

Advances in Topical Drug Delivery System: A Review

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Abstract:

The aim of this review article is to provide the scientific update of the advances coming in the drug delivery system via topical route of administration. The current review focus on the advanced methods and techniques which are available for administration of local therapy to the skin and its parts in form of Nanoemulsions liposome aerosols micronidles ethosome, nanoparticles aquasomes adhesives etc and devices like iontophoresis electroporation magnetophoresis etc This information can withstand as basis for further development and upgradation existing methods and technologies.

Keywords: *Recent techniques, Topical drug delivery, TDDS, Advances in skin delivery*

Introduction

Over the last decades the treatment of illness has been accomplished by administrating drugs to human body via various routes namely oral, sublingual, rectal, parental, topical, inhalation etc. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders like acne or the cutaneous manifestations of a general disease like psoriasis with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semi-solid formulation in all their diversity dominate the system for topical delivery, but foams, spray, medicated powders, solution, and even medicated adhesive systems are in use.¹ The delivery of a drug to a specific site, topical formulations are probably among the most challenging products to develop. An effective topical formulation needs to provide a stable chemical environment in a suitable dispensing container in order to accommodate multiple compounds that may have different, if not incompatible, physicochemical characteristics. Once applied, a topical formulation must interact with the skin environment, which can influence

the rate of the release of the compounds in order to achieve adequate skin absorption.

The excipients themselves will exert additional physical effects on the skin, such as drying, occluding, or moisturizing. Research and technology have brought a better understanding of the physics, chemistry, pharmacodynamic, and pharmacokinetics for drugs used to treat acne. These insights have resulted in new delivery systems that are capable of enhancing the efficacy, tolerability, and cosmetic acceptability of topical formulations.²⁻⁴

Topical drug delivery offers the advantages of ease of delivery, a cooperative patient, increased compliance as well as the avoidance of first-pass metabolism. Disadvantages are the lack of, or reduced rates of absorption and cosmetic considerations. New drug delivery technology and penetration enhancers may help to obviate some of these objections. There are important issues to consider as you contemplate development of a topical dermatological product. You may already have experience with oral or parenteral products, but there are challenges and issues which are unique to development of topical formulations.

A topical formulation must be aesthetically pleasing, in addition to being both physically and chemically stable, and this may require numerous excipients. The formulation must allow for optimal penetration of the drug into the skin, a complex tissue. Skin pH is approximately 5.5; thus the pH of the formulation may change following application to the skin.

A successful topical dermatological formulation can be considered to be one that satisfies the target product profile and is 1) Physically and chemically stable having adequate shelf life, 2) Releases drug from the formulation and delivers it into the skin as required for the target indication, 3) Is cosmetically elegant and acceptable to patients, 4) Contains only excipients that are necessary, FDA-approved or acceptable from a regulatory perspective, and acceptable for the disease state, 5) Is easy to apply and compatible with the desired packaging, and 6) Can be manufactured with a process that is scalable to commercial levels. There are challenges during almost every development program. It is important to be able to anticipate problems, prevent them where possible, and to understand how to correct those that do occur.⁵

Over the year it has showed promising result in comparison to oral drug delivery system as it eliminates gastrointestinal interferences and first pass metabolism of the drug but the main drawback of TDDS is it encounters the barrier properties of the Stratum Corneum i.e. only the lipophilic drugs having molecular weight < 500 Da can pass through it. So now a days, liposomes, niosomes, transferosomes and ethosomes are used to increase the permeability of drug through stratum corneum. Ethosomes have been found to be much more efficient in delivering drug to the skin, than that of liposomes or hydro-alcoholic solution. Ethosomes are the non invasive drug delivery carriers that enable drugs to reach the deep skin layers finally delivering to the systemic circulation. For optimal skin delivery, drug should be efficiently entrapped within ethosomal vesicles. Ethosomal drug delivery system is a new state of the art technique and easier to prepare in addition to safety and efficacy. Ethosomes have become a area of research interest, because of its enhanced skin permeation, improved drug delivery, increased

drug entrapment efficiency etc. Ethosomes are used to deliver many drug molecules like Acyclovir, Bacitracin, Testosterone, Insulin etc. Ethosomal drug delivery system thus became an active area of research and development for novel therapies.⁶

Novel Topical Drug Delivery Systems:

Following are the advances in the topical drug delivery systems

Aerosol Foams:

The aerosol foams gained the increasingly popular type of topical formulation for a variety of skin conditions including acne vulgaris. The vehicle base of the foam can have consistency like liquid or semi-solid which shares equal physicochemical characteristics of conventional carrier vehicle like gels, lotions and creams but it maintains desirable properties such as moisturizing, quicker drying effects, or high bioavailability of drug. The aerosol base is dispensed through a gas-pressurized can that discharges the foam. The product characteristics like thickness, viscosity, texture, bubble size, density, persistence, stable nature, and spread ability are determined by the type of formulation and the dispensing container that are selected to suit the specific therapy needs. The foams may be preferred for application on large hairy surfaces (e.g., chest and back) or on the face as cleansers, because they are easier to apply.

