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A NOVEL APPROACH FOR NIOSOMES AS A TRANSDERMAL DRUG DELIVERY: THE FUTURE SCENARIO

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ABSTRACT:

Transdermal drug delivery systems were developed as interesting research as well as one of the most regularly developed pharmaceutical goods on the global market in the field of pharmaceutical technology. Other delivery modes, like oral and intravenous, have limitations that this approach can solve. Nanocarriers, niosomes, electrosomes, liposomes, proniosomes, ethosomes and transferosomes are examples of vesicular targeted carriers for drug delivery. Niosomes and proniosomes, for example, are regarded to be improved carriers for increasing therapeutic efficacy and bioavailability while lowering side effects, making it a viable transdermal drug delivery system. Both are amphiphilic non-ionic surfactant-based vesicles. Niosomes are formed when non-ionic surfactant vesicles assemble. The type of nonionic surfactant employed, the method of production, the hydration temperature, and other variables all influence niosome formation. In this review paper, we sought to incorporate all of the basic data about niosomes, including different techniques of manufacture, distinct types of niosomes, factors impacting their production, and so on. Niosome toxicity is a term used to describe the toxicity of niosomes. Transdermal drug - delivery penetration enhancers, Mechanism of action of niosomes , and recent advances in the domain of niosomal research. The niosome's role as a pharmacological carrier in the skin is also highlighted.

KEYWORDS: Transdermal drug delivery,pharmaceutical technology, Niosomes, non-ionic surfactant, enetration enhancer.

INTRODUCTION

Niosomes are vesicular small lamellar Nanocarriers that are becoming more popular as a drug delivery mechanism owing to their distinct benefits. Niosomes are vesicles that form when a alkyl or dialkyl polyglycerol ether nonionic surfactant family and cholesterol are combined together and hydrated in aqueous media[1].The composition and physical properties of niosomes are identical to that of liposomes.liposomes have some disadvantages like stability, toxicity,that is why there was a need to develop niosomes.[2] Niosomes shows good biocompatibility and biodegradability. Niosomes act as a vehicle including both amphiphilic and lipophilic medicines, delivering them to the desired organ. (3) Nonionic surfactants are the main components of niosomes. Surfactants are utilised to create Niosomes because of their biodegradability, non-immunogenic properties, and biocompatibility., they are helpful to enhance the effectiveness of drugs which is encapsulated in a Niosomes[3]
Niosomes are a type of molecule that can be employed in a variety of medication delivery systems like pulmonary delivery (example-glucocorticoid), transdermal delivery (example-gallidermin, clomipramine), ocular delivery (example-tacrolimus, naltrexone HCl), It's also utilised to get drugs beyond the blood-brain barrier (example-temozolomide). Cosmetics Industry (L'Oreal) was the first to develop niosomes. , After this it was expored in Pharma Industry[2].

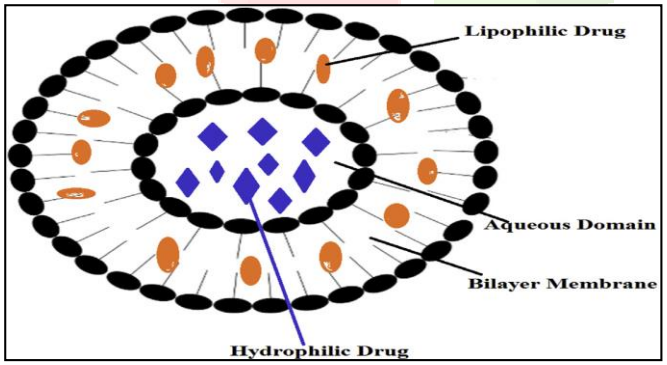


Fig 1: Niosomes

STRUCTURE OF NIOSOMES:

In a bilayer spherical shape, it is composed of nonionic surfactant and cholesterol[1]. Surfactant and cholesterol are mixed in appropriate proportions to generate a thermodynamically stable bilayered structure, and the temperature should be kept above the gel liquid transition point[2]. Niosomes are made up of a phospholipid bilayer on the outside and inside of the vesicle with hydrophilic ends facing each other and hydrophobic chains facing each other inside the bilayer. The hydrophilic pharmaceuticals are entrapped in the core aqueous medium or adsorbed on the bilayer surfaces, whilst the hydrophobic drugs are absorbed directly into the bilayer[2]. Niosomes are composed of the following ingredients:

