Proniosomes are Proved Secular Drug Delivery System by Dry Formulation for Non Ionic Surfactants

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Abstract
Proniosomes is a new proven secular drug system which are dry formulations covered by carrier like non-ionic surfactants. Proniosomes is formulated in such a manner that they can overcome the drawbacks of noisome like physical instabilities, fusion and aggregation. Proniosomes is administered by various routes like oral, intravenous, buccal, topical, transdermal etc. in which Proniosomes are formulated as gels for topical drug delivery. Proniosomal gels are translucent gels and liquid lamellar crystals of vesicular bilayers which can be formed by the addition of small quantity of gelling agent or water to the dry Proniosomes (mixture of non-ionic surfactant, lecithin and cholesterol). Proniosomal gels offer better resistance towards stress caused by skin flexion; mucociliary movement and better percutaneous absorption due to non-ionic surfactants are used. Because of their high stability, ease of application and better percutaneous absorption they are widely used for various category of drugs such as antifungals, NSAIDS, antihypertensive etc. As Proniosomal gels offer good attention towards the topical drug delivery, present review focuses on its preparation methods, applications and recent developments.

Keywords: Coacervation phase separation; Non-ionic surfactants; Proniosomal gel; Topical drug delivery.

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1 INTRODUCTION
Proniosomes are the proven secular drug distribution systems that are characterized as the dry plans covered by transporters, for example, non-ionic surfactants. Proniosomes can be changed over into niosomes after hydrating by heated water just before use. As niosomes are related by different downsides, for example, physical insecurities like combination, total of elements and spillage of the medication these are figured into Proniosomes. Proniosomes can convey together the hydrophilic and hydrophobic medications. The principal advantage of Proniosomes is that quantity of carrier essential for maintaining the surfactant ratio can be simply familiar. Proniosomal gels are the identical current proves secular drug delivery systems that proposal the drug delivery over current or percutaneous
course in a versatile manner. Proniosomal gels by combination of non-ionic wetter, lecithin and cholesterol. As proniosomes are in the form of vesicles and the components like non-ionic surfactants are used in the formulation of proniosomes itself acts as permeation enhancers and penetrate readily into the skin. Proniosomes in the dry by making the opportunity of unit medicating by converting them into beads, tablets, capsules and gels. Thus they provide an open platform to explore their suitability for drugs by various drawbacks to provide an effective and intended therapy.

**Formulation of proniosomal gels**

The essential components of proniosomal gels are as follows

**Non-ionic surfactants**

The non-ionic surfactants used in the preparation of proniosomal gels are selected based on the HLB worth of the wetter as the entrapment effectiveness of drug is pretentious by:

- The HLB value: The HLB value between 4-8 will usually give the vesicles by high compatibility.

**Phase transition temperature**

Spans 40 & 60 produce the vesicles by high temperature effectiveness and the leakage of drug by the vesicles is also condensed payable to tall change over temperature. The geometry of the vesicles can be predicted by the critical packaging parameter of the surfactant which must be between 0.5-1 for spherical vesicles.

**Lecithin**

In the formulation of proniosomal gels lecithin acts as a permeation enhancer and it enhances the % entrapment of the drug outstanding high phase transition temperature. Based on the penetration capability soy lecithin acts as a good permeation enhancer.

**Cholesterol**

Cholesterol is one of the important components in the formulation of Proniosomes which impart stability and permeability to the vesicles. The set-up effectiveness of the drug depends on the attentiveness of the cholesterol used. On the further increasing the concentration of cholesterol the disruption of the bilayer takes place and the entrapped drug leaks out.

**Aqueous phase**

The most widely used aqueous phases in the formulation of Proniosomes includes hot water, 0.1% glycerol and phosphate buffer of pH7 etc. The pH of the aqueous phase the stage a significant role in the set-up of the drug.

**Solvent**

The selection of the suitable solvent the stage an significant role in formulating the Proniosomes as they affect the vesicles size and drug permeation rate of the drug. The size of the vesicles depends on the type of solvent used and the order is as follows:

**Drug selection criteria**

The drugs by the following criteria are suitable for the formulation of
Proniosomal gels;
Low aqueous solubility, High dosage frequency, Low therapeutic index and drugs by more adverse effects\(^2\).

**Approaches of research of proniosomal gel\(^3\)**

- a) Coacervation stage technique.
- b) Slow spray coating technique.
- c) Slurry technique.

**COACERVATION PHASE SEPARATION**

Proniosomal formulae are set up by technique announced by Alsarra et al.\(^3\) by slight alteration, utilizing various sorts of non-ionic wetting agent, lecithin, and cholesterol. Suitable measures of peroxisomal segments combined by the medication stayed blended in by 2.5ml of total ethanol in a spotless and dry, wide-mouthed glass tube. In the wake of blending all the fixings, the exposed finish of the glass tube secured by cover to keep damage of dissolvable by it and take to in a water shower at 65 ± 3°C for 5 min, till the wetting agent are broken down totally. At that point, 1.6ml of pH of 7.4 phosphate cushion is included, and warming on the water shower for ~2 min till an unmistakable arrangement was watched. The blend is permitted to cool at room temperature until the scattering was changed over to peroxisomal gel.

**SLURRY STRATEGY**

Transporter material to a 250-ml flagon and the whole volume of surfactant arrangement was added to the jar to shape slurry. In the event that the surfactant arrangement volume is less, at that point extra natural dissolvable can get slurry. The flagon was joined to a rotator evaporator was applied until the free-streaming. The flagon was taken out from the evaporator and held under vacuum for the time being. The Proniosomes powder was put away in fixed compartments at 4°C. The time needed to create Proniosomes is free of the proportion of surfactant answer for be transporter material and seems, by all accounts, to be scalable.\(^3\)

**SLOW SPRAY COVERING TECHNIQUE**

This strategy includes planning of Proniosomes by splashing surfactant in a natural dissolvable onto transporter material and afterward dissipating the dissolvable. Since the transporter is dissolvable in the natural dissolvable, it rehashes the cycle until the ideal has been accomplished. The surfactant covering on the transporter is slim and hydration of this covering permits multilamellar when the transporter disintegrates. The subsequent pernicious is fundamentally the same as those delivered by traditional strategies and the size dissemination is more uniform. It is proposed that this preparation would deliver hydrolysis for hydrophobic drugs formulation\(^3\).
Fig 1. Strategy for planning proniosomes by splashing surfactant in natural dissolvable onto transporter material

Fig 2: Method of preparation of portrayal of proniosomes
PORTRAYAL OF PRONIOSOMES:

Differential examining calorimetry (DSC): the dsc thermo grams of the medication, excipients (range 60, gpc) and proniosomes are verified by a dsc q20 ta (m/s perkinelmer inc. usa) gadget by utilizing typical aluminum skillet. Precisely gauged tests (2-5 mg) are firmly fixed in the container. an unfilled container was utilized as a kind of perspective skillet. Tests are warmed at the filtering pace of 10°c/min with temperature range somewhere in the range of 20°c and 350°c.

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\text{Total no. of vesicles per cubic mm} = \frac{\text{Total no. of vesicles counted} \times \text{dilution factor} \times 4000}{\text{Total no. of squares counted}}
\]

(1)

Fourier transform infra-red spectroscopy (FTIR): Fourier transform infra-red spectroscopy of the medication, excipients and proniosomes are done by utilizing FT-IR instrument (Spectrum Two™ M/s PerkinElmer Inc,USA) at 25°C and wave number reach since3500 cm − 1 to 500 cm − 1. The examples are blended completely by potassium bromide (KBr) in the mass proportion of 2:98.

Readiness of ACE-stacked proniosomes

Micromeritics and Zeta likely estimation: The vesicles magnitude circulation examination of the created proniosomes done utilizing Delsa™ Nano C (M/s Beckman Coulter, India Pvt. Ltd., Mumbai, India) introduced at Institute of Microbial innovation (IMTECH), Chandigarh. The rule hidden the above examination is Dynamic Light Scattering (DLS) technique. An aliquot of 1ml of the postponement (proniosomes after hydration by PBS of pH 7.4) was weakened multiple times by refined water and the magnitude of vesicles is gotten by gadget programming. Zeta potential is dictated by estimating the electrophoretic development of the stimulating particles beneath an useful electric field by Doppler move of dispersed light at 25°C and the electric field quality stayed ar ound 23.2 V/cm. The normal zeta potential was legitimately acquired since the gadget programming.

Transmission electron microscopy (TEM): The surface morphology of niosomal vesicular postponement is analyzed by Hitachi H-7500, Japan, introduced at Central Instrumentation Lab (CIL), Panjab University, Chandigarh. 1% phosphotungstic corrosive (PTA) was utilized as a recoloring specialist. Imagesare reserved at an inflammation voltage of 200 kV.