Liposomes:

The liposomes are artificially prepared vesicles made of lipid bilayer which are frequently used as vehicles in pharmaceuticals and cosmetics for drug delivery in controlled manner to particular areas of skin or its layers. Liposomes are spherical vesicles whose membrane consists of amphiphilic lipids this lipid that are hydrophilic on one side and lipophilic on the other side i.e dual characteristics which enclose an aqueous core, same as to the bilayer membranes of living cells. Because liposomes offer an amphiphilic environment, they may encapsulate hydrophilic substances in their aqueous core and lipophilic substances in their lipid bilayer. This unique dual release capability enables the delivery of 2 types of substances once they are applied on the skin; each differs in its effects on skin permeability,

which may enhance the desired therapeutic benefit.^{7,8}

Nanoemulsions:

Nanoemulsions are a class of emulsions which may be water-in-oil or oil-in-water type of formulations that are identified and characterized by the dispersion of very small-sized droplets when mixed. The major requirement of nanoemulsions unique thermodynamic conditions without the nanoemulsions will not formed spontaneously, as they require unique thermodynamic conditions, specialized manufacturing processes, and specific surfactants that can stabilize the nano droplets. Nanoemulsions are suitable for the transport of lipophilic compounds into the skin and, therefore, they may be an ideal vehicle for use in acne to increase the penetration of the active compounds inside the lipophilic environment of the pilosebaceous unit. In addition, nanoemulsion particulates will not clog the pores and they can produce additional therapeutic effects, such as increased skin hydration and viscoelasticity.⁹

Polymers:

The polymers have played the milestone functioning in designing the topical formulation. The polymers are large molecules consisting of repeating structural units, or monomers that are connected by covalent chemical bonds. These compounds serve as the building blocks of natural like paper and amber, biological like proteins and nucleic acid, synthetic in form of plastics and polyethylene materials etc. Nowadays applications for synthetic polymers can be found in nearly every industry, and their versatility has given rise to technological advancements within the pharmaceutical sector that address a variety of medical needs. For example, in dermatology, there are new acrylic-acid polymers that turn into a gel in the presence of water by trapping water into microcells. Inside these aqueous microcells, hydrophilic compounds can remain in a solution, whereas non-hydrophilic compounds may be dispersed in suspension. The result is a stable gel-like formulation that is easy to use and releases the active compound once they are applied on the skin. Moreover, these polymer-based gels can be mixed with other excipients, such as moisturizers

and emollients, to provide additional clinical benefits. Recently introduced anti-acne formulations that combine clindamycin 1% with benzoyl peroxide 5% (Duac®, Stiefel Laboratories; BenzaClin®, Dermik) utilize this novel polymer-based gel technology that exhibits efficacy and excellent tolerability.⁷ following is the on of the polymer type used in topical formulation has wide application in the designing the advance formulation for skin delivery.

Dendrimer:

Dendrimers have found recent applications in novel topical and transdermal delivery systems, providing benefits such as improved drug solubilization, controlled release, and drug-polymer conjugates like prodrugs. The viscosity-generation-number property of a dendrimer solution allows for ease of handling of highly concentrated dendrimer formulations for these applications. Dendrimers have been shown to be useful as transdermal and topical drug delivery systems for nonsteroidal anti-inflammatory drugs (NSAIDs), antiviral, antimicrobial, anticancer, or anti hypertensive drugs. PAMAM dendrimers have been studied as carrier transdermal systems for the model NSAIDs: ketoprofen and diflunisal. It was found that the PAMAM dendrimer-drug formulations showed increased transdermal drug delivery compared with formulations lacking dendrimers. In vivo studies in mice showed prolonged pharmacodynamic responses and 2.73-fold higher bioavailability over 24 h for certain dendrimer-containing drug solutions.^{10,11}

Microsponges:

It is a unique technology for the controlled release of topical agents and consists of microporous beads, typically 10-25 microns in diameter, loaded with active agent. When applied to the skin, the MDS releases its active ingredient on a time mode and also in response to other stimuli like rubbing, temperature, pH, etc. MDS technology is being used in cosmetics, over-the-counter skin care, sunscreens and prescription products. These are biologically inert particles that are made of synthetic polymers with the capacity to store a volume of an active agent up to their own weight. Furthermore, the particles serve to protect the

entrapped active compound from physical and environmental degradation.