Non –ionic surfactant [4,1:] HLB value of surfactant is used selection of surfactant for preparation of niosomes.The formation of bilayered vesicles ,instead of micelles is depend on the HLB(Hydrophillic- Lipophillic balance)of the surfactant , gel liquid transition temperature and critical packing parameter. HLB value of surfactant should be between 4 to 8. Gel liquid transition temperature of the surfactant should be not less than 10^{o} C, it may cause oxidation s not used with iodidies,salicylates, tannins and phenolic salts[2]. The CPP is a critical parameter for identifying the sort of vesicles generated by surfactants. Surfactants with CPPs ranging from 1/2 to 1 prefer bilayeredvesicles.Nonionic surfactants are preferred which act as surface active agents because they provide more stability and compatibility and lesser toxicitycompared to other anionic ,cataonic and amphoteric counterparts. Examples of some nonionic surfactants used include polyoxyethylene-based ethers and esters, polyglycerol alkyl ethers,crown ethers, most often utilized non-ionic surfactants are span (20,40,60),Tween (20,40,60) etc.

Cholesterol: Cholesterol is a steroid derivative which used to form a proper shape and rigidity to noisome[1].It is a biosurfactant which regulate the membrane fluidity and permeability or penetration in vesicles[4] .Cholesterol must be added for bilayer formation when the HLB value of the surfactant is greater than 6, and for lower HLB values, it enhances the stability of the vesicles.Usually, cholesterol to non-ionic surfactant used is 1:1 M[2].
Hydration medium: Commonly used Hydration medium used is Phosphate buffer at physiological PH it depends upon solubility of the drug[5].

Charge molecule: To avoid aggregation of niosomes some charged molecules are added in formulation .Due to presence of charge on the surface repulsion of particles take place and hence prevents in coalescence and aggregation. Examples of charged particles are Diacetyl phosphate, phosphatidic acid, lipoamino acid, dihexadecyl phosphate (Negatively charged), - Stearyl amine, stearyl pyridinium chloride.(Positively Charged) etc. For the operation of generating niosomes about 2.5-5 mole percentage concentration of charged molecules is required[4].

Benefits of niosome[2,4,6]:

• Surfactants are biodegradable, biocompatible, non-toxic, and do not initiate immune responses.
• Niosomes are less toxic because non-ionic surfactant is a major component of niosomes and is non-toxic.
• Niosomes are osmotically active,
• Niosomes are chemically stable and can improve drug bioavailability.
• Niosomes are used for the delivery of sensitive and durable drugs because the drug is protected within the structure of the niosome.
• Niosomes contain both hydrophilic compounds in addition to hydrophobic compounds.
• Body structures such as size, shape, fluid, and efficiency of the entrapment can be influenced to adjust the parameters such as the use of additives and their combinations.
• Niosomes are used in a number of drug delivery systems such as transdermal, continuous and controlled drug delivery.
• Niosomes protect the drug from enzyme metabolism1.
• Niosomes limit their effect on cells by delaying the removal of the drug from the circulation system and improving the efficacy of the drug.
• Niosomes suspension in the aquatic environment may be dispersed in the dehydrated phase to control the level of drug delivery Control the normal vesicle in the dehydrated phase outside.
• Surfactants do not require special handling or storage conditions, which is why they are not expensive to prepare. Niosomes can be used in various medicine and cosmetic preparations.

Deficiency of niosomes[4,6]:

• Niosomes indicate physical instability.
• Consolidation may occur as a result of not using the usual preparation method
•Fusion of Niosomes vesicle occur due to presence of different charges
• Leakage of a blocked tree may occur
• May show inadequate drug delivery in some cases.

Types of niosomes[4]:

Niosomes are classified on the basis of
A) Depending on the type of lamellarity
1. Multilamellar vesicles (MLV) 1-5 μm in size.
2. Unilamellar vesicles large (LUV) 0.1 - 1μm in size
3. Unilamellar small vesicles (SUV) 25 - 500 nm in size.
B) Depending on size
1. Small Niosomes (100 nm - 200 nm)
2. Large Niosomes (800 nm - 900 nm)
3. Large Niosomes (2 μm - 4 μm)

Types	Vesicle size	Method of preparation
Small Uni-lamellar vesicle (SUV)	0.025- 0.05μm or 25-50nm	Sonication Method and French Press Extrusion Electrostatic Stabilization
Multi-lamellar Vesicle (MUV)	0.5-10 μm in diameter	Thin Film Hydration Method.
Large Uni-lamellar Vesicle (LUV)	100nm	Ether Injection Method and Reverse Phase Evaporation Method

Table 1: Types of Niosomes

METHODS PREPARATION OF NIOSOMES:

The number of bilayers, size, size distribution, and entrapment effectiveness of the aqueous phase, including the membrane permeability of the vesicles, should all bedetermined based on the niosomes' intended function.

a)Ether Injection method:

Baillie and others described this method in 1985; Deamer and Bangham described it in 1976 for the production of liposomes.(1,4,7)

Preparation steps:

Dissolve surfactant in diethyl ether. Then inject through 14 guazeneedle in warm water maintained at 60°C. Single layer niosomes is formed by evaporation of ether.

