REVIEW ARTICLE

Advancement of Niosomal Transdermal Targeting Drug Delivery System

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ABSTRACT

Traditional methods for applying medications to the skin include a variety of methods. Transdermal has been a popular method of drug delivery in recent years for a variety of medications that are challenging to administer in other ways. Transdermal drug delivery has a number of benefits, chief among them the prevention of first-pass metabolism and the stomach environment, which would render the drug inactive. In addition to discussing in depth the various formulation techniques and permeability enhancement for improved therapeutic efficacy, this review covers the fundamental anatomy of the skin that is pertinent to the transdermal route as a drug delivery method. The evaluation sums up the technologies that are now available on the market and discusses the path they are headed in. A transdermal patch offers a controlled release of medicine into the patient, typically through either membrane pores casing a reserve of medication or over body heat melting thin layers of medication entrenched in the adhesive. This is a bonus of transdermal drug transport over different drug transport styles, including like oral, topical, I. V., I. M., etc. The skin is a very real barrier; in this way, drug molecules are modest enough to permeate the skin and can be administered in this way. Typically, the basic disadvantage of transdermal administration systems. Transdermal patches for a wide run of solutions are now readily available. With properties like improved penetration of drug, a sustained sedate discharge by local depot, and modulating systemic absorption of drugs through the skin by a membrane which limits rate, niosomes are vesicular nanocarriers that are getting to be more and more well known as a potential transdermal drug delivery framework. Niosomes are non-ionic surfactant-based vesicles that are more stable, biodegradable, and generally harmless. Niosomes are ideal to liposomes since surfactants are more chemically stable than lipids. The concept of niosome, its benefits and disadvantages, composition, method of preparation, variables influencing niosomes, definition and characterization, and use of niosome are the main topics of this review study. Niosomes can be used to treat a variety of illnesses, including psoriasis, leishmaniasis, cancer, migraines, Parkinson's disease, etc. Niosomes can help in diagnosis. Niosomal administration can be done intramuscularly, intravenously, orally, or it can be used topically.

Keywords: Niosomes, Novel approaches, Transdermal drug delivery.

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INTRODUCTION

Transdermal drug delivery system one of the innovative drug delivery methods that is advancing the fastest is transdermal drug delivery. Although the idea for transdermal medication delivery has been around since 1924, it wasn't until the food and drug administration (FDA) approved scopolamine's transdermal distribution in 1979 which is transdermal delivery systems (TDDS) started to get widespread attention as a cutting-edge technique for controlled release. This medication delivery system was made to distribute drugs under control through the skin into the bloodstream while preserving consistent efficacy and lowering the dose and associated side effects.[1] The most popular route, oral administration, expedites patient satisfaction but is more likely to cause hepatic first-pass metabolism, necessitating a higher dose of medication. The main barrier to the inclusion of surfactants in lipid-based formulations is additional gastrointestinal irritability. The simultaneous dissemination of medicine throughout the body may result in unavoidable adverse effects. Therefore, the non-invasive, painless, and irritation-free topical delivery of definition may be a diverse strategy related to several benefits, counting the drug delivery to a particular location of activity with decreased systemic toxicity, evasion of first-pass metabolism and gastric irritation, increased release rate of the drug from formulation to induce superior percutaneous absorption, and for a minute topical application related to increasing bioavailability with sustained release drug delivery via the skin is a fascinating and difficult field. There are many

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transdermal delivery technologies on the market right now. However, the transdermal market is still only available for a few medications. The capacity which overcomes the problems related to penetration and skin irritation of the drug molecules will determine whether transdermal delivery technology progresses in the future.[2]