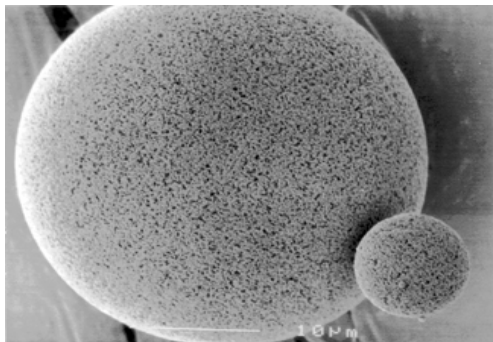


Fig.1 Surface Electron Microscopic (SEM) image of Microsponges

The microsponge technology can be utilized in a variety of formulations, but is more frequently manufactured as gels. Once applied on the skin, microsponges slowly release the active agents.

Emulsifier-free Formulations:

Emulsifier-free formulations are also a growing area of development for dermatologic and cosmetic products. The emulsifier-free formulations which are easy to process and suitable for O/W and W/O emulsions they offer a melting texture with non-tacky skin feel and ease of distribution. Most skin care products are emulsions, i.e., a mixture of 2 or more materials that are not miscible with each other; as such, according to the second law of thermodynamics, they are inherently unstable. As a result, they require the addition of surfactants i.e. emulsifiers that stabilize the formulation to guarantee an adequate shelf life. Furthermore, once these surfactant agents are applied on the skin, they tend to emulsify and remove the natural lipids of the epidermis. Consequently, the pharmaceutical industry has been developing surfactant-free emulsions as alternatives to conventional formulations by using stabilizers, such as polymeric emulsifiers or solid particles, in order to yield sufficiently stable products with a cosmetically pleasant appearance.

Fullerenes:

Fullerenes display a wide range of different biological activities. Strong antioxidant capacities and effective quenching radical

oxygen species (ROS) made fullerenes suitable active compounds in the formulation of skin care products these are the molecules which composed of entirely carbon that resemble a hollow sphere. It shows that once fullerenes come into contact with the skin, they migrate through the skin intercellular, as opposed to moving through cells.¹² Therefore; a fullerene could be used to “trap” active compounds and then release them into the epidermis once they are applied on the skin. Moreover, fullerenes, themselves, are thought to be potentially potent antioxidants. Data are reported in the literature showing that fullerenes are well tolerated and they hold substantial promise in dermatologic and cosmetic applications.^{13, 14}

Dynamic foams: Pharmaceutical foams are not new inventions and their application in topical therapy can be traced back three decades. However, foam formulations have been gaining in popularity with over 100 patents published globally in the last 10 years alone.

The use of foam technology to deliver a range of topical active agents has been claimed, including sun-screening compounds, corticosteroids, and antibacterial, antifungal and antiviral agents. Although foams present distinct application advantages and improved patient compliance, the real reason for the rapid growth of topical foam technology is that foams as elegant, aesthetic and cosmetically appealing vehicles provide an alternative, promising formulation strategy in the highly competitive dermatological market. Although there is a plethora of published data proving the safety profiles of topical foams there is a lack of sufficient clinical evidence to demonstrate any superiority of foams over other traditional topical vehicles such as creams and ointments for drug delivery.¹⁵

Solid Lipid Nanoparticles:

Solid lipid nanoparticles (SLN) have shown interesting potential as a drug delivery system for the topical delivery of various drugs. However, their performance when applied to the skin has not been fully investigated because of the complexity of their composition and structure.

Theoretically, drug can be targeted systemically to the vasculature in the dermis, locally to the

skin strata, or superficially to the surface of the skin. Therefore, the topical delivery vehicle should be designed according to the desired therapeutic purposes. To understand drug permeation behavior, it is essential to elucidate the pattern of drug release from the SLN formulations. A number of different drug release patterns have been outlined in the literature, and these patterns have been found to be related to the manufacturing process of the vehicle.¹⁶

Ethosomes:

The ethosomes are vesicular carrier comprise of hydroalcoholic or hydro/ alcoholic/ glycolic phospholipid in which the concentration of alcohols or their combination is relatively high. Typically, ethosomes may contain phospholipids with various chemical structures like phosphatidylcholine (PC), hydrogenated PC, phosphatidic acid (PA), phosphatidylserine (PS), phosphatidylethanolamine (PE), phosphatidylglycerol (PPG), phosphatidylinositol (PI), hydrogenated PC, alcohol (ethanol or isopropyl alcohol), water and propylene glycol (or other glycols) . Such a composition enables delivery of high concentration of active ingredients through skin. Drug delivery can be modulated by altering alcohol: water or alcohol-polyol: water ratio. Some preferred phospholipids are soya phospholipids such as Phospholipon 90 (PL-90). It is usually employed in a range of 0.5-10% w/w. Cholesterol at concentrations ranging between 0.1-1% can also be added to the preparation. Examples of alcohols, which can be used, include ethanol and isopropyl alcohol. Among glycols, propylene glycol and Transcutol are generally used. In addition, non-ionic surfactants (PEG-alkyl ethers) can be combined with the phospholipids in these preparations. Cationic lipids like cocoamide, POE alkyl amines, dodecylamine, cetrimide etc. can be added too. The concentration of alcohol in the final product may range from 20 to 50%. The concentration of the non-aqueous phase (alcohol and glycol combination) may range between 22 to 70%.¹⁷

Microneedles:

The needle or syringe combination has become the drug delivery mainstay for drugs and vaccines deemed ineffective by other routes and

has been optimized as a commodity scale product the world over.

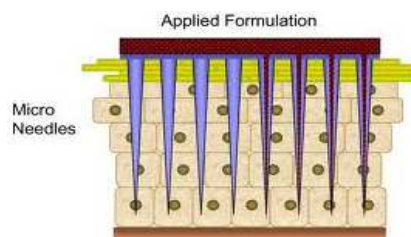


Fig.2. Figure of Microneedles functioning

It is therefore not surprising that the needle architecture to which we are so accustomed is the focus of the first microdevice for drug delivery: “Microneedles.” Microneedles are designed to be painless whilst overcoming the natural barrier function of the skin. Microneedle therapy is a way to rejuvenate the skin without destroying the epidermis. Methods for manufacturing these microneedle devices include micromolding, microfabrication, microshaping, and combinations thereof. Micro needles have a number of potential benefits for patients, clinicians, and the pharmaceutical industry as compared with alternative delivery methods. Micro needles have a number of potential benefits for patients, clinicians, and the pharmaceutical industry as compared with alternative delivery methods. Many people, particularly children, are ‘needle-phobes’. In addition, there are several patients, such as diabetics who are dependant on multiple injections on a daily basis. Many other disease conditions also require the delivery of therapeutic agents to the skin, while the outbreak of a pandemic would necessitate mass vaccinations. A solution to the problems posed by needle-based injections is the development of microneedles. This technology will help realise the development of new and improved devices, which will be smaller, cheaper, pain-free and more convenient with a wide range of biomedical and other applications. The ALZA Corp. has recently commercialized a microneedle technology named Macroflux which can either be used in combination with a drug reservoir or by dry coating the drug on the microprojection array; the latter being better for intracutaneous immunization.¹⁸⁻²⁰

Skin Abrasion:

The abrasion technique involves the direct removal or disruption of the upper layers of the skin to facilitate the permeation of topically applied medicaments. Some of these devices are based on techniques employed by dermatologists for superficial skin resurfacing (e.g. microdermabrasion) which are used in the treatment of acne, scars, hyperpigmentation and other skin blemishes.



Fig.3 figure of skin abrasion

Microscissuring is a process which creates microchannels in the skin by eroding the impermeable outer layers with sharp microscopic metal granules. Carlisle Scientific is currently in the process of developing a pen-like handheld device called the microscissioner.

In addition, MedPharm Ltd. has recently developed a novel dermal abrasion device (D3S) for the delivery of difficult to formulate therapeutics ranging from hydrophilic low molecular weight compounds to biopharmaceuticals. In vitro data has shown that the application of the device can increase the penetration of angiotensin into the skin 100-fold compared to untreated human skin. This device is non-invasive and histological studies on human skin show that the effects on the stratum corneum are reversible and non-irritating.

