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NANO ETHOSOMES: A PROMISING TECHNIQUE FOR TRANSDERMAL DELIVERY

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ABSTRACT

Using transdermal drug delivery routes offers a beneficial method of drug administration that patients find easy to use. The stratum corneum creates a natural barrier to skin which hinders multiple drug molecules from penetrating adequately. Scientific research teams generated different Nano carriers to improve drug penetration across the skin membranes. The pharmaceutical industry has adopted nano ethosomes as an innovative treatment delivery technique to boost drug absorption through the skin. Ethosomes function as a recognized nano carrier vesicles combine lipid foundations with both hydrophilic and lipophilic pharmaceutical elements which penetrate them through the skin barriers. Ethosomes combine phospholipids ethanol and water components which maintain high flexibility that allows them to pass through the tight junctions of stratum corneum. This abstract examines Ethosome characteristics which cover their components and preparation techniques alongside their operating mechanisms and identification variables and future potential uses. The review explores how Ethosomes have been used for delivering therapeutic agents including analgesics, anti-inflammatories, anti-depressants as well as hormones and skincare products. Ethosomes offer superior skin penetration while reducing systemic side effects so patients become more compliant which establishes them as beneficial elements for transdermal drug delivery methods. Mathematical expressions indicate that Ethosomes offer great potential to resolve transdermal delivery problems. Their distinctive characteristics allow skin drugs to pass efficiently through the skin barrier which creates a more controlled shipping system for multiple pharmaceutical and cosmetic substances. The abstract demonstrates the value of Ethosomes for transdermal drug delivery while creating new research possibilities focused on improving this approach.

INTRODUCTION

Persistent sadness and a loss of interest and pleasure are hallmarks of depression, a common mental illness. It is a mental illness marked by functional impairment and a melancholy or hedonistic mood that lasts for at least two weeks. Because of genetic, endocrine, and psychological factors, its frequency is 6.6% every year and 16.2% over the course of a lifetime. There is clinical and etiological variation in depressive illnesses, which are very common.[1] They originate from a variety of routes that change as a person develops and intersect with various physical and mental illnesses. Females are far more likely to have it, especially in adolescence and early adulthood. These illnesses are associated with a variety of biological and psychological abnormalities and

are greatly influenced by both genetic and environmental factors. There are treatments, but they are frequently only moderately successful, which emphasizes the need for greater prevention research and more potent treatments. More than 20% of people worldwide suffer from depression, which is a major cause of disability. Mood swings, diminished enjoyment, trouble focusing, poor energy, sleep issues, guilt feelings, and suicidal thoughts are some of its symptoms.[2] Although the precise mechanisms underlying depression are still unknown, a number of theories have been put out, including inflammatory, monoamine, GABAnergic, glucocorticoid, and neurotropic theories. Finding possible pharmacological targets for successful antidepressant treatments requires an understanding of these theories. Exercise, meditation, suggestion, and joy are the four therapeutic facets of prayer therapy that work together to help people overcome obstacles in life and promote mental health. The ultimate objective is to use the power of prayer to help people with depression become happy, healthy people.[3] Depression is often worsened by comorbid conditions. A well-researched and successful treatment for depression, cognitive-behavioral therapy (CBT) helps roughly two-thirds of patients. The effectiveness of acceptance and commitment therapy (ACT), which emphasizes psychological flexibility through six interconnected stages, is also becoming more widely acknowledged. The difficulties in identifying and treating depression can be addressed with the aid of a trans diagnostic viewpoint.

Despite the progress made in treating depression with serotonin and norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs), many therapeutic needs regarding side effects and efficacy remain unmet. These requirements include improved onset, less adverse effects such emesis or sexual dysfunction, and effectiveness in treating patients who are resistant to treatment. Numerous combination therapies and novel targets that may show improvements in one or more categories have been identified to meet these needs.[4] The kinds of goals and strategies being pursued are incredibly varied. Antidepressant medications in conventional dosage forms have poor absorption and side effects such hyperprolactinemia, orthostatic hypotension, and muscle tremor. Nanostructured lipid carriers (NLCs) ethosomes are intended to enhance bioavailability by means of transdermal drug delivery, hence circumventing the drawbacks of traditional dosage forms.

