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ADVANCES IN NIOSOME AS A DRUG CARRIER: A REVIEW

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ABSTRACT

In recent years a comprehensive research carried over niosome as a drug carriers. Various drugs are enlisted and tried in niosome surfactant vesicles. Niosomes proved to be a promising drug carrier and has potential to reduce the side effects of drugs and increased therapeutic effectiveness in various diseases. As of today more than fifty drugs are tried in niosomal formulations by intravenous route, per oral administration, transdermal route of administration, and inhalation preparation, ocular & nasal route of administration.

INTRODUCTION

Niosomes are vesicles mainly consist of nonionic surfactant. One of the reasons for preparing noisome is the assumed higher chemical stability of the surfactant than that of phospholipids, which are used in the preparation of liposome.

Niosome have been prepared from several classes of nonionic surfactants, e.g., polyglycerol alkyl ethers, glucosyl dialkylethers, crown ether and polyoxyethylene alkyl ether and esters.[1] One of the aims in developing delivery system is controlling the release of drugs from the carrier system in order to achieve a controlled uptake in the body. The noisome were prepared using various molar ratios of Brij 96 and cholestrol. The composition, the size, and the number of baitlayers of the vesicles have influenced the release. This shows that these parameters are important for the use of vesicles in pharmaceutical applications.

Surfactants

Surfactants that are used for the preparation of Niosomes are shown in table 1

Table1 : Nonionic Surfactants Used for the preparation of Vesicles

Nonionic Surfactants	Structural formula
Hexadecylpoly (3) glycerol	C16 H 33 O (CH2CH2 O)3 H | CH2 OH
Cholestrolpoly (24) ox ethylene ether Dialkylpoly (7) glycerol ether	C16 H33¬—CH—O (CH2CHO)7H | | CH2 CH2OH / C12H25O
Alkylglucoside	H (CH2) n—C6H11O6 n = 8,10,12,14,16,18

Cetyl mannoside	C16H33—C6 H11O6
Cetyl lactoside	C16H33—C6 H11O6
Alkyl galactoside	H (CH2) n- C6 H11 O6
Polyoxyetylenealkyl ether	H (CH2) n- (OC2H4) m OH n-12, 14,16,18 m-3, 4,5,6,7,8
Neutral crown ethers	
Polyoxyethylene glycerol-alpha, Alpha-diethyl ether	(H (CH2) N-OCH2)2 CHO (C2H4O)XH N-12, 14,16,18 x-6 to 30
n-Decylooxyethyleneoctadecylmyricylamine	H (CH2)18-N- (C2H4O)10H | H (CH2) 13-C= O
Cetyldiglycerolester	C15H31CO-(OCHCH2)OCH2CHOHCH2OH | CH2OH

Preparation of vesicles

The preparation methods should be chosen according to the use of niosomes, since the preparation methods influence the numbers of bilayers, size, size distribution and entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.[41]

1.Ether injection method

The surfactant/ cholesterol mixture is dissolved in diethyl ether and injected slowly through a needle into the aqueous phase at 60 degree centigrade. Large unilamellar vesicles are formed during the evaporation of the ether. The disadvantages of this method are that a small amount of ether is often present in the vesicles suspension and is very often difficult to remove.

2. Hand shaking (film) method

The surfactant/ cholesterol mixture is dissolved in diethyl ether in a round bottom flask, and the organic solvent is removed at room temperature under reduced pressure. The dried surfactant film is hydrated with an aqueous phase at 50 to 60 degree centigrade during gentle agitation. Large multilamellar vesicles are prepared.

3.Sonication

An aqueous phase is added to the surfactant/ cholesterol mixture in a glass vial. The mixture then probes sonicated for a certain time period. The resultant vesicles are small and uniform and unilamellar. In the case of niosomes the resulting vesicles size are in general larger than liposome's, niosomes being no smaller than 100 nm in diameter.

4. Method described by handjani-vila

Equivalent amounts of lipid (or mixture of lipids) and an aqueous solution of the active substance are mixed and agitated in order to get a homogenous lamellar phase. The resulting mixture is homogenized at a controlled temperature by means of agitation or ultra centrifugation

5. Reverse phase evaporation method

Lipids are dissolved in chloroform and ¼ volume of PBS

(Phosphate buffer saline). The mixture is sonicated and evaporated under reduced pressure. The lipids form a gel, which is then hydrated. The evaporation is continued until the hydration is completed.

