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Review on Novel Herbal Drug Delivery System – "Phytosomes"

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Abstract :-

The term "Phyto" means plant and "some" means cell It is also mentioned as herbosomes this is a new patented technology, where standardized plant extracts or water soluble phytoconstituents are complexed with phospholipids to produce lipid compatible molecular complexes, there by greatly increasing absorption and bioavailability. The recent development and conducted works of various researchers have been studied thoroughly to establish the transdermal route as a potential way to deliver phytoconstituents. Plant derived products or plant extracts are increasingly receiving attention as dietary supplements for the homeostatic management of inflammation, toxicities, cancers, weight loss and other chronic or acute degenerative disorders. But these products frequently face stability and bioavailability problems. Plant products after their isolation become prone to instability and are potentially unfit to cross the bio membrane as such. The phytosome technique reduces these tasks to reasonable extents. The phytosome or Herbosome technique increases the hydrophilicity of highly lipophilic drug there by making it suitable for drug delivery and increases the lipophilicity of hydrophilic phytoconstituents adequately to cross biological membrane. The topical application of phytosomes for cosmetic purpose has already been proven. This review also contains a comparative account of liposomes and phytosomes along with recent advancements in the field of phytosome technology with a special concern to transdermal drug delivery. The poor oral bioavailability of polyphenolic compound can be enhanced through the incorporation of them into phospholipid based self-assembled delivery system, i.e. popularly known as phytosome. There are number of products available in the market that contains phytosomal drug delivery system such as Ginkgo biloba, Silybum marianum, and Camellia sinensis.

Keywords: Phytosome; Plant; Phospholipid; Herbosomes; Bioavability

INTRODUCTION

Novel drug delivery systems is the new system Recent advances in the understanding of pharmacokinetic & pharmacodynamic behaviour of drug have offer a more rational approach to the development of optimal drug delivery system. The novel drug delivery systems (NDDS) are carriers which maintain the drug concentration in therapeutic range for longer period of time There are several advantages of novel drug delivery systems over conventional drug delivery.

1.Optimum therapeutic- drug concentration in the blood or in tissue may be maintained over a prolonged period of time.

2.Pre- determined release rates of extended period of time may be achieved.

3.Duration for short half- life drug may be increased

4.By targeting the site of action, side effects may be eliminated.

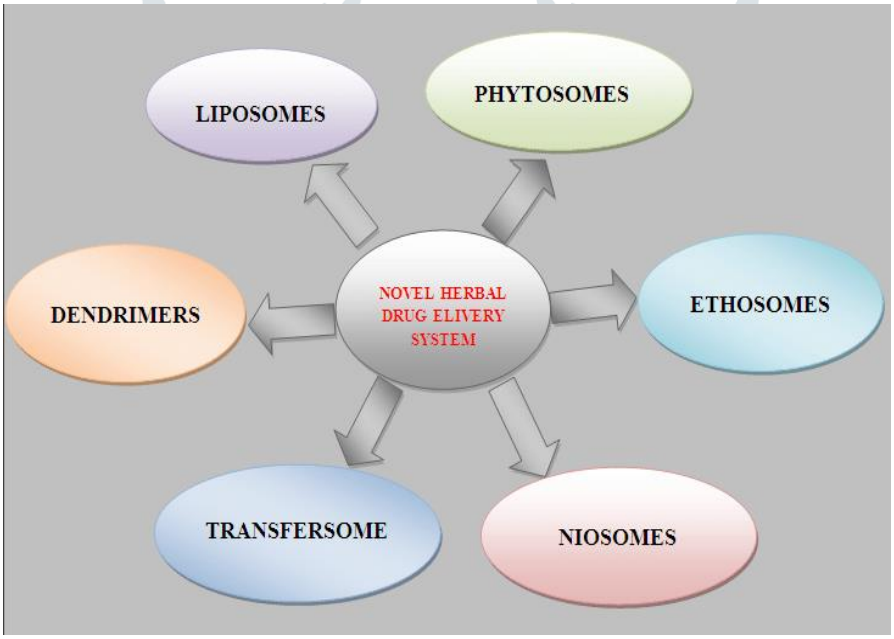
5.Frequent dosing and wastage of the drug may be reduced or excluded.