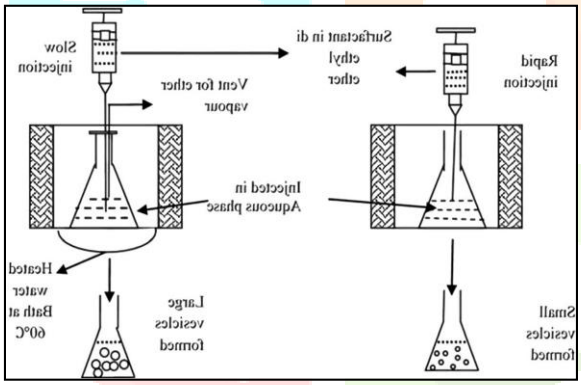


Figure 2: Diagram for Preparation of Niosomes by ether injection method[1, 9]

b) Hand Shaking Technique (Thin Film Hydration):

Azmin et al. and Baillie et al. described this method in 1985; it had previously been described by Bangham and others in 1965 for the production of liposomes.

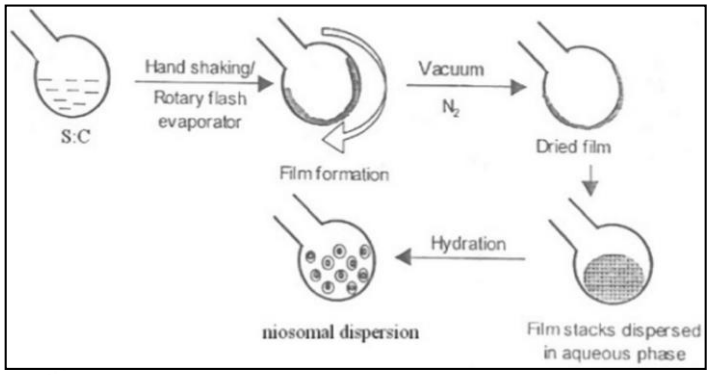
Preparation Steps:

Add surfactant+ choloroform (organic solvent) + Cholesterol in round bottom flask. Remove organic solvent by rotatory evaporator at RT. Then thin film is formed on wall of flask. Film is rehydrated by adding warm water and niosomes are produced.

Figure 1 : Diagram for Preparation of niosomes by by thin film hydration technique [1, 9]

C c) Sonication method :

Baillie et al. described this method for the

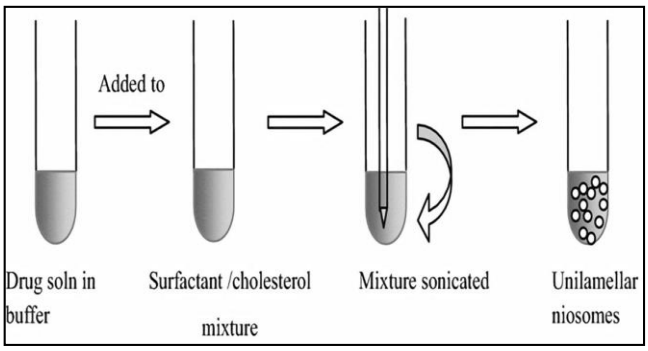


production of liposomes in 1986, after Huang had described it in 1969.

Preparation Steps:

Add drug in mixture of buffer + Surfactant/ Cholesterol.Then sonicate the above mixture for 3 mins at 60° C with the help of titanium probe yielding niosomes.

Figure 2: Diagram for Preparation of niosomes by Sonication method [10]



d)Microfludization method :

For the production of unilamellar vesicles, this is a new method. Two fluidized streams react at ultra-high velocities within the interaction chamber in this method. This method produces a smaller niosome with greater uniformity and reproducibility.

Preparation Steps:

two ultra-high-speed jet is present inside interaction chamber. The thin layer of Liquid in micro channels is impegmented and formation of niosomes occur.

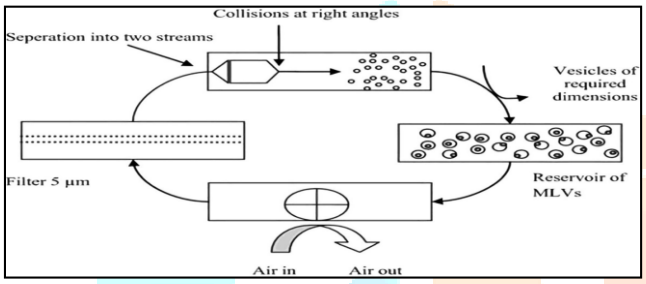


Figure 3: Diagram for Preparation of niosomes by microfludization[9]

e) Multiple membrane extrution method :

This method is used to control niosomal size.

