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An Overview on Design and Characterization of Cetrimide and Norfloxacine Loaded Niosomal Gel for Topical Uses: An Approach to Controlled Release Formulation

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ABSTRACT

In a recent search, many of the emerging technologies are developed which provide controlled and predetermined rate release of the drug inside the body. One of the modified techniques incorporated in the same lie is a liposomal-based drug delivery system. Such a system contains a vesicle base carrier system for loading an appropriate category of drug. Encapsulation of the drug in vesicular structures is one of the promising systems. Like as, liposomes, niosomes, ethosomes etc. It delivers the drug directly to the site of action, leading to a reduction of drug toxicity with no adverse effects. Vesicular drug delivery reduces cost by increasing bioavailability and also decreases drug insolubility. Niosomes is a novel drug delivery system, in which drug is encapsulated in vesicles, composed of a non-ionic surfactant. The niosomes are microscopic. Niosomes are nonionic surfactant-based vesicles. It can trap hydrophilic and lipophilic drugs. They are structurally similar to the liposome. Niosomes are formed by non-ionic surfactants and cholesterol. Their surface formation and modification are very easy because of the functional groups on their hydrophilic heads. They can improve the therapeutic performance of the drug molecules by protecting the drug from the biological environment. They can trap lipophilic drugs into vesicular bilayer membranes and hydrophilic drugs in aqueous compartments. The bilayer in the case of niosomes is made up of non-ionic surface-active agents. Niosomes may be unilamellar or multilamellar depending upon the method used to form the niosomes. Niosomes have advantages as drug carriers, such they are less costly, they are chemically stable. But there is some problem related to physical stability, aggregation, sedimentation, and leakage on storage. Niosomes have great drug delivery potential for targeted delivery of anti-cancer. They exhibit high stability and enable the delivery of drugs at the target site in a sustained or controlled manner.

INTRODUCTION

Niosomes are controlled drug delivery systems or controlled medication conveyance frameworks. Controlled medication conveyance is one that conveyance the medication at a foreordained rate, locally or fundamentally, for a predetermined timeframe. In the controlled medication conveyance framework the complete portion is low. Controlled medication conveyance diminished GI reactions. Controlled medication conveyance decreased dosing recurrence. They have better patient acknowledgment and consistency. They have less vacillation at plasma medicate levels. Controlled medication conveyance has a progressively uniform medication impact. Controlled medication conveyance frameworks of prescription have a few weaknesses:-

- Dose dumping
- Stability issue

Noisome are engineered infinitesimal vesicles. Such Vesicles are set up from self get together of hydrated non-ionic surfactant atoms. Niosome is a piece of novel medication conveyance framework. Niosome are utilized for focused medication conveyance. They are little molecules used to convey medication to the target site. Niosome is readied utilizing non-ionic surfactant. Niosome is commonly utilized for the treatment of tumors and malignancy. They have a bilayer structure. They have an infinitesimal structure of the size range between 10 to 1000 nm. Niosome comprises of non-immunogenic, biodegradable, and biocompatible surfactants. Niosome are steadier than liposomes. Niosome are less aggravation than liposomes. Niosome are exceptionally little in size.

1.1 Structure of niosomes

Niosomes are minuscule bodies that are exceptionally helpful media for conveying medications of variation classes. The structure of niosomes can be described by following under giving properties:

- Niosomes are infinitesimal lamellar structures.
- The basic parts are :

- Nonionic surfactant
- Cholesterol

- Charge actuation molecules

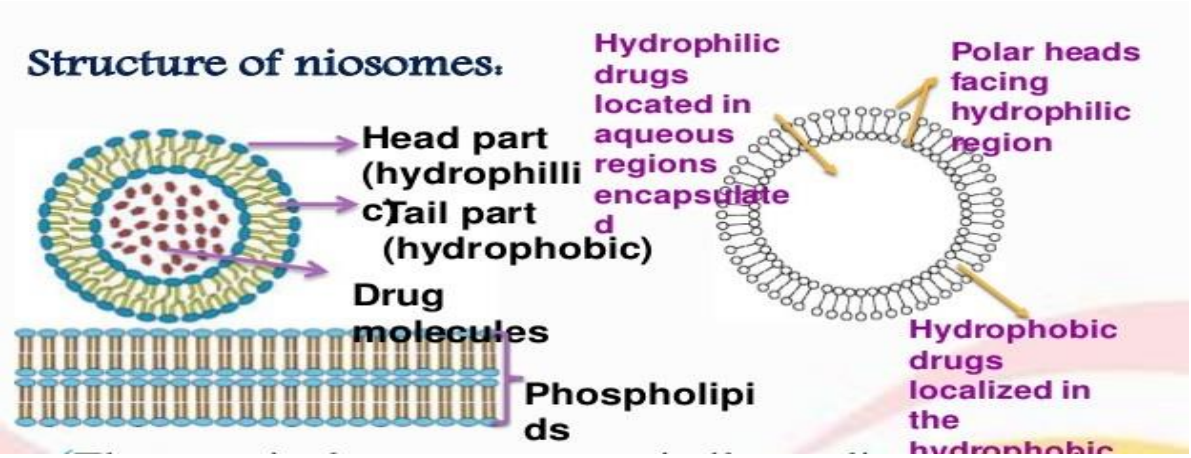


Figure No. 1.1 Structure of Niosomes Vesicle

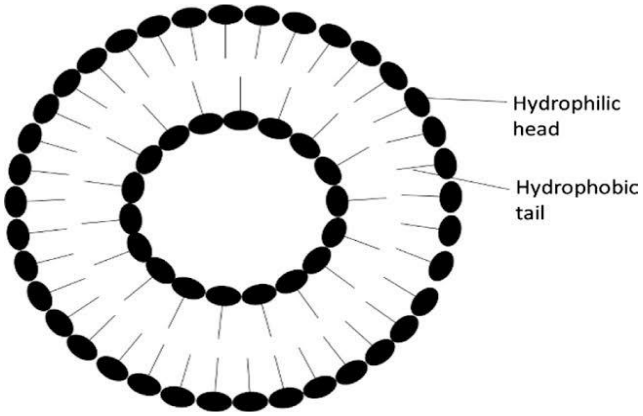


Figure No. 1.2 Structure of Niosomes Vesicle

1.2 Composition of Niosome

1. Cholesterol - They are used to provide rigidity and shape to niosome. Cholesterol is a waxy steroid. They prevent leakage.