Need for Transdermal Drug Delivery: Notwithstanding the difficulties, Transdermal drug delivery has a number of special benefits, including as a sizable and easily accessible surface area for absorption, simplicity in application, and ease of therapy cessation. Additionally, the development of safer penetration enhancers, vesicular carriers, and improved drug delivery technologies has rekindled interest in creating transdermal drug delivery systems for medications previously believed to be unsuitable for transdermal delivery.[5]

In recent years, there has been a growing interest in using lipid vesicles as drug delivery vehicles for skin care. It is widely acknowledged, therefore, that traditional liposomes are not very useful for this. Liposomes are appropriate for topical medication distribution since they are restricted to the stratum corneum's (SC) outermost layer. It has been demonstrated that only specialized vesicles can transport medications through the layers of the skin. Topical drug delivery using liposomal formulations has generated a lot of interest in recent decades. However, it has become clear that liposomes are not very useful as a vehicle for transdermal drug delivery because they only penetrate the top layer of the stratum corneum and do not penetrate deeply into the skin.[6] Two new vesicular systems, transferosomes and ethosomes, were recently introduced to address the issue of poor skin permeability. They combine edge activators, such as surfactants, and penetration enhancers, such as alcohols and polyols, respectively, to affect the properties of three vesicles and the stratum corneum.

Soft, pliable vesicles, ethosomes are primarily made of water, phospholipid, and ethanol in relatively high concentrations. A new vesicular carrier for improved distribution to and through the skin is represented by these soft vesicles. Ethosome vesicles have a size range of tens of microns to nanometers.[7] Because of its great deformability, this carrier exhibits intriguing characteristics relating to its capacity to pass through human skin intact. Since ethanol is known to disrupt the architecture of lipid bilayers, the ethosomes' high ethanol content makes them special. When incorporated into a vesicle membrane, ethanol allows the vesicle to pass through the stratum corneum. Lipid membranes are less densely packed than traditional vesicles

due to their high ethanol content. However, they are just as stable, allowing for a more flexible structure and better medication dispersion in stratum corneum lipid. Ethosomes have been demonstrated to improve penetration through the stratum corneum barrier in contrast to traditional liposomes, which carried drugs to the outer layers of the skin.[8]

Ethosomes have been shown in numerous papers to be effective in delivering transdermal agents. Additionally, it gives medium and widespread molecules a respectable amount of open space for dispersal. The ethosome can be measured in accordance with contemporary dimensions and is easy to prepare without the need of complicated materials. In the formulation and diagnosis, these vesicular frameworks are thought to be deep archives for supplying lipophilic molecules that differ from and pass through in vitro skin and in vivo. The concentration of pharmaceuticals in the region of action, which is determined by the dosage form and the degree of drug absorption in the area, determines the pharmacological responses, including both positive therapeutic efficacy and antagonistic effects of the drug.[9]

The most popular mode of administration is still transdermal drug delivery. In any case, the stratum corneum forms the primary barrier that prevents medication from penetrating all the way through the skin; therefore, the use of lipid vesicles that resemble ethosomes in delivery systems has recently drawn more attention. The type of liposomes with higher ethanol content was altered by ethosomes. Water, ethanol, and phospholipids make up ethosomes. They have the ability to penetrate the skin and enhance the distribution of chemicals to the deep skin and system. In addition to bilayers of the stratum corneum intercellular lipid, this ethanol fluidizes mutually ethosomal lipids. At that point, the soft, delicate vesicles penetrate the lipid bilayers that are dispersed.[10]