6. Alternative methods

The size and numbers of bilayers of vesicles consisting of polyoxyetylene alkyl ether and cholesterol can be changed in an alternative way. Temperature rise above 60 degree centigrade transform small unilamellar vesicles to large multilamellar vesicles (>1um), while vigorous shaking at room temperature results in the opposite effect by changing multilamellar vesicles into unilamellar ones. The transformation from unilamellar to multilamellar vesicles at higher temperature might be characteristics for polyoxyethylene alkyl ether (ester) surfactant, since it is known that polyethylene glycol (PEG) and water remixes at higher temperature due to breakdown of hydrogen bondings between water and PEG moieties.

Generally free drug is removed from the encapsulated drug by gel permeation chromatography dialysis method or by centrifugation method. Often weight density differences between niosomes and the external phase are smaller than in the case of liposomes, which makes separation by centrifugation very difficult. A possibility is to add protamine to the vesicles suspension in order to facilitate separation during centrifugation.

Entrapment efficacies

As in the case of liposomes, entrapment efficacies of hydrophilic and lipophilic compound depend on the preparation method. According to the result of Baillie et al, niosomes prepared by ether injection resulted in entrapment efficacies of carboxy fluorescein that were significantly higher than those of vesicles prepared by hand shaking method.

Both Baille et al and Hunter et al used glycerol surfactant and reported that the entrapment efficacy decreased as the amount of cholesterol added in the nonionic surfactant.

High entrapment efficacies were observed when incorporating an octapeptide, DGAVP, in noisome prepared from polyoxyethylene alkyl ether surfactant. By using the freezing/thawing method, values of up to 40% entrapment efficacy were reported, while only a low surfactant concentration (90mM) was used.

THERAPEUTIC APPLICATION

A. Administration of drugs by Intravenous route

Several drugs encapsulated in noisome were studied after i.v administration

1. Doxorubicin

Niosome prepared by C16G3 with and without cholesterol were administered i.v in S180 in tumor bearing mice. The vesicles were approximately 800-1000 nm in diameter. Doxorubicin was encapsulated in the niosome by the film method, the final encapsulated concentration being 1mg/ml. After a bolus injection in the tail vein of the rat, the concentration of doxroubicin in serum and the accumulation in lungs, liver, heart and spleen was determined. In serum a significant increase in doxroubicin concentration was observed then compared to the bolus injection of the free drug.[2]

2. Methotrexate

Intravenous administration of methotrxate loaded noisome prepared from the same surfactants, did not lead to increased accumulation of the drug in the liver compared to administration of free drug. This may be difference in size of the vesicles used in the two studies or to a modification of the drug in the liver compared to administration of free drug. It is known that size, charge and hydrophilic of the vesicles can change the distribution of the encapsulated drug when administered intravenously. Finally drug accumulation in the tumor was increased when administered in cholesterol containing vesicles.[3]

3. Sodium Stiboglucinate

Sodium stiboglucinate is a drug used in therapy of visceral leshmniasis; a protozoan infection of the RES.The distribution of the antimony drug was extremely affected by encapsulation into vesicles.[4]

4. Iopromide

The intravenous administration of iopromide C16G3 and C16C12G7 niosomes containing steraylamine and extruded through a 220 nm filter resulted in theses niosomes being found predominantly in the kidneys. It concludes that the incorporation of the surface positive charge enables targeting into the kidneys.[1]

5.Vincristine

Vincristine Span 40 niosomes increased the vincristine antitumor activity in S-180 sarcoma and Erlich ascites bearing mice. Span 60 bleomycine niosomes also increased the tumorcidal activity of bleomycine [1]

6. Diclofenac Sodium

Diclofenac sodium noisome reportedly prepared from polysorbate 60, cholesterol and DCP (22:73:5) & 3 μm in size were found to reduce the inflammation in rats with carrageen induced paw edema on intraperitoneal administration to a greater extent than the free drug. This increase in activity is a direct result of an observed increase in the area under the plasma time curve.[5]

7. Flurbiprofen

In a study involving flurbiprofen Span 60 niosomes there was also increased in bioavailability and increased reduction of carrageen induced rat paw edema when niosomal formulation was applied topically in a hydroxyprpopyl methylcellulose semisolid base containing 10% glycerin or orally as a suspension in saline.[6]

8. Centchroman

Centchroman is a non-steroidal contraceptive, which exhibits unique combination of weak estrogenic and potent ant estrogenic properties but does not affect hypothalamo-pitutary-ovarian axis. This particular drug, which has several advantages over the existing hormonal contraceptives poses to be an ideal candidate for novel controlled release contraceptive preparation. The studies and investigation examine some long acting, i.m injectable system for centchroman namely niosomes and poly (lactide-co-Glycolide) (PLGA) IN Triacetin (an insitu gel forming matrix). The formulation shows controlled drug release and enhanced stability whereas in vivo studies showed promising anti-fertility activity for PLGA-in Triacetin.[7]

9. Indomehacine

In order to achieve sustained ant platelet effect from indomethacine, it was incorporated in a non ionic surfactant vesicles (niosomes) The objective was to study the effect of niosomal-encapsulated indomethacine on platelet function as inhibition of aggregation and ATP release induced by variety of agonist Niosome were prepared from Tween-60 by the lipid hydration method. The niosomal drug proved to be more efficient in inhibiting platelet aggregation than the free drug, probably due to greater quantity of the drug reaching to the specific site of inhibition in the interior of the platelets and acting directly on the cyclooxygenase system to prevent thromboxane formation.[8]

10. Colchicine

To prepare noisome which have high encapsulation capacity for soluble drugs, starting from Span 60 and cholesterol, an improved method, evaporation sonication method was proposed. The corresponding niosomes shows a good stability at least 40 days. The results indicate that the Span 60 is the most ideal surfactant. Furthermore the release study of colchicines in vitro from niosomes exhibited a prolonged release profile as studied over a period of 24 hrs. The results demonstrated that niosomes prepared in this way not only have high encapsulation capacity but also expected that side effects of drugs may be reduced.[9]

11. Rifampicin

An attempt has been made to design a suitable noisome encapsulated drug delivery system for rifampicin and evaluated the same in vitro and in vivo. A modified lipid layer hydration method was employed to prepare this vesicular carrier. The formulated systems were characterized in vitro for size distribution analysis, drug entrapment, drug release profile and vesicular stability. At different conditions of storage. In vivo drug kinetics was evaluated in normal healthy albino rats for niosomal formulation upon subcutaneous injection and various pharmacokinetis parameter. Niosomal formulation elevated plasma elimination half-life and decreased elimination rate constant for rifampicin. In vivo suggested that encapsulation retarded the removal of the drug from circulation compared to free drug due to slow release into systemic circulation.[10]

12. Tretinoin

In this study comparison of tretinoin (TRA) in methanol and in vesicular suspension exposed both to UV &With the aim of evaluating the potential of niosomes as a topical carriers capable of improving the stability of photosensitive drugs. Tretinoin loaded niosomes were prepared from polyoxyethylene lauryl ether sorbitan esters (Span 40 & 60) and a commercial mixture of octyl/decyl polyglucosides. TRA loaded vesicles were prepared by film hydration method, extrusion and sonication method. After UV irradiation, TRA dissolved in photo degradation process. The photo protection offered by vesicles varied depending on the vesicles structure and composition.[11]

13. Transferrin and glucose ligands

To prepare polymeric vesicles and niosomes bearing glucose or transferring ligands for drug targeting. A glucose-palmitoyl glycol chitosan (PGC) conjugate was synthesized and glucose –PGC polymeric vesicles prepared by sonication of glucose-PGC/cholestrol. N-palmitoylglucosamine (NPG) was synthesized and NPG niosomes were also prepared by sonication of NPG/ Sorbitan monostearate/Cholestrol/ Cholesterol poly-24-oxyethylene ether. These two glucose vesicles were incubated with colloidal concanvalin a gold (Con-A-gold) washed & visualized by transmission electron microscopy (TEM). Transferrin was also conjugated to the surface of PGC vesicles & the uptake of these vesicles investigated. Glucose & Transferrin bearing chitosan based vesicles and glucose niosomes have been prepared. Glucose bearing vesicles bind Con A to their surface. Chitosan based vesicles are taken up by cells & transferring enhances the uptake.[12]

14. Zidovudine

A novel noisome preparation composed of non ionic surfactant, polyglyceryl-3-diisosterate and polysorbate-80 bilayers stabilized by myristyl alcohol and polysorbate-80 were in1: 2:1 molar ratio in which 85 % ziduvidine (3′-azido-3′-deoxythymidine, azidothymidine) was found to be encapsulated in aqueous core.