6.Better patient compliance may be ensured.

Novel drug delivery systems:- Various drug delivery systems have been developed and some of them under development with an aim to minimize drug degradation or loss, to prevent harmful side effects and to improve drug bioavailability and also to favour and facilitate the accumulation of the drug in the required bio-zone (site). There are no. Of novel carries which have been established and documented to be useful for controlled and targeted drug delivery. It is important to critically evaluate different terms used under the different broad categories of novel drug delivery system.

Types of Novel Drug Delivery System

Phytosomes is a novel approach of drug delivery system and it is advantageous in delivering the herbal drug at predetermined rate, delivery of drug at the site of action, Minimizes the toxic effects, Increase in bioavailability of drugs, Control of the distribution of drug is achieved by incorporate the drug in carrier system or in changing the structure of the drug at molecular level, Herbal drug are becoming more popular in the modern world for their applications and safety aspects. (Awasthi et al., 2011) Phytosomes is newly introduced patented technologies by Indian to developed and incorporate the standardized plant extracts. (Awasthi et al., 2011) The phytosomes process produces a little cell because of that the valuable components of the herbal extract are protected from destruction by digestive secretions and gut bacteria. Phytosomes are better able to transition from a hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane and from there into the cell finally reaching the blood. Phytosomes have improved pharmacokinetic and pharmacological parameter.



Phytosomes:-

Phosphatidylcholine (or phosphatidylser- ine) is a bifunctional compound. The phosphatidyl moiety is lipophilic and the choline (serine) moiety is hydrophilic in nature. This dual solubility of the phospholipid makes it an effective emulsifier. Thus, the choline head of the phosphatidylcholine molecule binds to these compounds while the lipid soluble phosphatidyl portion comprising the body and tail which then surrounds the choline bound material. Hence, the phytoconstituents produce a lipid compatible molecular complex with phospholipids, as shown (also called as phy- tophospholipid complex).

Properties of phytosomes Physico-chemical properties

As previously discussed, phytosomes are prepared by reaction of stoichiometric amount of phospholipid with the standardized plant extract as substrate. The spectroscopic data reveals that the phospholipid- substrate interaction is due to the formation of hydrogen bond between the polar head (i.e., phosphate and ammonium group) and the polar functionalities of the substrate.

The size of phytosome varies from 50 nm to a few 100 µm.

Phytosomes when treated with water, they assume a micellar shape resembling liposome and Photon Correlation Spectroscopy (PCS) reveals these liposomal structures acquired by Phytosomes.

Regarding the solubility of phytosomes, the complexes are often freely soluble in aprotic solvents, moderately soluble in fats, insoluble in water and relatively unstable in alcohol. But the phytosomes of certain lipophilic phytoconstituents like curcumin has shown increased water solubility upon complexation with phospholipids which has been discussed later in this paper. Ructures acquired by Phytosomes.

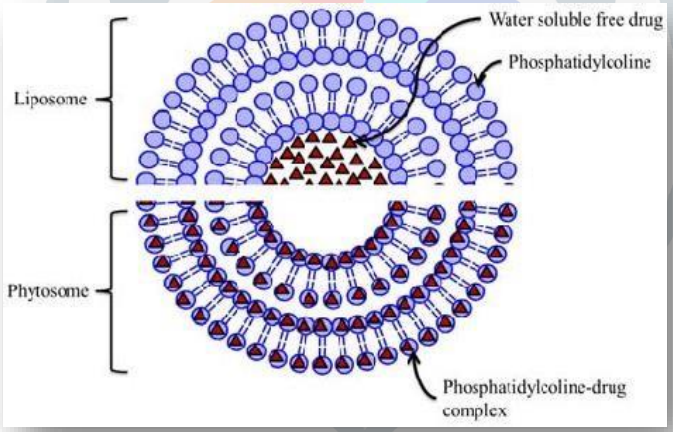
Biological properties:-

Phytosomes are novel complexes which are better absorbed and utilized, hence they produce more bioavailability and better result than the conventional herbal extract or non-complexed extracts, which has been demonstrated by pharmacokinetic studies or by pharmacodynamic tests in experimental animals and in human subjects.