Advantages over Liposomes: Ethosomes are a promising strategy for enhancing medication administration via the skin, and their notable benefits have drawn a lot of attention in recent years. The advantages of ethosomes as drug delivery vehicles for local distribution over traditional liposomes and hyper flexible liposomes have been well-documented by numerous analyses over the last era, which take into consideration the following:[11]

- Ethosomal systems were found to be superior in delivering drugs and fluorescent probe over the skin in terms of both extent and deepness when compared to liposomes and hydroalcoholic solution.
- Ethosomes were found to transmit active agents more meritoriously via the stratum corneum into deeper strata of the skin and subsequently retain them in the skin layers.
- Ethosomes were found to be more barrier-compatible than ultraflexible liposomes containing bilayer fluidizing agents like sodium cholate.
- Ethamomes have the ability to transport medications through the SC into deeper skin layers and even into the bloodstream more efficiently than liposomes.
- Unlike liposomes or the ethanolic drug solution, ethersomes are designed to increase the transdermal perviousness of the loaded drug.

Merits of Liposomes

- In contrast to the obstacles related to iontophoresis and phonophoresis, ethersomes are easy to use and safe for the skin.
- They also provide excellent patient compliance because they may be prepared in semisolid dose forms (gel or cream).
- Because the toxicological description of ethosomal constituents is well-established in scientific literature, the ethosomal system does not pose an excessive risk for drug development.
- It has been demonstrated that the ethosomal vector can increase the intracellular delivery of molecules with lipid and water affinity as well as increase the penetration of an antibiotic peptide.[12]

Demerits of Liposomes

- Since ethosomal formulation is intended for gradual and prolonged drug administration, input through bolus type cannot be accomplished.
- The drug's molecular size should be appropriate for transdermal administration.
- Adhesives might not work well on every skin type.
- Pricey
- The yield will be quite low.

- The use of permeation enhancers and other excipients to improve medication distribution may increase the risk of dermatitis or skin irritation.
- Wastage of products during the conversion of organic media to aqueous media

Methods of Preparation of Ethosomes

Hot method

Phospholipids and water at 40°C receive the drug solution made from ethanol and propylene glycol through hot method preparation. A five-minute mixture period leads to three cycles of five-minute sonication at 4 °C using the Probe Sonicator between which the preparation rests for five minutes. The pressure inside the high pressure homogenizer reaches 15,000 psi for three consecutive cycles to generate nano-sized ethosomes from the formulation.

Cold method

The cold method stands as the predominant and most common technique available for making ethosomes as drug delivery vehicles. Phospholipids and drug substances together with other lipid materials dissolve in ethanol before vigorous stirring takes place at room temperature inside a covered vessel. The mixture receives heat from 30°C water bath for the temperature treatment. The prepared mixture receives water at 30°C in a different vessel before being added to the stirring solution in five minutes under covered conditions. Decreasing the vesicle size in ethosomal formulations requires both sonication or extrusion methods. Proper storage needs to occur in refrigeration conditions for the formulation.[13]

Classical Dispersion Method

The Classical Dispersion Method dissolves Soya phosphotidylcholine through the combination of chloroform: methanol (3:1) within a round bottom flask. Lipid transition temperature directs the removal of organic solvents from the flask using rotary vacuum evaporator to create a thin lipid film on the flask wall. A final step includes drying the deposited lipid film by keeping it under vaccum overnight for removing traces of solvent mixture. The flask hydration process uses different drug solutions of increasing hydro ethanol concentration while rotating at appropriate temperatures.[14]

The Thin-Film Hydration Method

The thin film hydration method serves to produce liposomes through the use of hydroethanolic solution for hydrating the lipid film. An empty clean dry round-bottom flask receives the phospholipid dissolved either in pure chloroform or in 3:1 or 2:1 chloroform to methanol mixtures. The rotary vacuum evaporator eliminates organic solvents during procedures that take place above the lipid's transition temperature. After vacuum extraction the remaining solvent molecules disappear fully from the lipid film throughout an overnight period. During hydration the lipid film absorbs either water–ethanol solution or phosphate buffer solution combined with ethanol. An appropriate temperature for heating the lipid film during hydration is determined by its phospholipid properties while film rotation happens at specific intervals of 30 minutes, 1 hour, or 6 hours.[15]