Cyclodextrins:

Cyclodextrins are having hydrophilic outer surface and a somewhat lipophilic characteristics

of central cavity. Cyclodextrins are able to form water-soluble inclusion complexes with many lipophilic water-insoluble drugs. In aqueous solutions drug molecules located in the central cavity are in a dynamic equilibrium with free drug molecules. The lipophilic molecules in the aqueous complexation media will compete with each other for a space in the cavity. Due to their size and hydrophilicity only insignificant amounts of cyclodextrins and drug/cyclodextrin complexes are able to penetrate into lipophilic biological barriers, such as intact skin. In general, cyclodextrins enhance topical drug delivery by increasing the drug availability at the barrier surface. At the surface the drug molecules partition from the cyclodextrin cavity into the lipophilic barrier. Thus, drug delivery from aqueous cyclodextrin solutions is both diffusion controlled and membrane controlled. It appears that cyclodextrins can only enhance topical drug delivery in the presence of water²¹

Aquasomes:

Aquasomes are one of the most recently developed delivery systems that are finding a niche as peptide and protein carriers. These are nanoparticulate carrier systems with three-layered self-assembled structures. They comprise a central solid nanocrystalline core coated with polyhydroxy oligomers onto which biochemically active molecules are adsorbed. The solid core provides the structural stability, while the carbohydrate coating protects against dehydration and stabilizes the biochemically active molecules. This property of maintaining the conformational integrity of bioactive molecules has led to the proposal that aquasomes have potential as a carrier system for delivery of peptide-based pharmaceuticals. The delivery system has been successfully utilized for the delivery of insulin, hemoglobin, and various antigens²²

Emerging Novel Carriers for Topical Drug Delivery²²**Table.1 Emerging Novel Carriers for topical delivery**

Sr.No	Carriers	Application
1.	Archaeosomes	This Archaeosomes are vesicles composed of glycerolipids of Archaea with potent adjuvant activity and having application in Molecular shielding, specific targeting
2.	Aquasomes	The aquasomes are three-layered self-assembly compositions with ceramic nanocrystalline particulate core loaded with glassy layer of polyhydroxy compounds and having Potent adjuvant activity application
3.	Discomes	The dicomes are niosomes solubilized with nonionic surfactant solution (polyoxyethylene cetyl ether glass) and having application in ligand mediated drug targeting
4.	Cryptosomes	The cryptosomes are lipid vesicles with a surface coat composed of PC and of suitable polyoxyethylene derivative of phosphateidyl ethanolamine having application in ligand mediated drug targeting
5.	Enzymosomes	The enzymosomes are liposomes designed to provide a mini bioenvironment in which enzymes are covalently immobilized or coupled to the surface of liposomes and having application in targeted delivery to tumor cells
6.	Emulsomes	The emulsomes are nanosized lipid particles (bioadhesive nanoemulsions) consisting of microscopic lipid assembly with apolar core and having application in Parenteral delivery of poorly water-soluble drugs
7.	Ethosomes	Ethosomes are lipid-based soft, malleable vesicles containing a permeation enhancer and composed of phospholipids, ethanol, and water and applied to targeted delivery to deep skin layers
8.	Genosomes	Genosomes are artificial macromolecular complexes for functional gene transfer. Cationic lipids are most suitable because they possess high biodegradability and stability in the bloodstream and application in cell specific gene transfer
9.	Erythrosomes (Proteoliposomes)	This are human erythrocyte cytoskeletons used as a support to which lipid bilayer is coated and applicable to Effective targeting of macromolecular drugs
10.	Photosomes	Photosomes are generally photolyase encapsulated in liposomes that release the contents by phototriggered changes in membrane permeability characteristics and having application in photodynamic therapy
11.	Novasomes	It consist of consist of glyceryl dilaurate, cholesterol, and polyoxyethylene 10-stearyl ether at a weight-percent ratio of 57:15:28, respectively and applicable in Drug delivery to pilosebaceous compartment
12.	Transferosomes (elastic liposomes)	It is modified lipid-based soft, malleable carriers tailored for enhanced systemic delivery of drugs applicable to Noninvasive delivery of drugs into or across the deeper skin layers and/or the systemic circulation
13.	Vesosomes	It is the nested-bilayer compartments with "interdigitated" bilayer phase formed by adding ethanol to a variety of saturated phospholipids applicable to Multiple compartments of the vesosomes give better protection to the interior contents in serum
14.	Proteosomes	Proteosomes are high-molecular-weight multi-subunit enzyme complexes with catalytic activity that is specifically due to assembly pattern of enzymes applicable to better catalytic activity turnover than nonassociated enzymes, may serve as adjuvant as well as protein carrier
15.	Virosomes	It is liposomes spiked with virus glycoprotein, incorporated into the liposome bilayers based on retrovirus-derived lipids and having application as immunological adjuvants

Active methods for enhancing topical delivery to skin:

These active methods are applied by producing external energy to act as a driving force and/or act to reduce the barrier nature of the skin in order to enhance permeation of drug molecules in to the skin. Recent progress in these technologies has occurred as a result of advances in precision engineering (bioengineering), computing, chemical engineering and material sciences, and this all results in creation of devices for skin delivery of drug to achieve the desired therapeutic effect.²³ following are the active methods or devices for topical drug delivery.

