RECENT ADVANCES IN TOPICAL DRUG DELIVERY SYSTEM

Jotinder Kaur, Jasmeen Kaur, Sandhya Jaiswal, Ghanshyam Das Gupta*
ASBASJS Memorial College of Pharmacy, Bela (Ropar), Affiliated to IK Gujral Punjab Technical University, Jalandhar, India

ARTICLE INFO
Article history
Received 14/07/2016
Available online
08/08/2016

Keywords
Topical Drug Delivery;
Skin Penetration;
Lipophilicity;
Therapeutic Effect.

ABSTRACT
Optimum therapeutic outcomes requires not only proper drug selection but also effective delivery of drug. Over the past three decades, controlled drug delivery has become increasingly important in the pharmaceutical industry. The pharmacological response, i.e desired therapeutic and undesired therapeutic effect of a drug depends on concentration of drug reached to its site of action and in turn depends on dosage form. With conventional drug delivery systems, poor patient compliance is a major problem observed in clinical practice. Human skin is a readily accessible surface of drug delivery. The potential of using skin as a target has been recognized but its outermost layer acts as a barrier to the ingress of materials allowing only small molecules to penetrate over a period of time. Recently various strategies has been used to evade the stratum corneum and to increase flux through the skin membrane using different permeation enhancement techniques. For a drug to be delivered passively via skin needs to have enough lipophilicity and also a molecular weight less than 500 Da. These requirements have restricted the number of commercially available commodities based on transdermal or dermal delivery. Therefore the key function of a topical delivery system is to enhance the dermal permeability enabling it to cross the epidermis and retain in the dermis. The aim of this paper is to review non-invasive topical drug delivery employing sophisticated carrier systems leading to advancements in dosage forms.

*Corresponding author
Prof. (Dr.) G. D. Gupta
Director-cum-Member Secretary
Department of Pharmaceutical Res. Div.
ASBASJS Memorial college of Pharmacy, Bela
Ropar (Pb)-140111 (India)
drgdg@rediffmail.com

INTRODUCTION

Topical drug delivery can be defined as application of drug via skin to directly treat or cure the skin disorders. These systems are generally used for local skin infection like fungal infection or in place where other routes of the drug administration fails. Topical dosage forms are generally confined to a small area anywhere in the body through ophthalmic, rectal, vaginal and skin as route. Skin is one of the most easily accessible organ of human body. Skin of an average adult body covers a surface of about 2m² and receives around one-third of the blood circulating through the body. Over the pass three decades, controlled drug delivery has become increasingly important in the pharmaceutical industry. The surface of human skin is known to contain, on an average, 10-70 hair follicles and 200 to 250 sweat ducts on every cm² of the skin area. Skin is a very difficult barrier to the ingress materials allowing only small quantities of drug molecules to penetrate over a period of time. Transport of hydrophilic or charged molecules is especially difficult attributable to the lipid-rich nature of the stratum corneum and its low water content; this layer is composed of about 40% lipids, 40% protein, and only 20% water. Transport of lipophilic drug molecules is facilitated by their dissolution into intercellular lipids around the cells of the stratum corneum. Absorption of hydrophilic molecules into skin can occur through ‘pores’ or openings of the hair follicles and sebaceous glands, but the relative surface area of these openings is barely 1% of the total skin surface. This small surface area limits the amount of drug absorption. Percutaneous absorption of drug molecules is a key factor of particular importance in the case of topical drug delivery systems because the drug has to be absorbed to an adequate extent and rate to achieve and maintain uniform, systemic, therapeutic levels throughout the duration of use. In general, once drug molecules cross the stratum corneal barrier, passage into deeper dermal layers and systemic uptake occurs relatively quickly and easily. Drugs with the lipophilic character, are better suited for topical delivery. These systems ensure that the drug get into the body and reach the area where it is needed.

These preparations are applied onto the skin surface for providing local or systemic effects. Topical route favours safe and effective delivery of drug molecules with lower doses as compared to the conventional system. Drugs via skin reaches the desired area in optimum concentration, dropping the chances of side effects leading to increased bioavailability and increased patient compliance. Dermatological conditions i.e skin disease affects the population and has been observed as one of the top 15 medical conditions for which prevalence and healthcare spending have increased in the last decade. Advancements in the life sciences united with a growing market for dermatologicals have facilitated the emergence of better topical formulations and drug delivery systems. The present and emerging approaches of optimizing the topical dermatological agents delivery (i.e small and large molecules) includes the use of chemical enhancers, liposomes, bio-polymers (sodium hyaluronate), particulate carriers (microspheres and lipid nanoparticles), occlusion (via dressings and patches) topical peels, topical sprays and foams, temperature (heat), iontophoresis and ultrasound. These delivery approaches are a significant advancement over conventional systems (i.e creams, lotions, ointments and pastes) and are likely to enhance efficacy and tolerability, improve patient compliance (which include dermatology life quality), and also fulfil other required needs of the topical dermatological market. However, the limited dermal and transdermal delivery of many small and large molecules is a significant challenge because of the unyielding barrier properties of the skin. This paper reviews the application of a novel topical delivery system, employing sophisticated carriers built from nanoscale components, to the delivery of several therapeutic agents and discusses progress toward its clinical application.

Factors to be considered for designing topical dosage form:

Key factors to be considered for successful topical product

Container selection and stability:

Depending upon the physicochemical properties of drug-excipients, container could be selected (i.e tube, can, jar, etc.) to obtain a stable environment which maintain the shelf life of the product. The product could be liquid or semi-solid, monophasic or multiphasic (oil-in-water or water-in-oil), is basically dependent on the characteristics of the API(s) and condition of the skin to be treated.

Skin penetration:

Once a product is applied on the skin, a complex interaction occurs between the formulation, API and the skin. The penetration of the active compounds into skin follows Fick’s first law of diffusion, which describes the transfer rate of solutes as a function of concentration of the various ingredients, the size of the surface area of treatment, and the permeability of the skin. Even though, the skin’s permeability can also be influenced by numerous other factors such as the moisturizing, drying, or occluding effects of the excipients in the formulation which in combination can alter the release of the drug at the treatment site.

\[ J = -D \cdot \frac{dc}{dx} \]

Where, \( dc/dx \) is concentration gradient per unit length

D is the diffusion constant

Cosmetic acceptability:

In the present self-image conscious world, patients are looking for the topical products that are safe, efficacious, cosmetically approved and ease of application. In the case of acne, where the aesthetic aspect is one of the primary reason why patient hunt for dermatologic consultation. Acne patients are mainly our teenagers or youth adults, so care must be considered regarding these products to offer them ease and are minimally troublesome in daily routine which increases the level of fulfilment, and ultimately, the
efficacy of the therapy. For example, in prescription given to patient, vehicle consideration must be taken into account while applying the drug on large, hairy surface area in order to fulfil the requirement of better spreadibility and minimal remains or oiliness.  

