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PHYTOSOMES AS DRUG DELIVERY SYSTEMS: A REVIEW

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ABSTRACT

Phytosomes are advanced phospholipid-based vesicular drug delivery systems developed to improve the bioavailability, stability, permeability, and therapeutic efficacy of herbal active ingredients and phytoconstituents. Many plant-derived compounds such as flavonoids, polyphenols, terpenoids, and alkaloids possess excellent pharmacological activities but suffer from poor aqueous solubility, low membrane permeability, rapid metabolism, and poor oral absorption. Phytosome technology overcomes these limitations by forming molecular complexes between phytoconstituents and phospholipids, mainly phosphatidylcholine. The resulting phyto-phospholipid complexes exhibit enhanced lipid compatibility and improved passage across biological membranes. Phytosomes have demonstrated superior pharmacokinetic and pharmacodynamic performance compared to conventional herbal formulations. This review comprehensively discusses the concept, structure, preparation methods, characterization, advantages, limitations, and therapeutic applications of phytosomes. Special emphasis is placed on phytosomal formulations of curcumin, silymarin, quercetin, resveratrol, green tea polyphenols, and Ginkgo biloba extracts. Recent advances in nanophytosomes, targeted phytosomes, and topical phytosomal systems are also highlighted. Additionally, marketed products, regulatory considerations, and future prospects of phytosomal drug delivery systems are discussed.

1. Introduction

Herbal medicines have been used for centuries in traditional healthcare systems due to their therapeutic efficacy and relatively low toxicity. Phytoconstituents such as flavonoids, polyphenols, terpenoids, alkaloids, glycosides, and tannins exhibit a wide range of pharmacological activities including antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, cardioprotective, anticancer, neuroprotective, and antidiabetic effects. However, many herbal active ingredients suffer from poor water solubility, instability, rapid metabolism, low permeability, and poor oral bioavailability, limiting their clinical applications[1].

Novel drug delivery systems (NDDS) have been developed to overcome these challenges and improve the therapeutic efficacy of phytoconstituents. Among these systems, phytosomes have emerged as one of the most promising lipid-based nanocarriers for herbal drugs. Phytosomes are molecular complexes formed between phytoconstituents and phospholipids, mainly phosphatidylcholine. Unlike conventional liposomes, where the drug is merely entrapped within vesicles, phytosomes involve chemical interaction between phospholipids and herbal constituents through hydrogen bonding[2].

Phytosome technology was first developed by Indena S.p.A., Italy, in the late 1980s to enhance the absorption and therapeutic effectiveness of herbal extracts. The amphiphilic nature of phytosomes enables better transition of phytoconstituents across lipid-rich biological membranes, resulting in enhanced bioavailability and improved pharmacological response[3].

This review discusses the principles, formulation strategies, characterization, applications, advantages, limitations, and future perspectives of phytosomes as novel drug delivery systems.

2. Definition and Concept of Phytosomes

Phytosomes are phospholipid-based vesicular systems formed by complexation between standardized plant extracts or phytoconstituents and phospholipids in a stoichiometric ratio[4].

The term "phytosome" is derived from:

- "Phyto" = plant
- "Some" = cell-like structure

Phytosomes are also known as:

- Phytophospholipid complexes
- Herbosomes

The most commonly used phospholipid is phosphatidylcholine (PC), which possesses both hydrophilic and lipophilic properties.

3. Structure of Phytosomes

In phytosomes, phytoconstituents are chemically linked with phospholipid molecules through hydrogen bonding.

The phospholipid molecule acts as:

- Carrier
- Membrane stabilizer
- Bioavailability enhancer

Hydrophilic phytoconstituents bind with the polar head of phospholipids, while the lipid tail enhances membrane permeability.

4. Difference Between Liposomes and Phytosomes

Parameter	Liposomes	Phytosomes
Drug incorporation	Drug entrapped inside vesicle	Drug chemically complexed
Interaction	Weak physical entrapment	Hydrogen bonding
Stability	Comparatively less stable	More stable
Bioavailability	Moderate	Higher
Membrane permeability	Limited	Enhanced
Drug loading	Lower	Higher
Structure	Bilayer vesicle	Molecular complex

5. Need for Phytosomal Drug Delivery

Many herbal constituents exhibit:

- Poor lipid solubility
- Low membrane permeability
- Rapid degradation
- Poor gastrointestinal absorption
- Extensive first-pass metabolism

Examples include:

- Curcumin
- Quercetin
- Silymarin
- Resveratrol
- Catechins

Phytosomes improve:

- Solubility
- Stability
- Absorption
- Targeting
- