Section A-Research paper

NIOSOMES ON OCULAR DRUG DELIVERY SYSTEM:AN UPDATE

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Abstract

Ocular administration of drug is primarily associated with the need to treat ophthalmic diseases.The vesicle is made up of a bilayer of non-ionic surfactants, thus the name niosomes.Niosomes are extremely small and microscopic (on a nanometric scale). The niosomes are classified as a function of the number of bilayers (e.g. MLV, SUV) or as a function of size. (E.g. LUV, SUV) or as a function of the method of preparation (e.g. REV, DRV). Tthe characterization of noisome was experimented by different methods and the results was evaluated. Niosomes are vesicles composed of non-ionic surfactants, which are biodegradable, relatively nontoxic, more stable and inexpensive, an alternative to liposomes.

Introduction

Eye is the most easily accessible site for topical administration of a medication.Ideal ophthalmic drug delivery must be able to sustain the drug release and to remain in the vicinity of front of the eye for prolong period of time (1-4)

The first niosome formulation was developed and patented by L'OREAL in 1975.Niosomes are a novel drug delivery system that encapsulates the medication in a vesicular system made up of non-ionic surfactants. The vesicle is made up of a bilayer of non-ionic surfactants, thus the name niosomes.Niosomes are extremely small and microscopic (on a nanometric scale). Despite having a similar structure to liposomes, they have several advantages over them. The vesicles may act as a depot, releasing the drug in a controlled manner. They are osmotically active and stable, and also they increase the stability of entrapped drugs. They improve the therapeutic performance of the drug molecules by delayed clearance from the circulation, protecting the drug from biological environment and restricting effects to target cells. The surfactants used are biodegradable, biocompatible and non-immunogenic. They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of drugs. They can be made to reach the site of action by oral, parenteral as well as topical routes. Handling and storage of surfactants requires no special conditions.Disadvantages include: Physical instability of the noisome vesicles is a major disadvantage of the niosomal drug delivery system. (5) Aggregation: Aggregation of the niosome vesicles can be another

disadvantage to be considered. Fusion: Fusion of the niosomal vesicles to form loose aggregates or to fuse into larger vesicles will affect the uniformity of the size of the noisome vesicles. Leaking of entrapped drugs: leakage of the entrapped drugs from the polymer system will affect the intended properties of the niosomes. Hydrolysis of encapsulated drugs which limit the shelf life of the dispersion (6,7).

Table 1 Characterization and evaluation studies of various novel drug delivery system

NOVEL DRUG DELIVERY SYSTEM	DRUG NAME	METHOD OF PREPARATION	CHARACTERIZATION	EVALUATION
Archaeosomes	Corbevax	Immunization method.	Physicochemical properties offer the possibility for better antigen presentation by appropriate cells, being more effective to induce a comparable immune response.	In vivo studies by using wristar rat as a model(8)
	Immunoglobin –A	Polymeraization method	Bio degradable polymer-based system [loaded antigen]	In vivo studies by using guinea pig ileum method as a model(9)
Aquasomes	doxorubicin	oligomeric coatings methods	It was characterized by larger surface area, volume, and mass ratio that allows the drug to penetrate inside the cells and a prolonged drug release profile.(10)	Ex vivo studies by using mice as amodel.
	Methymoglobin	coprecipitation and self-precipitation method	It was characterized by oxygen carrying capcity .(11)	In vivo studies by using rat as amodel
	Dextrans	co-precipitation method	Nanoparticles made from chitosan (CS) and its N-trimethylated derivative, TMC, loaded with a model antigen ovalbumin (OVA) were	In vitro studies