Ultrasound (Sonophoresis or Phonophoresis):

Ultrasound involves the use of ultrasonic energy to enhance the transdermal delivery of solutes either simultaneously or via pre-treatment and is frequently referred to as sonophoresis or phonophoresis. The proposed mechanism behind the increase in skin permeability is attributed to the formation of gaseous cavities within the intercellular lipids on exposure to ultrasound resulting in disruption of the subcutaneous layer of the skin. The ultrasound or sonophoresis is a process that exponentially increases the absorption of topical compounds (transdermal delivery) into the epidermis, dermis and skin appendages. Sonophoresis occurs because ultrasound waves stimulate micro-vibrations within the skin epidermis and increase the overall kinetic energy of molecules making up topical agents. It is widely used in hospitals to deliver drugs through the skin²³

Laser radiation and photomechanical waves:

Lasers have been used in the clinical therapies for decades; therefore their effects on biological membranes are well documented. Lasers are frequently used for the treatment of dermatological conditions such as acne and to confer 'facial rejuvenation' where the laser radiation destroys the target cells over a short frame of time (~300 ns). Such direct and controlled exposure of the skin to laser radiation results in ablation of the SC without significant damage to the underlying epidermis. Removal of the subcutaneous layer of the skin by this

method it has been shown to enhance the delivery of lipophilic and hydrophilic drugs^{23,28}

Electroporation:

Electroporation are used to help deliver drugs or genes into the cell by applying short and intense electric pulses that transiently permeabilize cell membrane, thus allowing transport of molecules otherwise not transported through a cellular membrane. This procedure is referred to as electrochemotherapy when the molecules to be transported is a chemotherapeutic agent or gene electrotransfer when the molecule to be transported is DNA.²⁴ however, more clinical information on the safety and efficacy of the technique is required to assess the future commercial prospects

Iontophoresis:

The process of iontophoresis is increases the penetration of drugs into the skin by application of an electric current. The drug is applied under an electrode of the same charge as the drug, and a return electrode opposite in charge to the drug is placed at a neutral site on the body surface. Electrical energy assists the movement of ions across the skin using the principle "like charges repel each other and opposite charges attract"²⁶

Radio-frequency:

It includes the exposure of skin to high frequency alternating current equivalent to 100 kHz which reveals the formation of heat induced micro channels in the membrane of skin similar to when laser radiation is employed. The rate of drug delivery is controlled by the number and depth of the micro channels formed by the device, which is dependent on the properties of the microelectrodes used in the device²³.

Magnetophoresis:

Magnetophoresis is a phenomenon of enhancing drug permeation across the biological barriers by application of magnetic field. It has shown that magnetophoresis leads to enhanced transdermal drug delivery at in vitro and in vivo studies¹³ the predominant mechanism for drug permeation enhancement was found to be magnetokinesis and enhanced partitioning of drug into stratum corneum

Skin puncture and perforation devices:

These devices are made up of microfibrillation technology which is similar to Microneedles. This posses the blade or needle like structure which cuts the skin barrier which leads to formation of holes. After disruption of the skin skin, solution, patch, gel, ointment etc or iontophoresis, electroporation etc delivery methods can then be utilised.

Non Needle injections:

This method of delivery of drug is painless, skin delivery of the drug is achieved by forcing the liquid or solid particles at supersonic speed using suitable and controlled energy source e.g. Medijector[®]

Skin stretching devices:

In this case of topical delivery the tension is applied to the skin by the device in various directions as result permeation from the skin is increased hence the applied formulation or devices finds easiest way to deliver the drug into the skin.

Conclusion:

By concluding current review it shows that new and alternative drug delivery systems are currently focusing in various research activities. The dosage forms safety, efficacy and convenience of use are important for patient factors that need to be considered when developing novel or alternate drug delivery systems for topical application. In recent years, the transdermal route of drug delivery has evolved considerably and growing field as topical application as well as convenient properties. Most of the device-induced transdermal drug delivery techniques are still in the early stages of commercialization for optimization of better delivery of quality product to society.

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