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A PROMISING APPROACH OF NOVEL DRUG TECHNOLOGY: PRONIOSOMES

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Abstract:

Building and Engineering functional systems at the atomic level is known as nanotechnology, which is an emerging field of study centered on the manipulation ofmatter on a nanoscale scale.

Numerous innovative drug delivery systems, including liposomes, microparticles, niosomes, and proniosomes, have been developed as a result of nanotechnology.

Liposomes and niosomes possess certain drawbacks, such as the ability to leak, fuse, aggregate, distribute, transport, and store.

Proniosomes are a dry formulation of water soluble carrier coated with surfactant and drug encapsulated in proniosomal vesicles, which helps prolong the duration of retention of drug in systemic circulation and by reaching the target tissue shows its action which results in reduced toxicity. This helps overcome the drawbacks of both liposomes and niosomes.

The primary focus of this review is the drawbacks of niosomes and liposomes.

KEYWORDS: Liposomes, Niosomes, Proniosomes, Stability, Surfactant, Cholesterol, Characterization, Applications.

❑ INTRODUCTION:

- **PRONIOSOMES:**

Proniosomes are dry free-flowing formulations of surfactant-coated carrier, which on rehydration by agitation in hot water, produces a multi-lamellar niosomal suspension suitable for administration[13, 14]. Since these proniosomes are available in dry form of powders, they have a benefit in transportation, distribution, processing, packaging and storage.

It can offer the best possible flexibility, stability, and metered unit dosage in a capsule [15].

Several of the active pharmaceutical ingredients may be carried by these adaptable drug delivery systems [13, 16]. When compared to pre-niosomal formulations, these proniosomes exhibit greater stability, thereby mitigating the stability issues associated with niosomes.

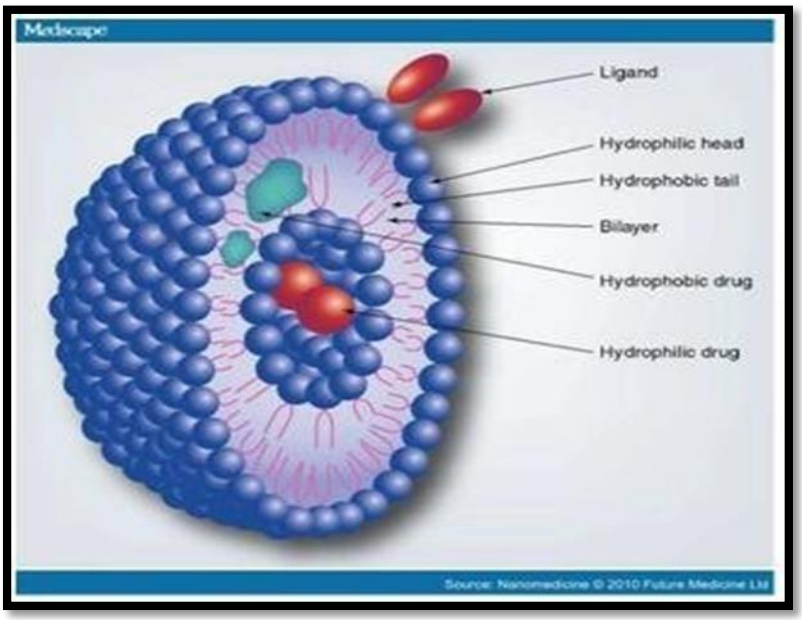

Figure 1: Structure of Proniosomes[26]

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❑ **Composition of proniosomes:**

- Phosphotidyl choline - eg. Soya/egg lecithin.
- Drug.
- Non-ionic surfactants

i) Fatty alcohol - cetyl alcohol, stearyl alcohol, cetostearyl alcohol,oleylalcohol.

ii) Ethers- decyl glucoside, lauryl glucoside, octyl glucoside, triton X-100

iii) Esters- glyceryl laureate, polysorbates, spans.

- Solvents - eg. Ethanol, butanol, iso-propanol.
- Cholesterol
- Aqueous phase - eg. Water, glycerol, phosphate buffer [18].

❑ **Ideal properties for the drug in proniosomal formulations :**

- Low aqueous solubility of drugs.
- High dosage frequency of drugs.
- Short half life.
- Controlled drug delivery suitable drugs.
- Higher adverse effects of drugs [18].

❑ **Comparison of proniosomes with niosomes:**

- Niosomes are microscopic lamellar vesicles formed by the mixture of non-ionic surfactants and cholesterol in the aqueous media, where as the proniosomes are dry formulations of surfactant coated carrier vesicles which are capable to get hydrated to produce niosomes immediatelybefore use.

- Niosomes can be degraded by hydrolysis while proniosomes are dryformulation and can not be degraded by
  hydrolysis.
- Use of unacceptable solvents in the preparation of niosomes.
- Incomplete hydration of lipid or surfactant film during hydration process for niosomal formulations[17].