			prepared by ionic gelation with tripolyphosphate. (12)	
Cryptosomes	Amygdalin and apricot kernels	Encryption method	It is characterized by particle size analysis, transmission electron microscopy, spectroscopy technique.(13)	In vitro studies
	cytarabine	Adsorption method	It was characterized by using sonication, all liposomes investi- gated in this study had a diameter of approx. 80 nm, as concluded from dynamic light scattering, by the choice of our specific experimental conditions. From electron micrographs we conclude that they were predominantly unilamellar.(14)	Liposomes for the sustained drug release in vivo
	doxorubiccin	Cytometric experiment methods	They are evaluated by middle sized, compact phospholipid vesicles with one or up to few lipid bilayers which are sterically stabilized with a small amount of large-head phospholipids.	It was evaluated by using in vivo studies.
Ethosomes	Metformin	Different concentration of ethanol adopting injection technique.	Ethosomes having 30 % v/v ethanol displayed superior entrapment for metformin % (55.3 ± 0.07); and a highly efficient permeation via mice skin (85.8 ± 3.7).	Invivo study by using the mice to achieve the wound healing action.

			entrapment efficiency, ex-vivo skin permeation, vesicle size, morphology and permeation kinetics.etc…(15)	
	Tocopherol acetate.	Modified cold method technique by using ultrasonic homogenizer ,TEM,centrifuge machine ,UV-VIS spectroscopy.	Particle size (PS), polydispersibility index (PDI), and zeta potential (ZP) of the TAEG formulations (N = 9). Entrapment efficiency,ph,conductivity and spreadility assessments.	Exvivo study: Franz cell method by using the albino rat.
	ceramide	High pressure homogenization method at 800 bar for 5min.	Particle size :80~130nmfor ethosome containing ceramide and vanilicacid . 150~170nm.(16)	Invitro method
	Indomethacin	Conventional thin film evaporqation and hydration method.	Particle size ,zeta ppotential ,polydispersity are measured by using instrument Zetasizer Nano (Nanozs 90, Malvern Panalytical.	Invitro study by porcine skin by frankz cell equipment.
	Kojic acid	Preparation is by using soy phosphatidylcholine, ethanol, propylene glycol, and water with cold method.	zeta potential, size, and entrapment efficiency of −23.4 mV, 148 nm, and 90.0008%and vesicles were spherical in shape(16).	Invivo method .
	Atorvostatin	Thin film hydration method	Emulsome size, polydispersity index, surface charge, and entrapment efficiency are of 359.4 ± 8.97 nm, PDI of 0.4752 ± 0.012, a zeta potential of -21.27 ± 0.53 mV, and a drug entrapment of 95 ±	Invivo permeation study by using albino rat.

			2.38%. (17)	
Bioemulsomes	Lefunoamide	Emulsomes were prepared by thin film hydration technique.	Particle size ,zeta potential , entrappment efficiency and invitro release.	Invivo study and invitro study were peformed. Invitro study by transmission electron microscopy,FTIR and DSC.invivostudy by using adult male spraugedawley rats.
SLN	Gefitinib	ultrasound melt emulsification method	The prepared sln was characterizd by the physiochemical Properties,entrapment efficiency and invitro release.	Ex-vivo permeability was performed by using the rabbit of 2 kg,under standard laboratory conditions. Invitro cytotoxicity:cytotoxic evaluation against the A549 cell lines were performed by MTT assay.
	Cinnacalcet	hot homogenization technique and ultra sonification	Entrappment efficiency ,particle size and time taken for diffusion was measured T85%	Pharmacokinetic study was carried out by using white albino rats of 2 kg.
	Sarcolipin-Protein	L.entiviral particles are prepared of the pmd2.g envelope plasmid and pspax2	It is characterized by glucose and oleic acid (OA) metabolism, mitochondrial function, and gene expressions. (18)	By using ,genetically altered mouse models, mice with loss of SLN were prone to gain