The Reverse-Phase Evaporation Method

The reverse phase evaporation method serves as an uncommon technique to produce unilamellar vesicles that stand above other methods in scale. To create the water-in-oil emulsion diethyl ether solution containing phospholipids requires combination with aqueous solution at 3:1 volume ratios while bathed ultrasonically at 0°C for 5 minutes. The reduced pressure treatment of solvent allows the gel formation while vigorous mechanical shaking transforms the gel into a colloidal dispersion.[16]

Trans membrane pH-Gradient Method

In all the methods just mentioned, the drug is added in either the organic or the aqueous phase, and it is spontaneously or “passively” loaded in the ethosomal system. In the transmembrane pH-gradient method, the drug is loaded “actively”, based on the pH-gradient difference between the acidic interior of the internal phase and the basic exterior of the external phase of the ethosomal system. The concept of this method was first applied in the preparation of liposomes, then it was used by Zhou et al and Fan et al in the preparation of ethosomal systems of total alkaloid extracts of *S. alopecuroides* and tetrandrine, respectively. The method is suitable only for water-soluble drugs that have protonizable amine functions.[17] This method involves three stages: preparation of the blank ethosomal system, active loading of the drug, and incubation (Last stage). In the first stage, the empty ethosomal suspension is prepared using any of the aforementioned methods, but the aqueous phase or the hydration process uses an acidic buffer

(usually citrate buffer, pH 3). The second stage involves the active loading of the drug into the empty ethosomal suspension, followed by continuous stirring. In order to make the external phase more alkaline and to establish the pH gradient between the acidic internal (pH 3) and basic external phases of the ethosomal system, an alkali, usually a sodium hydroxide solution of 0.5 M, is added to make the external pH 7.4.[18] In the third stage, the ethosomal system is incubated at a specified time and temperature (30°C–60°C) to give the opportunity for the unionized drug to actively pass the bilayer of the ethosomal vesicles and get entrapped. Before preparation of ethosomal systems using this method, some factors need to be taken into consideration, such as the physiochemical properties of the drug/agent to be incorporated, the pH of the internal and external phases, and the temperature and the duration of the incubation period. The different steps of ethosomal preparation using this method are illustrated.[19]

Characterization of ethosomes

Vesicle shape

The ethosomal vesicles' surface morphology is examined using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Mount the ethosomes onto double-sided tape that has been previously fastened to copper stubs and coated with platinum before doing an analysis at various magnifications.

Vesicle size and Zeta potential

Photon correlation spectroscopy (PCS) and dynamic light scattering (DLS) using a computerized inspection system are the two techniques used to evaluate the zeta potential and particle size of manufactured ethosomes.

Entrapment Efficiency

The most popular method for determining an ethosome's entrapment efficiency is ultracentrifugation. In a high-speed cooling centrifuge, the vesicles are separated for 90 minutes at 20,000 rpm while being kept at 4°C. Determine the amount of drug in the sediment by lysing the vesicles with methanol and separating the sediment and supernatant liquids.

Use the following formula to calculate the entrapment efficiency based on this:

$$\text{Efficiency of entrapment} = DE / DT \times 100$$

where DE stands for the drug's amount in the ethosomal sediment. DT stands for the theoretical amount of drug utilized to make the formulation, which is equal to the amount of drug in the sediment and the liquid supernatant.

Penetration and Permeation Studies

The method of confocal laser scanning microscopy (CLSM) is employed to ascertain the extent of ethersome penetration. Since ethosomes provide a method of dermal and transdermal distribution, they exhibit noticeably greater skin deposition, which may be caused by the combined action of ethanol and phospholipid.