To further highlight its benefits, typical transdermal formulations, such as ointments, creams, and lotions, have more drawbacks, including their pasty texture, poor spreadability, stability problems, etc., which eventually cause patient noncompliance. Researchers are also particularly concerned about stratum corneum penetration through the skin due to the systemic activity of transdermal administration.[3] topical medication delivery is made possible by targeting the skin directly. Both beauty products and pharmaceutical preparations now use semi-solid translucent gels. One of the many difficult areas for formulation scientists to work in is developing dosage forms for topical medication administration. Comparing the stratum corneum to the other epithelial barriers of the gastrointestinal, rectal, nasal, buccal and vaginal pathways, the stratum corneum is the supreme terrifying barrier because of its peculiar composition (proteins: lipids: water = 40:40:20%, respectively) and tight intercellular connections. Drugs are applied topically either for local or systemic effects, depending on their intended use. While other methods of medication administration fail or when treating a fungal infection, the topical drug distribution system is typically used.[4]

Advantages of Topical Drug Delivery System

- Avoids pre-systemic metabolism.
- The hazards and inconveniences during intravenous therapy were avoided.
- The absorption conditions, such as pH variations, the existence of enzymes, and the rate at which the stomach empties.
- Medication has the potential to stop when necessary.
- The capability of more targeted medicine delivery to a particular place.
- Avoidance of gastrointestinal compatibility
- These will enable the use of medications with a limited therapeutic window and short biological half-life

Disadvantages of Topical Drug Delivery

- Some medications have low skin permeability.
- The irritation could result from touch with dermatitis.
- Medicines with large particle sizes won't easily penetrate the skin.
- There is a chance of allergic reactions.[5,6]

Factors Affecting Topical Absorption of the Drug

- Physiological factors include skin thickness, sweat gland density, lipid content, pH, bloodstream, hydration, and inflammation.
- Partition coefficient, molecular weight (400 Da), degree of ionisation (only unionised pharmaceuticals get absorbed well), and carrier effect are all physiochemical factors.

Things to Take into Account While Selecting a Topical Preparation

- The effect of the carriers, an occlusive vehicle, increases the active ingredient's penetration and efficacy.
- Align the site and the sort of preparation. (Such as gel or lotion for places with hair).
- Align the preparation type with the kind of lesions. (Acute weepy dermatitis: refrain from using oily ointments)
- Capable of causing irritation or sensitization. Gels are irritating, although ointments and creams without alcohol are often less so. Transdermal and dermal drug delivery may have a number of physical and chemical advantages, including as minimal pre-systemic, patient compliance and comfort and local drug transport to the skin. Such a technique was employed to get over the skin's natural limiting factor for medication penetration.[7]

Niosomes

Targeted medicine delivery aims to concentrate a drug in the mark tissues while reducing the relative concentration. Medicine is thereby contained to the appropriate site. Because of this, the medicine has no impact on the primary tissues. Using diverse carriers, synthetic erythrocytes, polymers, microspheres, liposomes and niosomes have all been addressed.[8] Due to improved drug permeation, continuous drug-releasing local depots, and a membrane to limit the rate for modulating systemic absorption of pharmaceuticals *via,* the skin, niosomes and, vesicular nanocarriers, are gaining a lot of attention as future transdermal drug delivery systems. There are several theories put out to explain how niosomes can encourage medication transfer through the skin. This review points to supply a thorough collection of later studies for this intriguing field, with uncommon emphasis on methods utilized to maximise the potential of niosomes. Niosomal carriers are reasonable for the transdermal conveyance of a variety of pharmacological specialists, counting antioxidant, anti-inflammatory, anticancer, antimicrobial, and antibacterial molecules. Due to their distinct benefits, niosomes, vesicular nanocarriers, have gained much attention as probable drug delivery systems over the past 30 years. They have amphiphilic molecule-based lamellar (bilayer) structures encased in an aqueous compartment. Surfactants are amphiphilic molecules with hydrophobic (tails) and hydrophilic (heads) groups that have the ability to self-assemble into a diversity of geometries, such as micelles or a planar lamellar bilayer.[9,10] Sorbitan esters, analogs and sugar-based, polyglycerol, polyoxyethylene-based, or crown ether-based surfactants, sometimes in conjunction with membrane additives like cholesterol or its subsidiaries, might all be used as possible drug delivery methods. Because of their reduced tendency to irritate skin, non-ionic surfactants are chosen over cationic and anionic ones.[11] There are numerous ways to administer niosomal drugs, including intramuscular, intravenous, subcutaneous, dental, ophthalmic, pulmonary, and transdermal, depending on the drug, surfactant, ailment, and physiological site involved.[12] In addition to intraperitoneal and vaginal approaches, niosomal medications have also been