		packaging plasmid. Cell culture method.		weight, whereas skeletal muscle-specific overexpression of SLN protected mice from developing obesity.
	S-Adenosyl- L -Methionine	Microfluidization technique using high pressure homogenizer with y type interaction chamber.	SAMe-SLN: Particle size :241.7 ± 0.69 Zeta potential: 0.203 ± 0.01 PDI:− 29.2 ± 0.19 PY: 32.66 ± 1.48 55.3 Reconstituted SLN from SAMe-SLN: PARTICLE SIZE: 288.4 ± 3.41 ZETA POTENTIAL: 0.463 ± 0.01 PDI:− 22.5 ± 0.27(19)	Plasma pharmacokinetics were evaluated by adult male wistar rats.
	Sertraline	Emulsification-ultra sonication method.	PARTICLE SIZE: 110 nm size, POLYDISPERSITY INDEX:<0.2 PDI, ZETA POTENTIAL:>36 mV ZP, >72% EE	INVIVO STUDIES: Adult male Sprague-Dawley rats (250 ± 20 gm)
Niosomes	Doxycycline Hyclate	Doxycycline hyclatewas prepared by the thinfilm hydration method with different percentages of constituents.	Particle size, of 362.88 ± 13.05 nm to target follicles, entrapment efficiency of 56.3 ± 2.1%, the zeta potential of -24.46±1.39 mV, in vitro drug release of 54.93 ± 1.99% after 32 hours, and the lowest permeation of the drug through the rat skin among all other formulations. Improved cell	In vitro studies by using rat as a model

			viability,	
	Lornoxicam	LX niosomes were prepared by thin film hydration technique	They were characterized using Transmission Electron Microscopy (TEM), Differential Scanning Calorimetry (DSC), Particle Size analysis and Zeta potential determination.(20)	In vivo studies by using wristar rat
	Capecitabine	Entrapment efficiency method	Niosomes were characterized by particle size analysis, transmission electron microscopy, Fourier transform infrared spectroscopy and differential scanning calorimetry for surface morphology and drug excipient interactions.	In vitro studies by using guinea pig model
	5-Flurouracil	Inducible clindamycin resistance method	Fourier-Transform Infrared Spectroscopy (FTIR) analysis, proinflammatory cytokine levels, and oxidative stress markers of the tongues were monitored and collected after sacrifice.(21)	In vivo studies by using mice as a model
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Proteosomes	Ancestim	Haematopoetic stem cells method	differentiation into all mature blood lineages, that is, erythrocytes, platelets, lymphocytes	In vivo studies by using zebra fish model

Table 2 Applications and Route of administrations relating to novel drug delivery system

NOVEL DRUG DELIVERY SYSTEM	APPLICATIONS	ROUTE OF ADMINISTRATION
Archaeosomes	It is used for mucosal bacterial infection and for immunaization.(25)	Muosal
	It is udes for gene therapy	Nasal
	It can be used as a carrier for vaccines	Nasal
	It has a extensive application in immunology.(26)	Nasal
Aquasomes	It is used as a oxygen carrier	Paranteral
	It has a extensive application in insulin delivey.	Oral, intra muscular (27)
Dicomes	It is used for Enzymatic biotranformation	Parenteral
	It has a wide application inantidotal treatment , bioavailability,and increases the viscosity	Oral
Cryptosomes	It is a potential carrier of biological active compounds like PEG	Oral
	It is used for targeted drug delivery system	Parenteral
	It has awide application in deformability of property	intra - peritoneal route
Dendrimers	cyclodextrin	Topical
	Cationic peglyatedcarbosilanedendrimeric	Topical
Ethosomes	Used in treatment of melanoma and wound healing.	Topical
	Used in the moisturizing of the skin and also phtoprotective agent.	Topical
	Ethosomes containing Ceramide used in cosmetic industries.	Topical
	Used in hyperpigmentation treatment,skin whitening and moisturing property.	Topical
Emulsomes	Antifungal property .	Topical
	Used in arthritis treatment.	Intra articular
	The optimized SLN formulation and lyophilized CH shows oral bioavaibility 2 times .	Oral
	In the treatment of major depression.	Oral
	The SLN can be used as a potential	Oral

SLN	carrier for the delivery of poorly water-soluble drugs associated with poor oral bioavailability like sertraline.	
Niosomes	It has a wide application in acne treament	subcutaneous
	It is used in colon cancer and rectum cancer .	Transdermal
	It has a wide application in the treatment of cancer	Oral
	It is used to induce the melatonin niosomal gel	Transdermal
Novasome	It is used to treat the fungal infections	Topical
	It has a extensive application in hair follicles	Paranteral
	It has a extensive application in parathyroid hormone	intra muscular
Proteosomes	It regulates the degradation of cellular proteins.	intra arterial route