The phytotomies should not be confused with liposomes where hydrophilic drug molecules are entrapped within a cavity or spaces between the membranes.Phytosomes express their behavior in physical or biological system because of their physical size,membrane permeability, percentage entrapment, chemical composition, quantity and purity of the materials used.

The liposomes may involve several hundred phospholipid molecules for this entrapment and are usually now being used for cosmetic purposes.

phytosomes involves interaction of 1- 4 phospholipid molecules with the phytoconstituents which are chemically anchored to each other. Several researches have shown the phytosomes to be a better alternative for liposomes in terms of membrane permeability and stability.



Strength of phytosomes:-

Phytosomes show better stability as chemical bond is formed between phsospholipid molecule and phytoconstituent(s).

Dose of phytoconstituents is reduced due to more bioavailability of the phytoconstituents in the complex form.l Duration of action is increased.

Phytoconstituents complex with phospholipids are more stable in gastric sections and resist the action of gut bacteria.

Enhanced permeability of phytoconstituents across the biological membranes. 8 shows better absorption, hence shows significantly higher therapeutic effects.

Phoshatidylcholine used in the formation of phytosomes, besides acting as a carrier also possess several therapeutic properties, hence gives the synergistic effect when particular substance is given.

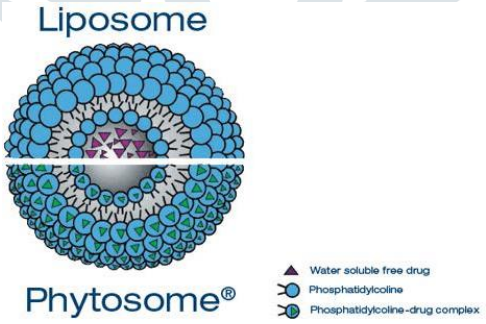
Drug entrapment is not a problem with phytosome as the complex is biodegradable.

Advantages

1) There is a dramatic enhancement of the bioavailability of botanical extracts due to their complexation with phospholipid and improved absorption in the intestinal tract.
2) They permeate the non-lipophilic botanical extract to allow better absorption from the intestinal lumen, which is otherwise not possible.[8]
3) The formulation of Phytosome is safe and the components have all been approved for pharmaceutical and cosmetic use.
4) They have been used to deliver liver protecting flavonoids because they can be made easily bioavailable by phytosomes. In addition to this, Phosphatidylcholine is also hepatoprotective and so provides a synergistic effect for liver protection. [9]
5) This technology offers cost effective delivery of phytoconstituents and synergistic benefits when used as functional cosmetics to protect the skin against exogenous or endogenous hazards in normal as well as stressful environmental conditions. [10]
6) They can be also used for enhanced permeation of drug through skin for transdermal and dermaldelivery. [11]
7) These are platform for the delivery of large and diverse group of drugs (peptides, protein molecules).
8) The vesicular system is passive, non-invasive and is available for immediate commercialization .[11]
9) Phosphatidylcholine, an essential part of the cell membrane used in phytosome technology, acts as a carrier and also nourishes the skin. [10]
10) There is no problem with drug entrapment during formulation preparation.
11) Also, the entrapment efficiency is high and moreover predetermined; because the drug itself forms vesicles after conjugation with lipid.
12) Relatively simple to manufacture with no complicated technical investment required for the production of Phytosomes.

Comparison between phytosome and liposome :-

There are number of research which has been carried out on phytosomes which state that phytosomes have good bioavailability, absorption, and excellent therapeutic efficacy over liposome. Comparison between phytosomes and liposomes is represented in along with their structure in Figure



Mechanism of phytosome technology:-

The lower absorption and bioavailability of polyphenolic constituents mainly due to two factors These chief constituents are number of ringed molecule and are not too much small that it will absorbed by diffusion process. Second factor is that flavonoid molecule or chief constituents of polyphenols have poor solubility with lipids.

