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NIOSOMES: INNOVATIVE SOLUTIONS FOR MODERN DRUG DELIVERY CHALLENGES

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ABSTRACT:

Recent years have seen the development of specific vesicular medication delivery vehicles, including ethosomes, proniosomes, transferosomes, etc. Niosomes and proniosomes in particular, are thought to be more effective carriers of drugs, improving therapeutic efficacy and bioavailability while lowering adverse effects and offering a viable method of transdermal drug delivery. Both are amphiphilic vesicles based on non-ionic surfactants. Because there is no appropriate therapeutic moiety or drug delivery system, many diseases go untreated, particularly when toxicity as well as side effects are the main cause for worry. Due to its affordability and ease of surface modification, it is serves drug delivery vehicle for a hydrophilic or hydrophobic type of drugs. An appropriate niosomal formulation must also be prepared with great care; this formulation is dependent on a variable, like the type of non-ionised surfactant, the production process or the production parameters.

Keywords: Niosomes, Hydrophilic, Hydrophobic, Non-ionic surfactant, Composition, Factors affecting, Fabrication methods, Evaluation.

INTRODUCTION:

Niosomes are mainly microscopic particles formed of a combination of cholesterol as well as non-ionic surfactant, charge-inducing substance. Because this type of surfactants is amphiphilic, they use energy, such as heat or physical agitation, for creating a closed bilayer vesicles in aqueous medium. While the hydrophilic part of the bilayer structure interacts with the aqueous solvent, the hydrophobic part of the assembly oriented away from it. By altering the vesicle's composition, dimensions, charge at the surface and concentration, one can modify their properties [1]. Niosome is a great choice for the cosmetics area because of improved skin penetration and stability of encapsulated medications, greater bioavailability of poorly soluble contents. They are efficacious for topical distribution because

they prolong residence duration of drug substances within the stratum corneum along with decreasing systemic absorption. They are still accepted above liposomes [2].

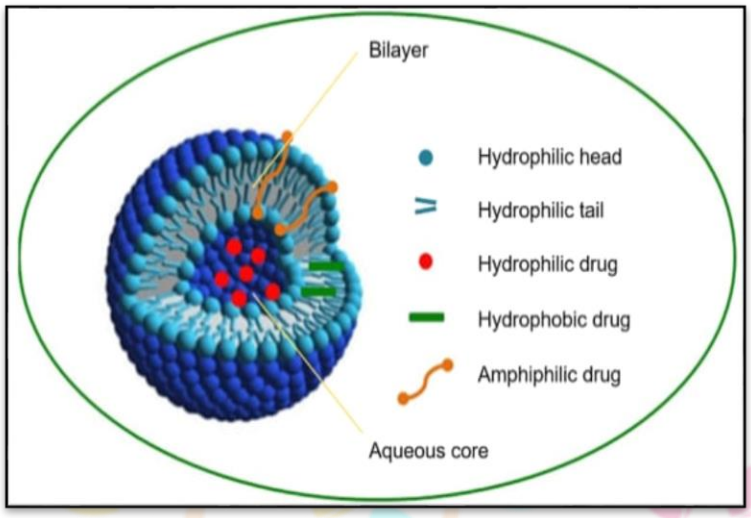


Fig.No.1: Structure of Niosome

Advantages of niosomes [3, 4, 5]:

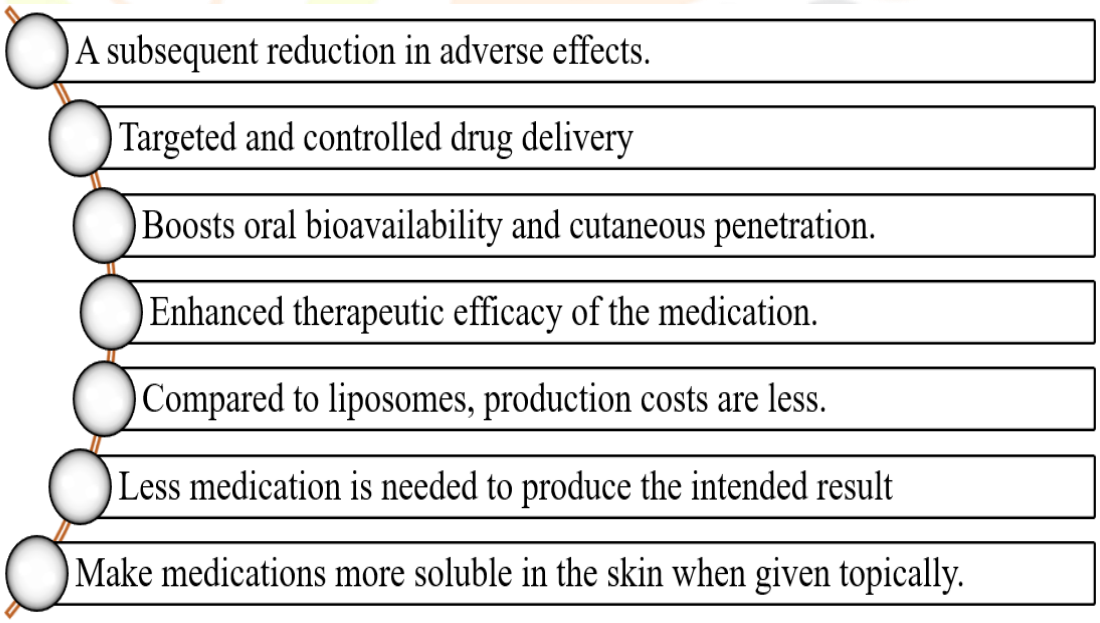


Fig. No.2: Advantages of noisome

Classifications of Niosomes [6]:

1. **General types of niosome:**

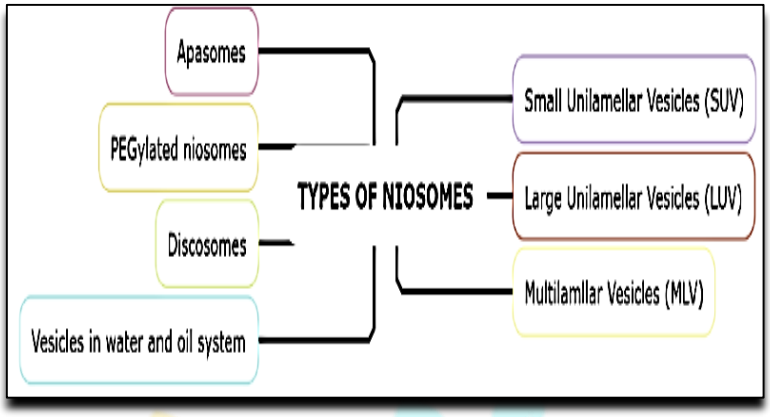


Fig.No.3: General types of niosomes

2. **According to size:**

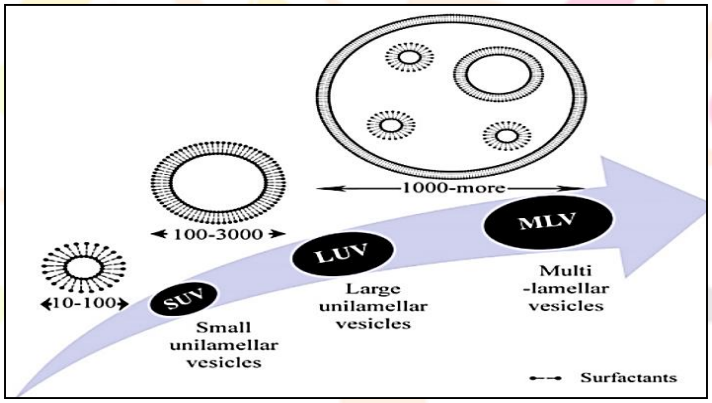


Fig.No.4: According to size

3. **Composition of noisome**:

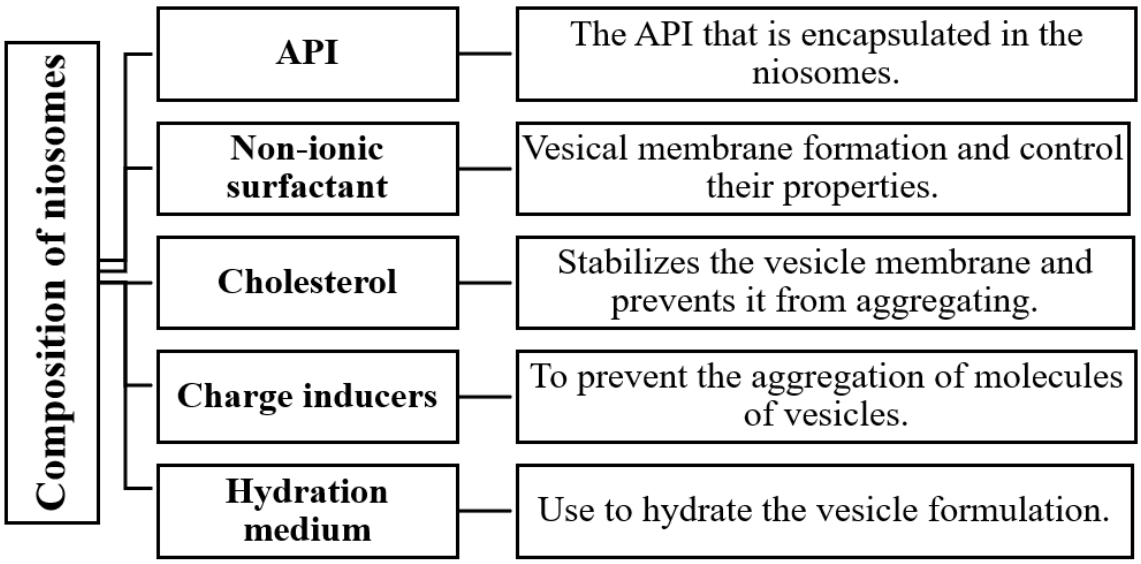


Fig.No.5: Composition of niosome

Materials used in niosome preparation [7]:

Table No. 1: Materials used in niosome preparation

Sl. No.	Nonionic surfactants	Examples
1.	**Alkyl ethers**	
	a. Alkyl glycerol ethers	Hexadecyldiglycerol ether (C16G2)
	b. Polyoxyethylene glycol alkyl ethers (Brij)	Brij 30, Brij 52, Brij 72, Brij 76, Brij 78
2.	**Alkyl esters**	
	a. Sorbitan fatty acid esters (Spans)	Span 20, Span 40, Span 60, Span 80, Span 65,Span 85.
	b. Polyoxyethylenesorbitan fatty acid esters (Tweens)	Tween 20, Tween 40, Tween 60, Tween 80,Tween 65, Tween 85
3.	**Alkyl amides**	
	a. Glycosides	C-Glycoside derivative surfactant
	b. Alkyl polyglucosides	Octyl-decylpolyglucoside (OrCG110), decylpolyglucoside (OrNS10)
4.	**Fatty alcohols or fatty acids**	
	a. Fatty alcohols	Stearyl alcohol, cetyl alcohol, myristyl alcohols
	b. Fatty acids	Stearic acid, palmitic acid, myristic acid
5.	**Block copolymer**	
	a. Pluronic	Pluronic L64, Pluronic 105
6.	**Lipidic components**	
	Cholesterol and l-α-Soya phosphatidyl choline	
7.	**Charged molecule**	
	a. Negative charge	Diacetyl phosphate, phosphatidic acid, lipoamino acid, dihexadecyl phosphate
	b. Positive charge	Stearylamine, stearylpyridinium chloride, cetylpyridinium chloride

Difference between niosomes and liposomes [8]:

Table No. 2: Difference between niosomes and liposomes

Characteristic	Liposomes	Niosomes
Stability	Chemically less stable	Chemically more stable
Cost	Expensive	Less expensive
Materials	Prepared from double chain phospholipids	Prepared from single-chain non-ionic surfactants
Storage	They require special storage & handling conditions	They do not need special storage conditions
Toxicity	Ionic drug carriers are less safe and toxic	Non-ionic carriers are safe and nontoxic