2. Non-ionic surfactant - They are used for the preparation of niosomes.

Examples : a - Tween (20, 40, 60, 80)

b - Spans (20, 40, 60, 80, 85)

c - Brijs (30, 35, 52, 58, 72)

Types of non-ionic surfactant:- **. Fatty alcohol**

. Ethers

. Esters

. Block copolymers

1.3 Advantages

1. They are osmotically dynamic.

2. They increment the soundness.

3. Increase skin penetrability when applied topically

4. Decrease the symptom

5. Increase the bioavailability

6. The surfactants utilized for the readiness of niosomes are biodegradable, biocompatible and non-immunogenic.

7. Niosomes are amphiphilic, hydrophilic, lipophilic in nature.

8. Niosome can discharge in the continued/controlled way.

9. They don't require any unique condition for the capacity of surfactant.

10. They increment the penetration of medication.

11. They improve the restorative profile.

12. Niosomes are acting as the best bio carrier for most drugs.

1.4 Disadvantages

1. Hydrolysis of entangled medication

2. Time expending

3. Requires particular hardware

4. Inefficient medication stacking

5. Aggregation

6. Physical shakiness

7. Leaking of ensnared tranquilize

1.5 Formulation Methodology of niosomes

The following methods can be used to formulate a niosomal carrier system:

1) Passive trapping techniques.

a) Sonication

b) Ether injection method

c) Reverse phase evaporation technique

d) The “Bubble method”

e) Handshaking method (thin film hydration technique/rotary evaporator)

f) Micro fluidization

2) Active trapping techniques

a) Transmembrane pH gradient drug uptake process

3) Miscellaneous method

a) Emulsion

b) Heating

c) Lipid injection

1.6 Factor influencing niosomal formulation

The following factors affect the formulation process of niosomal drug carrier system:

- Drug
- Charge
- Nature of surfactant
- Hydration Temperature
- Nature of encapsulated drug
- Resistant to osmotic pressure
- Content of Cholesterol

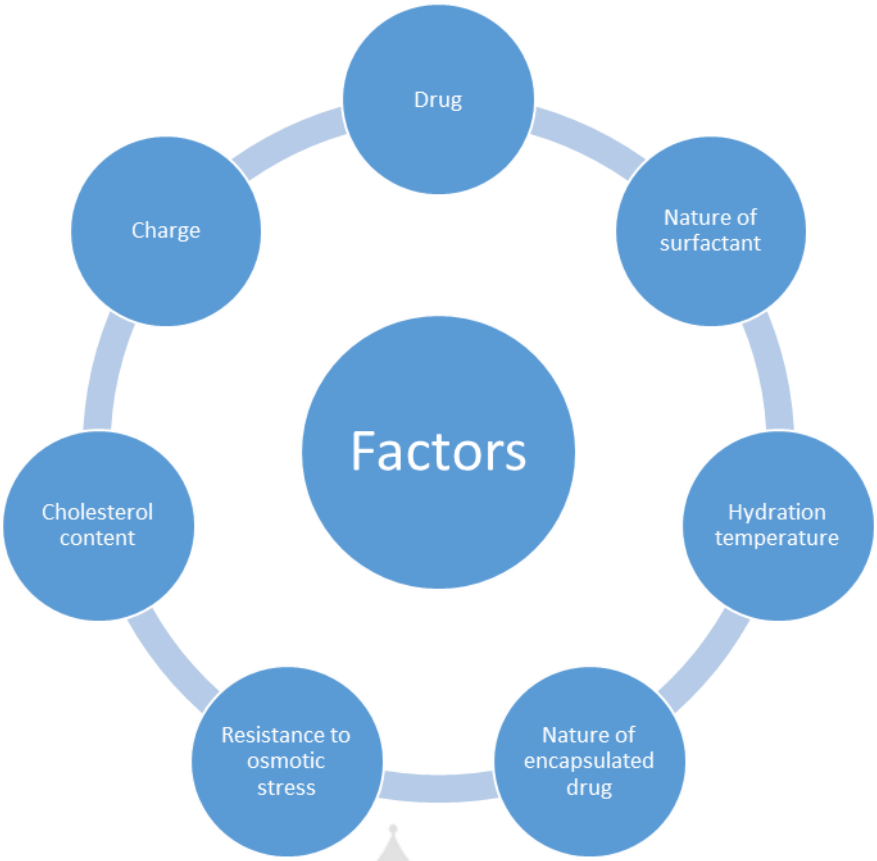


Figure No. 1.3: Diagram representing different factors affecting niosomes formation

i. **Nature of surfactant**- With the increment of the HLB value of surfactant they increase the size of niosomes. Entrapment efficiency is affected by the gel.

ii. **Nature of encapsulated drug**- The niosomal bilayer is greatly influenced by the physical chemical properties of the encapsulated drug. The entrapment of the drug occurs by interacting with the surfactant head groups leading to the increasing charge and creates mutual repulsion of the surfactant bilayer and thus increasing the size of the vesicles.

iii. **Hydration temperature**- The size and shape of niosomes are affected by hydration. Change in temperature affects the surfactant into vesicles.

iv. **Cholesterol content**- The Incorporation of cholesterol increases the entrapment and hydrodynamic diameter of niosomes. Cholesterol acts in two ways:

- Increase the chain order of the liquid state bilayer.
- Decrease the chain order of gel state bilayer.

1.7 Separation of unentrapped drug

The removal of unentrapped solute from the vesicles can be accomplished by various techniques, which includes: -

1) **Dialysis**: The aqueous niosomal dispersion is dialyzed in dialysis tubing against phosphate buffer or normal saline or glucose solution.

2) **Gel filtration**: The unentrapped drug is removed by gel filtration of niosomal dispersion through a sephadex-G-50 column and elution with phosphate buffered saline or normal saline.

3) **Centrifugation**: The niosomal suspension is centrifuged and the supernatant is separated. The pellet is washed and then resuspended to obtain a niosomal suspension free from unentrapped drug.

1.8 Application of niosomes

The application of niosomal technology is widely varied and can be treat a number of diseases.

1. **Niosomes as drug carriers** – niosomes is also used as carriers for iobitridol, a diagnostic agent used for X-ray imaging.

2. Targeting of bioactive agents-

a. To reticuloendothelial system (RES)

b. To organs, other than RES

3. **Antineoplastic treatment** – Many antineoplastic drugs cause side effects. Niosomes can alter the metabolism and half-life of the drug, decreasing the side effect of the drug.

4. **Use in studying immune response** – Niosomes are used to study the nature of the immune response.

5. **Ophthalmic drug delivery** – The eye disorder are cured by the installation of drugs into the eye.

6. **Leishmaniasis** – Leishmaniasis is a disease caused by parasites of the Leishmania type. It is spread by the bite of certain types of sandflies. The disease can present in three main ways: cutaneous, mucocutaneous, or visceral.

1.9 Therapeutic application of niosomes

1. For the controlled release of drug

i. To prolong the release rate

The release rate of the drug was found slower as compared to other dosage forms.

ii. In ophthalmic drug delivery

The practical result of the water-soluble antibiotic showed a substantial change in the release rate. As compared to normal drug solutions, drugs show slow release.