Topical route of drug administration:  
Even though the intact skin is less permeable than other tissues, many of the drug molecules do penetrate the skin to some degree at relatively slow rates. The penetration of the drug and other substances depends mainly on the physiochemical properties of the penetrating agent, the condition of the skin and the nature of the vehicle. Commercially available drugs that are applied topically provide local action includes anti-fungal, anti-septic, anti-inflammatory agents as well as skin emollients for the protective effects. Topically applied drug can diffuse through the skin through hair follicles, sweat glands or sebaceous glands but permeation through multiple lipid bilayers of stratum corneum is a dominant pathway though the rate is very slow. This route can also be used for systemic drug delivery.

Rationale for topical preparation  
In order to formulate an efficient and effective topical preparation, considerations should be given to the objective. This is directly concerned with the site of action and the desired effect of the formulation. Topical preparations may be used for: 1. Surface effects: cleansing (removal of germs and dirt), cosmetic (improvement of appearance), protective (prevention of moisture loss), antimicrobial (reduction of infection). 2. Stratum corneum effects: protective (sunscreens that penetrate this layer), keratolytic (a sloughing of the skin, helpful in the treatment of psoriasis), protective (moisturizing). 3. Viable epidermal and dermal effects: several classes of drugs can penetrate to these layers (anti-inflammatory, antihistamine anesthetic, antipruritic). Even though it is tough for drugs to penetrate the stratum corneum, once they are in the dermis, they can diffuse into the systemic circulation. It is difficult to formulate drug with only a local effect without successive uptake by the blood. 4. Systemic effects: few drugs, such as scopolamine, clonidine, nitroglycerin and estradiol, have been formulated in a manner to achieve systemic effects. 5. Appendage effects: some classes of drugs are intended to put forth their action in these portions (deplitary, antimicrobial, exfoliant, and antiperspirant). Infection remains a major reason of morbidity and mortality following the shock period in the burnt patients. Measures to lessen the risk of wound infection and subsequent sepsis include early removal where possible. The patient who is suffering from major burns is at risk from both systemic and cutaneous infections.

Advantages of topical drug delivery systems:  
- Avoidance of the first pass metabolism.  
- Convenient and easy to apply.  
- Avoidance of risks and inconveniences of the intravenous therapy and of diverse conditions of absorption like pH changes, presence of enzymes, gastric emptying time.  
- Easily terminate the medications, when needed.  
- Deliver drug more selectively to a specific site.  
- Avoidance of the gastro-intestinal incompatibility.  
- Providing utilization of drugs with short biological half life, narrow therapeutic window.  
- Improved patient compliance.  
- Provide suitability for self-medication.  
- Achievement of effectiveness with lower total daily dose of drug by continuous drug input.  
- Avoids fluctuation in drug levels, inter- and intra patient variations.  
- A quite large area of application in comparison with buccal or nasal cavity.  
- Ability to deliver drugs more selectively to a specific site.

Disadvantages of topical drug delivery systems:  
- Skin irritation or dermatitis may occur due to the drug or excipients.  
- Poor permeability of some drugs through skin.  
- Drugs with larger particle size can’t be easily absorbed through the skin.  
- Risk of allergenic reactions.  
- Can be used only for the drugs which need very small plasma concentration for action.

Physiology of human skin  
The skin is the largest organ of human body, accounting for about 15% of the whole adult body weight. Skin is one of the most readily accessible parts of the human body for topical administration. Penetration of molecules in the skin mainly occurs through three routes i.e through intact stratum corneum, through the sebaceous follicle and through sweat ducts. Topical drug delivery approach is used for localized action on the body through skin, ophthalmic, rectal and vaginal as topical routes. Skin performs various important functions:
- Protection against the physical, biological and chemical assailants.
- Prevention of excess loss of water from the body.
- Vital role in the thermoregulation.
- Enzyme in epidermis can denature the drugs.
The skin consists of three layers that are the epidermis, the dermis and the subcutaneous tissue. An average human skin surface contain, on an average 40-70 hair follicles and 200-300 sweat ducts on every cm² of the skin. The pH of the skin vary from 4-5.6 the skin of an average adult body covers a surface area of about 2m² and receives about one third part of the blood circulating through the body.

**Epidermis:**

It is a stratified squamous epithelium layer which is composed primarily of two types of cells; dendritic and keratinocytes cells. The epidermis layer harbour a number of other cells such as melanocytes, Merkel cells and Langerhans cells. But the keratinocytes cells type comprises the majority of the cells by far. The layers of epithelium are:

- **Stratum germinativum** (basal layer or rowing layer): It contains column-shaped keratinocytes that attach to the zone of basement membrane with their long-axis perpendicular to the dermis
- **Stratum spinosum** (prickly cell layer or squamous cell layer): Its thickness vary from 5-10 cells. Intercellular spaces between spinous cells are bridged by abundant desmosomes (adhering spot) to promote coupling between cells of the epidermis and provide resistance to the physical stresses
- **Stratum granulosum** (granular layer): It consists of living cells, these are responsible for further synthesis and modification of the proteins involved in keratinization. It is 1-3 cells layer in thickness
- **Stratum corneum** (horny layer): the corneocytes are rich in protein and low in lipid content (hydrophilic nature) are surrounded by a continuous extra cellular lipid matrix
- **Malpighian layer** (pigment layer): the layer whose protoplasm has not yet change into horny material
- **Stratum lucidium**

![Figure 1- Epidermal layer.](image)

**Dermis:**

It lies beneath the epidermis 1.5-4 mm thick (thickest of the three layers of the skin). It is like home for most of the skin’s structures including sweat glands and oil glands, hair follicles, nerve endings, and blood and the lymph vessels. The main components of the dermis are collagen and elastin. It stores much of the body’s water supply. The dermis also contains the scavenger cells from the immune system. In an event that a foreign organism tries to pass through epidermis, these cells will engulf and destroy it. It is an integrated system of fibrous, amorphous and filamentous connective tissue that accommodates stimulus induced entrance by nerve, vascular-networks, fibroblasts, appendages, mast cells. Its thickness ranges from 2000-3000 μm. The principal component of the dermis is collagen and it represents 70% of the skin’s dry weight.

**Subcutaneous tissue (Connective Tissue):**

The subcutaneous tissue or hypodermis is not actually considered as a true part of the structured connective tissue, which comprises of loose textured, fibrous, white, connective tissue containing blood and lymph vessels, secretary pores of the sweat gland and the cutaneous nerves. Most investigators consider that drug permeating through the skin enters the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug.
Drug transport across skin:

There are mainly two important layers in the skin: the epidermis and dermis. Blood vessels are profusely distributed beneath the skin in the subcutaneous layer. There are three primary mechanisms intended for drug absorption through the skin they are: intercellular, transcellular, and follicular. The other most common route of delivery is through the pilosebaceous route. Permeation tend to occur through intercellular matrix, but via transcellular pathway it has been shown to provide a quicker alternative route for highly polar molecules. In normal intact skin it is considered that the keratinized corneocytes and the large non-polar lipid intercellular cement of the horny layer are the major factors involved in maintenance of efficient barrier for drugs. The drug penetration for skin can be improved by using organic solvents such as propylene glycol, DMSO and surfactants. The permeation enhancers alters the barrier properties of the stratum corneum by type of mechanism which includes enhancing solubility, partitioning the stratum corneum and fluidizing the crystalline structure of the stratum corneum. New technologies now allow other drugs to be absorbed via skin. These can be used to treat not just the affected areas of the skin but the whole body by systemic route. The barrier resides in the outmost layer of the epidermis and the stratum corneum, as evidenced by just about equal rates of penetration of chemicals through the isolated stratum corneum or whole skin.

Factors Affecting Topical drug absorption:
Physiological Factors:
- Skin thickness - It varies from epidermis to subcutaneous layer. Epidermis has high thickness of about 100-150μm.
- Lipid content - It is an effective water barrier; percutaneous penetration increase when the lipid weight in stratum corneum is low.
- Density of hair follicles - hair follicle’s infundibulum has a large storage capacity i.e about 10 times more than the stratum corneum.
- Density of sweat glands
- Skin pH- Sweat and the fatty acid secreted from sebum, influence the pH of the skin surface.
- Hydration of skin - It can enhance permeation of drug.
- Inflammation of skin - It disrupts the continuity of stratum corneum and hence increases permeability.
- Skin temperature - Increase in temperature gives rise to increase in rate of skin permeation.
- Blood flow

Physiochemical Factors:
- Partition co-efficient - More the value of log p more easily will be the percutaneous absorption of the drug.
- Molecular weight i.e < 400 dalton
- Degree of ionization - Only unionized drug molecules get absorbed well.
- Effect of vehicles - Hydroalcoholic gel provides the most efficient absorption through skin.

Methods to enhance drug penetration:
- Physical Enhancement
- Chemical enhancement
- Super saturation enhancement
Physical enhancement:

Iontophoresis:
Iontophoresis is a system of enhancing the penetration of therapeutic agents through skin via electric current. The drug is placed under the electrode of similar charge as that of drug and a counter electrode is located somewhere else in the body. The active electrode repels the active substance and force it into the skin. Drug delivery enhancement can be done by following 3 mechanisms:
- The drug is forced into the skin via electronic repulsion of similar charges i.e anionic drug by negatively charged electrode and cationic drugs by positively charged electrode.
- Electric current enhances the permeation by inhibiting skin's protective barrier function
- Iontophoresis cause water (penetration enhancer) to enter the stratum corneum.

Electroporation:
It is a technique of creating transient pores in the lipid bilayer of skin by applying short (µ second) high voltage (50-1000 volts) pulses, which allows the passage of macromolecules from outside of the cell to intercellular space via diffusion and electrophoresis.

Sonophoresis:
It is a techniques that involves usage of ultrasonic energy (ie by using high or low frequency ultrasound waves) to enhance the skin penetration of active substances. Ultrasound alters the skin porous pathway via two mechanisms:
- Enlarging the radii of skin effective pores
- Creating additional pores

Microporation:
It is a technique of increasing the skin penetration by making use of micro needles that are applied to skin to pierce the stratum corneum. These are 10-200 µm in height and 10-15 µm in width. Microneedles are the drug coated projections of solid silicon.

Heat:
Heat enhances the drug penetration through skin by increasing the body fluid circulation, membrane permeability, and drug solubility, hence facilitating the drug transfer to the systemic circulation. With application of heat, the kinetic energy and the drug solubility of the drug molecules increases in cell membrane. It also changes the physicochemical properties of the drug formulation thereby increasing their permeation through skin.

Needleless injection:
It is a pain free technique of drug administration through skin which involves firning of the liquid and solid particles through stratum corneum at supersonic speed. The mechanism of skin penetration involves forcing the compressed gas through nozzle with resultant drug particles at sufficient velocity

Radiofrequency:
This technique involves skin exposure to a high frequency alternating current of 100 KHz which forms heat induced micro channels in cell membrane. The rate of drug delivery depends on the properties of the microelectrodes in skin contact.

Pressure wave:
These waves are generated by intense laser radiation and can penetrate through stratum corneum. The pressure waves are applied only for 100 µs -1 µs. When applied they form a continuous pathway across the skin which allows the transport of macromolecules into dermis and epidermis.

Magnetophoresis:
This technique involves the application of magnetic field which acts as external driving force to enhance drug delivery across the skin. The magnetophoresis cause alteration in structure of skin which increase the skin permeability

Chemical enhancement:
Water:
Hydration of stratum corneum is the principal measure to increase permeation of both hydro and lipophilic penetrants. Presence of free water molecules inside the tissue can alter the solubility of penetrant in stratum corneum. Increased rate of hydration may lead to swelling of stratum corneum and hence increase penetration.
Penetration enhancers:
The penetration enhancers facilitate the drug absorption by altering the barrier properties of stratum corneum. Penetration enhancer must be non-toxic, non-allergic, pharmacologically inert, tasteless, inexpensive and compatible with drug and excipients. Skin permeability can be enhanced by interaction of intercellular lipids causing disruption of their cellular organization and hence increasing their fluidity.

Prodrug:
Prodrugs are the inactive derivatives of therapeutically active drugs that are produced by undergoing metabolism. Prodrugs are more hydrophobic and have different physicochemical properties than the parent drug.

Supersaturation enhancement:
It is the method to increase the skin permeability by altering the structure of stratum corneum. The mechanism involved is based on the increased thermodynamic activity of the drug. Methods used to produce supersaturated systems includes cooling followed by heating; solvent removal; and formulating a less soluble compound by reacting two or more solutes.

Classification of topical drug delivery systems:

<table>
<thead>
<tr>
<th>Solids</th>
<th>Liquids</th>
<th>Semi solids</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Topical powders</td>
<td>• Lotion</td>
<td>• Ointments</td>
<td>• Transdermal delivery systems</td>
</tr>
<tr>
<td>• Poultices</td>
<td>• Liniments</td>
<td>• Creams</td>
<td>• Tapes and gauzes</td>
</tr>
<tr>
<td></td>
<td>• Solution</td>
<td>• Pastes</td>
<td>• Rubbing alcohol</td>
</tr>
<tr>
<td></td>
<td>• Emulsion</td>
<td>• Gels</td>
<td>• Liquid cleaner</td>
</tr>
<tr>
<td></td>
<td>• Suspension</td>
<td>• Suppositories</td>
<td>• Topical aerosol</td>
</tr>
<tr>
<td></td>
<td>• Tinctures</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• colloids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conventional topical drug delivery systems

Topical powders:
Powders differ from liquid skin care preparation in their physical characteristics. Very fine particle size produces large surface area per unit weight which covers a huge surface area of the body & results in strong light dispersion. There are various body powders, also known as dusting or talcum powder, face powder and compact. Medicated powders are used for preventing microbial growth on skin^2^.

Poultices:
A poultice, also known as cataplasm, is a soft moist mass, often heated and medicated, that is spread on cloth over the skin to treat the aching, painful or inflamed part of the body. It can be used on wounds such as cuts. Poultice can also be referred as porous solid filled with solvent used to remove stains from porous stone such as marble or granite. The word poultice originated from the Latin words puls or pulites meaning porridge^3^.

Lotions:
Lotions are the clear solution which contains 25-50% alcohol. In addition they may contain antiseptic, haemostypic and emollient substances. They may also contain extracts of menthol, alum, glycerin, boric acid, chloroform and potassium oxyquinoline sulfate. Most of the lotions are used as after-shave preparation. Types of lotions includes hand lotions, face lotions, body lotions, after shave lotions and antiperspirants.

Liniments:
Liniments (sometimes also called balms) are topical preparation for skin application. They are of similar or lesser viscosity than lotions and are rubbed on the skin to create friction. Liniments are usually sold to reduce or relieve pain and stiffness from sore muscles. These are typically formulated from alcohol, acetone, or from similar quickly evaporating solvents and contains counter irritant aromatic chemical compounds such as capsaicin, methyl salicylate or benzoin resin^1^.

Solutions:
Topical solutions are the liquid preparations that are usually aqueous but often contains other solvents like alcohol and polyols that contain one or more than one dissolved chemical substances intended for topical application to the skin^10^.
Emulsions:

Emulsions are biphasic preparations in which one phase i.e. the dispersed phase or internal phase, is finely dispersed in other phase i.e. continuous or external phase. Because there are two incompatible phases in close combination as physical stabilizing system the dispersed phase can either be a hydrophobic-based (oil-in-water), or be aqueous-based (water-in-oil). In most of the pharmaceutical emulsions, the stabilizing system comprise surfactant (ionic or nonionic), polymers (non-ionic polymers, biopolymers, or polyelectrolytes), or mixtures of these.

Suspensions:

Suspensions are heterogeneous systems that consists two phases. The continuous (external phase) is usually a liquid or semisolid and the dispersed (internal phase) is made up of particulate matter that is basically insoluble in, but dispersed throughout the continuous phase; the insoluble matter may be intended for physiological absorption or for internal or external coating. The dispersed phase may consist of discrete particles, or it may be a network of particles resulting from particle-particle interactions. Almost all the suspension system separate on standing. Therefore, the formulator’s main concern, is not basically to try to eliminate separation, but rather to decrease the rate of settling and to permit easy resuspend ability of any settled particulate matter.

Collodion:

Collodion (pyroxylin solution), is a solution of nitrocellulose in ether and acetone, sometimes with added alcohol. As the volatile solvents evaporates, a dry celluloid film is left on the skin. Because the medicinal use of a collodion depends upon the formation of a protective film, the film should be durable, flexible, tenacious in adherence and occlusive.

Tincture:

A tincture is in general an alcoholic extract of plants or animals material or solution of similar or of a low volatile substance (like iodine and mercurichrome). To qualify as an alcoholic tincture, the extract must have ethanol percentage of at least 25-60% (50-120 US proof). Sometimes alcohol concentration as high as 90% (180 US proof) is used in tinctures. In herbal medicines, alcoholic tinctures are made with various ethanol concentrations; 25% being the most common.

Ointments:

Ointments generally composed of fluid hydrocarbons meshed in a matrix of higher melting solid hydrocarbons. They usually contain medicament or medicaments dissolved, suspended or emulsified in an ointment base (vehicles). They are greasy in nature.

Creams:

Creams are generally semisolid dosage forms that contain one or more drug substances dissolved or dispersed in a suitable base. This term has traditionally been applied to semisolids that comprise a relatively soft, spreadable consistent formulation of either water-in-oil or oil-in-water emulsions. Recently the term has been restricted to products consist oil-in-water emulsions or aqueous microcrystalline dispersions of long chain fatty acids or water washable alcohols and more cosmetically and aesthetically acceptable.

Pastes:

Pastes or ointments, are intended for external application to the skin. They differ from ointments primarily in the way that they generally contains larger percentage of solid material as a result they are thicker and stiffer than ointments because of the large percentage of solids. Pastes are generally more absorptive and less greasy than ointments. Because of the stiffness and absorptive qualities of paste, they remain on place after application with little tendency to soften and flow. Therefore these are effectively employed to soak up secretions from the site of application. Pastes are therefore preferred over ointments for acute lesions that have a tendency toward crusting, or vesiculation. Because of their stiffness and impenetrability, pastes are generally not suited for application to hairy parts of the body. Eg. zinc-oxide paste.