Challenges for the successful ocular drug delivery

There are numerous challenges in the therapy of ocular diseases, the main problem related to ocular therapeutics is the strain to keep up the effective drug concentration at the desired site for achieving the desired therapeutic effects for required period of time. (44) These days' ophthalmologist are exacting on improvement in the retention time of drugs for ocular delivery system. Nanotechnology based carrier systems may be working for the ocular delivery of drugs via the topical routes since these delivery systems encapsulates the drug molecules and carry it to various parts of eye. Presence of numerous barrier (ie., anatomical and protective) which empowers the therapeutic efficacy of drugs. Barriers in the eye for the ocular therapeutic: Barriers in the anterior segments(44).

Cornea(44,45)

In the eye, the cornea behaves as a main barrier for the absorption of topically administered drugs. It is the primary pathway for transporting topically applied ocular drugs. The absorption of small lipophilic molecules takesplace through the cornea whereas large lipophilic molecules are absorbed through conjunctiva and sclera. The ophthalmic drugs are removed from the eyes by the lacrimal drainage or through the systemic absorption, which leads to the entirely absorption of a very small amount of topically administered dose. Moderate charge contains molecules that has the capacity to pass through the cornea. Hydrophilic molecules entry is restricted through the tight junctions formed by the corneal epithelium, it also restricted by the stromal fibres which are charged and which act as the sieve for the large molecules. Due to the tight junction of conjunctival epithelium which

inhibits the pathway of the molecules. Intercellular spaces in the conjunctiva epithelium are broader than the cornea so it easily permeates the larger molecules. Cornea contains 7 different cell layers'epithelium, bowman's later, stroma, dua's layer, Descemet's membrane and endothelium.

Sclera and choriocappillaries(45)

It act as the obstacle for the diffusion of macromolecule. Many molecules have the capacity to pass by the sclera, but the high molecular weight molecules can't easily pass through the sclera was portrayed by the numerous studies conducted in the invitro level. Choriocappillaries consists of fenestrated endothelial cells which also present a barrier in the penetration of macromolecules.

Stroma(45,46)

In the cornea hydrophilic as well as the lipophilic area is present, but main part of cornea is stroma which is hydrophilic. In stroma lipophilic drugs can't easily penetrate to the epithelium, for hydrophilic drugs stroma act as the depot, whereas lipophilic drugs the epithelium may act as depot.

Conjuctiva(46)

With comparison to cornea, presence of conjunctival blood Capillaries and lymphatics the absorption is said to be non-productive, which lead to the loss of dug in the blood circulation so that it may lead to decrease in the ocular bioavailability.

Barriers in posterior segment

Retina and blood retinal barrier(47)

Retina, which is considered as the photosensitive layer itself behaves as the substantial diffusion barrier for large molecules. The presence of inner and outer plexiform layers causes the high resistance to the diffusion of molecules. The blood retinal barrier(BRB)has the work to separate the neurosensory layer from the blood circulation. BRB divided into 2 segment namely, inner and outer retinal barriers. The outer retinal barrier is composed of the retinal pigment epithelium (RPE), Hexagonal monolayer. The RPEis found in between the choriocappillaries and photo receptors, which mainly transmit the nutrients to the photo receptors and the wastage are out through the sub – retinal spaces.

Protective barrier(47)

The absorption of topically administered drugs in ocular route is confined by various protective mechanism which encourages the safety and good functioning of the eye.

Lacrimation(48)

The lachrymal film is the main barriers for the drug penetration, it's other functions includes cleansing property, it hydrates, lubricates, and behave as the protective mechanism against

then pathogens. It also said to be dynamic fluid involves in the constant renewable process and blocks the retaining time of the drugs on the surface of eye.