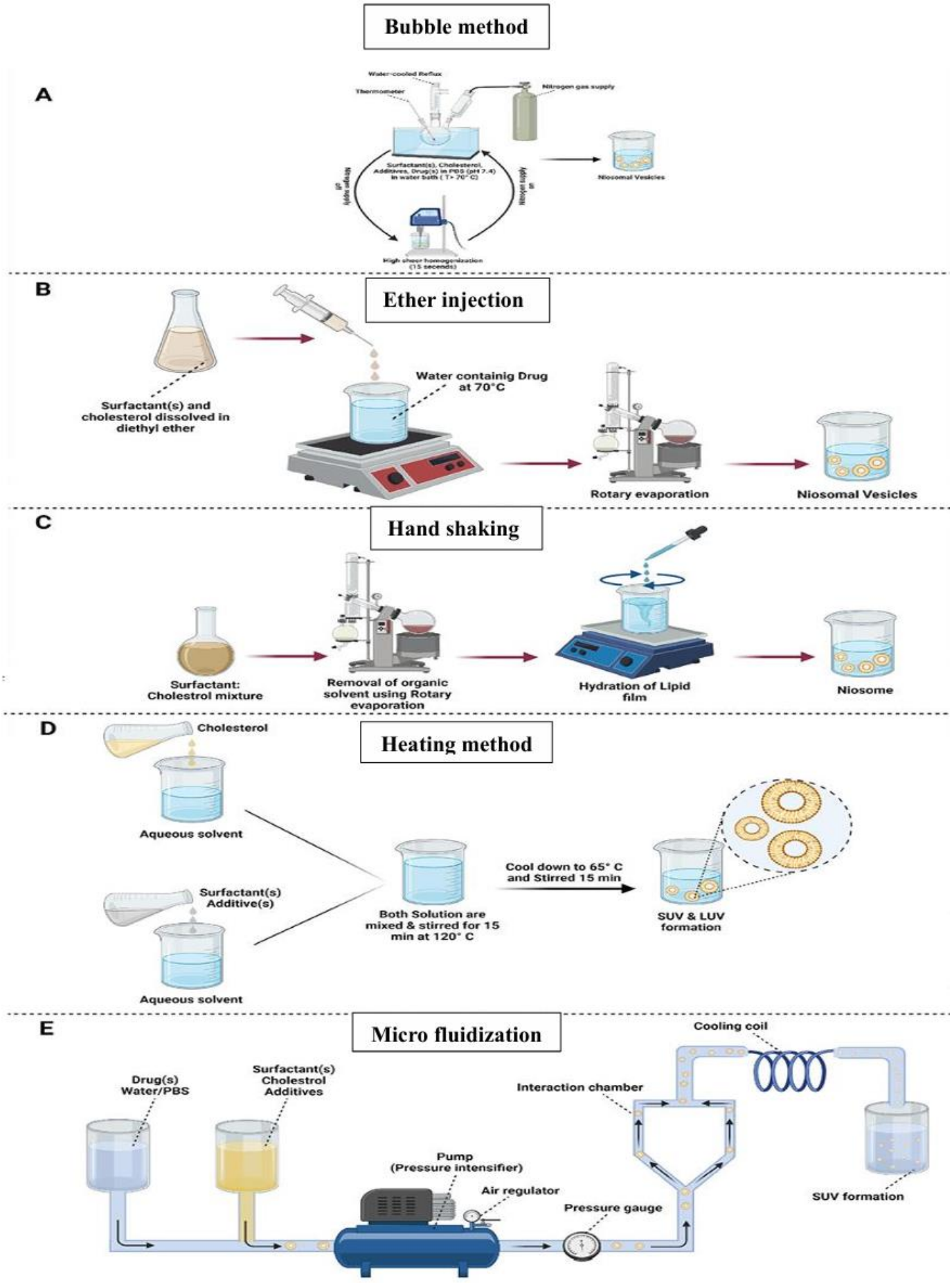
Methods of fabrication of Niosome [9, 10, 11, 12, 13, 14, 15]:

Table No. 3: Methods of Preparation

Methods	Description
Bangham method	Vesicle mixture (into chloroform and ethanol (1:2)) -> solid thin layer, rehydrated by buffer.
Micro-fluidization method	Liquidized streams are passed through micro channels at ultra-velocities, energy needs to be within the field.
Development of Niosomes from proniosomes Proniosomes:	Animate solvent + annex of cholesterol + drug + surfactant + others -> heated -> lucent solution + annex aqueous phase -> heated -> kept overnight -> collect proniosomes. niosomes: formulation from maltodextrin based proniosomes -> free floating powder + slurry of maltodextrin and surfactant-> remoisturize by the annex of water.
The Bubble method	Consist of three flask -> contain water chilled reflux, thermometer & nitrogen supply -> surfactant + cholesterol + put up in buffer pH- 7.4 + dispersion mixed -> bubbled.
Heating Method	cholesterol + surfactant + charged molecules + annexed the aqueous medium + polyol -> heated + magnetic stirrer.