METHOD OF PREPARATIONS OF PHYTOSOMES:-

1. Antisolvent precipitation technique

The specific amount of drug and soya lecithin were taken into a 100 ml round bottom flask and refluxed with 20 ml of dichloromethane at a temperature not exceeding 60oC for 2 h. The mixture is concentrated to 5-10 ml.

Hexane (20 ml) was added carefully with continuous stirring to get the precipitate which was filtered and collected and stored in vacuum desiccators overnight. The dried precipitate is crushed in mortar and sieved through #100 meshes. Powdered complex was placed in amber colored glass bottle and stored at room temperature.

2. Rotary evaporation technique:-

The specific amount of drug and soya lecithin were dissolved in 30 ml of tetrahydrofuran in a rotary round bottom flask followed by stirring for 3 hours at a temperature not exceeding 40oC. (Awasthi et al., 2011) Thin film of the sample was obtained to which n-hexane was added and continuously stirred using amagnetic stirrer. The precipitate obtained was collected, placed in amber colored glass bottle and stored atroom temperature.

3. Solvent evaporation method:-

The specific amount of drug and soya lecithin were taken into a 100 ml round bottom flask and refluxed with 20 ml of acetone at a temperature 50 - 60oC for 2 h. The mixture is concentrated to 5-10 ml to obtain the precipitate which was filtered and collected. (Mazumder et al., 2016) The dried precipitate phytosomes complexes was placed in amber colored glass bottle and stored at room temperature

Applications of Phytosomes:

1.There are many plant drugs that are incorporated to Phytosomes process as herbal extracts including Ginkgo biloba, grape seed, hawthorn, milk thistle, green tea, and ginseng.

2.Most of the phytosomal studies are focused to Silybum marianum which shows that it contains premier liver-protectant flavonoids.

3.The fruit of the milk thistle plant (S. marianum, Family steraceae) contains flavonoids known for hepatoprotective effects.

4.It was found that Silymarin has been shown to have positive effects in treating liver diseases of various kinds, including inflammation of the bile duct, hepatitis, cirrhosis and fatty infiltration of the liver.

5.The antioxidant capacity of silymarin significantly boosts the liver's resistance to toxic insults. 6..Silymarin primarily contains three flavonoids of the flavonol subclass.

8.Silybin predominates, followed by silydianin and silychristin.

9.Silybin is a flavonolignan which is probably produced within the plant by the combination of a flavonol with a coniferyl alcohol. It is now known that Silybin is the most potent of the three.

10. Silybin protects the liver by conserving glutathione in the parenchymal cells , while PC helps repair and replace cell membranes .

11. These constituents offer the synergistic benefit of sparing liver cells from destruction.

12. In its native form within the milk thistle fruit, Silybin occurs primarily complexed with sugars, as a flavonyl glycoside or flavonolignan Silybin has been extensively researched and found to have impressive bioactivity, albeit limited by poor bioavailability.

CONCLUSION:-

The novel drug delivery system research area of herbal drugs is an innovative work that target for phytoconstituents and plant extracts regarding the therapeutic and cosmetic usefulness of plant products particularly conits poor lipid solubility and larger molecular size limiting their ability to pass across the lipid-rich taining flavonoids and poly phenolic compounds. However, due to its poor lipid solubility and larger molecular size limiting their ability to pass across the lipid-rich biological membranes, resulting poor bioavailability.

Different reports show a promising future of phytosome as an advanced form of herbal products that are better absorbed, utilized, and as a result produce better results than conventional herbal extracts. The complexation of phytoconstituents and phospholipids makes the phytoconstituents more stable in the complexform due to liopophilic nature and offering the herbal drugs with sufficient lipid penetrability, form due to liopophilic nature and offering the herbal drugs with sufficient lipid penetrability, higher concentration, sustained therapeutic levels and increased cosmetic value. It was confirmed that Curcumin phytosoml showed a better diffusion as well as stability profile, hence providing an attractive carrier for the delivery of various phytoconstituents present in it. In conclusion, the application of phytosomal formulation as topical pharmaceutical agent and cosmetics with improved safety and efficacy results in proper utilization of herbal drugs and cost effective pharmaceutical product.

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