How the drug act on the lacrimation(48)

Initially the drug is administered topically which quickly diluted in the lachrymal fluid. Next the excess over solution stays on the lower eyelid, where small amount of drug is present which drains into the nasolacrimal duct. Lastly, after the above steps the remaining drug again it further diluted by increasing in the lacrimation and physiological tear turnover which is activated by the application of the drug

Metabolism(49)

The ocular tissues have the metabolic enzymes such as esterase's, aldehyde, and ketone reductase, which involves in the degradation of the drugs applied so that their therapeutic efficacy is reduced.

Ocular drug delivery and its challenges (50-52)

The ocular drug delivery deviates through the number of anatomical and physiological barriers,which have been a bottleneck for the ophthalmologist. The ocular barriers statistical and dynamic barriers decrease the absorption of the therapeutic agent and the entry of xenobiotic. Generally, the major topic is linked with victorious ocular delivery is to sustain the fruitful therapeutic concentration of the drug(50-51).

Numerous safeguarding and automatic action are decreased at the concentration of drug in the high flown or taking up in areas. Incompetent concentration of drug in ocular tissue may generate increasein prospect of failed therapy, so that lowest level effective drug concentration should be hold on keep at the steps or soaking up site. For the use of ocular diseases, the topical administration of the drug is favour. But the ocular openness ofa bid formulation is usually poor because eye accommodate inherent guarding device which prevent the managing of any foreign substance. At this time new drug delivery systems are being visual finerchance of ophthalmic drug delivery. Application of nanotechnology-based drug delivery systems supply better scope for the delivery of therapeutic molecule when try outer appearance at the ocular region. These systems save the encapsulated remedy with high success as well as make smooth its intensity into the several tissues of the eye. further, hope of drug delivery in controlling manner can be obtained by these nanostructure, thus it is a likely tool for the therapy in some chronic ocular diseases. But alive of several barriers in the eye sector usually may convey the sang in delivery of drug which out turn less therapeutic benefits (52-54).

Advantages of ocular drug delivery systems (55)

It increases the ocular residence improving bioavailability increased drug release for better efficacy, less visual and systemic side effect, extravascular pressure, reduction of the number of administration better patient compliance and accurate dose in the eye a better therapy.

Limitation of ocular delivery system (55,56)

They are easily administered by the physicians, they are easily administered The by the patient himself, have the quick absorption effect, less visual and systemic side effect and increased shelf life.

Challenges for the successful ocular delivery system

Method of healing of ocular diseases is having wide provocation which requires to be control for the effectual care of these situation. Normally, the important issue situated with ocular therapeutics is the strain of keep a productive drug concentration at the appropriate site for getting the reach therapeutic activity for a wanted period of time. In recent days, ophthalmologists are focusing on amplify of support time of drugs for ocular delivery systems. Nanotechnology based carrier systems may be with a job for the ocular delivery of drugs via topical routes since these delivery systems encapsulate the drug molecule and over several it to several regions of eye. Presence of various barriers control the therapeutic efficacy of drugs(57).

Recent developments in ocular delivery system

Anterior segment ocular drug delivery technologies

Punctum plugs

Punctum plugs are also known as occludes or lacrimal plugs. These are biocompatibledevices used to block tear drainage when inserted into the tear ducts. PPDS was recently developed from a thermosensitive hydrophobic acrylic polymer used for treatment of dry eye disease. TX-TP known as travoprost punctum plug insert to deliver travoprost to the ocular tissues for 90 days used in treatment of reduction of intraocular pressure and ocular hypertension. TX-DP is used in the treatment of chronic allergic conjunctivitis and in eye surgery (58,60).

Cul-de-sac-implants

It is a pocket like depression where bulbar and palphebral conjunctiva which meet in upper and lower eyelid.Devices such as lacrisert and ocusertare used as implants (59).

Drug eluting contact lenses

Light transparent corneal dressings acting as reservoirs.Timolol maleate and dorzolamide hydrochloride with loaded lenses have shown sustained drug release.Bioinspired hydrogels are also currently used (61).