Pharmacokinetics and tissue distribution studies were conducted on this noisome preparation using rabbits and albino rats, as animal model. AZT than with AZT solution. Such levels were maintained for prolonged time. T½ increased clearance become slowly and as a result AUC &AUMC increased and consequently MRT increased following niosomal AZT treatment.[13]

15. Insulin

Pharmacokinetic profile and hypoglycemic effect, after intraperitoneal injection of insulin and insulin encapsulated in niosomes were determined in diabetic rats. Niosomes of different doses and different lipid compositions were prepared by lipid layer hydration method. Plasma samples were collected at specified.

Time interval and plasma concentration of insulin was determined by HPLC method. Blood glucose levels were estimated spectrophotometricaly using commercial glucose assay kit. In-vitro release and pharmacokinetics profile of niosomal formulation and free insulin were evaluated. Niosomes significantly reduced the blood glucose level in diabetic rats. Fall in blood glucose level were almost 92 % of initial value. In case the niosomal formulation the half-life was prolonged by 4-5 hours in contrast to free 2 hours for free drug. Niosome maintained the plasma insulin level up to 12 hrs but free drug was cleared quickly.

More than 80 % of the drug was successfully encapsulated to give formulation with sustained release characteristics. Entrapment efficiencies with increasing lipid concentration and decreased with increasing drug concentration. The result showed that insulin entrapped in niosomes prolongs the existence of drug in the body therefore increasing its therapeutic value.[14]

16. Cisplatin

The use of cisplatin is limited due to its toxic effects. In the study noisome of cisplatin by using Span-60 & Cholesterol were prepared and investigated for antimetastatic activity in experimental metastaic model of B16 F 10 melanoma. Theophylline and its combination effect with free cisplatin and niosomal cisplatin were also carried out in the same model. Treatment with niosomal cisplatin and combination of the same with theophylline showed significant reduction in the number of lung nodules as compared to untreated control as well as the free cisplatin .The treatment with activated macrophages reduced the secondary growth of tumor in lung. Niosomal cisplatin showed a significant protection against weight loss and bone marrow toxicity as compared to free cisplatin. These results suggest that cisplatin encapsulated in niosomes has significant antimetastatic activity and reduced toxicities than that of free cisplatin. However theophylline failed to show antimetastatic effect alone or in combination with cisplatin or with active macrophages.[15]

17. Amarogentin

Niosomes were prepared by non-ionic surfactant of the Span series e.g. Span 20, was used. For niosomal amarogentin, the reagent i.e. Span-20, Cholesterol, Phosphatidic acid were dissolved as before in a chloroform –methanol mixture and amarogentin (500 µg in methanol) was added. The dry film was swelled, sonicated & centrifuged to remove excess amarogentin. The amarogentin in niosomal forms was found to be more efficacious.[16]

18. Daunorubicin Hydrochloride

The central aim of this study was to modify the reverse

evaporation process, such that enhanced drug entrapment, with increased stability, prolonged release, could be achieved and translated these advantages into increased therapeutic efficacy of daunoroubicin hydrochloride.[17]

19. Amphotericin –B

The potential ant fungal agent Amphotericin-B was incorporated into nanosphere at various concentrations. The targeting efficiency of drug-loaded nanosphere was compared with that of free drug in terms of percentage, increase in targeting to various organ like liver, lung & spleen.[1]

20. 5-Fluorouracil

Niosomes of Span (Sorbitan Monostearate) have prepared of 5-Flurouracil (FU) using different Spans. Niosome s was prepared by Hand Shaking Method, Reverse Phase Evaporation Method & Ether Injection Method using series of spans. The niosomal preparation shows higher & sustained plasma drug level profile compared to free drug solution.[18]

21. Camptothecin

The camptothecin niosomes were spherical in shape. Their size distribution was narrow. The entrapment efficiencies were higher. Its antitumor activity was better than camptothecin in free form.[19]

