INTRODUCTION
In the past few decades, significant attention has been focused on the development of novel drug delivery system named as Controlled Drug Delivery System. This formulation shows the prolonged action and it gives continuous release of their active ingredients at a predetermined rate and predetermined time. Recently, different carrier systems and technologies have been broadly studied with goal of controlling the drug release and improving the usefulness and selectivity of the formulation. Now-a-days, the vesicular systems like niosomes or liposomes are developed and having specific advantages while avoiding demerits.
associated with conventional dosage forms. To overcome the disadvantage of vesicular system, Proniosomes are intended. Proniosomes are coated with surfactant and can be hydrated to form niosome dispersion by brief agitation with hot aqueous medium. And also an additional convenience for the conveyance, circulation; storage and scheming

**Proniosomes as drug carriers**

Proniosomes are promising drug carriers, because of better chemical stability and also many disadvantages associated with liposomes. Proniosomes are dry formulations of surfactant coated carrier vesicles, which can be rehydrated to form niosome, and resulting niosomes are very similar to conventional niosomes of uniform in size. Being dry, free flowing product, proniosomes minimizes stability problems during storage and sterilization. And also exhibit the merits of ease to transportation, distribution, and storage. And it makes proniosomes a pronouncing versatile delivery system

**ADVANTAGES OF PRONIOSOMES OVER THE NIOSOMES**

1. Proniosomes avoids the problems of physical stability drug.
2. It avoids encapsulation of hydrolysis drugs.
3. Additional convenience in transportation, distribution, storage and dosing.
4. Can carry both hydrophilic drug and hydrophobic drug.
5. Extensively used in various drug delivery system like drug targeting controlled release and permeation enhancement of drug

**TYPES OF PRONIOSOMES**

**Dry granular type of proniosomes**

Dry granular proniosomes are involves the coating of water-soluble carrier such as sorbitol and maltodextrin with surfactant. The subsequent coating process is a dry formulation in which each water-soluble particle is covered with thin film of surfactant. It is essential to prepare vesicles at a temperature above the transition temperature. The non-ionic surfactant being used for the formulation. There are further categorized as follows:

**Sorbitol based proniosomes**

Sorbitol based proniosomes formulation involves sorbitol as the carrier, which is further coated with non-ionic surfactant and is used as niosomes within minutes by addition of hot water followed by agitation.

**Maltodextrin based proniosomes**

A proniosome formulation based on maltodextrin was recently developed. Maltodextrin based proniosomes prepared by slurry method. Maltodextrin is a polysaccharide easily soluble in water and it is used as carrier material in formulation.

**Liquid crystalline proniosomes**

When the surfactant molecule are kept in contact with water, there are three ways through which lipophilic chains of surfactant can be disordered in to a liquid state called as lyotropic liquid crystalline state. These three ways are
1. Increasing temperature at kraft point (Tc),
2. Addition of solvent which dissolve lipids,
3. Use of both temperature and solvent.

The liquid crystalline proniosomes and proniosomal gel act as reservoir for transdermal delivery of drug.

**COMPONENTS OF PRONIOSOMES**

**Surfactant**

Surfactants are the surface active agent usually they contains both a water insoluble (lipophilic) and a water soluble (hydrophilic) component. They are used in variety of purposes like acting as solubilizers, wetting agents, emulsifiers and permeability enhancers. The most common non-ionic amphiphiles used for vesicle formation are alkyl ethers, alkyl esters, alkyl amides and esters of fatty acids.

**CARRIER MATERIAL**

The carrier when used for preparation of proniosomes permits the flexibility in the ratio of surfactant and other components that are incorporated. And it increases the surface area and.

To whom correspondence should be hence efficient

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loading. The carriers should be safe and non-toxic, free flowing, poor solubility in the loaded mixture solution and good water solubility for ease of hydration.

**MEMBRANE STABILIZER**

Cholesterol and lecithin are mainly used as membrane stabilizer. Steroids are important components of cell membrane. Cholesterol is a naturally occurring steroid used as membrane additive. It prevents aggregation by the inclusion of molecules Phosphatidyl choline is a major component of lecithin. Depending upon the source they are obtained and are named as egg lecithin and soya lecithin. It acts as stabilising as well as penetration enhancer.

**SOLVENT AND AQUEOUS PHASE**

Alcohol used as solvent in Proniosome formulation which are having pronounced effect on vesicle size and drug permeation rate. Vesicles formed from different alcohols are having different size and they follow the order: Ethanol > Propanol > Butanol > Isopropanol. Ethanol has a greater solubility in water hence leads to formation of highest vesicles size instead of isopropanol which forms smallest size of vesicle.

**DRUG**

The drug selection criteria could be based on the following assumptions.