given *via* other routes. It has been proposed that niosomes could be used as a transdermal medicine delivery system. Improved bioavailability, more even plasma levels, a longer time of activity driving to a decrease in dosing recurrence, decreased and improved treatment due to the maintenance of plasma levels up to the conclusion of the dosing period as contradicted to a drop in plasma levels to ordinary sorts are fair a couple of the major benefits offered by transdermal drugs.[13] Administration via transdermal route increased the drug's ability to enter the skin when it was embedded in noisome. Terbinafine hydrochloride was thin-film hydrated using polysorbate 20, 40, 60, and 80 non-ionic surfactants and cholesterol to produce terbinafine hydrochloride niosomes with continuous drug concentration. *Aspergillus niger* strain was used to test the formulations' antifungal activity *in-vitro*, along with the results were concomitant to a pure drug solution as standard. Due to the medication's-controlled release, both formulations demonstrated a consistent inhibition zone expansion. Comparing gels having drug entrapped in pure drug and commercial formulations, whole gels have the maximum zone of inhibition (12 mm) at initially, subsequently sustained release (12–16 mm).[14] While transdermal patches are equally effective as oral dose forms, they also have a few advantages over them. Transdermal delivery has a first-pass metabolic effect in comparison to the oral method. As a result, transdermal administration increases bioavailability. Second, transdermal administration allows a prolonged drug release, which may make it simpler for patients to take their drugs consistently. Finally, when medications are applied *via* transdermal route, their peak concentrations are decreased.[15,16]

Novel Topical Drug Delivery System

Aerosol Foams

A growing number of topical formulations, including aerosol foams, are being used to treat various dermal problems like acne vulgaris. The foam's vehicle base can be a semi-solid or liquid that retains the same physicochemical properties as common vehicles like gel, creams and lotions while still retaining useful qualities like moisturizing or fast-drying properties or increased drug bioavailability. The formulation type and the dispensing pack that are chosen to meet the treatment needs can impact the item properties (i.e., surface, bubble measure and thickness, tirelessness, solidness, and spreadability). Foams may be recommended in cases of acne since they are simpler to apply and can be used as cleansers on the face or on big hairy surfaces (such the chest and back).

Liposomes

Liposomes are habitually utilized as vehicles in cosmetics and pharmaceuticals for optimised and delivery to the specific layers of the skin. These are vesicles of spherical shapes consisting of a membrane with amphiphilic lipids (i.e., which can be lipophilic and hydrophilic both) which encase an aqueous core, comparable to the living cells of bilayer membranes. Since they offer an environment of amphiphilic nature, which encapsulates lipophilic substances in the lipid bilayer and hydrophilic substances in the aqueous core and special dual release capability which empowers the delivery of 2 sorts of substances which may cause enhancement in the desired therapeutic effect after application on skin with different impacts on skin penetrability.[17,18]

Nanoemulsions

The dispersion of very small-sized drops while mixing an emulsion, such as oil-in-water or water-in-oil, is what distinguishes nanoemulsions from other types of emulsions. Since they require particular thermodynamic circumstances, specialized production methods, and particular surfactants that can stabilize the nano-droplets, nanoemulsions do not spontaneously develop. Nanoemulsions are effective in delivering lipophilic substances to the skin, making them a potential treatment option for acne by facilitating the entry of active substances into the lipophilic nature of the pilosebaceous unit. Moreover, nanoemulsion particles can have extra therapeutic effects including improved skin hydration and viscoelasticity and won't clog pores.[19]

