels, sprays, medicated plasters and powders.	Transdermal products can be related to patches or semisolid vehicles which provide necessary drug permeation through the skin and exert systemic effect.
These products aim the skin itself as target site and the maximum drug retention in the skin with minimum systemic exposure is favorable.	Local concentration may not reach high levels.
Only small amounts of drug are absorbed into the systemic circulation, avoiding toxic effects.	Drug absorption is high, resulting in therapeutic plasma levels.
Applied dose (amount applied per unit area) varies with applying individual. Absorption may change with application technique such as the pressure applied, etc.	Currently available transdermal systems are very pratical, and applied dose is constant and is usually defined by the manufacture.

Functions of topical delivery system

- To support & restore the barrier function of the skin.
- To help hydrate the skin because of their emollient properties.
- To protect from the external environment or heal an intact or injured area of the skin.
- To transport an active moiety into the skin.

Desirable characteristics of drug for topical use

The drug should be uniformly and consistently distributed throughout the product.

- The texture of the formulation is very important. The product should be free from grittiness as it is applied to the skin.
- Physical, chemical and microbiologically stability should be maintained over the shelf - life of the product.
- The product should not cause any skin irritation or sensitization.
- The product should be cosmetically elegant and aesthetically appealing to the patient.
- The viscosity of the formulation influences spread ability and retention on the skin surface, and hence needs to be adjusted depending on the formulation and intended use of the product.

Topical delivery includes two basic types of product

- External topicals that are spread, sprayed or otherwise dispersed on to cutaneous tissues to cover the affected area.
- Internal topicals that are applied to the mucous membrane orally, vaginally or on anorectal tissues for local activity.

For the most part topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. Although some unintended drug absorption may occur, it is of sub therapeutic quantity and generally of minor concern.

Advantages of Topical Drug Delivery Systems

- Avoidance of first pass metabolism.
- Convenient and easy to apply.
- Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time etc.
- Achievement of efficacy with lower total daily dosage of drug by continuous drug input.
- Avoids fluctuation in drug levels, inter- and intrapatient variations.
- Ability to easily terminate the medications, when needed.
- A relatively large area of application in comparison with buccal or nasal cavity
- Ability to deliver drug more selectively to a specific site.
- Avoidance of gastro-intestinal incompatibility.
- Providing utilization of drugs with short biological half-life, narrow therapeutic window.
- Improving physiological and pharmacological response.
- Improve patient compliance.
- Provide suitability for self-medication.

Disadvantages of Topical Drug Delivery Systems:

- Skin irritation of contact dermatitis may occur due to the drug and/or excipients.
- Poor permeability of some drugs through the skin.
- Possibility of allergenic reactions.
- Can be used only for drugs which require very small plasma concentration for action
- Enzyme in epidermis may denature the drugs
- Drugs of larger particle size not easy to absorb through the skin

Classification of Topical Drug Delivery Systems

Classification of Topical Drug Delivery Systems based on physical state

A) Solid

- Powder
- Aerosol
- Plaster

B) Liquid

- Lotion
- Liniment
- Solution
- Emulsion
- Suspension
- Aerosol

C) Semi-solid

- Ointment
- Cream
- Paste
- Gel
- Jelly
- Suppository

Permeation through skin

Most of topical preparations are meant to be applied to the skin. So basic knowledge of skin and its physiology function and biochemistry is very important for designing topicals. The skin is the heaviest single organ of the body, combines with the mucosal lining of the respiratory, digestive and urogenital tracts to from a capsule, which separates the internal body structures from the external environment. The pH of the skin varies from 4 to 5.6. Sweat and fatty acids secreted from sebum influence the pH of the skin surface. It is suggested that acidity of the skin helps in limiting or preventing the growth of pathogens and other organisms.

Factor affecting topical permeation

(i) Physicochemical properties of drug substances

- Partition coefficient
- pH-condition
- Drug solubility
- Concentration
- Particle size
- Polymorphism
- Molecular weight

ii) Penetration enhancer

Percutaneous absorption can be enhancing in two ways either

by chemical enhancer or by physical method.

iii) Chemical penetration enhancer

By definition, a chemical skin penetration enhancer increase skin permeability by reversibly damaging or by altering the physicochemical nature of the stratum corneam to reduce its diffusional resistance. Among the alterations are increased hydration of stratum corneam and a change in the structure of the lipids and lipoproteins in the intercellular channels through solvent action or denaturation. These may conveniently be classified under the following main heading:

Solvents

These compounds increase penetration possibly by swelling the polar pathway and/or by fluidizing lipids. Examples include water, alcohols, methanol and ethanol; alkyl methyl sulfoxide, dimethyl sulfoxide, alkyl homologs of methyl sulfoxide, dimethyl acetamide and dimethylformamide; pyrrolidones- 2 -pyrrolidone, N-methyl, 2- pyrrolidone; laurocapram (Azone), miseellancous solvents- propnylene glycol, glyeerol, silicone fluids, isopropyl palmitate.