22. Adriamycin

The effect of encapsulation of adriamycine into niosomes, and its resultant chemical purity, was studied by means of HPLC & high speed scanning spectrophotometer and the process shown not to adversely affect the drug. Efficiency of entrapment of neither aqueous solutions of the drug dependent on neither vesicles composition nor method of production, and evidence of a degree of surfactant-adriamycine was provided by the high entrapment values. Light induced drug degradation was reduced by niosome encapsulation.[20]

23. Cytarabine Hydrochloride

Niosome vesicles of cytarabine hydrochloride were prepared by a lipid hydration method that excluded dicety phosphate. The sizes of the vesicles obtained ranged from 600 to 1000 nm, within the objective of producing more blood levels in-vivo. The study of the release of drug from niosomes exhibited a prolonged release profile as studied over a period of 16 hrs. The drug entrapment efficiency was about 80 % with Tween 80, Span 60 and Tween 20, for Span 80, it was 67.5 %. The physical stability profile of vesicular suspension was good as studied over a period of 4 weeks.[22]

24. DNA Vaccine

The result shows that DNA can be effectively entrapped within a range of nonionic vesicles formulation using the dehydration-rehydration method. These vesicles containing DNA, may be a useful system for subcutaneous delivery of DNA vaccine.[21]

B. Peroral administration of drugs

1. Vaccine delivery system

The feasibility to develop a per oral vaccine delivery system based on nonionic surfactant vesicles (niosomes) was evaluated using BALB/c mice. Ovalbumin was encapsulated in various lyophilized noisome preparation consisting of sucrose ester, cholesterol and dicetylphosphate. Two different formulations were compared with this study. ELISA monitored the specific antibody titers within serum, saliva and intestinal washings on days 7,14,21 and 28 after intragastric administration. Only encapsulation of ovalbumin into 70 % stearate sucrose ester, 30% palmitate sucrose ester (40%, mono, 60%di/triester) niosomes resulted in significant increase in antibody titers. Administration of ovalbumin and empty niosomes did not exert a similar effect; neither did administration of any control formulation. [22]

2. Protein and peptide delivery

More gut labile compounds such as proteins have been administered by this route and intestinal transport of a niosomal formulation of the peptide 9-desglycinamide-8 -arginine vasopressin (DGAVP) has been studied in vitro.[23]

3. Ergot alkaloid

Peptide ergot alkaloid is poorly absorbed after oral administration. The incomplete intestinal absorption of the alkaloid was increased significantly when administered in bile duct cannulated rats as a micelle solution together with POE-24 cholesterol ether. In-vitro diffusion studies suggested that diffusion of ergot alkaloid across the mucous barrier is facilitated by micelle entrapment of the drug.[1]

4. Polysaccharide coated niosomes

Niosomes were prepared and appended with a polysaccharide cap using hydrophobic anchors. Hydrophobized polysaccharides, o-palmitoyl pullulan (OPPu) & choles-

terol pullulan (CHPu) were anchored onto propranol HCL containing preformed niosomes. The coated noisome were characterized for average particle size, size distribution, shape, encapsulation efficiency and invitro release profile and were compared with their uncoated counterparts. Inviter coated release studies however revealed that significant lowering of drug release.[24]

5. Ciprofloxacin & Norfloxacin

An attempt has been made to design suitable noisome-encapsulated drug delivery system for ciprofloxacin & norfloxacin. Encapsulation of ciprofloxacin & norfloxacin in niosomes was investigated and the nasal & intestinal adsorption of the products studied. More than 80 % of the drug was successfully encapsulated to give products with sustained release characteristics. Encapsulation in niosomes also improved the stability of the antibacterial compounds. Although the systemic availability of these niosome-encapsulated was not increased after nasal administration, intestinal absorption was significantly higher in comparison with that of plain inclusion complexes.[25]

6. Insulin

Niosomes of sorbitan monostereate (Span-20, 40,60 & 80) were prepared using the film hydration method without sonication. Unlike the other surfactant, span 80 did not form niosomes in the absence of sufficient amount of cholesterol.