2. To improve the stability and physical properties of the drugs

i. To increase oral bioavailability

With the formation of niosomes, the oral bioavailability will increase.

ii. For improvement of stability of peptide drugs

The in vitro release of insulin from niosomes formulated by span 40 and span 60 in the simulated intestinal fluid was lower than the niosomes formulated by span 20 and span 80.

iii. To promote transdermal delivery of drugs

There are some drugs such as estradiol, lidocaine that are used for topical and transdermal drug delivery systems by formulating them as niosomes.

iv. As a tool for improvement of stability of immunological products

Low toxicity and more stability of the incorporated active moiety.

3. For targeting and retention of drugs in blood circulation

i. For liver targeting

Methotrexate was reported to be selectively taken up by liver cells after administration as a niosomal drug delivery system.

ii. To improve the efficacy of drug in cancer therapy

Niosomes can also be used for the administration of drug-like 5-FU.

CHAPTER- 2

2.1 LITERATURE REVIEW

1. Kaur Dhanvir, Kumar Sandeep et al (2018), in the current investigation was presumed that the Niosomes have been concentrated as an option in contrast to liposomes. A few focal points over liposomes, for example, their moderately higher synthetic steadiness, improved virtue and generally lower cost in examination with liposomes. Non-ionic surfactant vesicles change the plasma freedom energy, tissue dissemination, digestion, and cell connection of the medication rate discharge.

2. Anbarasan B. et al (2011), presumed that the dainty film hydration strategy is a helpful technique for the fruitful consolidation of hydrophilic medications. The plans were portrayed regarding size, entanglement effectiveness, in-vitro tranquilize discharge, and soundness under explicit conditions. It has been presumed that the Niosomes arranged with Tween 60 (F16) has greater capture proficiency and discharge medicate gradually (67.95±0.65) in a supported way when contrasted with different details. The medication discharge design from Capecitabine stacked Niosomes follows Higuchi's model and first request discharge. The drawn-out arrival of the medication from the niosomes proposes that the recurrence of organization might be diminished. Further, as the particles are in nanometeric size range, the bioavailability might be expanded and viable focusing on might be accomplished. Future examinations in creatures, human volunteers, pharmacological and toxicological examinations in creatures, and human volunteers may assist with abusing the niosomes as prosperous medication transporters for focusing on drugs all the more proficiently. Henceforth, we can presume that niosomes give controlled arrival of medication and these frameworks are utilized as medication transporters for the conveyance of cytotoxic medications with fewer symptoms.

3. Jothy Arul et al (2015), Niosome is utilized as a colloidal vesicular transporter in sedate conveyance. It is comprised of non-ionic surfactant vesicles which are biodegradable and non-harmful. It is financially savvy and stable contrasted and other colloid transporters. It has applications in oral, topical, parental, and novel medication conveyance is controlled and focused on conveyance. In the prior 70's the niosomes were utilized in the field of beautifying agents. Lancome propelled an enemy of maturing niosomal cream in 1986. In epic medication conveyance, it has applications in the treatment of malignant growth, utilized as a bearer in hemoglobin, conveyance of the peptide tranquilizes through the oral course, in

treatment of leishmaniasis, in ophthalmic conveyance, in beauty care products, and as a transporter in dermal medication conveyance. This survey article centers around niosome structure, organization, points of interest, sorts of niosomes, techniques for arrangement, portrayal, and its application. It likewise bargains in insight regarding the job of niosome as a transporter in dermal medication conveyance.

4. Ahmed Usama et al (2016), communicated that Niosomes have been accounted for as a potential way to deal with improving low skin saturation appeared by ordinary vehicles. In this examination, a dangerous based conveyance arrangement of meloxicam (MX) was created and portrayed for in vitro execution. Niosomes were set up by turn around stage dissipation strategy (REV) utilizing diverse nonionic surfactants and cholesterol in various molar proportions (1:1, 2:1, 3:1,1: 2 and 1:3) and distinctive medication stacking (5, 10 and 15 mg). The pre-owned surfactants included Tweens (20, 40, and 80), Brij (35 and 58), and Myrj 52. The readied frameworks were portrayed to capture productivity and in-vitro discharge. In like manner, chosen frameworks were assessed for vesicle size, and planned into various hydrogel bases (sodium carboxymethyl cellulose, hydroxypropyl cellulose, and sodium alginate). In-vitro sedate discharge from the various plans was concentrated over a time of 8 hr. Impact of definition added substances on sedate discharge was likewise researched. The calming movement of the chose plans was assessed by the paw edema test. Results indicated high embodiment productivity which ran from about 81.93% to 99.23%. The most elevated ensnarement productivity was gotten with 1:1 surfactant: cholesterol proportion and 15 mg tranquilize stacking, so niosomes arranged by this proportion were chosen for additional investigations. Molecule size extended from 4.047 to 12.334 µm for various niosomal frameworks. In vitro tranquilize discharge from various gel definitions containing 0.3% MX was contrasted with that from similar plans containing 0.3% niosomally captured sedate. In all details the medication discharge was increasingly supported in the event of niosomally ensnared sedate. Consolidation of glycerol and propylene glycol as plan added substances into gel details uniquely upgraded the medication discharge, yet the discharge from gels containing niosomally entangled medication was as yet postponed.

5. Dhakar et al., (2018), inferred that the elevated level of power over the engineering of a dendrimer, their shape, fanning length and thickness, their surface usefulness, and inside void space (porosity, etc makes dendrimer perfect transporters for different applications like medication conveyance, remedial and analytic specialist. Poor solvency, bioavailability and porousness biocompatibility, and poisonousness can be overwhelmed by using it. The high

thickness of surface gatherings permits the connection of focusing on bunches just as gatherings that change the arrangement conduct or harmfulness of dendrimers. Bioactive specialists may be epitomized into the inside, truly adsorbed or synthetically appended to the dendrimer surface, with numerous choices for fitting vector properties to the particular needs of the dynamic material and its helpful applications. At long last, certain anionic surface-changed dendrimers are demonstrated to work as protected and viable topical nanopharmaceuticals against HIV and genital herpes. Ideally, this survey of dendrimer-based clinical applications unmistakably delineates the capability of this new considerably more elevated level of good faith for 'fourth design class of polymers' and reaffirms the future job of dendrimers in the medication conveyance, analysis, and treatment.

6. Shankyan Anchal et al (2012), current audit work is an endeavor to communicate that niosomes are novel medication conveyance framework that offers an enormous number of points of interest over other customary and vesicular conveyance frameworks. In particular focused on conveyance, a decrease of portion, steadiness, and similarity of non-ionic surfactants, simple change, deferred leeway, appropriateness for a wide scope of Active Pharmaceutical Agents, and so on. From the above arrangement of work it very well may be inferred that niosomes have appropriateness for typifying a differed assortment of medications and furthermore the advantages offered by niosomes are likewise generally misused. Niosomes have advanced for treatment of numerous frightful illnesses proficiently with decreased reactions and better patient consistence. In this manner niosomes present itself as a flexible device in therapeutics.

7. Gevariya, Hitesh B., (2013), communicated that the Niosomes in topical visual conveyance are favored over other vesicular frameworks due to the accompanying reasons: (1) synthetic soundness; (2) low harmfulness as a result of their non-ionic nature; (3) taking care of surfactants with no extraordinary precautionary measures or conditions; (4) the capacity to improve the exhibition of the medication by means of better accessibility and controlled conveyance at a specific site; (5) being biodegradable, biocompatible and non-immunogenic. The benefit of vesicular frameworks doesn't just dwell in giving drawn out and controlled activity at the corneal surface yet additionally includes giving controlled visual conveyance by keeping the digestion of the medication from the chemicals present at the tear/corneal epithelial surface.

8. Mehta Akul et al., (2010), was presumed that, Niosomes are a novel medication conveyance framework, in which the prescription is exemplified in a vesicle. The vesicle is made out of a bilayer of non-ionic surface dynamic operators and subsequently the name niosomes. The niosomes are extremely little, and tiny in size. Their size lies in the nanometric scale. Albeit basically like liposomes, they offer a few points of interest over them. Niosomes have as of late been appeared to significantly increment transdermal medication conveyance and furthermore can be utilized in focused medication conveyance, and along these lines expanded investigation in these structures can give new techniques to sedate conveyance.

CHAPTER 3

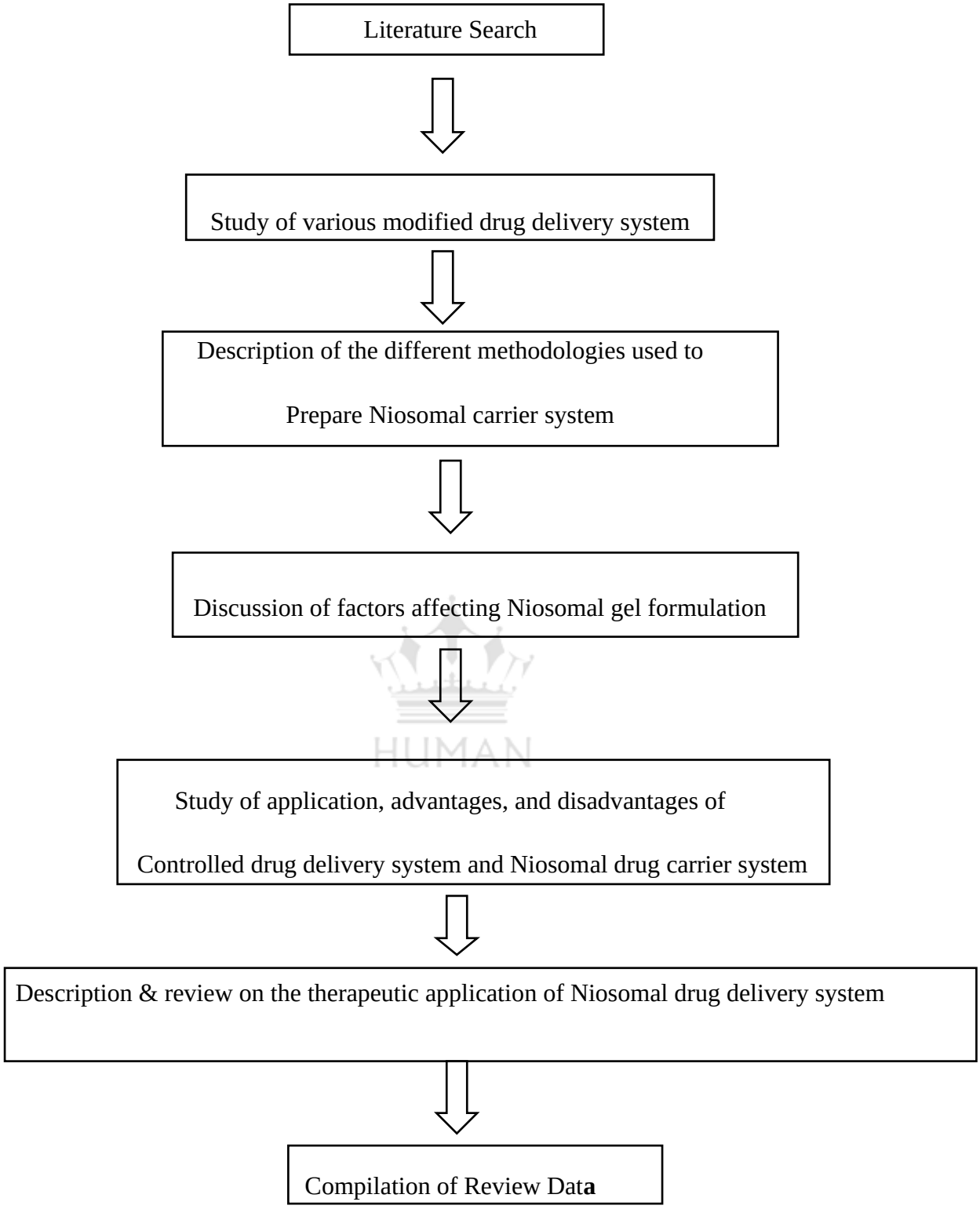
3.1 AIM AND OBJECTIVE

AIM: Design and Characterization of Cetrimide and Norfloxacine loaded niosomal gel for topical use: An approach to controlled release formulation.

OBJECTIVES:

1. To discuss the modified drug delivery system and its application.
2. To study the various types of controlled drug delivery patches.
3. To study in detail structure and composition of niosomal gel formulation.
4. To study the various factors which are affecting niosomal drug delivery process.
5. To discuss the different methodology to prepare niosomal gel system.
6. To express various application and properties of Transdermal drug delivery system.
7. To discuss about various marketed available transdermal drug delivery system.
8. To conclude about the best selected formulation and methodology to prepare a therapeutically efficient niosomal drug carrier system.

3.2 PLAN OF WORK



CHAPTER- 4

4.1 MATERIAL AND METHOD

MATERIALS

Chemicals used generally to prepare a drug loaded Niosomal gel system are listed in table no.:1.1.