Surfactant

These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs. The ability of the surfactant to alter penetration is a function of polar head group and the hydrocarbon chain length. Commonly used surfactants are as follow

Anionic surfactant

It can penetrant and interact strongly with skin. Examples include are Dioctylsulphosuccinate, Sodium lauryl sulphate, Decodecylmethylsulphoxide etc.

Cationic surfactant

Cationic surfactants are reportedly more irritating than anionic surfactants and they have not been widely studied as skin permeation enhancer.

Nonionic surfactant

Nonionic surfactants have least potential for irritation. Example includes are Pluronic F127, Pluronic F68 etc.

Bile salts

Sodium taurocholate, Sodium deoxycholate, and Sodium tauroglycocholate.

Binary system

These systems apparently open the heterogeneous multilaminated pathway as well as the continuous pathways. Examples include are prolylene glycol -oleic acid and 1, 4-butane diol- linoleic acid.

Miscellaneous chemicals

These includes urea, N, N-dimethyl-m-toluamide, calcium thioglycolate etc.

Physical method of topical drug delivery

Iontophorosis: Intophorosis is a process or a technique involving the transport of ionic or charged molecules into a tissue by the passage of direct or periodic electric current through an electrolyte solution containing the ionic molecules to be delivered using an appropriate electrode polarity.

Electroporation: The process involves the application of transient high voltage electrical pulse to cause rapid dissociation of the stratum corneam through which large and small peptides, oligonucleotides and other drugs can pass in significant amounts. Electroporation or elecro-permeabilization involves changes in membrane cells due to application of large transmembrane voltage. The change in the membrane involves structural arrangement and conductance leading to temporary loss of semi-permeability of cell membranes suggesting formation of pores.

Sonophoresis: Sonophoresis involves the usage of the frequency ultrasound waves. The ultrasound application has resulted in permeation of low frequency ultrasound was shown to increase the permeability of human skin to many drugs including high molecular weight protein by several orders of magnitude.

Phonophoresis: The movement of drugs through living intact skin and into soft tissues under the ultrasound perturbation is called phonophoresis. The technique involves placing an ultrasound-coupling agent on the skin over the area to be treated and massaging the area with an ultrasound source.

Vesicular concept: Drug enclosed vesicle made from phospholipids and nonionic surfactants are used for transport of drug into and across the skin. The various vesicles used for this purpose are liposomes, niosomes and transfersome. The lipid vesicle serve as a rate limiting membrane barrier for system absorption of drug, non-toxic penetration enhancers for drug, organic solvents for solubilization of poorly soluble drugs and can incorporate both hydrophillc and lipophillic drugs.

Micro fabricated micro needles technology: This technology employed micron-sized needles made silicon. These microneedles after insertion into the skin create conduits for transfer of drug through the stratum corneum. The drug after crossing stratum corneum diffuses rapidly through deeper tissues and taken up by capillaries for systemic adminitration.

Physicochemical properties of topical

Release characteristics: The mechanism of drug release depends on whether the drug molecules are dissolved or suspended in the delivery system. The interfacial partition coefficient of drug from delivery systems to the skin pH of the vehicle

Composition of drug delivery system: Example polyethylene glycols of low molecular weight decrease permeation.

Nature of vehicle: Liphophilic vehicle increase permeation where aslipophobic vehicle decrease permeation.

Common Topical Ingredients
Hydrophobic vehicle
Hydrocarbons
Liquid petrolatum (mineral oil, liquid paraffin, paraffin oil)
White petrolatum (petroleum jelly, Vaseline)
Yellow petrolatum (petroleum jelly)
Squalane (perhydrosqualene, spinacane)

Silicones
Liquid polydimethylsiloxanes (dimethicone, silastic, medical grade silicone oil)

Alcohols
Lauryl alcohols (1-dodecanol, dodecyl alcohols)
Myristyl alcohols (tetradecanol, tetradecyl alcohols)
Cetyl alcohols (hexadecanol, ethal, palmityl alcohols)
Stearyl alcohols (stenol, cetosteryl alcohols)
Oleyl alcohols (ocenol)