Ocular iontophoresis

This works by electroporation,electrophoresis,and electro osmosis.route of administration is by trans scleral and trans corneal.Dexamethasone sulphate formulation is used in anterooruvetis,caatract,inflammation and scleretis(62).

Posterior segment ocular drug delivery technology(62)

Durasert drug delivery system
It consists of surrounded ploymer layers with drug core in the centre part.Vitrasert with ganciclovir an antiviral agent used in treatment of cytomegalovirus retiniis.

Encapsulated cell technology
These are very much advantageous fo their biologically active prolonged acting molecules. Rexenus(NT-501) undergoing phase 3 clinical trials for glaucoma,and retinitis pigmentosa(63)

Suprachoroidal drug delivery
The drug delivery through the suprachoroidal route by the hollow microneedles and cannulas shows more biooavailability. In this,triamcinolone acetonide and bevacizumab delivery system through this suprachoroidal route has been evaluated for its efficacy, safety and pharmacokinetics. It has undergone phase 3 clinical trials and are investigated for treatin the posterior uvetis and DME(diabetic macular edema) with other anti VEGF agents (64)

Types of niosomes(35,36)
The niosomes are classified as a function of the number of bilayers (e.g. MLV, SUV) or as a function of size. (E.g. LUV, SUV) or as a function of the method of preparation (e.g. REV, DRV).

Multilamellar vesicles (MLV)
It consists of a number of bilayer surrounding the aqueous lipid compartment separately. The approximate size of these vesicles is 0.5-10 μm diameter. Multilamellar vesicles are the most widely used niosomes. These vesicles are highly suited as drug carriers for lipophilic compounds.

Large unilamellar vesicles (LUV)
Niosomes of this type have a high aqueous/lipid compartment ratio, so that larger volumes of bio-active materials can be entrapped with a very economical use of membrane lipids.(durak)

Small unilamellar vesicles (SUV)
These small unilamellar vesicles are mostly prepared from multilamellar vesicles by the sonication method, French press extrusion.

Table 3 Drugs used in ocular drug delivery system(65,66)

Route of administration	Drugs
Intravenous	Ipramide,daunorubicin,indamethacin
Transdermal	Piroxicam,erythromycin,cyclosporin
Oral	Polysaccaharide coated niosomes,insulin
Ocular	Timolol ,cyclopentolate
Oncology	Methotrexate,doxorubicin
Nasal	Sumatriptan , influenza

Method of preparation

Ether injection method

This method is based on slow injection of surfactants: cholesterol solution in ether through 14-gauge needle into a preheated aqueous phase maintained at 60^0c.vapourization of ether resulting into a formation of ether gradient at ether water interface which lead to a formation of single layer vesicles.depending upon the condition used,the diameter of the vesicle ranges from 50-1000nm. (66-68)

Hand shaking method

Surfactant and cholesterol are dissolved in a volatile organic solvent(diethyl ether, chloroform or methanol) in a round bottom flask The organic solvent is removed under vacuum at room temperature using rotary evaporator leaving a thin layer of solid mixturedeposited on the wall of the flaskThe dried surfactant film can be rehydrated with aqueous phase at temperature slightly above the phase transition temperature of thesurfactant used, with gentle agitation. This process forms large multilamellar noisome.

The Bubble Method

It is novel technique for the one step preparation of liposomes and noisome without the use of organic solvents .The bubbling unit consists of round-bottom flask with three necks positioned in water bath to control the temperature .Water-cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through the third neck .Cholesterol and surfactant are dispersed together in this buffer (pH 7.4) at 70°C, the dispersion mixed for 15 seconds with high shear homogenizer and immediately afterwards "bubbled at 70°C using nitrogen gas(69-70).