Gels:

Gels are relatively newer class of dosage forms formed by entrapment of large amount of aqueous or hydro-alcoholic liquid in a network of colloidal solid particles which may consists inorganic substances such as aluminum salts or organic polymers of natural or synthetic origin. Depending upon the nature of the colloidal substances and the liquid in the formulation, the appearance of gel will range from entirely clear to opaque. Most of the topical gels are prepared with organic polymers such as carbomers which impart an aesthetically pleasant, clear sparkling appearance to the product and are easily washed off from the skin with water. Gels are basically two component semisolids systems. In a typical polar gel, a natural or synthetic polymer builds a three dimensional matrix all the way through a hydrophilic liquid. Typical polymers used includes the natural gums such as tragacanth, pectin, carrageenan, agar and alginic acid; semi synthetic materials such as methylcellulose hydroxyl ethyl cellulose, hydroxy propyl methyl cellulose, and carboxy methylcellulose; and the synthetic polymer, carbopol may be used. They are of two types i.e. single phase gels and double phase gels.

Suppositories:

Suppositories are the solid dosage forms proposed to deliver medicine into rectal, vaginal, or urethral orifice. Suppositories can be prepared by cold compression or fusion technique. A suitable base is selected for its compatibility, melting point, stability, and esthetics. Commonly used bases are glycerin, cocoa butter, hydrogenated vegetable oils, and polyethylene glycol.
Miscellaneous

Transdermal drug delivery system: Transdermal drug delivery systems are defined as self contained, discrete dosage forms which when applied to intact skin delivers the drug through the skin at controlled rate to systemic circulation. TDDS in comparison to conventional pharmaceutical dosage forms, offers many advantages such as reduced side effects, improved patient compliance, sustained drug delivery and elimination of first pass metabolism.

TDDS are classified as follows:
- Matrix system
- Matrix dispersion system
- Reservoir system

Liquid cleaner: Cleaning agents are substances (liquids, powders, sprays, or granules) used to remove dust, dirt, stains, bad smells, and clutter on surfaces. Purposes of cleaning agents includes health, beauty, removing offensive odour, and avoiding the spreading of dirt and contaminants. Some cleaning agents can clean and kill bacteria at the same time.

Topical aerosol: It is a disperse phase system in which very fine solid drug particles or liquid droplets get dispersed in the propellant (gas), which acts as continuous phase. An aerosol system expels the contents from the container which depends upon the pressure development by compressed or liquefied gas. Dispersed Phase - Solid / Liquid and Continuous phase - Gas /Propellants.

Tapes and gauzes: Gauze is a bandage which is simple natural fibre strip of material, or a woven strip of material with a permeable barrier to prevent adhering to wounds. A gauze bandage can be in any number of widths and lengths, and can be used for about any bandage application, including holding a dressing in place.

Surgical tape or Medical tape: It is a type of pressure sensitive adhesive tape used in medicine and first aid to hold a bandage or other dressing on wound. These tapes usually have a hypoallergenic adhesive which is designed to hold firmly on the skin, dressing materials and underlying layers of tape, but can be removed easily without damaging the skin. They allow air to reach the skin (breathable). Some breathable tapes like Kinesiology Tape, and other elastic bandages with adhesive are made of cotton. Surgical tape is usually white because it contains zinc oxide, which is added to help prevent infections. Tapes made up of microporous material, such as 3M Micropore, are widely used.

Novel topical drug delivery systems:
- Organogels
- Foams
- Emulgels
- Microsponges
- Mucoadhesive/ bioadhesives
- Novel vesicular carriers
  - Liposomes (liposomal gel)
  - Niosomes (Proniosome gel)
  - Transfersomes
  - Ethosomes
- Micelles
- Novasomes
- Hydrogels
- Jellies
- Protein and peptide delivery
- Microemulsion/nanoemulsions
Organogels  
Organogel, a viscoelastic system can be regarded as a semi-solid preparation which contains an immobilized external apolar phase. The apolar phase gets immobilized within spaces of the three-dimensional network structure formed by the physical interactions amongst the self assembled structures of compounds regarded as gelators. Generally, organogels are thermodynamically stable in nature and have been explored as matrices for delivering bioactive agents. In the current manuscript, attempts have been made to understand the properties of organogels, various types of organogelators and some applications of the organogels in controlled delivery. The organogels may be regarded as bi-continuous systems consisting of gelators and apolar solvent, which may or may not contain water-molecules entrapped within the self-assembled structures of the gelator. The gelators, when used in concentration < 15 % (approx.), may undergo physical or chemical interactions to form self assembled fibrous structures which get knotted with each other resulting in the formation of a three-dimensional network structure. The three-dimensional structure thus formed prevents the flow of external phase. Some general examples of gelators are sterol, lecithin, sorbitan monostearate and cholesteryl anthraquinone derivates. The thermo reversible property of the organogels has generated a good deal of interest for the potential use of the organogels as drug delivery system. The thermodynamic stable nature of the organogels has been attributed to the impulsive formation of fibrous structures by virtue of which the organogels reside in a low energy state.¹⁸,¹⁹

Properties of organogels:¹⁸,¹⁹
- Viscoelasticity (organogels seem to follow Maxwell model of viscoelasticity)
- Non-birefringence (property of organogels of restricting the polarized light to pass through its matrix is regarded as non-birefringent)
- Thermoreversible (the organogels are heated above the critical temperature at which they loose its solid matrix like structure and starts Flowing)
- Thermostable (The organogels are intrinsically thermostable in nature. The stability of the organogels may be attributed to the ability of the gelators to undergo self-assembly under suitable conditions to form organogels.)
- Optical clarity (Depending on the composition of the organogels, they can be transparent or opaque in nature.)
- Chirality: The presence of chirality in the low molecular weight gelators have been found to affect the growth and the stability of the solid fiber networks.
- Biocompatibility: In the beginning organogels were developed using various non biocompatible organogels which rendered the organogels non biocompatible.