Sterols; sterol esters
Lanolin (hydrous wool fat, lanum)
Anhydrous lanolin (wool fat, anhydrous lanum, agnin)
Semi synthetic lanolin's

Carboxylic acids
Lauric acid, Myristic acid, palmitic acid, stearic acid, oleic acid

Esters; polyesters
Cholesterol esters (stearate), Ethylene glycol monoesters, Propylene glycol monoesters, Glyceryl monoesters, Glycerylmonostearate, Sorbitol monoesters, Sorbitain monoesters, Sorbitol diesters, Sorbitan polyesters (spans, arlacels), Glyceryl tristearate, Lard, Almond oil, Corn oil, Caster oil, Cottonseed oil, Olive oil,Soyabeanoil,Hydrogenated oils, Sulfated oils, Isopropyl myristate, Isopropyl palmitate.

Ethers; polyethers
Polyethylene-polypropylene glycols (pluronics)

Water-miscible vehicle, co solvent
Polyols; polyglycols
Propylene glycol (1, 2-propanediol)
Glycerin (glycerol)
Liquid polyethylene glycol

Esters; polyesters
Solid polyethylene glycol (hard macrogol, carbowax)
1, 2, Phenols-hexanetriol, Sorbitol solution 70%
Polyoxyethylenesorbitain monoesters (stearate- tweens)
Polyoxy ethylene sorbitan polyesters (tweens)

Ethers; polyethers
Polyethylene glycol monocetyl ether (cetomacrogol 1000)
Polyethylene-polypropylene glycols (pluronics)

Structural matrix former
Hydrocarbons
White petrolatum (petroleum jelly, vaseline)
Yellow petrolatum (petroleum jelly)
Paraffin (paraffin wax, hard paraffin)
Microcrystalline wax
Ceresin (mineral wax, purified ozokerite)

Silicones
Fumed silica (cab-O-sil)
Bentonite (colloidal aluminum silicate)
Veegum (colloidal magnesium aluminum silicate)

Polyols, polyglycols
Solid polyethylene glycol (hard macrogol, carbowax)

Alcohols
Cetyl alcohols (hexadecanol, ethal, palmityl alcohols)
Stearyl alcohols (stenol, cetosteryl alcohols)

Sterols; sterol esters
Cholesterol (cholesterin)
Lanolin (hydrous wool fat, lanum)
Anhydrous lanolin (wool fat, anhydrous lanum, agnin)
Semi synthetic lanolin's

Carboxylic acids
Lauric acid, Myristic acid, palmitic acid, stearic acid, oleic acid

Esters; polyesters
Bees wax, White bees wax (bleached bees wax), Carnauba wax, Myricin, Cholesterol esters (stearate), Polyoxyethylenesorbitain Monoesters (stearate- tweens), Lard, Hydrogenated oils.

Suspending, jelling, or viscosity inducing agents:
Silicones
Fumed silica (cab-O-sil)
Bentonite (colloidal aluminium silicate)
Veegum (colloidal magnesium aluminium silicate)

Polycarboxylates; polysulfates; polysaccharides
Agar, Alginates, Carragen, Acacia, Tragacanth, Methylcellulose, Carboxy methylcellulose, Hydroxy ethyl cellulose, Carboxy vinyl polymer, gelatin, pectin, xanthan, polyacrylic acid.

Others
Ethanolamin, Triethanolamin.

Water-in-oil (w/o) emulsifier
Sterols; sterol esters
Cholesterol (cholesterin)
Lanolin (hydrous wool fat, lanum)
Anhydrous lanolin (wool fat, anhydrous lanum, agnin)
Semi synthetic lanolin's

Carboxylic acids
Na+, K+, ethanolamin salts of Lauric acid, Myristic acid, palmitic acid, stearic acid, oleic acid.

Ethers; polyethers
Polyethylene-polypropylene glycols (pluronics)

Oil-in-water (o/w) emulsifier
Esters; polyesters
Polyoxyethylene sorbitain monoesters (stearate- tweens)
Polyoxyethylene esters (stearate- polyethylene glycol monoesters, Myrj)
Polyoxy ethylene sorbitan polyesters (tweens)

Ethers; polyethers
Polyethylene glycol monocetyl ether (cetomacrogol 1000)
Polyethylene-polypropylene glycols (pluronics)

Others
Sodium lauryl sulfate, Borax (sodium borate), Ethanolamine, Triethanolamine