The size of vesicles depended on the cholesterol molar ratio or charge incorporation. The amount of Insulin released in simulated intestinal fluid from Span 40 & 60 was lower than Span 20 & 80 vesicles. Vesicles containing Span 60 showed the highest protection of insulin against proteolytic enzyme & good stability in the presence of sodium desoxycholate and storage temperature.[26]

C. Transdermal drug delivery system

1. Flurbiprofen

Dose dumping results in more side effects due to conventional therapy of anti-inflammatory drugs. In view of this, the formulation of suitable transdermal delivery system of flurbiprofen is attempted. In the present study an attempt is made to improve the therapeutic efficacy of flurbiprofen in transdermal preparation incorporating drug-entrapped niosomes.

1% w/w flurbiprofen were incorporated in semisolid gel base guar gum (10%), methyl cellulose (4%), hydroxy propyl methyl cellulose (60%), Carboxy methyl cellulose (5%) and sodium alginate (14%) with each base containing (0.1%) methylparaben as a preservative.

Niosomes of flurbiprofen were prepared using Span 60 (71.25 mg), cholesterol (71.25 mg) and dicetyl phosphate (7 mg) to get a ratio of 47.5: 47.5: 5 respectively. The lipids were dissolved in diethyl ether (10-15 ml) and 50 mg of flurbiprofen was added to the solution.

The solvent was evaporated using a rotary flash evaporator, leaving a thin layer of solid mixture deposited on the wall of the round bottom flask. Adding 5 ml of water in divided quantities and intermittently mixing on vortex until a good dispersion of the mixture was obtained hydrated this film. The free drug was separated by dialysis method, using 0.9% sodium chloride solution. The percentage entrapment of flurbiprofen was 65 % w/w.[6]

2. Piroxicam

Niosomes which are the nonionic surfactant vesicles can be used as a drug carriers with modified tissue distribution characterstics.0.5% Piroxicam prepared in a niosomal formulation in transdermal preparation improve the therapeutic efficacy.[6]

3. Estradiol

The permeation of estradiol from vesicular formulations through human stratum cornea was studied in vitro. The vesicles were composed of nonionic n alkyl polyoxyethylene ether surfactant. The thermodynamic activity of estradiol present in each formulation was kept constant by saturating all formulations with estradiol The effects of both the particle size and the composition of formulation on estradiol permeation across excised human stratum cornea were investigated.[27]

4. Levonorgestrol

A proniosome based transdermal drug delivery system of levonorgestrol was developed and extensively characterized both in-vitro & in-vivo. The proniosomal structure was liquid crystalline-compact noisome hybrid, which could be converted into niosomal formulation upon hydration. The study demonstrated the utility of proniosomal transdermal patch bearing levonorgestrol for effective contraception.[28]

5. Nimesulide

A noisome based transdermal drug delivery system of

Nimesulide was developed and extensively characterized and evaluated for in-vitro performance followed by in-vivo evaluation in rats by carrageen induced rat paw edema method. Niosome prepared were by lipid film hydration technique using tweens and spans. Preparation of niosome was optimized for highest entrapment. Finding of this investigations conclusively demonstrate prolongation of drug release and increase in amount retention into the skin and across the skin after niosomal encapsulation of nimesulide. Developed niosomal gel formulation has also demonstrated enhanced anti-inflammatory activity compared to plain drug gel and marketed formulations.[29]

6. Dithranol

Dithranol is one of the mainstays in the topical treatment of psoriasis. However the use of dithranol in psoriatic condition is inconvenient and troublesome, as it has irritating, burning, staining and necrotizing effect on the normal as well as diseased skin. The entrapment of drug in vesicles is viewed to help in the localized delivery of the drug and an improved availability of drug at their site of action will reduce the dose and turn, the dose dependent side effects like irritation and staining. The invitro permeation study using mouse abdominal skin shows significantly enhanced permeation with vesicles as indicated by flux of dithranol from niosomes as compared with the cream base.[30]

7. Ketoconazole

Ketoconazole niosomes were prepared by ether injection technique using surfactant (Tween 40 or 80); cholesterol and drug in five different ratios by weight .The noisome were characterized by size, shape, entrapment efficiency and invitro drug release (by exhaustive dialysis). The formulations were also tested for in vitro drug release (cup plate method) and in vivo antifungal activity (in rabbits) and compared with free ketconazole. The results of the present study indicate that niosomes have the potential to reduce the therapeutic dose of ketoconazole by improving its performance.[31]