Preparation steps:

Surfactant+ cholesterol+dicetyl phosphate in cholesterol is mixed to form thin film rotary evaporator. produced film hydrates with membrane of aqueous polycarbonate material through which resultant suspension is extruded.

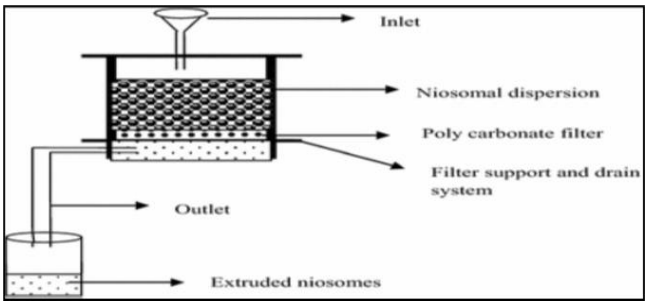


Figure 4: Diagram for Preparation of niosomes by multiple extrusion method [10]

f) Reverse Phase Evaporation Technique (REV):

To make Diclofenac Sodium niosomes using Tween 85 this method was used by Raja Naresh et al.

Preparation steps:

Cholesterol + surfactant are dissolved in ether solution + chloroform. Sonicate mixture at 5oc and again sonicated after adding PBS. To the aforesaid combination, aqueous-phase drug is added. Then Viscous niosomes suspension is diluted with PBS. At 40°C and low pressure, the organic phase is removed.Heated on a water bath for 60oC for 10 mints formation of niosomes occur.

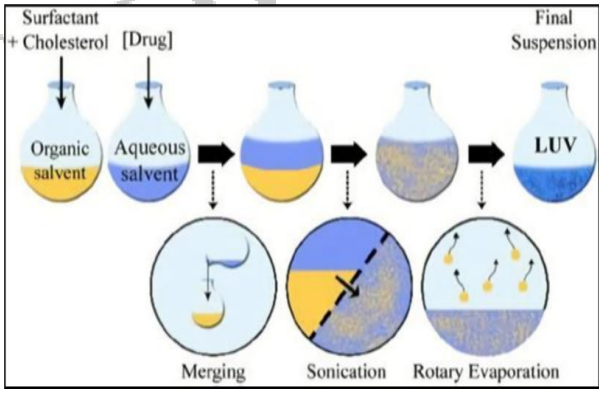


Figure7: Diagram for Preparation of niosomes by reverse phase evaporation method [11]

g) Transmembrane PH gradient Drug uptake Process:

Surfactant + cholesterol + chloroform mixed and solvent is evaporated under reduce pressure. On the RBF's walls, a thin film is deposited. 3 cycles of freezing and thawing, followed by sonication, to hydrate with citric acid . Add solution of aqueous drug and vertexing. Raised PH to 7.0-7.2 by 1M disodium phosphate RBF as bubbling unit with three necks in water bath. Three necks provide reflux, thermometer, and nitrogen supply. Add Cholesterol + surfactant dispersed in buffer pH 7.4 at 70°C . To make Niosome, the above dispersion is homogenised for 15 seconds and subsequently bubbled using nitrogen gas at 70°C.

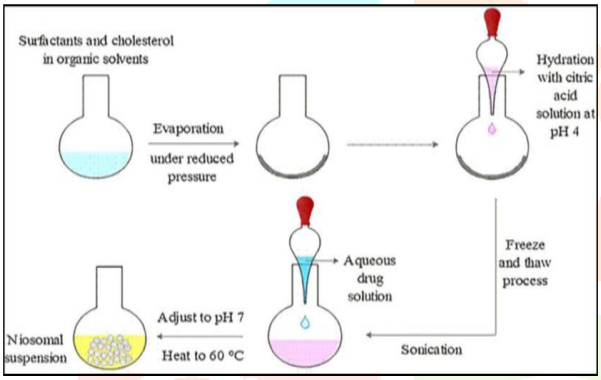


Figure 8: Diagram for Preparation of niosomes by Trans membrane Ph gradient [12]

h) The Bubble Method

This is a novel method for preparing liposomes and niosomes that does not require the use of an organic solvent. This bubbling unit has a round bottomed flask with three necks that is placed in a water bath to keep the temperature consistent.

The first and second necks house the water-cooled reflux and thermometer, while the third neck houses the nitrogen supply. Surfactant and cholesterol were combined in a PH-7.4 buffer at 70°C for 15 seconds in a high shear homogenizer, and then immediately bubbled at 70°C with nitrogen gas.