Preservative
Antimicrobial
Benzalkonium chloride, Benzoic acid, Benzyl alcohol, Bronopol, Chlorhexidine,
Chlorocresol, Imidazolidinyl urea, Paraben esters, Phenol, Phenoxyethanol, Potassium sorbate, Sorbic acid

Antioxidants
a-Tocopherol, Ascorbic acid, Ascorbylpalmitate, Butylated hydroxyanisole, sodium ascorbate, sodium metabisulfite

Chelating agents, Citric acid, Edetic acid
Buffer
Citric acid and salts, Phosphoric acid and salts, H_3PO_4 / NaH_2PO_4, Glycine, Acetic acid, Triethanolamine, Boric acid

Humectant
Glycerin (glycerol), propylene glycol (E 1520), glyceryl triacetate (E1518), sorbitol (E420), xylitol and maltitol (E965), polydextrose (E1200), quillaia (E999), lactic acid, urea, lithium Chloride.

Sequestering antioxidant
Citric acid and salts
Ethylene diaminetetra acetic acid (Versene, EDTA)

Table 3: Characteristics and properties of dermatological formulations

Dermatological formulation	Properties and Characteristics
Paste	Semisolids with a high % of dispersed solids (>50%) in a fatty vehicle for external application. Opaque and viscous.
Ointment	Hydrocarban based semisolids contain dissolved or suspending drug. Hydrophillicointment contain bases that are miscible with water, may contain water.
Cream	Viscous semisolid emulsions (w/o or o/w) with opaque appearance. Multiphasic system.
Gel	Liquid phase is immobilized in a three –dimensional polymeric matrix of a gelling agent. Transparents or translucent non –greasy thick semisolid.

The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three-dimensional "house of cards" structure. Gels consist of two-phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains.

Typical properties of gel as a dosage form

- Gels are soft, solid-like, or semisolid in nature, and consist of at least two components, one of these being a liquid that is present in a substantial quantity. Although the liquid content is high, on a time scale of seconds, a gel should not flow under the influence of its own weight.
- Some gel systems are transparent and others are translucent, since the ingredient involved may not be completely dispersed or they may form aggregates which disperse light.
- The common characteristic of all gels is that they contain continuous structures that provide solid –like properties. Gel exhibits a number of different characteristics, including imbibition, swelling, syneresis and thixotropy.
- Where the gel mass consists of network of small, discrete particles, the gel is classified as a two- phase system. In these two –phase systems, if the particle size of the dispersed phase is large, the product is referred to as a magma.
- Single phase gels consist of organic macromolecules uniformly distributed throughout a liquid in such a manner that no apparent boundaries exist between the dispersed macromolecules and the liquid. Single - phase gels may be made from synthetic macromolecules or from natural gums (mcilages).
- The continuous phase is usually aqueous but it can also be alcoholic or oleaginous.

Classification

Table 1.4: Classification of GEL

Class	Description	Example
Inorganic	Usually two- phase systems	Aluminium hydroxide gel, bentonite magma
Organic	Usually single – phase Systems	**C**arbopol, tragacanth
Hydrogels	Organic hydrogels	Pectin paste, tragacant jelly
	Natural and synthetic gums	MC,Na, CMC, F-127
	Inorganic hydrogels	Bentonite gel (10% t0 25%)

Organogels	Hydrocarbon type	Petrolatum, mineral oil/polyethylene gel, Plastibase
	Animal/vegetable fats	Lard, cocoa butter
	Soap base greases	Aluminium stearate with heavy mineral –oil gel
	Hydrophilic organogels	Carbowax bases (PEG ointment)

Advantages of gel formulations

- As the dosage form is applicable to all topical membranes they have a variety of application in the administration of medication by oral, topical, rectal, intranasal and vaginal route.
- Gels can also be used subcutaneously and for administration to the stomach or colon.
- The contact time of a gel formulation on skin or mucosa is typically much longer than that of an aqueous solution owing to the more favorable adhesive and/or rheological properties.
- An extended contact time at the site of administration might increase the absorption of the substances, opening up the possibility of giving a lower dose of the administered drug, using longer dosing intervals, or both.
- Gels as a dosage form with favorable properties offers high patient compliance.
- Compared to ointments and creams the oil content is usually very low in a gel, which makes the cosmetics properties favorable in many places.