1. Low aqueous solubility of drugs.
2. High dosage frequency of drugs.
3. Short half-life.
4. Controlled drug delivery suitable drugs.
5. Higher adverse drug reaction drugs

**METHODS OF PREPARATION OF PRONIOSOMES**

Proniosome preparation mainly comprised of nonionic surfactants, coating carriers and membrane stabilizers. The formulation may be prepared by following methods.

**Spraying method**

This method involves preparation of proniosomes by spraying surfactant in organic solvent onto the carrier and then evaporating the solvent. It is necessary to repeat the process until the desired surfactant loading achieved. The surfactant coating on the carrier is very thin and hydration of this coating allows vesicles to form as the carrier dissolves. The resulting niosomes have uniform size distribution similar to those produced by conventional methods.

**Slurry method**

Proniosomes were produced by slurry method by using a different carrier. In slurry method, the whole volume of surfactant solution is added to maltodextrin powder in a rotary evaporator and vacuum is applied until the powder appears to be dry and free flowing product. Drug containing proniosomes-derived niosomes can be prepared in manner similar to that used for the conventional niosomes, by adding drug to the surfactant mixture prior to spraying the solution on the carrier (sorbitol, maltodextrin, and mannitol) or by addition of drug to the aqueous solution used to hydrate the proniosomes.

**Coacervation phase separation method**

In this method, accurately weighed amount of carrier, cholesterol, surfactant and drug are taken in a clean and dry wide mouthed glass vial (5 ml) and solvent to be added to it by simple mixing. In order prevent the loss of solvent, open end of the glass vial can enclosed by a lid and heated on water bath at 60-70ºC for 5 min. The mixture should be allowable to cool at room temperature the dispersion gets converted to a proniosomes.

**FORMATION OF NOISOME BY PRONIOSOME**

The niosomes can be prepared from the proniosomes by adding the aqueous phase with the drug to the proniosmes with brief agitation at a temperature greater than the mean transition phase temperature of the surfactant.

\[ T > T_m \]

Where,

\[ T = \text{Temperature} \]
\[ T_m = \text{Mean phase transition temperature} \]
REVIEVE OF LETTRETURE

Akhilesh Dubey et al., developed Lornoxicam loaded Maltodextrin based proniosomes by slurry method with different surfactant to cholesterol ratio. They reported proniosomal formulation showed higher entrapment efficiency and in-vitro release and release follows super case II transport diffusion⁹.

Parthibarajan et al., reported Methotrexate entrapped Proniosomes by slurry method using cholesterol, the non-ionic surfactant span 80 and the carrier maltodextrin. They reported proniosomes exhibited a prolonged release over a period of 24hrs and concluded that the encapsulation of Methotrexate Proniosomes could be meant for targeted drug delivery thereby reduces the toxicity associated with conventional dosage forms¹⁰.

Akhilesh et al., Investigated Glipizide loaded sorbitol, maltodextrin and mannitol based proniosomes by slurry method with different surfactant to cholesterol ratio. The proniosome formulations were evaluated for FT-IR study, angle of repose and scanning electron microscopy. They reported, formulation based maltodextrin showed higher entrapment efficiency of 82.64 ± 1.25 and in-vitro release of 98% at the end of 24hrs and zero order kinetics release¹¹.

Raja K et al., have reported Glipizide loaded maltodextrin based proniosome with different surfactant to cholesterol ratio. They used slurry method to prepare proniosomes. Their results showed that the release was followed by the zero order kinetics with super case II transport diffusion. They reported the proniosome formulation showed appropriate stability¹².

Sandeep Loona et al., prepared proniosomes of Metformin hydrochloride using different ratios of span 60 span and span 40, they characterized the proniosomes for their encapsulation efficiency, size, zeta potential analysis, in vitro drug release, vesicular stability at different storage conditions. They have concluded that formulation with 9:2:9 ratio of span 60, cholesterol, lecithin give maximum encapsulation efficiency, good zeta potential and lowest drug release percent after 24 hrs¹³.

APPLICATION OF PRONIOSOMES

- Drug targeting
- Anti-neoplastic treatment
- Leishmaniasis
- Delivery of peptide drugs
- Uses in studying immune response
- Proniosomes carriers for haemoglobin
- Proniosomes carrier for cardiac disorders
- Sustained release
- Localized drug action
- Hormonal therapy
- Nsaid application.