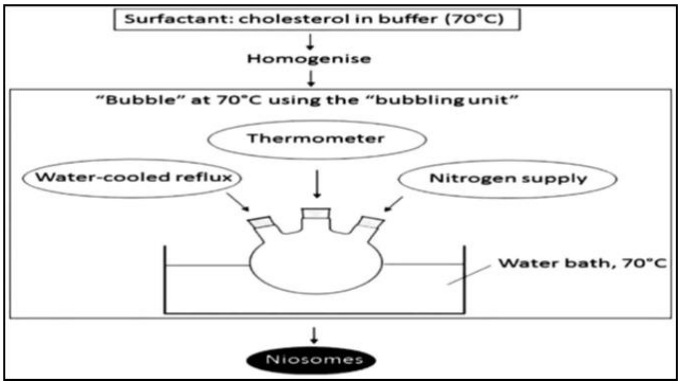


Figure 5: Diagram for Preparation of niosomes by bubble method[13]

TRANSDERMAL DRUG DELIVERY:

Transdermal targeting aims to reach the bloodstream and is attracting the attention of many pharmaceutical research teams working on diseases like cancer, psoriasis, alopecia, acne, inflammation. The drug is penetrated into the systemic circulation through the skin's blood vessels and then circulated throughout the body. The transdermal route has a number of benefits over other drug delivery methods: The risk and inconvenience of intravenous therapy are avoided by avoiding peak and trough serum levels. gastrointestinal degradation and first-pass hepatic metabolism (pH, enzymatic activity, and interactions with food, beverages, and other orally administered drugs),leads to enhance bioavailability of drug and its efficacy[14].This method has been utilised to administer a variety of medications, both hydrophilic and hydrophobic. Because of the advantages described above, pharmaceutical researchers are effective in designing and investigating transdermal drug delivery systems, specifically in changing or breaching the stratum corneum to promote drug absorption through the skin[15] .The new approach to enhace transdermal delivery with the help of niosomal vesicles.

FACTORS AFFECTING DRUG ABSORPTION THROUGH THE SKIN FOR TRANSDERMAL DELIVERY[15]:

- The volume of lipid in different layers of the skin at which the transdermal patch is put may affect the pace of medication absorption.

- The amount of capillary blood capillaries in different regions of the skin may have an impact on how quickly drugs are absorbed into the circulation.

- The presence of hair follicles and sweat ducts may help to an increased amount of drug permeating into the body as a result of transfollicular drug delivery.The vasodilation of skin capillaries and blood flow is affected by body temperature, which results in higher absorption rates.

- The degree of ionisation of a medication has a significant impact on its absorption via the skin.

- The melting point of the medication may also have an effect its skin penetration. Because a drug's solubility in the SC is greater when it shows low melting point, it has a higher chance of permeating the skin.

TOXICITY OF NIOSOMES:

Nonionic surfactants are less toxic and more biocompatible than their anionic, amphoteric, but cationic equivalents, and their toxicity is linked to niosomal components14.These properties are greatly reduced when the similar surfactants are available in the form of vesicular systems14.The toxicology of niosomes and the varieties of surfactants utilised have received little attention in the literature. A study of the toxicology effect of surfactant type of niosomal formulations on human keratocytes showed that ester type surfactants are less hazardous than ether type surfactants due to enzymatic destruction of ester boundaries. CxEOy surfactant toxicity on nasal mucosa and human kerationocytes using a ciliotoxicity model. The findings revealed that increasing the alkyl chain length of the surfactant lowers toxicity while increasing the polyoxyethylne chain length increases ciliotoxicity. As per the study results, ciliotoxicity is linked to the formation of a liquid state as polyoxyethylene chain length increases, whereas an increase in surfactant alkyl chain length leads to the formation of a gel, which is safer than a liquid state. The ability of niosomes to disrupt erythrocytes has recently been shown to be dependent on the length of the alkyl chain in the surfactant and the size of the colloidal aggregates in solution. Shorter carbon chains are thought to solubilize better into erythrocyte membranes, destroying their molecular organisation; niosomes have more difficulty interacting with biological membranes, resulting in significant hemolysis. Niosomes produced with bolaform surfactants showed promising safety and tolerability evidence in vitro in human keratinocytes and in vivo in human volunteers who were topically treated with a drug-free bolaformniosome formulation[16].