Transition Temperature

Vesicular lipids' transition temperature (T) is measured twice using DSC in an aluminum pan with a steady nitrogen stream and a heating rate of 10°C per minute.

Surface Tension Measurement

It makes use of the Du Nouy ring tensiometer. To determine a drug's surface tension activity in an aqueous solution, the ring approach is utilized.

Vesicle Stability

Ethosomal preparations can be evaluated for drug-retentive behavior by storing them at various temperatures, such as 25 ± 2°C (room temperature, RT), 37 ± 2°C, and 45 ± 2°C, for varying lengths of time (1, 20, 40, 60, 80, and 120 days). Following nitro-gen flushing, the ethosomal preparations were stored in sealed vials with a 10 ml volume. Using DLS and TEM to track the vesicles' size and shape allowed for a quantitative assessment of the stability of ethosomes.[20]

Drug Content

A modified high performance liquid chromatographic method can be used to quantify the drug.

APPLICATIONS OF ETHOSOMES FOR DEEP DERMAL AND TRANSDERMAL DELIVERY

In vivo studies: The ethosomal carrier's ability to deliver diverse compounds with distinct physicochemical properties into the deep layers of the skin or throughout the skin has been extensively investigated. This article examines research done in clinical trials or animal models.

Treatment of Microbial and Viral Skin Infections: Numerous skin illnesses have been studied using ethosomal systems that

incorporate antibiotic medications. The effectiveness of bacitracin and erythromycin ethosomal systems was developed and evaluated in animal models of deep skin infections. When S. aureus was injected intradermally into immunocompetent ICR male mice, the pharmacodynamic effect of the tested topical therapies was assessed by isolating S. aureus colonies from the skin wounds seven and ten days after the experiment started. The ethosomal erythromycin system-treated mice had no S. aureus bacteria in the inoculation sites, as contrasted to the untreated mice's 090 × 107 and 057 × 107 cfu/g tissue on days 7 and 10, respectively. Additionally, no dermatonecroses and the preservation of normal skin structures were seen in the histological analysis of the injured skin tissue on days 7 and 10 after the treatment. Inspection of the injured regions in mice that were not treated and mice who received erythromycin hydroethanolic solution, on the other hand, revealed that the infection had progressed, leading to a substantial dermatonecrosis of the skin and surrounding tissues as well as the first crust forming over the necrotic area. These findings suggest that the erythromycin ethosomal system effectively eliminates the bacteria at the inoculation site in the deep layers of the skin. Therefore, topical use of antibiotic ethosomal system may be a good substitute for systemic injection of the drug in the treatment of deep skin infections.

A pilot clinical research was conducted to investigate an additional antibiotic-containing ethosomal system. The effectiveness of a novel clindamycin ethosomal gel (CLSA) for the treatment of mild to moderate acne vulgaris was examined in this study, which involved forty patients. In ethosomes, CLSA comprises a combination of salicylic acid and clindamycin phosphate. When compared to a placebo, the acneic condition dramatically improved after eight weeks of twice-daily CLSA gel treatment, which significantly reduced the amount of comedones, pustules, and lesions overall. Seventy-one percent of participants said that their condition had improved; no worsening was reported. In addition, 14 out of 17 participants who had previously received topical treatment favored the clindamycin ethosomal gel above previous commercial topical treatments due to its better tolerability and fewer adverse effects