Table No. 1.1: List of chemicals

Sr. No.	Chemical	Applications
1.	SPAN 80	Surfactant
2.	Diglycerol ether	Surfactant
3.	Cholesterol	Entrapment efficiency enhancer
4.	Sodium Lauryl Sulphate	Permeation Enhancer
5.	Diacetyl phosphate (DCP)	Stability Enhancer
6.	Carbopol 934	Gelling agent
7.	Propylene glycol	Permeation Enhancer
8.	HPMC K100	Thickening agent
10.	Chitosan	Natural Polymer
6.	Carbopol and Sodium alginate	Synthetic Polymer
7.	Ethanolor Chloroform	Vehicle
9.	Drug (Cetrimide)	Antiseptic
10.	Drug (Norfloxacine)	Antibiotic

4.2 DRUG PROFILE

1. Cetrimide

Cetrimide is a quaternary ammonium compound utilized as sanitary surfactants. Inside the watery arrangement, Surfactants are changed over into a bioactive action, the capacity of which is the surface impact, just as an anion with a more fragile action. The substance is combined for quite a while with certain, just as collagen, in this way shaping cetrimide-protein buildings. That is the reason arrangements utilized for the treatment of dermatological sicknesses with a low degree of cetrimide don't have noteworthy retention. It is likewise having the property of amazing disinfectant, for sanitizing careful instruments, cleaning wounds, and so on.

IUPAC Name of Glimepiride: hexadecyl(trimethyl)azanium;bromide

Chemical formula: $C_{19}H_{42}BrN$

Mol. Wt.: 336.4g/mol

Structure:

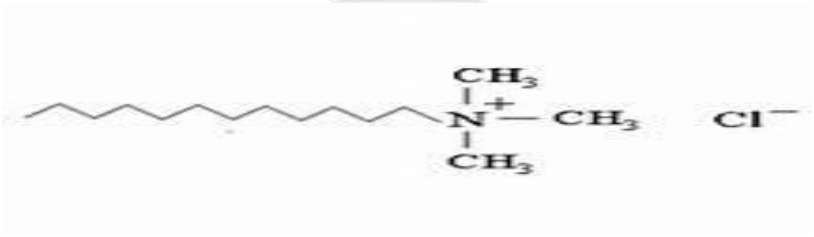


Figure No. 1.4: Structure of Cetrimide

Category: Antiseptic

Uses:

- Seborrheic Dermatitis and Scalp psoriasis
- Wound cleansing
- Minor burns

Storage: Store at below 25 °C.

Physiochemical Properties:

State: Solid

Description: White and Free Flowing Powder

Solubility: Unreservedly Soluble in Water, in Ethanol (95%) and in Chloroform, Practically Insoluble in Ether

Loss on Drying: Not More Than 2.0 %, Determined On 1.0g By Drying In An Oven At 100°C to 105°C For 2 Hrs.

Melting point: 245-250 °C

Dosage Form strengths:

Wound cleansing - Topical: Adult: Apply 0.1-1% aqueous solution or 0.5% cream onto affected area.

Seborrhoeic dermatitis - Topical: Adult: Apply 10% shampoo solution onto the scalp.

Mechanism of action: This medicine is a sort of germicide that is demonstrations through three modes, in particular, protein denaturation, film harm, and catalyst inactivation. At low levels, the drug goes about as bacteriostatic, while in higher fixations it is a bactericide.

Symptoms: Nausea, spewing, and so on. The significant symptom incorporates:

- Rash
- Skin rankling
- Redness of skin
- Burning sensation

Safety measures:

- Inordinate utilization may expand the danger of hypersensitive responses.
- Avoid contact with eyes, center ear, meninges, mind, body cavities.
- Consult with your primary care physician before utilizing this drug.

- Caution is required for pregnant and breastfeeding ladies.
- For outside utilize as it were.

2. Norfloxacine

Norfloxacin is an antibiotic in a gathering of medications called fluoroquinolones (flor-o-KWIN-o-lones). Norfloxacin battles microscopic organisms in the body. Norfloxacin is utilized to treat distinctive bacterial diseases of the prostate or urinary tract (bladder and kidneys). Norfloxacin is likewise used to treat gonorrhea.

IUPAC Name of Glimepiride:

1-ethyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic acid

Chemical formula:

$C_{16}H_{18}FN_3O_3$

Mol. Wt.: 319.33 g/mol

Structure:

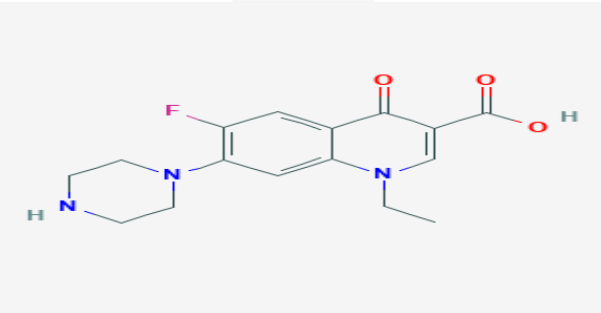


Figure No. 1.5: Structure of Glimepiride

Category: Antibiotic

Uses:

- In Uncomplicated urinary tract infections (including cystitis)
- In Complicated urinary tract infections (restricted use)
- In Uncomplicated urethral and cervical gonorrhea (however this indication is no longer considered to be effective by some experts due to bacterial resistance).

- In Prostatitis due to *Escherichia coli*.
- Syphilis treatment: Norfloxacin has not been shown to be effective in the treatment of syphilis.
- Antimicrobial agents used in high doses for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis.

Storage: Store at below 25 °C

Physiochemical Properties:

State: Solid

Description: White Powder

Solubility: Freely soluble in glacial acetic acid, and very slightly soluble in ethanol, methanol and water

Melting point: 221 °C

Bioavailability: 30 to 40 %

Protein Binding: 10-15%

Metabolism: Hepatic

Elimination Half-life: 3-4 hrs

Excretion: Renal and Fecal

Mechanism of action: Norfloxacin is a wide range anti-toxin that is dynamic against both Gram-positive and Gram-negative microbes. It works by restraining DNA gyrase, a sort II topoisomerase, and topoisomerase IV, compounds important to isolate bacterial DNA, subsequently repressing cell division. Norfloxacin doesn't tie to DNA gyrase however binds to the substrate DNA.

Side effects:

- Headache with chest torment and extreme discombobulation, swooning, quick or beating pulses.
- Dark pee, earth-shaded stools, jaundice (yellowing of the skin or eyes).

- Muscle shortcoming or inconvenience relaxing.
- Diarrhea, Sudden shortcoming or sick inclination, fever, chills, sore throat, mouth wounds, simple wounding or dying;
- Depression, disarray, visualizations, distrustfulness, tremors, feeling fretful or on edge, strange musings or conduct, a sleeping disorder, bad dreams.
- Seizure (seizures)
- Increased pressure inside the skull- - extreme cerebral pains, ringing in your ears, sickness, vision issues, torment behind your eyes.