Drug Targeting

One of the most useful aspects of proniosomes is their ability to target drugs. Proniosomes can be used to target drugs to the reticule-endothelial system. The reticule-endothelial system (RES) preferentially takes up proniosomes vesicles. The uptake of proniosomes is controlled by circulating serum factors called poisonings. These poisonings mark the proniosomes for clearance. Such localization of drugs is utilized to treat tumors in animals known to metastasize to the liver and spleen. This localization of drugs can also be used for treating parasitic infections of the liver. Proniosomes can also be utilized for targeting drugs to organs other than the RES. A carrier system (such as antibodies) can be attached to proniosomes (as immunoglobulin bind readily to the lipid surface of the noisome) to target them to specific organs¹⁴.

Anti-neoplastic Treatment

Most antineoplastic drugs cause severe side effects. Noisome can alter the metabolism; prolong circulation and half-life of the drug, thus decreasing the side effects of the drugs. Noisome entrapment of Doxorubicin and Methotrexate (in two separate studies) showed beneficial effects over the entrapped drugs, such as decreased rate of proliferation of the tumor and higher plasma levels accompanied by slower elimination. Podophyllotoxin- (PPT-DPPC) dipalmityl phosphatidyl choline proliposomes (PPT-DPPC-PL) for improvement of the stability of PPT-DPPC¹⁵.
Leishmaniasis
Leishmaniasis is an illness it caused by parasite of the genus Leishmania invades the cells of the liver and spleen. Commonly prescribed drugs for the treatment of Leishmaniasis is (antimonials) derivatives of antimony, which in higher concentrations can cause cardiac, liver and kidney damage. Use of pronoisome in assessments conducted showed that it was possible to administer higher levels of the drug.

Delivery of Peptide Drugs
Oral peptide drug delivery has long been faced with a challenge of bypassing the enzymes which breakdown the peptide. Use of proniosomes intended to successfully protect the peptides breakdown from gastrointestinal tract. In a study, oral delivery of a vasopressin derivative entrapped in proniosomes showed highest entrapment of the drug and significant increase in the stability of the incorporated peptide.

Used in Studying Immune Response
Proniosomes are used to study the immune response due to their immunological selectivity, low toxicity and greater stability. Niosomes are being used to study the nature of the immune response provoked by antigens.

Pronosomes as Carriers for Haemoglobin
Using a photo initiator, such as eosin and visible light. These hydrogel are constrained to surgical sites nearby to a light source as they form with difficulty after injection into the body. Ion-mediated gelation has been described for a number of polymers, e.g. chitosan/phosphate ions or alginites/calcium ions. The concentrations of the counter ion available under physiological situations are usually lacking for cross-linking of the above mentioned polymers. There are two important factors which limit the use of calcium-alginate. The first factor is their potential immunogenicity and the second one is longer time in-vivo degradability.

Pronosomes used in Cardiac Disorders
Proniosomal carrier system used for the treatment of hypertension for example captopril that is capable of efficiently delivering entrapped drug over an extended period of time.

Sustained release drug delivery
Sustained release action of proniosomes can be applied to drugs with low therapeutic index and low water solubility since those could be maintained in the circulation via proniosomal encapsulation.

Localized drug action
Drug delivery through proniosomes is one of the approaches to achieve localized drug action. Localized drug action results in enhancement of efficacy of the drug and at the same time it will reduces its systemic toxic effects e.g. Antimonials.

Hormonal Therapy
A proniosome based transdermal drug delivery system of levonorgestrel (LN) was developed and widely characterized both in vitro and in vivo. The biological assay for progestational activity included endometrial assay and inhibition with the formation of corpora lutea.

NSAID application
Non-steroidal anti-inflammatory drug like Ketorolac tromethamine (KT) administered intramuscularly and orally in divided multiple doses for short-term management of postoperative pain. Therefore, an alternative noninvasive mode of delivery of the drug is needed. So that, Transdermal route of delivery is an unconditionally an attractive route of administration to maintain the drug blood levels of KT for an extended period of time.

Table No.1: List of common non-ionic amphiphiles used in pronosome formulation

<table>
<thead>
<tr>
<th>S.No</th>
<th>Non-ionic Amphiphiles</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alkyl ethers and alkyl glycercylethers</td>
<td>Polyoxyethylene 4 lauryl ether (Brij30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polyoxyethylene stearyl ethers (Brij 72,76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polyoxyethylene cetyl ethers (Brij 52, 56, 58)</td>
</tr>
<tr>
<td>2</td>
<td>Sorbitan fatty acid Esters</td>
<td>Span 20, 40, 60, 80</td>
</tr>
<tr>
<td>3</td>
<td>Polyoxyethylene fatty acid esters</td>
<td>Tween 20, 40, 60, 80</td>
</tr>
</tbody>
</table>
Table No.2: Carriers used for the preparation of Proniosomes