Advantages:²⁰,²¹
- Ease of preparation.
- Cost reduction due to less number of ingredients.
- Longer shelf life.
- Thermodynamically and chemically stable.
- Process is very simple and easy to handle.
- Since it consists of both hydrophobic and hydrophilic components, both the drugs (hydrophilic and lipophilic) can be incorporated.
- Organic solvents could be of natural origin example sunflower oil, mustard oil etc.
- Organogels provide opportunity for incorporation of broad range of substances with varied physicochemical characters viz: chemical nature, solubility, molecular weight and size etc.
- The structural integrity of organogels is maintained for longer time periods.
- They enhance the skin permeability and transport of the molecules

Applications:³⁶
- Organogels as matrix for transdermal transport of drugs
- Organogel as antiphoretic transdermal drug delivery system
- Organogels for rectal drug delivery
- Organogels for ophthalmic drug delivery
- Organogels for delivery of vaccines.
Foams

According to European Pharmacopoeia medicated foam is a preparation that consists of large volume of gas dispersed in a liquid usually containing one or more active substance; a surfactant and various other excipients. In the US Pharmacopeia a foam aerosol is defined as an emulsion that contains one or more active ingredients, aqueous or non-aqueous liquids, surfactants, and the propellants. An aerosol foam is usually packed in container as an emulsion in which the liquefied gas propellant is dispersed as droplets throughout the aqueous phase. When the emulsion is discharged the propellant vaporises into a gas that is trapped by the aqueous solution and this forms a foam. By summarising the above information, topical foams can be defined as: dynamic dosage forms intended for application to the skin that usually contains active agents, propellant, surface active agents, solvents and other excipients. Prior to application of dose they are sealed in a pressurised container in the form of emulsion or suspension or solution. On valve actuation, the propellant evaporates from the pressurised system producing a liquid or semi solid foam product that expands with air. Topical foams contain active ingredients, propellant, surfactants, solvents, co solvents and viscosity modifying agents. Although most of the topical foams incorporate corticosteroids. The active agents can also be selected from antibacterial, antifungal, antiviral agents, anti-inflammatory agents, local anesthetic agents, skin emollients and protectants, depending on the skin conditions to be treated.

Foams can be generated by various approaches.
- whipping (mechanical agitation of a liquid or a solution)
- bubbling (injecting a stream of gas or liquid or the mixture into a liquid)
- sudden pressure reduction (rapidly actuating the valve of pressurised systems i.e a solution or emulsion or suspension. For pharmaceutical or topical use, foams are often generated in situ using the method of sudden pressure reduction.

The future of novel topical foams:

Dynamic topical foams have already been a useful addition to conventional topical formulation approaches, as can be seen from the growing number of topical foam products in the market and the increasing number of foam patents filed in recent years. The attractiveness of elegant topical foams currently lies in their application advantage and aesthetics which patients prefer. However, consideration of their potential ability to enhance or assist drug delivery to the skin when engineered properly should not be neglected.

Types:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Water containing foams</td>
</tr>
<tr>
<td></td>
<td>a. Hydrophilic emulsion foam</td>
</tr>
<tr>
<td></td>
<td>b. Lipophilic emulsion foam</td>
</tr>
<tr>
<td></td>
<td>c. Nanoemulsion foam</td>
</tr>
<tr>
<td></td>
<td>d. Aqueous foam</td>
</tr>
<tr>
<td></td>
<td>e. Hydroethanolic foam</td>
</tr>
<tr>
<td></td>
<td>f. Potent solvent foam</td>
</tr>
<tr>
<td></td>
<td>g. Suspension foam</td>
</tr>
<tr>
<td>2.</td>
<td>Water free foams</td>
</tr>
<tr>
<td></td>
<td>a. Ointment foam</td>
</tr>
<tr>
<td></td>
<td>b. Hydrophilic ointment foam</td>
</tr>
<tr>
<td></td>
<td>c. Oil foam</td>
</tr>
<tr>
<td></td>
<td>d. Saccharide foam</td>
</tr>
</tbody>
</table>

Emulgels:

Emulgels are emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. It is stable and superior vehicle for hydrophobic or poorly water soluble drugs. In short, emulgels are the combination of emulsion and gel.

Emulgel is composed of two parts:
- Emulsion
- Gel

Emulsion:

Emulsions are biphasic system in which one immiscible liquid is dispersed into other, because of which the system becomes unstable that is then stabilized by emulsifying agents. Emulsion can be either o/w or w/o these are used as vehicles to deliver drug. Emulsions are stabilized by using emulsifying agents. They can be easily washed off from skin and have a good penetration ability.
Gel:

The term “gel” represents a physical state with properties in between those of solids and liquids. However, it is often used wrongly to describe any fluid system that exhibits some degree of stiffness. A gel consists of a polymer which swells in the presence of fluid. The rigidity of the gel is determined by the amount of fluid it entraps. These gels are wet and soft and look like a solid material. These are capable of undergoing large deformation in their physical state i.e. from solid to liquid.

Types of emulgels:⁶

- Macroemulsion gel
- Nanoemulgel
- Microemulsion

Advantages of emulgels:²⁴,²⁵

- Prevention of systemic adverse effects of drug i.e. first pass metabolism in the body
- Systemic circulation is prevented or minimized
- Improve patient acceptability
- Suitable for self-medication
- Provide target drug delivery on the body
- Ability to easily terminate medication
- Can easily pass through skin having dual behaviour i.e. hydrophobic plus hydrophilic
- They are suitable to apply on hairy skin due to absence of greasiness and lack of residues upon application
- Better stability and release of drug
- Better loading capacity
- Production feasibility and low preparation cost
- No intensive sonication needed
- Emulgels can be used to prolong the effect of drugs having shorter t₁/₂

Liposomal gel:²⁶

Liposomes established themselves as a promising novel drug delivery vehicle in several different basic sciences and as a feasible alternative in several applications. Liposomes are microscopic spheres with an aqueous core surrounded by one or more external shells consisting of lipids arranged in a bilayer configuration. Liposomes are acceptable and better-quality carriers having capability to encapsulate hydrophilic and lipophilic drugs and protect them from degradation. It also has affinity with keratin of horny layer of skin and can penetrate deeper into skin and hence give better absorption. Liposomes when applied on skin may act as a solubilizing matrix for poorly soluble drugs, penetration enhancer and as local depot at the same time diminishing the side effects of these drugs. Topical liposome formulations could be more efficient and less toxic than conventional formulations. The liposome gel formulations can perform therapeutically better effects than the conventional formulations as prolonged and controlled release topical dosage forms, which may lead to improved efficiency and better patient compliance.

Advantages:²⁶

- Precipitation at the injection site and in the blood circulation can be prevented.
- Phospholipids are one of the few solubilizers that are well tolerated intravenously.
- Provide selective passive targeting to tumour tissues.
- Increase safety and therapeutic index.
- Increase stability via encapsulation
- Site avoidance effect.