For the treatment of Herpes labialis, another skin infection, an ethosomal system containing the synthetic acyclic nucleoside analog acyclovir (ACV) was created and evaluated. 20 The effectiveness of an ethosomal formulation, a commercial acyclovir cream (Zovirax®, GlaxoSmithKline S.p.A.), and a solution of the free medication was compared in forty patients who experienced 61 assessable episodes in this randomized double-blind clinical research. Thirty-one participants in the parallel arm received ethosomal acyclovir (EA), ten Zovirax® creams (ZC), and nine vehicle (V). Eight participants received EA followed by ZC in the crossover arm, while seven people received ZC followed by EA.This study measured the amount of time (in days) till crust formation, the amount of time (in days) until crust loss, the percentage of abortive lesions among all assessable lesions, the amount of time (in days) until the reported pain intensity was reduced for the first time, the amount of time (in days) until the pain was completely resolved, and the percentage of lesions where the reported pain intensity decreased from day 1 to day 2 and from day 1 to day 3. All of the assessed clinical metrics significantly improved with the use of the ethosomal acyclovir system. When compared to Zovirax cream, 80% of lesions crusted in the parallel arm on the third day following the onset of the herpes outbreak following ethosomal drug system treatment, compared to 10% in the Zovirax group. The EA group took 1.6 days to develop crust, while the ZC and V groups took 4.3 and 4.8 days, respectively. Furthermore, compared to just 10% in the ZC group, 33% of the lesions in the EA group were abortive. On day 2, the EA group's days to crust loss in the crossover arm dropped dramatically from 4.2 to 5.9 compared to the ZC group. Only 15% of the lesions treated with ZC crusted, compared to 60% of the lesions in the EA group.20 A new topical acyclovir cream called Supra-Vir was released as a result of the clinical study's findings, which showed that ethosomal acyclovir was more clinically effective than ZC.

Anti-Inflammatory Ethosomal Systems: Paolino and associates examined the efficacy of ammonium glycyrrhizinate (AG) ethosome in treating inflammatory skin conditions on human volunteers who have erythema caused by the drug methyl-nicotinate. Using a reflectance visible spectrophotometer, which is used to quantify the erythema index (EI), the anti-inflammatory impact of the ethosomal AG system after either pre-treatment or therapy of skin erythema was compared to aqueous or hydroethanolic medication solutions. In comparison to the other formulations, the results demonstrated that AG ethosomes significantly

decreased the severity and duration of erythema. Sites treated with AG ethosomes three hours after topical treatment did not exhibit any erythema, however sites treated with the drug's aqueous or hydroethanolic solutions did exhibit chemically induced erythema.Notably, an investigation into the potential impact of empty ethosomes revealed no anti-inflammatory properties. Erythema index decreased after the skin was pre-treated with the ethosomal AG system for 1, 3, and 5 hours, suggesting that the system was successful in counteracting the emergence of erythema. The greatest impact was seen after five hours of system pre-treatment.

Ethosomal methods have been studied for transdermal delivery of anti-inflammatory medications in addition to deep skin administration. A novel medication possibility for the treatment of rheumatic disorders is cannabidiol (CBD), a highly lipophilic chemical. By measuring the amount of medication accumulated in the skin and other body organs, the CBD ethosomal system was created and tested for in vivo skin penetration.21 The substance was found to have significantly accumulated in the skin and underlying tissue, according to the results. Following a 24-hour treatment period, CBD was found in the hip muscle, liver, and pancreas, as well as in the hip skin (3743± 13.58 g/cm2), abdominal skin (11007± 24.15 g/cm2), and abdominal muscle (11.537 g CBD/g muscle).

Drug plasma concentrations measured during 72-h system application in ICR mice indicated that steady state levels of the drug were achieved after 24 h and lasted until the end of the experiment 72 h. 43.33% of the initial drug's dose penetrated the skin into systemic circulation. Furthermore, the anti-inflammatory effect of ethosomal CBD system applied topically 19 h before the carrageenan injection completely prevented the development of the edema, as evaluated in carrageenan-induced aseptic paw edema in male ICR mice by hourly measurements of paw thickness for up to 4 h

Ethosomal Systems for Menopausal Syndromes: Ethosomal compositions have been tested for their efficiency in the treatment of androgen deficiency associated with menopause in men and menopausal syndromes in women. A testosterone ethosomal patch system, Testosome, was designed for the treatment of androgen deficiency in men.3 An in vivo study, comparing testosterone serum levels in rabbits, following single or multiple (once a day for five days) application from either Testosome or Testoderm® patch (Alza) was carried out. Results of single patch application showed no significant differences between the tested groups. However, following daily application of the patches to rabbit pinna skin for 5 consecutive days, the AUC and When compared to Testoderm, the Cmax values for Testosome were 2.2 and 2.4 times greater.