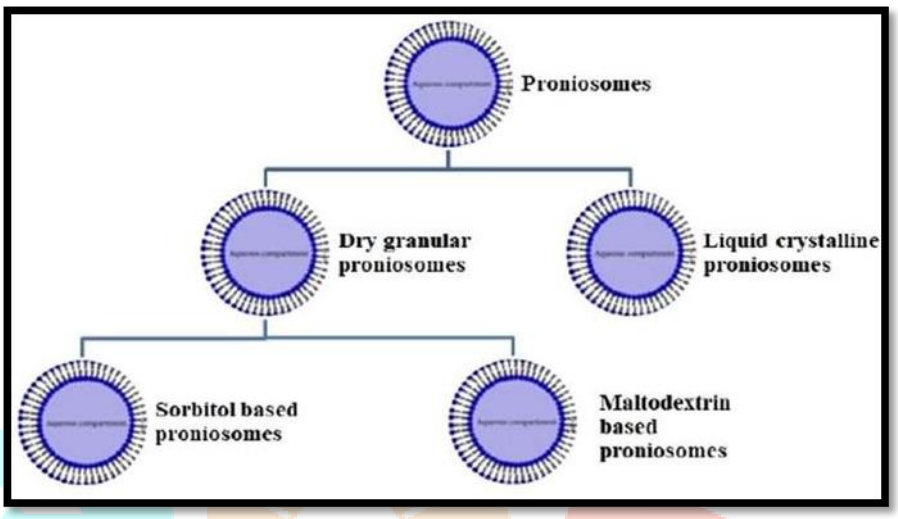

Figure 2: Types of Proniosomes[27]

❑ METHODS OF PREPARATION:

❖ Slurry method:

First, a stock solution of cholesterol and surfactants was made with the appropriatesolvent.

The 100ml RBF containing the carrier (maltodextrin/lecithin) should be filled withthe solvent and the required volume of the above prepared stock solution per gramof carrier and drug.

Next, add the chloroform, which causes the slurry to form.

This RBF was connected to a rotary flash evaporator, which was used to evaporatethe solvent at 50–60 revolutions per minute, 45 ± 2 °C temperature, and 600 mm Hg pressure, until the flask's contents were dry and freely flowing.

Lastly, the niosomal formulation needs to be kept in a tightly closed container at 4 °C, or refrigeration temperature[12].

❖ **Spray coating Method –**

A hundred milliliters of RBF must contain the necessary amount of carrier.

Next, a mixture of surfactant and cholesterol was made, and this was sprayed onto the carrier in the RBF that is attached to the evaporator.

It was kept in a tightly closed container at 4°C after the surfactant and cholesterol mixture were sprayed on the carrier one after the other until the aliquot coated the carrier and the solvent evaporated[19]. The powder was then dry and free-flowing.

❖ **Co acervation phase separation method –**

The proniosomal gel is prepared using this technique.

The prescribed dosage of the medication, cholesterol, surfactant, and carrier should be weighed and placed in a sterile glass vial with a widemouth. The solvent is then added to the mixture mentioned above.

With the aid of the glass rod, all of the mixture's ingredients must first be heated before being combined.
With the aid of the lid, the open end of the vial is sealed to prevent solvent loss.

This mixture is heated on a water bath at 60–
70°C for five minutes, or until the surfactant dissolves completely. After that, it is allowed to cool to room temperature, which is necessary for the dispersion to turn into proniosomal gel[20].

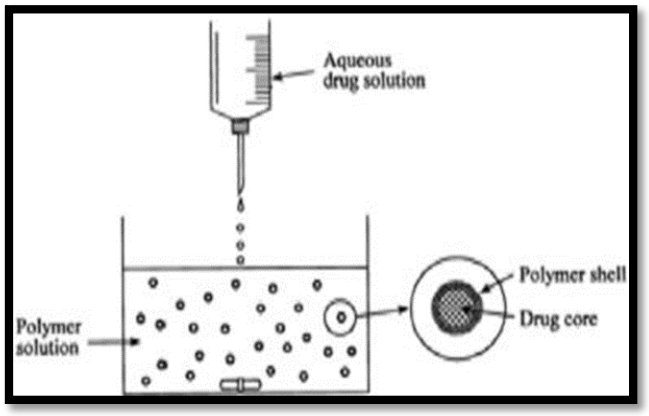

Figure no:03 Co acervation phase separation method[28]

❑ **Conversion of proniosomes to niosomes:**

When surfactant is added to a carrier surface, it creates a dry surfactant film that can enclose particles that dissolve in water.
Niosomal vesicles, which can ensnared both hydrophilic and hydrophobic drug particles, are formed upon additional water addition or hydration of proniosomes (Fig).