<table>
<thead>
<tr>
<th>S.No</th>
<th>Carrier materials investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Maltodextrin</td>
</tr>
<tr>
<td>2</td>
<td>Mannitol</td>
</tr>
<tr>
<td>3</td>
<td>Sorbitol</td>
</tr>
<tr>
<td>4</td>
<td>Sprayed lactose</td>
</tr>
<tr>
<td>5</td>
<td>Glucose monohydrate</td>
</tr>
<tr>
<td>6</td>
<td>Lactose monohydrate</td>
</tr>
<tr>
<td>7</td>
<td>Sucrose stearate</td>
</tr>
</tbody>
</table>

Table No.3: Proniosome as carrier of various drug molecules

<table>
<thead>
<tr>
<th>S.No</th>
<th>Name of therapeutic agent</th>
<th>Route of delivery</th>
<th>Therapeutic category</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Levonorgestrel</td>
<td>Transdermal</td>
<td>Contraceptive agent</td>
<td>The study demonstrated the utility of proniosomal transdermal patch bearing levonorgestrel for effective contraception.</td>
</tr>
<tr>
<td>2</td>
<td>Flurbiprofen</td>
<td>Transdermal</td>
<td>NSAID</td>
<td>The drug release rate from cholesterol free proniosomes was to be high.</td>
</tr>
<tr>
<td>3</td>
<td>Captopril</td>
<td>Transdermal</td>
<td>Antihypertensive</td>
<td>Prolonged release of captopril.</td>
</tr>
<tr>
<td>4</td>
<td>Estradiol</td>
<td>Transdermal</td>
<td>Female hormone</td>
<td>The non-ionic surfactant in proniosomal formulation helps in enhancement of drug permeation through the skin.</td>
</tr>
<tr>
<td>5</td>
<td>Losartan potassium</td>
<td>Transdermal</td>
<td>Antihypertensive</td>
<td>Enhanced bioavailability and skin permeation.</td>
</tr>
<tr>
<td>6</td>
<td>Chlorpheniramine Maleate</td>
<td>Transdermal</td>
<td>Anti-histamine</td>
<td>Span 40 proniosomes showed optimum stability, loading efficiency and particle size and release kinetics suitable for transdermal delivery of drug.</td>
</tr>
<tr>
<td>7</td>
<td>Ketorolac Tromethamine</td>
<td>Transdermal</td>
<td>NSAIDS</td>
<td>The drug entrapment was high within the lipid bilayers of vesicles.</td>
</tr>
<tr>
<td>8</td>
<td>Tenoxicam</td>
<td>Transdermal</td>
<td>NSAID</td>
<td>Tenoxicam loaded proniosomal formula proved to be non-irritant, with significantly higher anti-inflammatory and analgesic effects.</td>
</tr>
<tr>
<td>9</td>
<td>Piroxicam</td>
<td>Transdermal</td>
<td>NSAIDS</td>
<td>Span 60 based lecithin vesicle showed significant decrease in paw swelling. There is an increased drug delivery from lipid vesicles.</td>
</tr>
<tr>
<td>10</td>
<td>Vinpocetine</td>
<td>Transdermal</td>
<td>Cerebro-vascular and cerebral Degenerative diseases</td>
<td>Proniosomes were prepared to optimize the extent of drug permeation through the skin.</td>
</tr>
<tr>
<td>11</td>
<td>Ketoprofen</td>
<td>Transdermal</td>
<td>NSAIDS</td>
<td>Demonstrat permeation enhancement of ketoprofen compared to plain gel.</td>
</tr>
<tr>
<td>12</td>
<td>Aceclofenac</td>
<td>Oral delivery</td>
<td>NSAIDS</td>
<td>The polynomial equation and contour plots developed by central composite design allowed to prepare proniosomes with optimum characteristic.</td>
</tr>
<tr>
<td>13</td>
<td>Indomethacin</td>
<td>Oral delivery</td>
<td>NSAIDS</td>
<td>The release rate of the drug from the vesicle was in the controlled manner.</td>
</tr>
<tr>
<td>14</td>
<td>Gliclazide</td>
<td>Oral delivery</td>
<td>Anti-diabetic</td>
<td>Higher surfactant concentration shows the higher entrainment efficiency.</td>
</tr>
</tbody>
</table>
CONCLUSION
From the above article concluded that the concept of including the drug into niosomes for a better targeting of the drug at proper tissue destination. Proniosomes based niosomes are thought to be better candidates drug delivery as compared to liposomes due to various factors like cost, stability etc. Proniosomes have been tested to encapsulate lipophilic as well as hydrophilic drug molecules. The use of proniosomal carrier results in delivery of high concentration of active agent(s), regulated by composition and their physical characteristics.

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CONFLICT OF INTEREST
We declare that we have no conflict of interest.

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