Sonication Method	Drug solution + buffer +surfactant or cholesterol -> sonicated and unsafe of titanium probe for yield.
Method of Multiple Membrane Extrusion	Fine film by evaporating - cholesterol + surfactant + dicetyl phosphate into chloroform -> hydrate film with the drug polycarbonate (aqueous) -> resultant solution extruded through the passage of series.
Production of niosomes by utilizing the polyoxyethlene alkyl ether	Water and (PEG) -> remixed at high temperature -> breakdown of h-bonds -> free drug is removed -> difficult separation.
Method of Emulsion	Oil in water made of-> animate solution + cholesterol + viscous solution of drug -> evaporating animate solution.
Niosomes development using micelle	mixture of micellar solution (dicalcium hydrogen phosphate, PCSD, C16 G2, incubated with esterase, PCSD is therefore to cleave by estracse to make out -> sebaic acid, polyethylene & cholesterol.
Method of Lipid Injection	Surfactant + lipids mixture -> melted -> injected to highly agitated viscous phase -> drug is dissolved into molten liquid -> mixture is injected into heated viscous phase + surfactant.

Schematic methods of fabrication of niosomes [16]:



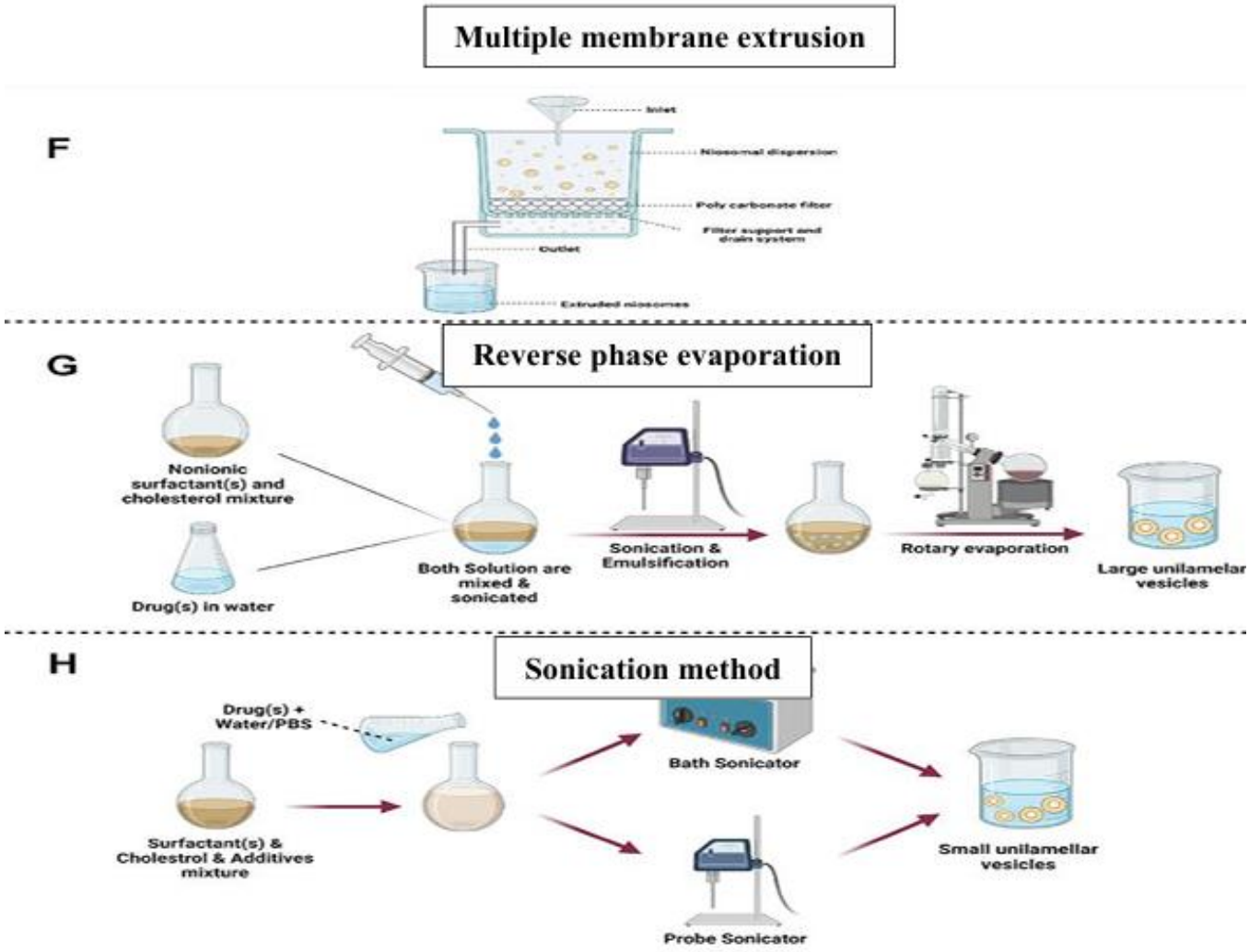


Fig.No.6: Methods of preparation

Factors affecting on formation of niosomes [17]:

1. **Nature of surfactant:** One important factor in managing drug entrapment in the vesicle a surfactant creates is its HLB value. Niosomes cannot be produced by a surfactant having an HLB level between 14 and 17, a surfactant with an HLB value of 1.7-8.6 reduces entrapment efficiency, and an HLB value >6 requires the addition of lipid or cholesterol. To make niosomes more stable, surfactants with lower HLB values must include cholesterol. HLB value calculated from the following equation:

CPP = v/lc x a0

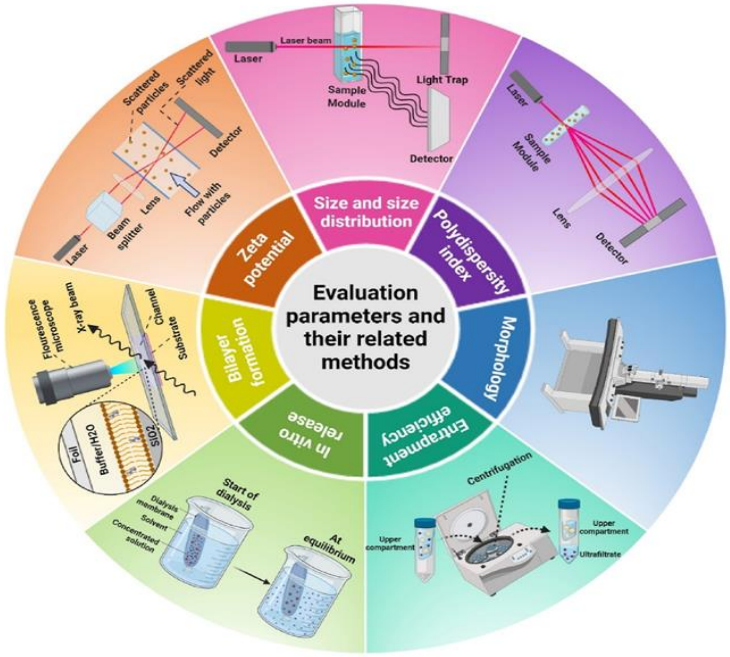
2. **Nature of encapsulated drug:** The drug's physicochemical characteristics affect the stiffness and charge of the niosome bilayer. Compared to hydrophilic medicines, hydrophobic medications leak from the bilayer less frequently. Drugs that are hydrophobic have better transdermal penetration and formulation stability. However, hydrophilic medications are more likely to leak from the bilayer, which reduces the preparation's stability. The niosomes effectively encapsulate amphiphilic medicines.

3. **Cholesterol contents:** High levels of cholesterol limit the release rates of medications because increasing the rigidity of bilayer.

4. **Temperature of hydration:** It must be above the gel to sol/liquid phase transition temperature. It might have an impact on the size and form of niosomes.

5. **Method of preparation:** Various techniques are employed to prepare the niosome suspension: hand shaking yields larger vesicle than ether injection, while reverse phase evaporation yields smaller vesicles. The transmembrane pH gradient technique produces niosomes with higher entrapment efficiency and improved drug retention of entrapped drug.