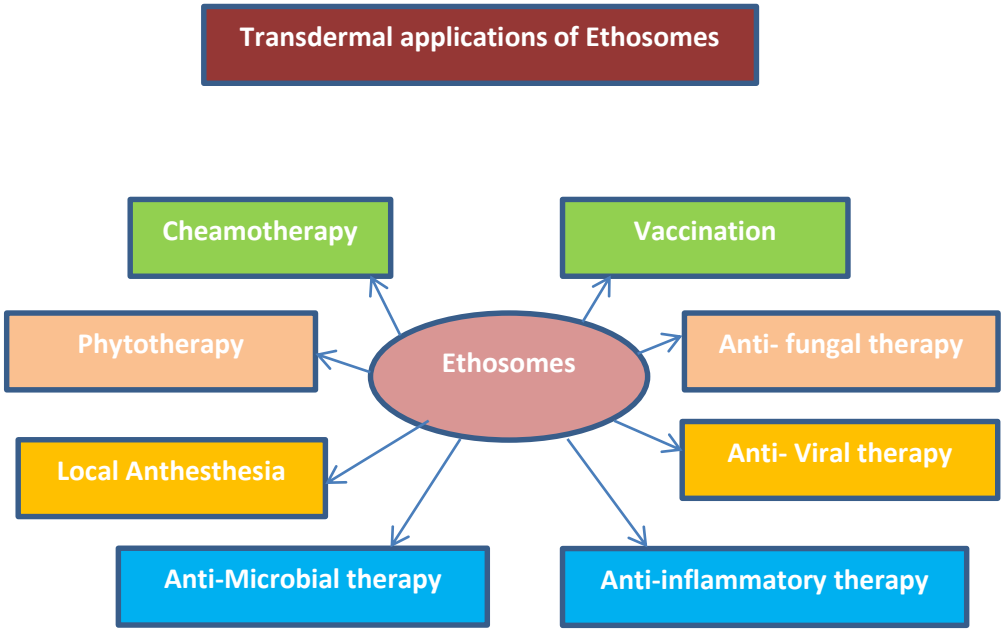
Management of Erectile Dysfunction: In a "in-office" pilot clinical investigation, ethosomal prostaglandin E1 systems were applied to the glans penis of 16 males who had experienced 17 episodes of erectile dysfunction. A doctor assessed the patients' erection and asked them to score their erectile response to gauge their capacity for sexual activity. 15 minutes after the application, the cavernous arteries were subjected to a duplex examination to measure the pulsative index (PI) and peak systolic velocity (PSV) of the left and right cavernous arteries. The length of time the erection lasted was noted. The study's findings demonstrated that 12 out of 15 males examined had better peak systolic velocity and increased penile stiffness after a single topical administration of the PGE1 ethosomal system. After applying the empty ethosomal vehicle, there were no alterations in penile blood flow or erectile response seen. The erection lasted anywhere from 10 to 60 minutes. Notably, none of the participants in either of the study groups have reported experiencing penile erythema or any other negative side effects. This pilot study's findings suggest that topical administration of prostaglandin E1 (PGE1 ethosomal systems) may be a viable local therapeutic strategy for erectile dysfunction.