Reverse Phase Evaporation Technique (REV)

Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. The clear gel formed is further sonicated after the addition of a small amount of phosphate buffered saline (PBS). The organic phase is removed at 40°C under low pressure. The resulting viscous noisome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield noisome. (71)

Applications of niosomes

Haemoglobin carrier

Noisome acts as a carrier for haemoglobin since the niosomal suspension shows a visible spectrum which is super imposable onto the free haemoglobin. As the vesicles havean ability to permeate to O2 molecule, the haemoglobin dissociation curve can be altered similarly to non-encapsulated haemoglobin. (73,74)

Ophthalmic drug delivery(75,76)

Compared to other delivery system ophthalmic system has very complications to achieve the maximum bioavailability of a drug from ocular dosage forms like ophthalmic solutions,ointments and suspension etc. which is mainly due to the transient residence time, nonporous corneal epithelium and lacrimal fluid production and also non-productiveabsorption. But the good bioavailability of drug has been put forward by Carter et al. He described that multiple dosing with sod. stibogluconate loaded niosomes was to found to be successful against the parasites in the liver, speen and bone marrow as compared simple solution of sodium stibogluconate.

Table 4 Drug loaded niosomes in ocular delivery (78)

DRUG	SURFACTANTS	ENHANCEMENT
Atenol,timolol,betanol,cyclosporine.	Brij 35,78,98,100	When compared with conventional form it increase the corneal permeability.
Cyclosporine A	Polysorbate 80,polyoxyl 40 stearate,polyoxyl 60 hydrogenated castor oil	Increase in corneal permeability
Diclofenax sodium	Span 20,40,60,80	Non-irritant
Pilocarpine	Pluronic F127	Increase in miotic response in comparison with aqs solution
Levofloxacin	SPAN 20,40,60,80	Prolonged drug release with less side effects.
Gentamycin sulphate	Polysorabate 60,80 and brij 35	Prolonging the drug release
Cyclopentolate	Polysorbate 20	Enhancemen in ocular penetration
Acyclovir	Span 20,40,60,80	More effective against herpes simplex keratitis
Acetazolamide	Span 20,40,60,80	Enhancement of bioavailability and lowers IOP

Transdermal delivery of drugs(79,80)

When drugs are incorporated in the niosomes the penetration of drug through the skin is improved.

Neoplasia (85)

Doxorubicin, aanthracyclic antibiotic shows the broad spectrum antitumouractivity, produces a dose depend antireversible cardio toxic effect.thelifespan is seen to be increased and rate of proliferation is said to be decreased when administered by niosomal delivery.

Leishmaniasis(82)

Niosomes can be utilized for focusing of medication in the treatment of maladies.

Immunological Application (86)

Niosomes acts as a potent adjuvant in terms of immunological selectivity,low toxicity and stability reported by Brewer and Alexander.

Niosomes as drug carriers

Lobitridol,which is used as a symptomatic operator utilized for xray imaging in which nioosmes act as a carrier.topical niosomes may fill in as solubilization grid, as a neighbourhood station for maintained arrival of dermally dynamic mixes,as entrance enhancers or as a rate restricting layer obstruction for the tweak of foundational ingestion of medications.

Delivery of peptide drugs (84,85)

The stability of peptide increased by niosomes for oral delivery of 9-desglycinamide, 8-arginine vasopressin entrapped in niosomes in an invitro intestinal loop model and reported that the stability of peptide increased by niosomes.

Anti-inflammatoryagents (78,81)

Diclofenac sodium niosomal formulatopn with 70% cholesterolexhibits greater anti-inflammatory activity and also nimesulide,flurbiprofen formulations shows greater action compared to free drug.

Niosomes in gene delivery (82)

Novel niosomes explaining the 2,3 di propan-1-amine cationic lipid,joining with squalene and polysorbate 80 to assess the transfection efficiency in rodent retinas.

Liposomes at 15\1 proportion were 200nm in measure,25mV in eta potential and displayed circular morphology,at this condition ,niosomes fixed the DNA from enzymatic processing.

TT(tetanus toxoid) (83)

Katare et al developed the polysaccharide capped niosomes for oral immunization and considered the niosomes as a best approach for TT for oral immunization.