Evaluation parameters of niosomes [16]:



Applications of niosomes [18]:

1. **Peptide medication delivery:** By avoiding enzymes that breaks the peptide has long been a problem for oral peptide drug delivery. Research is being done on the effective use of niosomes to shield peptides from gastrointestinal peptides degradation. The stability of the peptide was shown to be greatly enhanced by the trapping of a vasopressin derivatives in niosomes, as demonstrated by an oral delivery method used in an in-vitro investigation.
2. **Transdermal delivery:** Primary disadvantage of this route is the delayed skin penetration. However, niosome-based transdermal delivery of drugs has been shown to enhance the penetration rate.
3. **Cosmetic delivery:** L'Oreal's beauty applications were the source of the initial information about non-ionic surfactant vesicles. The benefits of niosomes can be used in cosmetic as well as skin care applications because of having capacity of promoting skin permeation, increasing stability of encapsulated medications and improve the bioavailability of less-absorbed substances.
4. **Hormone delivery:** It was investigated how estradiol in vesicular preparations permeated the stratum corneum of human *in vitro*. Two methods are suggested to have a significant function in vesicle–skin interactions, that

is, the impact of vesicular structures brought about through their absorption in the stratum corneum suspension interface and penetration-enhancing action of the surfactant molecules.

5. **Vaccine delivery:** Non-ionic surfactant vesicles, or niosomes, are a fascinating class of vaccine carrier systems since they are only marginally immunogenic on their own. The use of niosomes as a topical and oral vaccination delivery technology is becoming more popular immunization. Investigations were conducted on the effects of different ratios of the surfactants, cholesterol, & dicetyl phosphate on the appearance, size, and effectiveness of entrapment as well as the release of antigen in vitro from niosomes. When the immune-stimulating properties were examined, topical liposomes and intramuscular recombinant HBsAg were shown to elicit lower levels of endogenous cytokines and serum antibody titers, respectively, than topical niosomes.

Marketed products [19]:

Table No. 4: Marketed formulations of niosomes

SR.	Brand	Name of the product
1.	Lancôme-Foundation and complexation	Flash Retouch Brush on Concealer
2.	Britney Spears-Curious	Curious coffret: Edp Spray 100ml +Dualended Parfum & pink lipgoss + Body souffle 100 ml
3.	Loris Azzaro - Chrome	Chrome Eau De Toilette Spray 200 ml
4.	Orlane – Lipcolor and Lipstick	Lip Gloss

Patent citation [19]:

Table No. 5: Patent of niosomal formulation

Publication number.	Priority date.	Publication date.	Assignee.	Title.
US4873088A	06-09-1983	10-10-1989	Liposome Technology, Inc.	Liposome drug delivery method and composition.
US4891208A	10-04-1985	02-01-1990	The Liposome Company, Inc.	Steroidal liposomes.
US5741515A	20-10-1994	21-04-1998	Bayer Aktiengesellschaft	Ketoprofen liposomes
US6403056B1	21-03-1997	11-06-2002	Imarx Therapeutics, Inc.	Method for delivering bioactive agents using cochleates
US6428811B1	11-03-1998	06-08-2002	Wm. Marsh Rice University	Temperature-sensitive polymer/ nanoshell composites for photothermally modulated drug delivery
US20020143385A1	13-03-2000	03-10-2002	Jun Yang	Stent having cover with drug delivery capability

CONCLUSION:

A novel and promising method of drug delivery is represented by niosomes. To create an efficient drug delivery system, they are drug carriers. They present an excellent chance to combine hydrophilic and lipophilic medicines or both. Niosomes have shown the enhanced stability for the medication that is entrapped, lower dosage as well as allow targeted drug delivery to a particular location. Niosomes are stable as well as affordable, they seem to be the preferable drug delivery technique over liposomes. Academicians and researchers generally recognize this carrier. Generally niosomes offer a wide range of medication delivery applications, including transdermal drug delivery, targeted delivery of anti-inflammatory, anti-cancer, and anti-infective medicines, as well as recent uses as adjuvants for vaccines and diagnostic tools. Given that niosomes have performed better than all other formulations and drug delivery systems, their safety and effectiveness make them the ideal drug delivery technique to use and enhanced adherence from patients.

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