NIOSOMES AS TRANSDERMAL DRUG DELIVERY SYSTEM:

Niosomes were widely used in cosmetic industry for dermatological purpose in 1975. First patented niosomes in cosmetic brand was L'Oréal5. However recently, Transdermal medication delivery has been established utilising Niosomes[16]. When applying niosomes to the skin it is essential to know type of effect require is (dermal drug delivery) local effect within the skin or (Transdermal drug delivery) Systematic effect . Niosomes, when used topically, local effect is observed in epidermis and by increasing residence time they reduce systemic absorption of drug.For permeation of drug in stratum corneum retention time can act as rate limiting step.Using transdermal route it allows drug to avoid gastrointestinal degradation by not allowing drugs to pass hepatic first pass metabolism. Another advantage of using transdermal drug delivery is better patient compliance due to non invasive and large surface area . The major disadvantage is low penetration rate through skin. Only few number of

drugs show selective effect to cross the skin. Transfer of drug is a passive process it shows three routes transappendageal, intracellular and transcellular. Many methods are used to conquer barrier of stratum corneum which may lead to drug transport. This can be conquered improving the drug transport through skin by addition of penetration enhancers[5,14,16].

NIOSOMES AS PENETRATION ENHANCER:

Ideal properties of penetration enhancers:

- Nontoxic, nonirritating, and nonallergenic
- pharmacologically inert
- a quick onset of action; a predictable and the active substance's action should last a reasonable amount of time
- The CPE has a reversible influence on SC's barrier property.
- Compatible with both the delivery system chemically and physically
- Easily integrated into the distribution system
- Inexpensive and acceptable from a cosmetic perspective

Penetration enhancers may work through one or more of the lipid-protein partitioning mechanisms. theory: change the intercellular communication Corneocytes have a lipid structure between them ,as a result of which the diffusivity is increased; and intracellular protein domains can be altered within the horny layer, resulting in an increase in the drug's partitioning into the skin tissue12.As a result, appropriate penetration enhancers can enhance transdermal drug delivery by increasing drug diffusion coefficient in the SC, increasing drug concentration in the vehicle, enhancing partitioning between the drug formulation and the SC, and decreasing skin thickness, which is the significantly less likely. Niosomes have been extensively studied for transdermal drug delivery over the last decade, and they appear to be promising vehicles for active substances and skin layer targeting. Niosomes are gaining popularity in the domain of topical drug delivery due to their outstanding characteristics and the properties induced by their presence in a formulation, such as improved drug absorption, a local depot for long-term release of drug, and a rate-limiting barrier for controlling systemic drug administration via the skin14.

Chemical penetration enhancers:

Penetration enhancers can work in one of three ways.

1. Disruption of the stratum corneum's tightly packed lipid structure.

2. Interaction with a protein found outside the cell.

3. Improved drug, coenhancer, or solvent partitioning in the stratum corneum

Changing the polar route requires altering protein structure or causing solvent swelling. The fatty acid enhancers improved the fluidity of the lipid protein part of the stratum corneum. Some enhancers function on both polar and nonpolar pathways by changing the multilaminate pathway for penetration.Through skin proteins, enhancers can increase drug diffusivity[17].

MECHANISM OF ACTION OF NIOSOMES ON TRANSDERMAL DRUG DELIVERY :

There are several mechanism proposed by niosomes for transdermal drug delivery

1) Diffusion through stratum corneum layer:

Drug thermodynamic activity is increased because of encapsulated drug vesicles are adsorbed and fused to the skin's surface.Then a thermodynamic activity gradient is created, which increases the surface diffusion pressure for drug permeation, acting as a driving force for drug penetration across the stratum corneum (sc)

2) Water present in the skin structure plays very important role in mechanism Water in the skin structure plays a critical part in the mechanism. By preventing transepidermal water loss, which causes the stratum corneum's densely packed cellular structure to soften, the stratum corneum becomes more hydrated. This mechanism is more significant since the stratum corneum's lipid lamellar gaps have a smaller diameter than niosome vesicles.

3) Aggregation, fusion, and adhesion help lipophilic drugs cross the stratum corneum. On the skin's surface, niosomes adsorb and/or fuse, resulting in a large thermodynamic activity gradient at the drug's interface.Fusion of allows mixing of niosomes and cytoplasm.where as adsorption of niosomes on skin cells can occur as a result of attracting physical forces or as a result of ligands on the niosomal membrane binding to specific receptors on the cell surfaces, allowing the drug to be transferred directly from the vesicles to the skin.

4) The structure of the stratum corneum may be altered by niosomes, making the intercellular lipid barrier of the stratum corneum looser and more permeable.

5) The non-ionic surfactant that makes up niosomes works as a penetration enhancer, which could help boost drug penetration from niosomes. The type of surfactant utilised while using niosome vehicles to change permeability is critical[5,7,16].

NEW DEVELOPMENTS IN NIOSOMAL FORMULATIONS FOR TRANSDERMAL DRUG DELIVERY:

In a range of disease models, transdermal drug delivery from niosomes was being studied, and current efforts are focused on developing procedures, introducing new compositions, and final preparations. Elastic vesicles, a new category of highly flexible niosome, have been proposed and reported to be effective at delivering molecules through the skin, because edge activators (such as ethanol) give vesicles elastic properties, allowing them to penetrate deeper into the skin's layers more easily[14,18] .Besides this, the liquid nature of niosomes is a major drawback because when applied they may show leakage from the site of application.