Polymers

Polymers are made up of monomers, or repeating structural units, which are joined by covalent chemical connections. These substances are the building blocks of biological, natural, and manufactured materials like proteins, nucleic acids, polymers, and polyethylene. Instances of natural materials include paper and amber. Synthetic polymers are used in almost each industry today, and their adaptability has led to technological developments within the pharmaceutical business that cater to a range of medical needs. For instance, novel acrylic-acid polymers are used in dermatology to create gels that trap water inside micro-cells when moisture is exposed. Hydrophilic chemicals can stay in a solution inside of these aqueous micro-cells, but non-hydrophilic compounds may be disseminated in suspension. As a result, a gel-like formulation that is stable and simple to use releases the active ingredient(s) once it is applied to the skin. These polymer-based gels can also be combined with other excipients, like moisturizers and emollients, to offer more clinical advantages. This innovative polymer-based gel technology is used in recently released anti-acne formulations that contain clindamycin 1% and benzoperoxide 5% (Duac®, Stiefel Laboratories; BenzaClin®, Dermik). These formulations demonstrate the efficiency and outstanding tolerability.

Microsponges

Micro-sponges are synthetic polymer-based units that are physiologically inert and have the ability to clutch a volume of an active ingredient more than their own mass. The particles also defend the entrapped active chemical from deterioration caused by the environment and physical forces. Although the micro-sponge technology can be used to many different formulations, gels are the form in which they are most usually produced. Micro-sponges progressively discharge the active ingredient after being used on the skin.[20]

Emulsifier-free Formulations

Emulsifier-free formulations are a significant region of development for dermatologic and cosmetic products. Since the majority of skincare artifacts are emulsions, which are mixtures of two or more immiscible substances, they are intrinsically unstable according to the second law of thermodynamics. In order to ensure sufficient shelf life, they necessitate the addition of surfactants (also known as Emulsifiers) which stabilize the formulation. The natural lipids of the cuticle tend to be emulsified and removed once these surfactant agents are smeared to the skin. Therefore, to produce passably stable products with an appealingly pleasing look, the pharmaceutical industry has been creating surfactant-free emulsions by way of alternatives to standard formulations by employing stabilizers like solid particles or polymeric emulsifiers.[21]

Fullerenes

Carbon-only compounds called fullerenes have the appearance of hollow spheres. Fullerenes travel through the skin intercellularly instead of by means of cells once they come into touch with it, as demonstrated by Rouse *et al.* As a result, active substances could be "trapped" by a fullerene and subsequently released into the epidermis later being applied to the skin. Additionally, fullerenes themselves are believed to be powerful antioxidants. According to data published in the literature, fullerenes are well accepted and have a lot of potential for use in dermatologic and aesthetic procedures.[22]

