

# Phytosomes: a strategy to improve transdermal absorption of phytoconstituents

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**Abstract:** Herbal medicines have been used in treatment of various diseases and disorders since a very long time. Despite of the fact of their usage and benefit, a question is raised on their low lipid solubility, large size and decreased stability. To their rescue is the phyto-phospholipid complex under an advanced novel technology called Phytosomes with a promising effect of increasing quality and delivery of plant extracts. They are definitely advantageous over conventional herbal extracts and has offered researchers to deliver lipid insoluble plant metabolites to skin and other desired target in the human body. This review highlights the use of phytosomes in successfully delivering drugs by increasing their solubility and bioavailability, especially to skin.

**Index Terms:** Phytosomes, phospholipid, drug-phospholipid complex, TDDS.

## I. INTRODUCTION

Transdermal drug delivery system is the method of delivering drug into the systemic circulation through skin. Conventional methods of delivery of drug to the skin or through skin involves use of different dosage forms like creams, ointments, skin and dermal patches with advantages like eliminating first pass metabolism, better patient compliance and steady states of plasma concentration. Despite of the advantages major drawback is poor absorption of many drugs. This poor absorption of drugs through skin can be attributed to many reasons like skin metabolism, skin temperature, skin hydration, disease state, age and gender related factors[1].

Namely only eight drugs are available in the market which are used via transdermal route because many of the drugs cannot easily penetrate the layers of skin, the key reason for this stands to be the stratum corneum which is being compared to a brick wall in which corneocytes acts as bricks and intercellular lipid lamellae acts as the mortar, both responsible for the barrier properties. To disrupt this barrier many strategies have been developed to improve drug transport, nanoparticles and other vesicular systems being one of the most useful method[2].

Different systems like nanoparticles, nanoemulsions, solid lipid nanoparticles, liposomes, niosomes, transferosomes, ethosomes and phytosomes has been proposed as an attempt to deliver drugs through the skin. They present advantages like enabling drug retention and also in some cases delivering a drug at a predetermined rate. This is attributed to their physicochemical properties like surface charge, size, shape, rigidity etc[3].

One among these important vesicular systems is **Phytosomes**, also knowns as herbosomes and are structurally similar to liposomes. They are cell-like structures made of phospholipids which surrounds hydrophilic phytoconstituents of plants. This system of delivery of plant derived drugs is an efficient way in improving bioavailability and efficacy of these drugs.

## II. PHYTOSOMES

Phytosomes where, phyto means plant and some means cell like, is formed by a method in which plant extract is encored by phospholipids forming a complex. The phospholipid used here mainly is phosphotidylcholine. Phospholipid acts as an emulsifier with a structure containing two lipophilic tails and a hydrophobic head. Phytosomes enhance bioavailability and improve absorption of the drug by combining the phospholipid and the active component of the herbal extract making it a competent carrier[4].

## III. PROPERTIES OF PHYTOSOMES

Phytosomes is an innovative drug delivery that has made a crucial improvement in the delivery of phytochemicals. Although they are compared structurally to liposomes, they differ from them based upon their stoichiometric ratio (generally a 1:1 or 1:2 of phospholipid:phytoconstituent) through which carriers are bonded to active moiety, for example through hydrogen bonds which increases their stability. Phytosomes are stable because of the chemical bonding which also imparts it with better encapsulation efficiency.

When herbal extracts are formulated using phytosomes rather than as free drug they show better PK and PD profiles, which in case are also better than liposomes.

In addition to increased bioavailability and solubilty, phytosomes also improves permeability rate to a great extend in some cases of herbal extracts. It inhibits both physical and chemical degradation of phytochemicals and does not generate toxic effects.[4]

## Phytosomes and phytoconstituents

Phyto-pharmaceuticals or herbal medicines relates back to a long time in history of medicines due to their therapeutic importance. Phytoconstituent in nature is not high in terms of bioavailability incomplete In-vitro activity of herbal extracts is excellent but their low lipid solubility and high molecular size make their in-vivo activity very less efficient with low bioavailability. To overcome this limitation the novel technology of “Phytosomes” is used based on their physicochemical and spectroscopic characteristics[5].