This drawback can be conquered by introducing niosomes into an appropriate vehicle, which can be achieved by adding gelling agents to niosomal dispersions, resulting in a niosomal gel[14,19]. Niosomal gels have been encountered to improve therapeutic drug retention by the skin and to provide high and sustained drug concentrations in the skin[14,20].

El-Menshawe and Hussein's study is about meloxicam loaded into niosomes being delivered transdermally. When comparing animals treated with meloxicam vesicular gel to animals treated with free meloxicam, their findings showed that niosomes made from Span 60 and cholesterol had fewer side effects and a significant increase in edoema inhibition[14,21].

For topical use, Manosroi et al created novel elastic niosomes with entrapped diclofenac diethylammonium, an NSAID. Different bilayer vesicular formulations were formulatedusing dipalmitoylphosphatidylcholine, Tween 61, or Span 60 mixed with various molar ratios at 0%–25% (v/v) of cholesterol and ethanol. Elastic Tween 61 niosomes were chosen to entrap diclofenac diethylammonium because they offered advanced physicochemical characteristics, including no sedimentation, layer separation, or particle size change.The drug was entangled with 65 percent and 93 percent efficiency in conventional and elastic Tween 61 niosomes, respectively. The flux of diclofenac diethylammonium in the skin of the gel containing these elastic niosomes was relatively high than that of the commercial Emulgel product, whichincorporates an equivalent amount of drug[14,22].

Another NSAID encapsulated in niosomes is rofecoxib.. In the study by Das and Palei, niosomes were integrated into a topical gel base for long-term therapeutic effect. Various sorbitan esters like (Span 20, Span 40, and Span 60) and cholesterol were used to make the vesicles. These

niosomes can be utilized as drug delivery carriers for rofecoxib delivery to the skin, according to the findings. The niosomal gel provided for a prolonged release of the medication, which allowed rofecoxib to maintain its action while reducing side effects[14,23].

To enhance the low skin permeation and poor bioavailability of conventional topical formulations containing baclofen, a centrally acting muscle relaxant, niosomes were loaded with the drug.The lipid film hydration method was used to make vesicles using a varied molar ratios of nonionic surfactant and cholesterol. The need for niosomal formulations to transport baclofen resulted in improved muscle relaxant activity[14,24].

Papain is a protease enzyme derived from Carica papaya latex that is commonly used in dermatology to heal scars. Manosroi et al. evaluated the transdermal release of papain from gel formulations incorporating niosomes or nanospheres. They found that niosomes (particularly elastic niosomes created from Tween 61/cholesterol with sodium cholate as an edge initiator) might improve papain transdermal absorption via rat skin and scar reduction in a rabbit ear model, suggesting that they could be useful in the development of topical scar treatments[14, 25].

Nifedipine act as a calcium channel blocker that is commonly used to treat angina and high blood pressure. It requires frequent first-pass metabolism after oral administration, limiting both the amount of drug absorbed in the GIT and the drug's bioavailability in the systemic circulation. Yasam et al presented the transdermal route as a novel means of nifedipine delivery. In this study, proniosomes were made by modifying the ratios of Span 40, lecithin, aqueous phase, and polymer. The role of niosomes as permeation enhancers was identified in ex vivo percutaneous permeation studies in rat skin. Result showed that nepfedipine is nt irritant and do not causes erythema[14, 26].

RECENT APPLICATION OF NIOSOMES AS TRANSDERMAL DRUG DELIVERY SYSTEM :

Niosomes were created and patented for the dermatological purposes in 1975, and many products depend on this technology have since appeared on the market, including Lancome Noisome Plus as an anti-ageing formulation. The usage of niosomes for transdermal drug delivery has recently been developed. Current efforts to prove the superiority of niosomes as a topical carrier, with a focus on clinical application, were reviewed in this paper.

A) Local anesthesia :

Topical anaesthetics are utilized by dermatologists to relieve pain before cutaneous procedures, pain caused with laser pulses, and soft tissue augmentation. Ineffective local anaesthetic formulations resulted in severe dermatitis, systemic toxicity, and other complications. or insufficient local analgesia. Local anaesthetics are used to create numbness through topical preparation. Because drug penetration through the skin is low, niosomes act as a carrier to improve drug penetration by encasing them in vesicles that can easily pass through the skin. When compared to liposomes, lidocane hydrochloride, a local anaesthetic prepared by niosomes (lidocane entrapped with tween20 and cholesterol), performed better[16,27].