Microsponges:

Microsponge are uniform, spherical, porous polymeric microspheres having numerous interrelated voids of particle size range 5-300 μm. These have the capacity to entrap a wide range of active ingredients such as essential oils, emollients, fragrances, sunscreens and anti-infective, etc. are used as a topical carrier system. Microspheres having average size of 25 μm in diameter and embedded in the vehicle, act like microscopic sponges, which stores the active drug until its release is triggered by application to the surface of skin. Micro pores within the spheres comprise a total pore density of approximately 1 ml/g and pore length 10 ft for extensive drug retention.²⁷ A Microsponge Delivery System is patented, extremely cross-linked, porous, polymeric microspheres that can entrap wide range of active material and then release them onto the skin over a time and in response to trigger. This system was employed for the improvement of performance of topically applied drugs. It is a unique technology for the controlled release of topical agents and consists of micro porous beads, typically 10-25 microns in diameter, loaded with active agent. When microsponge delivery system is applied to the skin, the release of drug can be controlled via diffusion or other variety of triggers, including moisture, rubbing, pH, friction, or ambient skin temperature.
Microsponge technology offer:\textsuperscript{27,29}
• Enhanced product performance.
• Extended drug release.
• Reduced irritation and improved patient compliance.
• Improved product elegance.
• Improved formulation flexibility.
• Improved thermal, physical, and chemical stability.
• Flexibility to develop novel product forms.
• Microsponge systems are non-mutagenic, non-irritating, non-allergenic and non-toxic.
• MDS allows the incorporation of immiscible products.
• In contrast to other technologies like microencapsulation and liposomes MDS has wide range of chemical stability, higher payload and ease of formulation.
• Liquids can be converted into powders by improving material processing.
• MDS can improve bioavailability of drugs.
• It can also improve efficacy in treatment.
• Site specific action produced on target organ.

Mucoadhesives /bioadhesives:\textsuperscript{30}
The oral mucosa has many properties that makes it an attractive site for drug delivery but they also offer several challenges for researchers investigating novel delivery techniques to conquer many different formulations which includes sprays, tablets, mouthwashes, gels, pastes and patches. They are presently used for delivery into or across the oral mucosa. The term bio adhesion refers to any bond formed between two biological surfaces or a bond in between a biological and a synthetic surface. In case of bio adhesive drug delivery, the term bio adhesion is used to describe the adhesion between polymers (either synthetic or natural) and soft tissues or the gastrointestinal mucosa. In cases where the bond is formed with the mucus, the term mucoadhesion may be used synonymously with bio adhesion. The term bioadhesion can be defined as the state in which two materials, at least one biological in nature are held together for an extended time period by interfacial forces (Good, 1983). In biological systems, bioadhesion can be classified into following 3 types:
• Type 1- adhesion between two biological phases, eg. platelet aggregation and wound healing.
• Type 2- adhesion of a biological phase to an artificial substrate, eg. cell adherence to culture dishes and bio-film formation on prosthetic devices and inserts.
• Type 3- adhesion of an artificial material to a biological substrate, eg. adhesion of synthetic hydrogels to soft tissues and adhesion of sealants to dental enamel.

Advantages:
• Due to the increased residence time it enhances absorption and hence the therapeutic efficacy of the drug
• Avoids the first pass metabolism
• Prolongs the residence time of the dosage form at the site of absorption
• outstanding accessibility
• Rapid absorption because of enormous blood supply and good blood flow rates
• Increase in drug bioavailability due to first pass metabolism avoidance
• Drug is protected from degradation in the acidic environment in the GIT
• Improved patient compliance & ease of drug administration
• Faster onset of action is achieved due to mucosal surface

Vesicular carriers:\textsuperscript{31,35,38}
The field of pharmaceutical science has been developing steadily over the years, and today it has become priceless in helping to keep us healthy and prevent disease. In the past few decades substantial attention has been focused on the development of topical drug delivery because of number of advantages offered by this route. TDDS system offers a number of advantages like longer duration of action, dosing flexibility, reduced side effects, uniform plasma levels, high patient compliance etc. At the same time it also bear some drawbacks like possibility of local irritation effect, itching and most important low permeability of drugs in the stratum corneum. Stratum corneum is the top layer of the epidermis consists of keratinized, flattened leftovers of once actively dividing epidermal cells impermeable to water and behaves as a harsh flexible membrane. Many technologies and systems have been investigated to avoid this barrier and one of the most promising technique is to formulate novel vesicular carriers for delivery through the skin. These novel drug delivery systems bear great potential for dermal delivery. Among them lipid and non-lipid vesicular systems such as liposome, noisome, transfersome and ethosome have been suggested to overcome the problems related to conventional topical formulations. These vesicular systems are well ordered assemblies of one or quite a few concentric lipid bilayers formed when certain amphipillic building blocks are confronted with water. Some commonly used materials for the formation of vesicles are phospholipids, cholesterol and non-ionic surfactants. Vesicle shape, size, structure and entrapment efficiency of these vesicular carriers depends on the composition of vesicles and all these parameters provide major impact on the efficacy of the systems.
Vesicular system offers number of advantages in drug delivery through the skin such as non-toxicity, biocompatibility, incorporation of both hydrophilic and lipophilic drugs, controlled drug delivery extent and rate, act as a depot formation for sustained release of the drug, increased permeation of drugs through the skin and penetration enhancer because of their unique composition etc.

**Principal components used in different vesicular systems for topical drug delivery are:**

- Liposomes
- Niosomes
- Ethosomes
- Transferosomes

**Liposomes:**

Liposomes can be defined as a colloidal, vesicular structures composed of one or more lipid bilayers surrounding a number of aqueous compartments. These are spherical vesicles with particle size ranging from 20 nm to several µm that are composed of a phospholipid bilayer membrane and are used to deliver drugs into cells.

**Applications:**

Liposomes are used as a carrier in immunology, vaccines adjuvant, eye disorders, brain targeting, infective disease and in tumor therapy. They are also used in topical drug delivery system as they are capable of improving the drug deposition within the skin at the site of action where the goal is to reduce systemic absorption, minimizing side effects and increases the patient compliance.