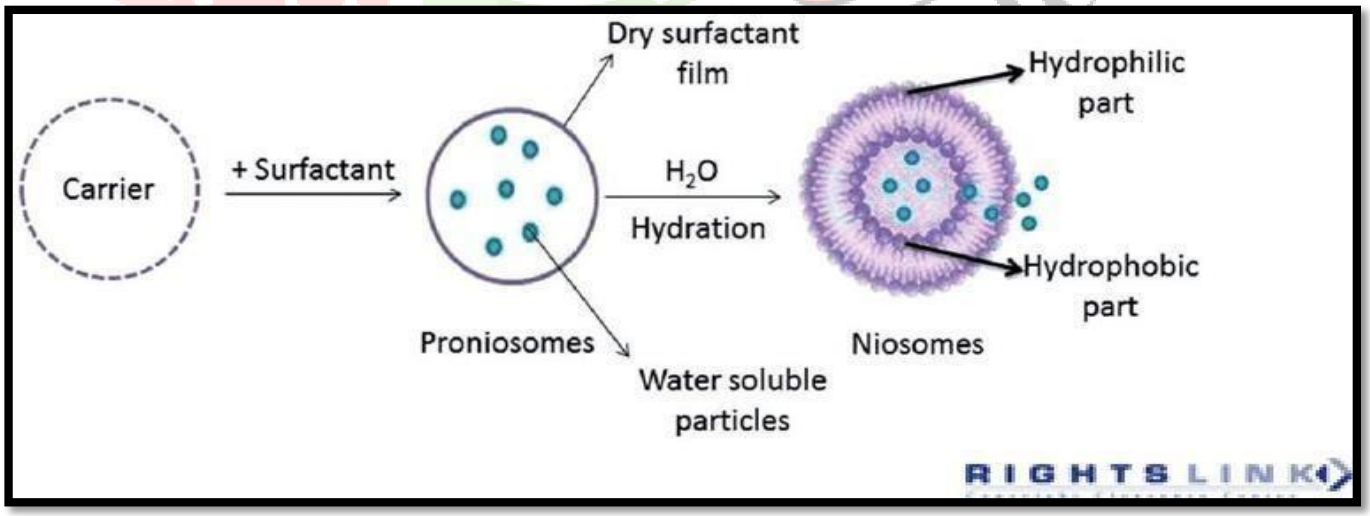

Figure 4: Conversion of Proniosomes to Niosomes[29]

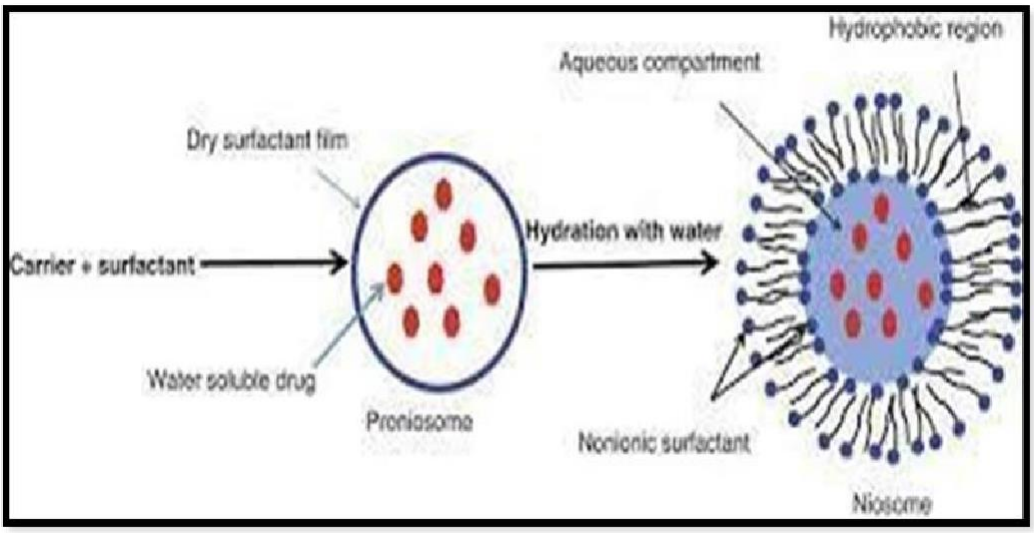

Figure 5: Bilayer Proniosomes[30]

❑ CHARACTERIZATION OF PRONIOSOMES:

- **Angle of repose measurement:** There are two techniques available for measuring the angle of repose.

Funnel Method: The funnel is set two centimeters above the surface.
The proniosomal powder was added to the funnel and allowed to descend through the 12-cm-wide funnel outlet orifice to form a surface cone.
The cone's height (h) and the base's diameter (r/2) were then measured in order to determine the angle of repose[21].