Phytosomes has successfully increased bioavailability of herbal extracts or phytochemicals like ginkgo biloba, grape seed, hawthorn, green tea and milk thistle. In case of dermal applications, phytosomes made of **Rutin** using phosphatidylcholine increases the dermal absorption of rutin which can be used in the treatment of athletic-aches, arthritis and rheumatism (Das and Kalita, 2014). It was determined from a clinical study that, **green tea catechins** showed better absorption in phytosomes when compared to free catechins and increased antioxidative properties in the human volunteers (Pietta et al., 1998).

Formulations containing six boswellic acids were shown to increase tissue penetration in rats when prepared in phytosomes and can be successfully used for their anti-inflammatory activity (Huishi et al., 2013). **Silybin-phospholipid** complex was found to be more suitably encapsulated in phytosomes than liposomes (Angelico et al., 2014). In vitro and in vivo delivery of hydrophobic molecules of **curcumin** has been effective. **Quercetin**, a water insoluble component was efficiently encapsulated (approximately 98%) with a diameter of 80nm in phytosomes. Absorption of many other polyphenolic compounds like **silymarin** was improved. Delivery of herbal drugs using phytosome technology has also been used in certain cosmetics.

## IV. ADVANTAGES OF PHYTOSOMES

Phytosomal technology is used since 1989 as better carrier of drugs than conventional herbal extracts mainly because of following advantages[6];

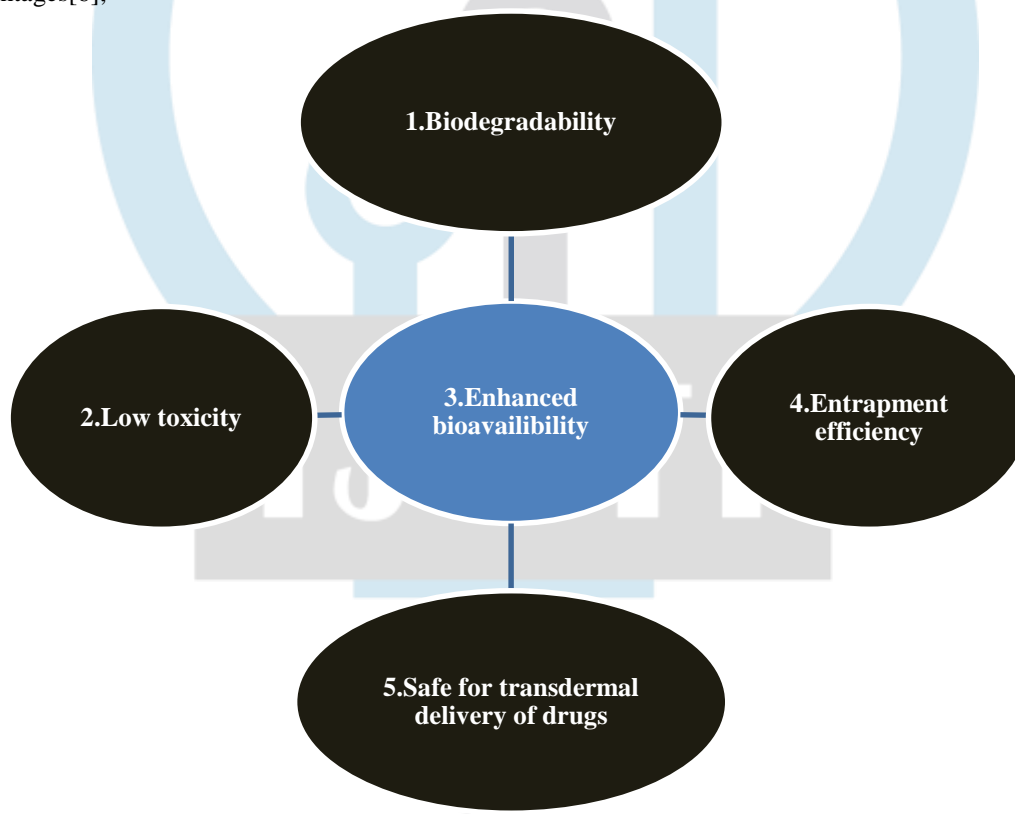


Figure 1: Advantages of phytosomes

## V. MATERIALS AND METHODS

### Methods of preparation of phytosomes:

The common approach followed in all the different procedures in the preparation of phytosomes is a reaction between active drug and phospholipid (natural or synthetic) in a solvent.