Confocal laser checking microscopy (CLSM): The coumarin-6 (3-(2-Benzothiazolyl)- N, N-diethylum belliferylamine, 3-(2-Benzothiazolyl)- 7-(diethylamino) coumarin) stacked proniosomes are set up by blending
Coumarin-6 at convergence of 0.15 μmol/mL by 240 mg of Span 60, 800 mg of MLDX, and 160 mg of cholesterol. Color stacked proniosomes by no drug are useful to the extracted pig eye for 6 h surveyed by washing it by PBS pH 7.4 and the static slides are readied. Restriction of fluorescence in the visual sheets subsequently research is inspected utilizing a confocal laser checking magnifying lens (Olympus FV10i, M/s Olympus Singapore Pvt. Ltd, Singapore). All confocal pictures are gained in similar set boundaries.

**Joining of proniosomes in auxiliary vehicle**

To consolidate the readied proniosomes in topically pertinent vehicle, this are additionally developed by 1% w/w of Proniosomal gel.

Delivery examines: Ex vivo transcorneal pervasion considers are completed utilizing newly extracted pig corneas. The cornea was mounted among cinched contributor and recipient sections of an all-glass changed Franz dissemination cell so that its epithelial surface confronted the benefactor section. The corneal territory accessible for dissemination was 0.50 cm². The recipient section was loaded up by 10 ml newly arranged tear liquid (pH 7.2), and entire air bubbles are ousted from the section. An aliquot (1 ml) of definition [Aceclofenac (0.1% w/v) ophthalmic arrangement (pH 7.2), was set on the cornea, and the kickoff of the giver cell is fixed by a glass spread slip. Recipient liquid is kept at 37°C by consistent blending utilizing a Teflon-covered attractive mix globule. Penetration learning is proceeded for 360 min, and tests are pulled back by recipient and investigated for aceclofenac contented by dissecting tests by HPLC. Consequences are communicated as sum saturated or in vitro visual accessibility.

**Evaluation:**

Filtering electron microscopy

Proniosome powder is fastened to twofold sided carbon tape, situated on an aluminum stub, and abundance powder is taken out. The stub is put away under vacuum for the time being. The examples are falter covered by Au/pd under an argon environment at 180 mA for 1 min. Electron micrographs are acquired utilizing a field emanation SEM working at 1 or 2 kV.

**Transmission Electron Microscopy**

The monography of hydrated niosome scattering is resolved utilizing communication electron microscopy. A droplet of niosome scattering is weakened 10-overlay utilizing deionised water. A droplet of weakened niosome scattering is useful to a carbon covered 300 work copper lattice and is left for 1 min to permit a portion of the niosomes to cling to the carbon substrate. The rest of the scattering is taken out by engrossing the drop by the edge of a bit of channel paper.
Subsequently double flushing the network a drop of 2% watery arrangement of uranyl acetic acid derivation for 1 sec. The rest of the arrangement is taken out by engrossing the fluid by the tip of bit of channel daily and the example is air dehydrated. The example is seen by a JEOL 100 CX spread electron magnifying lens at 80kv.

**Angle of response**

The point of rest of dehydrated Proniosome powder is estimated by a pipe technique. In this strategy, the channel is static at a place so the 13mm passage opening of the pipe is 10cm over a level dark surface. The powder is poured however the channel to frame a cone on a superficial level, and the point of rest is then determined by estimating the tallness of the cone and the width of its corrupt.

**MOLECULE SIZE AND PARTICLE SIZE DISTRIBUTION**

A little aliquot (100 microliter) of niosome scattering is scattered in 50ml of water and is estimated quickly by a Sald-1100 Laser Deflection molecule size analyser. The molecule size reach is set to 0.1-45 micrometer and the refractile file choice is set to 0.2-1.7 micrometer. The molecule size appropriation of niosome is determined inside.

**Release of Drug from Proniosome**

In vitro release is determined using dialysis tube. One end is seated by cellophane membrane. Measured amount of niosome are placed in the dialysis tube. Dialysis tube is placed into a beaker containing simulated fluid at 370. Beaker is placed on magnetic stirrer and is shaken at 100rpm at temperature of 370. Aliquots are reserved by recipient compartment at certain period inter missions. The drug is reserved samples is estimated by the suitable analytical method\(^4\).

**CONCLUSION**

Proniosomes provide a promising drug delivery by great potential towards physical and chemical stability, ease of preparation and economical viability. They had attained a great courtesy for the distribution of drugs concluded topical and transdermic routes since of their nontoxicity, penetration enhancement due to surfactants. As proniosomes are in the form of vesicles and the components like non-ionic surfactants are used in the formulation of proniosomes itself acts as permeation enhancers and penetrate readily into the skin. Proniosomes in the dry by making the opportunity of unit medicating by converting them into beads, tablets, capsules and gels. Thus they provide an open platform to explore their suitability for drugs by various drawbacks to provide an effective and intended therapy.

**REFERENCES**