Cylinder Method: Using a cylinder with an outlet orifice fixed at an elevation above the surface, proniosomal powder was poured into it in a manner akin to the funnel method. The powder descends from a cone through the outlet orifice. The cone's height (h) and the base's diameter (r/2) were measured in order to determine the angle of repose in more detail[21]. Repose angle (妾) = Tan -1 (h/r)

- **Scanning electron microscopy (SEM)** :
  Using scanning electron microscopy (SEM), the proniosomes' particle size is the most crucial factor.
  Through the use of SEM, the size distribution and surface morphology (i.e., roundness, smoothness, and formation of aggregates) of proniosomes were examine
  After spreading the proniosomal powder on a doublesided tape that was attached to an aluminum stub, the mixture was put inside a SEM vacuum chamber (XL 30 ESEM with EDAX, Philips, Netherlands).With the use of a gaseous secondary electron detector (working pressure of 0.8 torr, acceleration voltage of 30 kV), the morphological characteristics of the samples were examined[21].

- **Optical microscopy:** Under an optical microscope (Medilux – 207 RII, Kyowa- E1 etner, Ambala, India), the niosomes were mounted on a glass slide. The morphological observations were conducted using a microscope that had an X 1200 magnification. A digital single lens reflex (SLR) camera was used to take a photomicrograph of the preparation under the

microscope [21].

- **Measurement of vesicle size :**

In the same preparation medium, niosomal dispersions are diluted approximately 100 times. Before measuring the size of the vesicles, the sample was thoroughly mixed. The laser diffraction particle size analyzer from Sympatec, Germany was used to measure the size of the vesicles. Within the apparatus is a small volume sample holding cell (Su cell) and a HeNe laser beam with a wavelength of 632.8 nm that is focused with a minimum power of 5 mW using a Fourier lens (R-5).
Proniosome-derived niosomes had an average particle size of roughly 6×10-6 m,whereas conventional niosomes have a particle size of about 14×10-6 m [21].

❑ STABILITY STUDIES:

To determine the stability of proniosomes, the prepared proniosomes are stored at various temperature conditions like refrigeration temperature (i.e., 2-8°C), room temperature (25 ± 0.5°C) and elevated temperature (45 ± 0.5°C)for a period of 1- 3 months. Drug content and difference in the average
vesicle diameter was monitored periodically. As per ICH guidelines stability studies for dry proniosomes powders which are meant for reconstitution should be studied for accelerated stability at 40°C/75% RH as per international climatic zones and climatic conditions. After storing for particular period, the product should be evaluated for appearance, color, assay, pH, particulate matter, sterility, preservative content and pyrogenicity[2, 23, 25].

❑ APPLICATIONS OF PRONIOSOMES

Proniosomes as drug carriers : Proniosomes act as Drug carriers for above mentioned drugs, which are only few examples. Drug delivery has been studied by different methods of administration which includes IV, peroral, transdermal, aerosoles and intramuscular. In vivo behavior of proniosomes will be similar to liposomes[27].

❖ **Clinical applications**:

- **In cardiology** – Proniosomes as carriers for captopril drug for treatment ofhypertension in the form of transdermal delivery which results in an extended release of the drug in the body. Encapsulation of drug is carriedout using sorbitan esters, cholesterol and lecithin [21].
- **In diabetes-** Furosemide proniosomes are injected transderrmally which reduces the glucose levels[21].

- **Hormonal therapy** – Levonorgestrel proniosomes was given in transdermal drug delivery system. Bioassay for progestational activity was performed including endometrial assay and blockage of development of corpora lutea[21]. **Immune response** - Niosomes and proniosomes are being used to study the nature of the immune response due to their immunological
selectivity, low toxicity and greater stability [21].
- **Peptide drugs-** Oral peptide drug delivery has a limitation of bypassing the enzymes, which leads to breakdown of peptide and protein bonds [21].
- **Anti-neoplastic Treatment -** Niosomes have the ability to alter the
metabolism, prolong circulation and half-life of the drug leading to minimalside effects. Doxorubicin and methotrexate niosomes shows an
advantageous effects over the unentrapped drugs in decreasing the rate ofproliferation of the tumor [21].

❑ CONCLUSION:

Proniosomes, which resemble liposomes in structure, are a promising drug delivery technology. As such, they may serve as a substitute for other vesicular systems. It is well known that niosomes derived from proniosomes are free from several issues, including issues with physical stability like fusion, leakage, and aggregation. They also offer extra advantages for distribution, storage, dosing, and transportation. Based on the aforementioned article, it can be inferred that researchers and academicians generally accept the idea of entrapment or drug incorporation into proniosomes for improved targeting ofthe appropriate tissue target.

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