8. Enoxacin

The skin permeation and partitioning of a fluorinated quinolones antibacterial agent, enoxacin in niosomes, after a topical application were elucidated in the present study. In vitro percutaneous absorption experiment were performed on nude mouse skin with Franz diffusion cells. The influence of vesicles on the physicochemical property and stability of the formulation measured. The enhanced delivery across the skin And noisome encapsulated enoxacin had been observed after selecting the appropriate formulation. The optimized formulations could also reserve a large amount of enoxacin in the skin. The ability of noisome to modulate drug delivery without significant toxicity makes the vesicles useful to formulate topical enoxacin.[32]

9. DNA Loaded non-ionic surfactant vesicles

Niosomes have been shown to effectively entrap and deliver DNA vaccine. Niosomes incorporated DNA based on dehydration rehydration method gives higher efficiency employed through topical route. DNA encoding hepatitis B surface antigen was encapsulated in niosomes. The study signifies the potential of niosomes as DNA vaccine carriers for topical immunization.[33]

10. Radiopaque contrast agents for X-ray imaging

Niosomes are considered as a carrier of iobitridol, a diagnostic agent for X-ray imaging. The noisome prepared using the film –hydration method followed by sonication. Method allows the increasing encapsulation and the stability of vesicles were carried out.[34]

11. Ketorolac

Permeation of potent nonsteroidal anti-inflammatory, Ketorolac, across excised rabbit skin from various proniosome gel formulation was investigated using Franz diffusion cells. Each of the prepared proniosome significantly improved drug permeation and reduced lag time. Proniosome prepared with the Span-60 provided a higher Ketorolac flux across the skin.[35]

C. Inhalation Niosomal Preparation

In this study the potential of encapsulating all-trans retinoic (ATRA) in niosomes and delivering it as inhaled aerosol. Niosome may provide a means to reduce the toxicity of ATRA & alter the pharmacokinetis in a manner similar to liposomes. In addition the low cost of the surfactant used for preparing niosomes & their greater stability compare with liposome makes them attractive alternative. Various nonionic surfactant were used to achieve optimum encapsulation & nebuilization efficiencies, and the best formulation were obtained with combination of (Span 20+ Tween 80) using ATRA concentration of 1mg/ml.[36]

D.Occular Niosomal Preparation

1. Timolol Maleate

Non-ionic surface-active agents based discoid vesicles (Discomes) bearing timolol maleate were prepared. Niosomes were incorporated with Solulan C in order to effect vesicles to discome transition. The discomes were relatively large in size, 12- 60 micron. They were found to entrap relatively high qty of timolol maleate. The prepare system were characterized for size, shape & drug release profile in-vitro. They were found to release the contents following biphasic profile particularly in the case where the drug was loaded using PH gradient technique. The prepared system could produce or sustain a suitable activity profile upon administration into the ocular cavity; however, systemic absorption was minimized to a negligible level. The discomes were found to be a promising and of potential for controlled ocular administration of water-soluble drugs.[37]

2. Cyclopentolate

Cyclopentolate was encapsulated within niosomes prepared from polysorbate 20 and cholesterol & found to penetrate the cornea in a pH dependent manner with in these niosomes. Permeation of cyclopentolate increased at pH 5.5 but decreased at pH 7.4. Contrary to these findings, in-vivo there was increased mydriatic response with the niosomeal formulation. It is concluded that the increased permeability characteristics of the conjunctiva and sclera membranes.[38]

E. Nasal Drug Delivery System

1. Sumatriptan

Niosome of Sumatriptan succinate was prepared using lipid hydration method. The prepared niosomes were evaluated for entrapment efficiency, size analysis and invitro release studies. Further niosomes were evaluated for nasal absorption using an ex-vivo model. The niosome reported to enhanced the drug absorption & prolongation.[39]

2. Influenza Viral Vaccine

The goal of this study was to develop nonionic surfactant vesicles of influenza antigen for nasal mucosal delivery. The study describes the encapsulation of viral influenza vaccine antigen in nonionic surfactant vesicles using dehydration-rehydration technique and investigations of the influence of the varying proportion of surfactant, cholesterol, and dicetylphosphate.[40]

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