Common side effects may include:

- Nausea, heartburn, stomach cramps, mild diarrhea;
- Vaginal itching or discharge;
- Mild dizziness; or
- Mild headache.

Contraindications:

- Noroxin (norfloxacin) is contraindicated in people with a past filled with extreme touchiness, tendinitis, or ligament crack related to the utilization of norfloxacin or any individual from the quinolone gathering of antimicrobial operators.
- Quinolones, including norfloxacin, have been appeared in vitro to restrain CYP1A2. Accompanying use with drugs processed by CYP1A2 (e.g., caffeine, clozapine, ropinirole, tacrine, theophylline, tizanidine) may bring about expanded substrate tranquilize fixations when given in normal dosages.
- A concomitant organization with tizanidine is contraindicated.
- Norfloxacin is additionally viewed as contraindicated inside the pediatric populace.

4.3 METHODOLOGY

1) Passive trapping techniques.

a) Sonication

b) Ether injection method

c) Reverse phase evaporation technique

d) The “Bubble method”

e) Handshaking method (thin film hydration technique/rotary evaporator)

f) Micro fluidization

2) Active trapping techniques

a) Transmembrane pH gradient drug uptake process

3) Miscellaneous method

a) Emulsion

b) Heating

c) Lipid injection

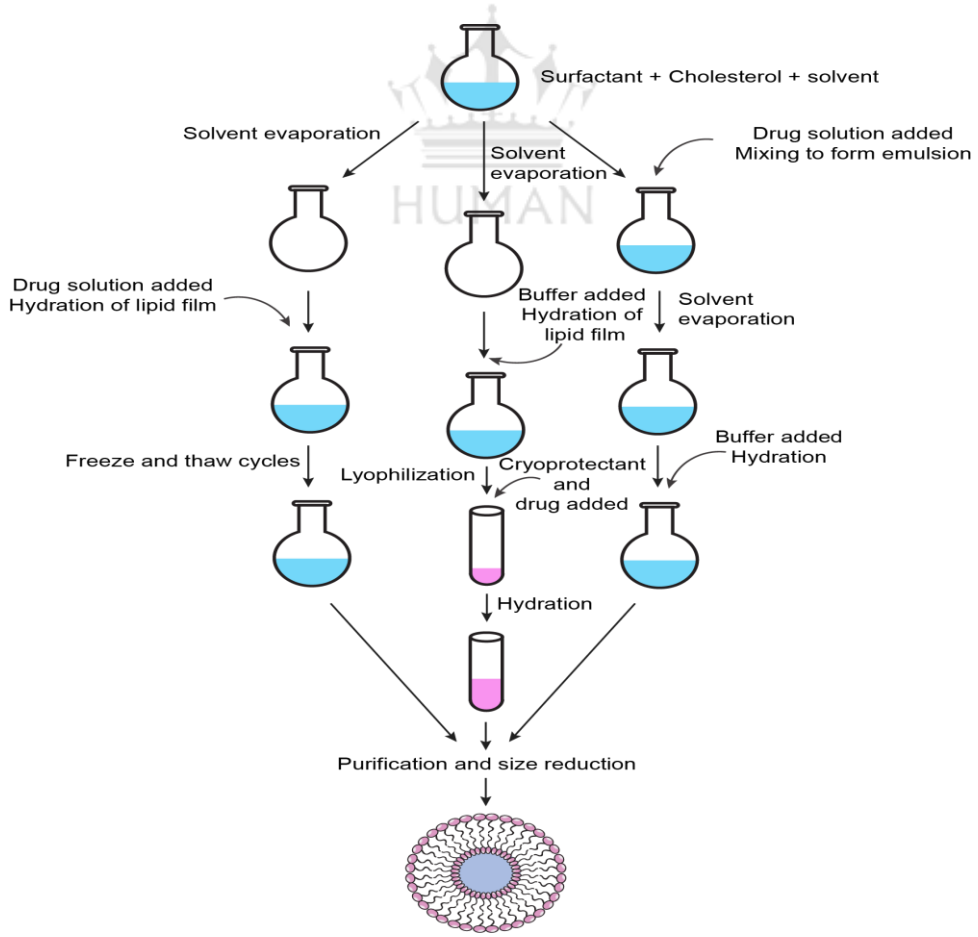


Figure No. 1.6: Diagrammatic representation of Processing of Niosomes

The detail descriptions of such methods are given below.

1) Passive trapping techniques - This technique is very important for the preparation of niosomes in which drug is incorporated during the preparation.

a) **Sonication-** a mixture of drug solution, surfactant, and cholesterol

↓

Sonicated with a titanium probe sonicator at 60^0C for 3 minutes.

b) **Ether injection method-**

Step 1: The surfactant dissolved in solvent diethyl ether and warm water at a temperature of 60^0C.

Step 2: Above mixture via 14gauge needle injected into the aqueous solution.

Step 3: This mixture allowed for evaporation and a single layer of vesicles were formed.

Step 4: The formulated vesicles within the range of 500 to 1000 nm in range.

c) **Reverse phase evaporation technique-**

Step 1: The surfactant and cholesterol mixture dissolved in an organic solvent.

Step 2: Above mixture mixed properly and W/O type emulsion was formed.

Step 3: This mixture allowed for drying at 40^0C.

Step 4: To this mixture added a phosphate-buffered saline solution which clears the gel.

Step 5: Formulated gel allowed for sonication.

Step 6: The sonicated solution was diluted with phosphate-buffered saline solution and then heated on a water bath at a temp. of 60^0C for 10 minutes.

d) The "bubble" method

Step 1: To prepare niosomes based carrier system Surfactant and cholesterol placed in a round bottom flask and mixed with three neck positions in the water bath.

Step 2: Water cool reflux is in the first neck and thermometer is in the Second neck and nitrogen supply in the third neck.

Step 3: The Cholesterol and surfactant are dispersed in buffer (pH 7.4) at a temperature of 70^0C.

Step 4: This mixture allows for mixing by homogenizer for about 15 seconds.

Step 5: This mixture Bubbled at 70^0C using nitrogen gas.

e) Handshaking method (thin film hydration technique/rotary evaporator)

Step 1: To prepare niosomes based carrier system Surfactant and cholesterol are placed in a round bottom flask and mixed. For powerful mixing, a volatile organic solvent was also added mixed completely.

Step 2: This mixture allowed for evaporation at 20^0C by placing into the rotary evaporator and then allowing for drying.

Step 3: The dried surfactant film rehydrated with an aqueous phase at 0 to 60^0C with agitation.

Step 4: When agitation is completed Vesicles started to form.

f) Micro fluidization

Two fluidized streams interact with each other at high velocities and in the microchannel. The impingement of a thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. The greater uniformity, smaller size, and better reproducibility.