**Niosomes:**

They consist of microscopic lamellar structures formed with a mixture of non-ionic surfactant and cholesterol having a bilayer structure formed by self-assemble of hydrated surfactant monomers. There are mainly two types of components i.e. non-ionic surfactants and the additives. There are a number of advantages presented by the niosomes as a drug delivery system such as high bioavailability, biocompatibility, biodegradable, controlled and sustained release of drugs due to depot formation, more stable than liposomes and increased permeation of drugs via skin.

**Proniosome gel:**

Potential of proniosomes of entrapping a wide range of active compounds without showing any problems of physical stability makes them versatile delivery system. They also provide the ease of the transportation, distribution, storage, and dosing. Proniosomes upon hydration with water get readily converted into niosomes of uniform size.

**Applications:**

1. Antifungal agents
2. NSAID’s
3. Anti acne drugs
4. Cosmetics
5. Muscle relaxants

**Ethosomes:**

Ethosomes are novel lipid carriers that are the modified forms of liposomes containing high ethanol content. They contain phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water having a size range from 10 nm to microns. Size of ethosomes depends upon the means of preparation and application of techniques like sonication. Ethosomes are mostly used for the delivery of drugs through transdermal route. These vesicular systems have higher penetration rate through the skin as compared to liposomes. Unlike liposomes, that are mainly known for the delivery of drugs to the external layers of skin. Ethosomes have been shown to enhance permeation of drug through the stratum corneum barrier. They act as a carrier of drugs and offers a number of advantages like, high patient compliance (as the ethosomal drug is administrated in semisolid form like gel or cream), non-invasive and can be broadly used in pharmaceutical, veterinary, cosmetic fields.

**Applications:**

1. Delivery of HIV drugs
2. Delivery of anti fungal drugs
3. Delivery of NSAID’s
Transfersomes: A novel vesicular drug carrier system called transfersomes that is composed of phospholipid, surfactant, and water to enhance transdermal delivery. Transfersomes are a form of elastic or deformable vesicle, which were first introduced in the early 1990s. In terms of delivering of drugs through transdermal route, there are some problems encountered with some other vesicular systems like poor skin permeability, breaking of vesicles, leakage of drug, aggregation and fusion of vesicles. To overcome all the above mentioned problems, a new type of vesicular carrier has been developed called "transfersome" which is capable of transdermal delivery of both low and high molecular weight drugs. Transfersomes are artificial vesicles and they are more deformable than standard Liposomes. Transfersome have been reported to improve the transdermal delivery of drugs, when applied onto the skin non-occlusively.

Advantages:
- They can encapsulate both hydrophilic and lipophilic moieties.
- Prolong half lives of drugs by increasing duration in systemic circulation due to encapsulation.
- Ability to target organs for drug delivery.
- Biodegradability and lack of toxicity.
- Prolong half lives of drugs by increasing duration
- Transfersomes have a unique structure which is capable of entrapping hydrophilic, lipophilic, amphiphilic drugs.
- They have high entrapment efficiency (in case of lipophilic drug near to 90%).
- This high deformability gives better penetration of intact vesicles.
- They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin.
- Transfersomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility. They act as depot, releasing their contents slowly and gradually.
- They can be used for both systemic as well topical delivery of drug.
- They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes.
- They protect the encapsulated drug from metabolic degradation.
- Ease of scale up do not involve lengthy procedure and unnecessary use or pharmaceutically unacceptable additives

Applications: Transfersomes are used as a carrier for protein and peptides like insulin, bovine serum albumin, vaccines, etc. They improve the site specificity, overall drug safety and lower the doses several times than the currently available formulations for the treatment of skin diseases.

Micelles:
A micelle is defined as a group of surfactant molecules dispersed in a liquid. In an aqueous solution, micellization occurs due to the mounting of hydrophilic head of surfactant molecules toward water and sequestering of the hydrophobic tails toward the inside. Micelles were reported to be promising carriers for delivering an antifungal drug topically.

Microemulsions:
Microemulsions are defined as thermodynamically stable mixtures of oil and water stabilized by surfactants and co-surfactants, with size in the nanometer range. Owing to their ability to solubilize many poorly soluble drugs, microemulsions have been found very promising in the delivery of antifungal drugs which are characterized by their lipophilicity.

Novasomes:
Novasomes are an innovation of the liposomal drug delivery system or a variation of other similar drug delivery systems. Novasome can be defined as lamellar vesicles of 200 to 700 nm in diameter consisting of 2 to 7 bilayered membrane each composed of amorphous core and amphiphilic molecule. The core accounts for most of the Novasome vesicular volume thus accommodating a high capacity of water immiscible and water soluble drugs.

Characteristics:
- The ability to have a negative, positive or neutral charge.
- A large volume of water soluble drugs can be incorporated.
- Uniform sized vesicles can be predicted.
- Depending on the various conditions it can adhere to skin or hair shaft
- The release rate is predictable
- Enhanced product stability
- Up to 80% of the drug can be loaded in the Novasome
- Frequent applications can be allowed.
- It contains a high capacity core with seven membered bilayer surrounding.
- Prevents the skin from drying away
• Smaller volume can accommodate large amounts of drug

Hydrogels:
Hydrogels are three-dimensional cross-linked polymer network that can respond to the fluctuations of the environmental stimuli. These biomaterials can incorporate large quantum of biological fluids and swell. When swelled, they are soft & rubbery and resemble the living tissue, exhibiting excellent biocompatibility. Today, drug delivery experience several challenges where hydrogel could be one potential answer. Thanks to the unique properties of hydrogel for which they are widely exposed to different biomedical fields. Hence the preparation techniques of Hydrogel biomaterial and the evaluation of the properties are of utmost significance.

CONCLUSION
The present review discusses efforts to produce topical drug delivery systems incorporating novel carriers. With the advent of new technologies, effective formulation and topical delivery strategies had overcomed the stratum corneum barrier leading to release drug at the target site. When compared to other conventional systems, these prove to be better in terms of efficacy, feasibility, shelf life and patient compliance. So, it is concluded that transforming topical delivery system into novel formulation by utilizing carriers can help in productive research which provide new hope to treat and diagnose several diseases. In future these carrier system can become a milestone for delivery of hydrophilic drug via skin.

ACKNOWLEDGEMENT
Authors are thankful to Punjab technical university, Jalandhar, Punjab and ASBASJSM college of pharmacy ,Bela, ropar, Punjab for the academic support.

REFERENCES
9. eprints.utm.my/3153/1/The_physiology_of_the_Skin.pdf