Analgesic and Antipyretic Ethosomal Systems: A recent study used two animal models—tail flick nociception mice and Brewer's yeast-induced fever rats—to examine the in vivo analgesic and antipyretic therapeutic benefits of transdermal ethosomal ibuprofen. When ibuprofen gel was applied to the animal's skin, the fevered rats' body temperature gradually dropped. By using the tail flick test on mice, the analgesic effects of ethosomal ibuprofen gel and oral therapy were contrasted. At 120 and 360 minutes following treatment, the ethosomal ibuprofen method produced a statistically significant greater impact. The effect lasted for at least six hours. The information gathered for this study indicates that the antipyretic and analgesic properties of the ethosomal ibuprofen gel can be

further studied in people. Transdermal delivery may also be helpful for pediatric patients who frequently refuse to take the entire dosage of the medication or experience vomiting, in addition to providing a convenient and effective treatment with continuous drug input to the systemic circulation and preventing potential gastrointestinal ulceration and bleeding.

Ethosomes for Parkinsonism disease: A cationic anti-M1 muscarinic medication called trihexphenidyl (THP) is used to treat Parkinson's disease. Over 2 percent of the elderly population suffers from Parkinsonism. THP is taken orally three to four times a day and has a brief half-life of three hours. For elderly patients with Parkinsonism who have trouble swallowing oral medications due to neurological symptoms and motor abnormalities, this oral route is not recommended. One appealing way to get around the issues with oral delivery of THP is by topical administration. SC is a lipophilic barrier that prevents ionic molecules from entering. Therefore, ethosomes were created and described in order to make transdermal distribution of THP effective. THP ethosomes had a high drug entrapment efficiency of 75 ± 0.5% and were tiny (109 ± 2 nm). When THP ethosomes were administered transdermally to and via the dorsal skin of naked mice, the flow of THP from ethosomes was 51 times higher than that of liposomes. The quantity of medication that has collected on the skin was also greater for ethosomes than liposomes following 18-hour testing. Additionally, it was discovered that the THP ethosomes remained stable for over two years.

Ethosomes for vaginal delivery: In order to deliver the antifungal medication metronidazole vaginally, PH-responsive ethosomes were developed and tested. The Franz diffusion cell, a semi-permeable membrane made of regenerated cellulose, and a medium of phosphate buffer pH 5.5 were used for the in vitro permeation investigation. According to the study, metronidazole may be delivered continuously via the ethosomal gel at a maximum flow of 143.67 ± 2.73 mg/cm^2



Stability of Ethosomes

Ethosomes are colloidal dispersions that exhibit both optical characteristics and storage-related cracking and creaming behaviors. Ethamomes' phospholipid contents are vulnerable to oxidation and hydrolysis, which compromises their stability. The optical characteristics of colloids on long-term stability investigations are measured by the new optical analyzer Turbiscan LabVR Expert. In addition to providing information on the type of destabilization process occurring, this technique may distinguish between stability issues caused by coalescences, sedimentation, or creaming.() This nondestructive technique quantifies the change in mean size (coalescence) or droplet volume fraction (migration) upon instability, which causes changes in transmission and backscattering signals over time. An unstable formulation is indicated by variations in the graphical scale of backscattering more than ±10%. Ethamomes with varying concentrations of linoleic acid have been studied for long-term stability using the Turbiscan optical analyzer. The findings revealed neither sedimentation, flocculation, coalescence, or clarity, nor any change in the colloidal suspension's backscattering profile. It was discovered that ethosomal formulations of minoxidil, testosterone, and trihexphenidyl HCl were stable for two years. However, it was discovered that an ethosomal gel containing erythromycin was only stable for a year. 5-fluorouracil transethosomal gel was shown to be stable for two months when stored under accelerated circumstances and for eleven months when kept at room temperature. While small unilamellar vesicles exhibited aggregation as a result of their increased surface area being exposed to the medium, multilamellar and large unilamellar ethosomal vesicles loaded with benzocaine remained stable over time in terms of entrapment yield and particle dimensions. Since few investigations were carried out for longer than a year, it is necessary to assess the ethosomal systems' long-term stability.

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