2) Active trapping techniques- This includes the loading of the drug after the formation of niosomes. The niosomes are prepared and the drug is maintaining the pH gradient or ion gradient to facilitate of the drug into niosomes. Advantages of niosomes from are 100% entrapment, absence of leakage, cost-effectiveness and high drug lipid ratios.

a) Transmembrane pH gradient drug uptake process-

Step 1: In this methodology, in a round bottom flask the surfactant and cholesterol in an accurate ratio (1:2) were dissolved in a suitable organic solvent and allow for evaporation by using a solvent evaporator.

Step 2: Due to evaporation, a thin film is formed at the walls of the evaporation flask. This film allows for hydration by using a vortex mixer with the addition of 300 mM citric acid (pH4.0).

Step 3: By vortex mixing vesicles are formed and allowed for frozen and then sonicated.

Step 4: To make niosomal suspension preparation, an aqueous solution containing 10mg/ml of the drug was added and pH is increased up to 7.0-7.2 with the addition of disodium phosphate.

Step 5: Prepared mixture allowed to heat for 10 min at 60^0C and niosomes are formed.

3) Miscellaneous method –

a) **Emulsion method**- In this method oil in water emulsion is prepared from an organic solvent of surfactant, cholesterol, and an aqueous solution. Then the organic solvent is evaporated and niosomes are dispersed in the aqueous phase.

b) **Heating method**- This method is non-toxic and based on patent procedure. An aqueous medium such as buffer distilled water. In which a mixture of non-ionic surfactant, cholesterol and charge-inducing molecules are added in the presence of the glycerol. The mixture is heated until the vesicles were form.

c) **Lipid injection method**- The mixture of lipid and surfactant is melted and injected into a heated aqueous phase. Drug dissolve in molten lipid and the mixture will inject into agitating, heat aqueous phase containing surfactant.

4.4 EVALUATION METHODS OF NIOSOMAL GEL:

1. Entrapment Efficiency:

The capture effectiveness of the niosomal gel is unfaltering by UV Visible spectrophotometer. This strategy is valuable to identify the medication contained in the niosomes. Weakening of arranged gel has been finished with the assistance of 10 ml of methanol with overwhelming mixing by utilizing a mechanical attractive stirrer. Toward the finish of weakening a homogeneous arrangement has been acquired and kept aside. This arrangement at that point experiences centrifugation at 1200 rpm for 30 min by utilizing gadget centrifugation. The supernatant fluid was isolated and takes into account UV

examination under UV Visible spectrophotometer at 296 nm with reasonable weakening. The Entrapment productivity rate was determined by utilizing the below referenced equation.

% Entrapment efficiency = (Amount of drug entrapped / Amount of drug added) X 100

Percentage Yield

Formula to detect the percentage yield:

Percentage yield = (Practical yield / theoretical yield) X 100

2. Drug Content

Niosomal gel after the arrangement is additionally assessed for tranquilizer content assurance. In this test acquired buildup was weighed up to 1gm and weakened with support arrangement having of pH 6.8 and make the volume up to 50 ml. This is considered a stock arrangement. From the stock arrangement, 5ml was pipette out in 25 ml volumetric cup, and the volume was made up 25 ml by including phosphate cushion pH 6.8. At that point, the readied weakened same examine under UV Visible spectrophotometer at 296nm. After the UV investigation, the substance of medication was determined by using standard bend of the detailing drug.

3. pH:

The mechanical gadget advanced pH meter was utilized to decide the pH of various kinds of niosomal framework. The gadget is recently aligned before the investigation was performed. Multiple times or in a triplicate the pH of various arrangements was resolved through a pH meter and the result were recorded.

4. Viscosity

To distinguish the thickness of niosomal gel plan a Brookfield Viscometer was utilized. The gels were poured in a measuring utensil and turned at 50 rpm, and the comparing perusing that appeared on the viscometer by the revolution of the shaft was noted. The consistency was communicated in a unit called as centipoises (cps). This process is performed in triplicate.

5. Spreadability

To assess the niosomal gel detailing the test for spreadability were additionally performed. For such test examination the 350mg (approx.) of gel was gauged, and afterward, applied on

the glass plate to decide the spreadability of the gel. Another glass plate was dropped over the recently applied glass plate at the stature of 5 cm. Following one moment the distance across of circle was estimated. Same test marvel was acted in triplicate, and normal qualities were determined.

6. SEM Analysis

To decide the surface attributes of Niosomal sedate bearer framework Scanning Electron Microscopy (SEM) was led. By utilizing this SEM assessment investigation state of the figured niosomes can likewise be resolved. A drop of examining niosomal gel was mounted on spotless and clear glass stub, air-dried and pictured under SEM.

7. In-Vitro Drug Release

To gauge the in-vitro sedate discharge pace of planned niosomal gel detailing an adjusted mechanical assembly Franz dissemination cell of vertical structure is utilized. The distinctive quality detailing of niosomal gel was taken and taken into account test investigation. For this 3 mg of newly arranged gel was spread on the benefactor side of the cellulose nitrate film grade 110 (each example done in a triplicate way). The cellulose film is doused with isopropyl liquor to make it increasingly hydrophobic. In the receptor vessel, 1litre of saline phosphate cradle (pH-7.4) with methanol was filled and set the gathering for test investigation. The investigation was done at 37 ±0.5oC temperature and the speed of the instigator kept up as 400-500 rpm for 11-12 hrs. After a normal time frame, a 5ml example was gathered and supplanted with a similar cushion arrangement. Gathered examples were checked and held it for examination under UV Visible spectrophotometer. A reasonable weakening has been made for each example and focus was estimated at 296nm. Then calculate the final drug release rate with particular period of time.

8. Release Kinetic Studies

The discharge dynamic investigation of niosomal formulation has been directed by utilizing disintegration profile. The active examinations were assessed by the accompanying condition referenced beneath.

• Zero request: Mt = Mo+ Kot

• First request: ln Mt = ln Mo+ K1t

• Higuchi model: Mt = KH √t

• Korsmeyer–Peppas model: Mt/Mo = Kktn

Where Mt is the measure of medication broke down at time t, Mo the underlying measure of medication, K1is the primary request discharge steady, K0 the zero request discharge consistent, KH the Higuchi rate steady, Kk the Korsmeyer–Peppas model discharge consistent and n is the diffusional discharge example demonstrative of the working discharge system. The relationship coefficient (R2) esteem was utilized as a marker of the best fitting, for every one of the models considered.

9. Ex-Vivo Diffusion Studies for Best Formulation

To play out the Ex-vivo dispersion considers a male solid pale-skinned person rodents weighing 150-180 g were yielded for stomach skin. The readied plan which shows the best test outcome was applied to the creature's skin.