EVALUATION PARAMETERS OF NIOSOMES BASED ON DELIVERY SYSTEM(56,57)

Based on the Rheological Properties

The rheological properties of niosomal dispersions are influenced by a large number of factors, such asthe volume fraction of the dispersed phase, flocculation processes and

deformation of the vesicle membranes, the size and nature of the distribution of niosomes, and the electroviscosity effect. It was bound up with by using Ostwald U tube viscometer.It was one of the most important parameter inophthalmic preparation the nanocarrier of noisome is first diluted with some amount of water to a required quantity of concentration and then allowed it to stand for 1 hr t 25ºC. (42)

Based on the Stability Studies

Niosome formulation provided sustained release of piroxicam. The drug leakage from stored niosomeswas observed at the level of 1.56-6.63 %. Individual vesicle images were obtained for all samples byoptical microscope. However, particle size of niosomes was increased upon storage.After a period ofmonth, the in vitro studies was carried out on the selected particular formulation and it was observedfor three months (35,40).

Based on the Ocular Irritancy of Niosomes

The ocular based irritancy was studied by using rabbit as a model,the average weight of the rabbit should be 2.8-3.5.it could be assessed by examining the model for any swelling,redness,spam,or anyanother increased secretion of teras ,abdominal fluid,etc.the following control and test sample wasimprinted into the both eyes (left and right eye)by using one as control .further the eyes wasunconnected ,riveted and gash erect ,arid,limid,imbue in soft and hard paraffin ,segment at 8µmcompactness with the microtone and tint with the haemotoxylin and eosin by using the method ofoptical microscopy ,look into the photographed tinted division for corneal histological examinations (45,46).

Based on the Particle Size Analysis

Niosomes had an average particle size of 110.2±0.7 nm, polydispersity index of 0.229±0.008, and zetapotential of −64.8±1.2 mV. Experimental data revealed that 30 µg/mL of $SnCl2{\cdot}H2O$ was the optimalconcentration of reducing agent required for the radiolabelingprocess.The surface cytology wasresolved on by using the method of SEM -scanning electron microscopy .From each batchapproximately 30 niosomes was selected and and further it was measured from the rach batch and theaverage of the mean was ontemplate (51-59)

Based on the Studies of Intra Ocular Pressure (45,40)

Intraocular pressure (IOP) is the fluid pressure of the eye. As pressure is a measure of force per area, IOPis a measurement involving the magnitude of the force exerted by the aqueous humor on the internalsurface area of the anterior eye (60-72).Here we are selecting an adult male by denoating a normal bloodpressure of rabbit the weight of each rabbit should be approximately 1.8-2.5 kg are used. Tonometer isused to observe the intraocular pressure. At the outset of imprinting a plop of a local ansathetic aftersome period of imorintation of drug in both left and right eye and further the intra ocular pressureis measured. The IOP can be theoretically determined by the Goldmann equation, which is IOP = (F/C) +P, where F represents aqueous flow rate, C represents aqueous outflow, and P is the episcleral venouspressure. A change or fluctuation in any of these variables will inevitably alter the

IOP.IOP difference (ΔIOP) for each eye is calculated as follows, ΔIOP = IOPdosed eye – IOPcontrol eye (73-80).

Based on the AquesousHumor Analysis Study

Albino rat is used to determine the aquesouhumor ,the average weight of aquesoushumor should be1.5-2.0 kg .by injecting the 30/30 mixture ketamine hydrochloride and xylazinehydrochloride to the ratsforanesthesia .by adding one or two peral of oxybuprocaine to drop off further endure overhead of the corneoscleral limbus just beyond the cornea needle of 29G is loaded .for the upcomimgobservation s the samples are collected and the collected samples are stored at 20 0 c.by using highperformance liquid chromatography with Ultra violet detector amount of the drug in the aqueoshumorn(81-86).

Conclusion

Compared to liposomes, niosomes are osmotically active and are stable chemically.niosomes do not contain any special conditions for handling, protection or storage or any other purpose. the other stutures and characteristic are facilitated by this particular, methodniosomes often regulars the various advantageous method for drug delivey system and has found a wide range of variety in pharmaceutical field. It was concluded that niosomes are very effective against the drug delivery system, they improve the patience compliance and reducing the dosing frequency

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