Limitations of gels formulations

- Applization to mucosa or skin, the mucoadhesives and rheological properties of a gel of may increase the residence time on the tissue. The advantages of this can only be utilized if the drug substance is released from the gel throughout the contact time.
- Given that the gel formulations under consideration are mostly comprised of water, the diffusion rate of free, small molecules in these gels is similar to that in pure water. Gels are therefore quickly emptied of the drug, resulting in no obvious benefits in the form of an extended residence time at the site of application.
- To prolong the release of drug substances for gels formulations many strategies have been suggested; the drug can be formulated as solid particles in the gels, rendering a suspension; the drug substance may interact with the gel polymer or the drug can be distributed to vesicular carriers or micelles, which are incorporated in the gel.

Gel forming substances

Polymers are used to give the structural network, which is essential for the preparation of gels. Gel forming polymers are classified as follows:

(i) Natural polymer

a) Proteins: Collagen, Gelatin
b) Polysaccharides: Agar, Alginate acid, Sodium or Potassium carageenan, Tragacanth, Pectin, Guar Gum, Cassia tora, Xanthan, Gellum Gum.

(ii) Semisynthetic polymers

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

iii) Synthetic polymers

A) Carbomer: Carbopol 940, Carbopol 934
B) Poloxamer
C) Polyacrylamide
D) Polyvinyl alcohol
E) Polyethylene and its co-polymers

iv) Inorganic substances

A) Aluminium hydroxide
B) Besitonite

v) Surfactants

A) Cebrotearyl alcohol
B) Brij - 96

Evaluation of topical gel

The topical gel formulation are evaluated for varies parameters mentioned below.

Measurement of pH

The pH of various gel formulations is determined by using digital pH meter. One gram of gel is dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation is done in triplicate and average values are calculated.

Drug content

1g of the prepared gel is mixed with 100ml of suitable solvent. Aliquots of different concentration are prepared by suitable dilutions after filtering the stock solution and absorbance is measured. Drug content is calculated using the equation, which is obtained by linear regression analysis of calibration curve.

Viscosity study

The measurement of viscosity of the prepared gel is done with a Brookfield Viscometer. The gels are rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding dial reading is noted. The viscosity of the gel is obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogues.

Spreabability

One of the crieteria for a gel to meet the ideal quantities is that it should possess good spreadability. It is the term expressed to denote the extent of area to which gel readily spreads on application to skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load lesser the time taken for separation of two slides, better the spreadability. It is calculated by using the formula:

S = M. L / T
Where,
M = wt. tied to upper slide
L = length of glass slides
T = time taken to separate the slides

Extrudability study
The formulations are filled in the collapsible tubes after the gels are set in the container. The extrudability of the formulation is determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 second.

Skin irritation study
Guinea pigs (400-500 g) of either sex are used for testing of skin irritation. The animals are maintained on standard animal feed and had free access to water. The animals are kept under standard conditions. Hair is shaved from back of guinea pigs and area of 4 cm^2 is marked on both the sides, one side served as control while the other side is test. Gel is applied (500 mg / guinea pig) twice a day for 7 days and the site is observed for any sensitivity and the reaction if any, is graded as 0, 1, 2, 3 for no reaction, slight patchy erythema, slight but cofluent or moderate but patchy erythema and severe erythema with or without edema, respectively.

***In-vitro* Diffusion studies**
The diffusion studies of the prepared gels can be carry out in Franz diffusion cell for studying the dissolution release of gels through a cellophane membrane. Gel sample (0.5g) is taken in cellophane membrane and the diffusion studies are carried out at 37 ± 1° using 250 ml of phosphate buffer (pH 7.4) as the dissolution medium. Five milliliters of each sample is withdrawn periodically at 1, 2, 3, 4, 5, 6, 7 and 8 h and each sample is replaced with equal volume of fresh dissolution medium. Then the samples are analyzed for the drug content by using phosphate buffer as blank.

***In-vivo* studies**
Inhibition of carrageenan induced rat paw odema. Three groups of 6 male wistar albino rats are used one for marketed sample (reference). Other for test formulation and one group for control, the volume of unilateral hind paw test animal are measured. On each paw, 100 mg of preparation is carefully rubbed twice at 1 and 2 h. before carrageenan administration. They are placed in cages with copography meshes. 0.1ml of 1 % w/v carrageenan is injected subcutaneously into the paw and volume of hind paw measured at hourly interval for 5 h. using a mercury plethysmometer. Percentage of inhibition is calculated.

Stability
The stability studies are carried out for all the gel formulation by freeze - thaw cycling. In this syneresis is observed by subjecting the product to a temperature of 4 °C for 1 month, then at 25°C for 1 month, then at 40°C for 1 month. After this gel is exposed to ambient room temperature and liquid exudates separating is noted.

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