In this procedure about of 3mg of gel of niosomal sedate was applied through the benefactor compartment on the creature skin. Thus, promoted gel (MR) of Cetrimide or norfloxacin of 3mg was taken and applied through the benefactor compartment on another dispersion cell. In both the dissemination cells, the store compartment was loaded up with 10 ml of methanol and 40 ml phosphate support arrangement (pH 7.4) at 37±0.5°C at 400 rpm/min for 12 hrs. At ordinary time stretches the Samples were pulled back from the supply compartment and break down under the UV Visible spectrophotometer at 296nm after appropriate weakening to distinguish the medication discharge rate. Each time the supply compartment was renewed with a similar amount of new phosphate cushion arrangement (pH 7.4). The measure of medication content was evaluated in arranged niosomal gel definition and contrasted and the advertised gel. After examination result was recorded and directed.

10. FTIR

Fourier-change Infra-Red spectroscopy can likewise be performed to acquire an Infrared range of ingestion or discharge of strong, fluid, or gas substances. The trademark tops with no moving and expanding with the mix of HPMC polymer (comparative outcomes acquired with different polymers) were recorded.

11. DSC examination

Differential Scanning Calorimetry (DSC) strategies were utilized to examine the similarity on the dynamic medication of plan, various polymers, and their syntheses. DSC bend of the unadulterated medications was thought about with1:1 proportion physical blends. Warm circle of the mixes for example softening point, the nonappearance of a generous move in unexpected melting point, or nonattendance in the showcase originating from new exothermic/endothermic top in the mix demonstrated appropriateness in the center sedate just as polymers.

CHAPTER- 5

CONCLUSION

Niosomes are turning into a developing procedure for a controlled medication conveyance framework. It is a productive transporter framework for the development of medication regarding changed and NDDS forms. These were utilized in the advanced pharmaceutical industry because of their mind-blowing reward over customary vesicular conveyance frameworks. The fundamental goal of the advancement of niosomes is to direct the arrival of medication in a controlled and supported way, further modifications in the appropriation profile of medication, and focusing to the unequivocal body site with the least dosages and less patient consistence. Niosomal tranquilizes conveyance framework can be utilized as a transporter vehicle for various courses of medication organization. For example, Ocular, Topical and Nasal medication Delivery Systems. Therefore, it is working as a successful instrument for the treatment of topical skin contamination treatment. This medication conveyance defeats the difficulties combined with the existing acknowledged medication conveyance framework. In this manner, it shows a promising future. As per the degree of treatment, different medications are financially open as Niosomal gel formulation.

CHAPTER 6

REFERENCES

1. Kaur Dhanvir., Kumar Sandeep, Niosomes: present scenario and future aspects, Journal of drug delivery and therapeutic 2018;8(5):35-43
2. Madhav NVS., Saini A, Niosomes: A novel drug delivery system, International journal of research in pharmacy and chemistry 2011;1(3):2231-2781
3. Arul jothy M., Shanmuganathan S., Nagalakshmi, An overview on niosomes as carrier in dermal drug delivery, Journal of pharmaceutical sciences and research 2015;7(11):923-927

4. Pei Ling Yeo., Soi Moi Chye., Anna Pick Kiong Ling., RhunYian Koh, Niosome: A mini review on its structure, properties, methods of preparation and medical applications, Journal of chemical and pharmaceutical research 2016;8(10):231-239
5. Ahmad Usama., Gihan Fetih., Tahani EI-Faham, performance of meloxicam niosomal gel formulation for transdermal drug delivery, British journal of pharmaceutical research 2016;12(2):1-14
6. Rampal Rajera., Kalpana Nagpal., Shailendra Kumar Singh., Dina Nath Mishra, Niosome: A controlled and novel drug delivery system, Biol.Pharm.Bull 2011;34(7):945-953
7. Lohumi Ashutosh., Rawat Suman., Sarkar Sidhyartha., Sipai Altaf Bhai., Yadav M. Vandana, A novel drug delivery system: niosomes review, Journal of drug delivery and therapeutic 2012;2(5):129-135
8. S.B.Shirsand., Ganesh G.Keshavshetti, Recent advances in miosomal drug delivery- A review, Research journal of life sciences, bioinformatics, pharmaceutical and chemical sciences 2019;5(3):514-531
9. V.Pola Chandu., A.Arunachalam., S.Jegnath., K.Yamini., K.Tharangini., G.Chaitanya, Niosomes: A novel drug delivery system, International journal of novel trends in pharmaceutical sciences 2012;2(1):25-31
10. PranshuTangri., Shaffikhurana, Niosomes: Formulation and evaluation, International journal of biopharmaceutics 2011;2(1):47-53
11. Naresh Kalra., G.Jeyabalan., Gurpreet Singh., Suresh Choudhary, Non ionic surfactant vesicles and their therapeutic potentials, journal of innovations in pharmaceuticals and biological sciences 2016;3(2):193-201
12. M.N.Navya., S.Parthiban., J.AdlinJinoNeasalin., A.Vikneswari, niosomes as novel vesicular drug delivery system- A review, Asian journal of research in biological and pharmaceutical sciences 2014;2(2):62-68
13. Srivastava NS., Thakur S., Kaur J, Niosomes: A novel approach for topical delivery of drugs, International journal of pharmacy and technology 2016;8(2):11712-11731
14. S.Nagalakshmi., N.Damodharan., J.Thanka., S.Seethalakshmi, Niosomes in ocular drug delivery system: A review of magic targeted drug delivery, international journal of pharmaceutical sciences review and research 2015;32(1):61-66
15. Badari Srikanth Reddy., Jakkani Surya Chandra Padman., Voruganti Santosh, Niosomes as nanocarrier system: A review, International journal of pharmaceutical sciences and research 2012;3(6):1560-1568
16. Kothare Ashwini., bhaskarPayal., Rane Pritishikha., Gavhane Mayuri., Kad Dhanashree, Niosomes: A versatile drug delivery system, World journal of pharmaceutical sciences 2018;6(10):30-39
17. Namrata Mishra., Vinamrata Srivastava., Anu Kaushik., Vivek Chauhan., Gunjan Srivastava, formulation and in vitro evaluation of niosomes of aceclofenac, Journal of scientific and innovative research 2014;3(3):337-341
18. Goyal A, Kumar S, Nagpal M, Singh I, Arora S, Potential of Novel Drug Delivery Systems for Herbal Drugs. Indian Journal of pharmaceutical Research and Education, 2011; 45(3): 225-235.
19. Vyas SP, Khar RK. Targeted and controlled drug delivery novel carrier systems; CBS Publishers and Distributors, New Delhi; 2011. p. 249-79
20. Saraswathi t. S., Mothilal M. et al., Niosomes as an emerging formulation tool for drug delivery-a review, International journal of therapeutic application, 2018, p. 249-79