B) Psoriasis:

Psoriasis is an autoimmune disorder of the skin (like the epidermis and dermis) caused by T-lymphocytes. It is characterised by leukocyte infiltration and localised deregulated skin growth, resulting in scaling erythematous plaques. Regardless of whether that psoriasis is rarely life-threatening, it causes patients to lose their confidence and suffer from itching, painful, and disfiguring skin lesions. Regardless of the fact that topical formulations based on conventional excipients have some drawbacks that limit their use in therapy, topical therapy is the most commonly used in patients. The usage of niosomes as a delivery mechanism for topical drugs, the potential to improve topical product efficacy and safety has vastly improved. Anthralin, Methotrexate, Corticosteroids, Vit-D3, coal tar, and Tacrolimus are some of the drugs used topically to treat psoriasis. Methotrexate is an anti-cancer drug utilized in treatment of psoriasis that has several side effects, one of which is hepatotoxicity, when taken systemically. As a result, topical application as an alternative to reduce the negative effects can be chosen. After 12 weeks, the lesion on the niosomalchitosin Methotrexate gel has shrunk by three times. As a

result , niosomal Methotrexate gel can be applied to use in topical treatment of psoriasis[16,28].

C) Hyperpigmentation:

Noisomal preparation can help with hyperpigmentation disorders. N-acetyl glucosamine is a niosomal preparation used to treat hyperpigmentation because it's capable of delivering all hydrophilic and hydrophobic medicines topically, as well as inhibiting thyrosine enzymes in melanocytes, which helps to treat hyperpigmentation[16].

D) Acne:

Acne is the most often occurring multifactorial skin disease, having a high frequency of 70 to 80 percent in adolescence. While topical therapy plays a major role in acne treatment, the efficacy and patient satisfaction of several topical antiacne agents are harmed by side effects. Because of their efficient dermal drug delivery, niosomes is added in topical preparations[29].When combined with other factors anti-acne agents, benzylperoxide, a synthetic drug-macrolide antibiotic, was used to treat acne. Benzyl's negative effects.When peroxide is utilized as a dermal delivery system, it causes itching and skin irritation. Irritation, redness Benzyl peroxide incorporated into niosomal .The activity of an HPMC gel was tested for its ability to attract bacteria in the treatment of acne. With improved drug permeation, the results showed good drug skin retention, extended release, and reduced drug toxicity[16, 30].

E)Vitiligo:

Vitiligo is a dermatological illness characterised by well-circumscribed milky white macules generated by damaged melanocytes with in skin. Regardless of the fact that vitiligo can't be a life-threatening disorder, it can have a significant negative impact on one's quality of life, in rare situations, this has resulted in attempted suicide[16, 31, 32]. Because the usability and patient compliance of traditional topical dose forms are harmed by side effects or low efficacy, innovative dermal drug delivery systems can play an important part in vitiligo treatment. Tyrosinase, an enzyme implicated in melanogenesis, from human tyrosinase gene. Depigmented skin, also known as vitiligo, can be caused by a tyrosinase gene mutation[33, 34].

F) Hair Loss - Alopecia:

The biochemistry, metabolism, and immunology of the pilosebaceous unit, which includes the sebaceous gland, hair follicle, and hair shaft, is unique. Targeted medication delivery could help current therapeutic techniques to address follicular disorders. In an increasing number of topical trials, niosomes have been found to target drug delivery towards the pilosebaceous unit.

Minoxidil-loaded niosomes with varied surfactant and cholesterol molar ratios were recently generated using the ethanol injection method. The data suggest that raising cholesterol levels in niosome vesicles improves minoxidil skin retention and has an impact on entrapment efficiency and niosome size, resulting in better cutaneous therapy.The developed niosomal formulation was discovered to be a viable solution for cutaneous application minoxidil targeting[35].

CONCLUSION:

The transdermal drug delivery system was considered to be an an efficient method solve the problems associated with traditional oral dosage forms, such as poor bioavailability, high dosing frequency, and untargeted drug action. Niosomes are promising controlled delivery systems for all hydrophilic and lipophilic drugs. Their use as percutaneous permeation enhancers, and their more recent applications as drug delivery systems for transdermal drug targeting. In recent years, more research has led in development of niosomes and proniosomes, a new versatile non-ionic surfactant-based vesicular approach for efficient drug delivery through the skin. This review provides a quick overview of their role as a percutaneous permeation enhancer, and advantages, disadvantages,toxicity mechanism and their most recent applications in transdermal drug delivery. It demonstrates a promising method for delivering the drug in a controlled and long-term manner. There are no special handling or storage requirements for these. Because the various type of surfactant is the most crucial consideration affecting the formation of vesicles, their toxicity, and their stability, researchers should be more cautious when selecting a suitable surfactant for noisome preparation.

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