Advanced Techniques

The activators, such as ethanol, give vesicles their elastic properties and enable easier penetration into the deeper layers of skin, elastic vesicles, a novel type of highly flexible niosomes, have been postulated and are reported to be successful at transporting molecules over the skin. Niosomal gels provides high and sustained drug concentrations in the skin.[21] Topical nonsteroidal anti-inflammatory medicines (NSAIDs) have been developed with NSAIDs, whose ability to enter the skin is crucial. By adjusting the cholesterol content of the kind of surfactant utilized for efficiency as topical anti-inflammatory delivery systems,[23] an aceclofenac targeting system incorporating niosomes was worked *via* the skin. The carrageenan-induced rat paw edema method was used to assess the transdermal transport of meloxicam loaded into niosomal gel formulations, and the results demonstrated the advantage of niosomal gels over conventional gels.[24] In comparison to the commercial emulgel product, which contains a similar quantity of medication,[25-27] the innovative elastic niosomes with entrapped diclofenac diethyl ammonium demonstrated a higher flow of the drug in the skin. Another NSAID that has been enclosed in niosomes is rofecoxib. A topical gel base containing the niosomes was used for a long-lasting therapeutic effect for topical administration. A promising pro-niosome gel formulation that goals lower the daily dose of medicine required to be taken to increase patient compliance. The transdermal formulation of tenoxicam is characterized by improved safety and great therapeutic efficacy with a high drug loading (55.4%, weight by weight), flurbiprofen was created as a pro-niosomal transdermal gel using cholesterol and a number of non-ionic surfactants (span 20, 40, and 60).[28] Baclofen acts as centrally acting muscle relaxant, was loaded into niosomes to increase the poor bioavailability and low skin penetration of traditional topical preparations containing this medication.[29] Topical use of capsaicin results in rapid skin absorption. Several lotions and patches with capsaicin as the active ingredient are sold without a prescription. When compared to formulations based on micro-emulsions, it showed that niosomes produced superior percutaneous capsaicin permeation.[30] Aiming to create novel cosmeceutical products niosomes based on Polysorbate 60 and containing resveratrol, alpha-tocopherol, and curcumin as single operators and in combination were created.[31] Papain, a protease protein inferred from *Carica papaya* latex, is frequently employed in skin care to heal scars. Simvastatin, a lipid-lowering medication, is used to treat hypercholesterolemia in both people and animals.[32] Simvastatin exhibits substantial presystemic metabolism in the liver after oral administration, which results in limited bioavailability and a minute half-life of just 2 hours a pro-niosomal method for simvastatin transdermal administration.[33] By adjusting the ratios of span 40, lecithin, polymer and aqueous phase, nifedipine-containing pro-niosomes for transdermal delivery were created.[34] A transdermal distribution of niosomes laden with sulfadiazine sodium, an antibiotic often applied topically to treat infected burns, has been reported.[35] To assess the impact of the chemical makeup of various surfactants and reticulated drugs on the carriers' physicochemical characteristics and pre-cutaneous drug penetration profiles, novel multicomponent formulations were explored. Tyrosol, propranolol hydrochloride, and sodium sulfadiazine salt were chosen as the model drugs, and pluronic L64 or aerosol OT was used as the surfactant. To create lamellar lyotropic liquid crystal phases, lyotropic liquid quartzes were created at a set proportion of pluronic L 64 or aerosol OT to water, and the appropriate surfactant was utilized to plan the vesicular frameworks (niosomes) that were included to the gel. Ritonavir must be used in conjunction with lopinavir, a very effective protease inhibitor used to treat acquired immunodeficiency syndrome (AIDS), because of lopinavir's limited systemic bioavailability and significant pre-systemic metabolism. As a transdermal drug delivery technique for tumour therapy, niosomes were employed.[36]

As a result, new methods for preparation, loading, and adjusting niosomes can enhance their ability. Further study and creation of commercially viable niosomal preparations are required in these domains. Researchers should be aware of how crucial it is to prepare niosomes with the proper surfactants because the choice of surfactant affects the toxicity, stability, and potential applications of the final product.

CONCLUSION

Systems for transdermal medicine distribution have been employed as reliable means of delivering medications. The scientists with high rates of accomplishment are utilizing

their potential in a controlled release on a worldwide scale. Transdermal delivery is a remarkably efficient method of administration if a medication has the proper balance of physical chemistry and pharmacology. Many fresh studies are being conducted today to incorporate newer medications *via* the system due to the TDDS's many benefits. For the regulated percutaneous administration of both hydrophilic as well as lipophilic medicines, niosomes have been shown to be promising. Niosomes potential can be increased by employing fresh formulation, drug loading, along with modification techniques. To create niosomal formulations that can be sold commercially, these areas require additional investigation and study. The simple elements of a niosomal transdermal patch, such as drug reservoirs, liners, adherents, permeation enhancers, plasticizers, backing laminates and solvents, are crucial to the drug's release through the skin. Transdermal patches come in a variety of forms, including matrix, reservoir, membrane matrix hybrid, and drug-in-adhesive TD patches. These patches are prepared using various techniques employing the core N-TDDS components.

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