The different methods are as follows:

1. Anti-solvent preparation method:

In this method the desired phytoconstituent and the phospholipid is taken in a flask containing organic solvent and at a particular temperature it is refluxed on a magnetic stirrer. later, the mixture is concentrated and followed by addition of anti-solvent. suitable anti-solvents can be selected for example, n-hexane. Then the complex forms as a precipitate. Under vacuum the precipitate is filtered and stored.

### 2. Solvent Evaporation Technique:

This is the most commonly used technique for preparation of phytosomes in which the mixture of phytoconstituent and phospholipid is taken in a flask containing organic solvent maintaining a temperature of about 40°C for about 1 hour.

Using a rotary evaporator the organic solvent is then removed which leaves a thin film in the flask. The phytosomes so obtained are sieved and kept in a desiccator for about 12 hrs. The resultant are then flushed with nitrogen and stored in ambered colour container.

### 3. Mechanical Dispersion Method:

Also known as ether injection method, this method involves dissolving the active drug in aqueous solution and lipid in organic solvent like diethyl ether. The ether solution is then slowly injected to the aqueous solution of the drug in order to encapsulate them.

The drug-lipid complex is formed once the organic solvent is removed under reduced pressure.

There are other novel methods of preparation like super critical fluids which involves anti-solvent process (PCA), gas anti-solvent technique (GAS) etc [7].

## VI. CHARACTERIZATION AND OPTIMIZATION TECHNIQUE

There are certain criteria like stability, drug release, vesicular size, shape, entrapped concentration etc that formulated phytosomes should be evaluated for which performing characterization is an important aspect.

### Visualization:

To observe particle size, surface attributes etc of the drug-phospholipid complex, scanning electron microscopy is used to obtain high resolution images which can be resolved and visualized. As a result, the atomic state is described by posterior scattered electrons and surface topography by secondary electrons.

TEM can be used to study the composition, crystallographic features and internal structure of the complexes. [8]

### Entrapment Efficiency:

Centrifugation is used to measure entrapment efficiency in which known amount of drug-lipid complex and equivalent quantity of encapsulated drug is made into a solution using phosphate buffer pH 6.8. Centrifugation is then carried out at 5000 rpm for about 30 mins. The supernatant is collected and using UV or HPLC Absorbance is measured and percentage is calculated using the following formula;

Entrapment Efficiency (%) =  $\frac{\text{Actual amount of drug}}{\text{theoretical amount of drug}}$

### Vesicle stability:

Zeta potential and polydispersity index can be used to describe the stability of the prepared phytosomes. Generally size of the phytosomes depends upon the formulation prepared but with PDI < 0.5 and zeta potential  $\geq \pm 30$  mV they are considered stable. [9]

### Drug Content:

Drug content can be measured using HPLC and other methods using spectroscopy.

### Spectroscopic Evaluations:

Spectroscopy is used to confirm the complex formation of the prepared phytosomes. To validate the complex formed between the active herbal extract and the phospholipid used various spectroscopic methods like: <sup>1</sup>H NMR, <sup>13</sup>C NMR, FTIR etc are used. [10]

## VII. CONCLUSION:

Phytosomes are not only a choice for formulating herbal extracts by improving their absorption but also an important step-ahead in development of formulation technology. This review is an attempt to put forward the simple preparation and vast advantages that phytosomes provide in transdermal route along with many other routes for the delivery of drugs to different parts of the body. After being used for several years, today phytosomes has proved themselves to be successfully used in many therapies like anti-cancer, anti-tumor, cardiac disorders and many others through their better drug targeting approach.

## VIII. ACKNOWLEDGMENT

I would like to thank everyone associated with this review article.

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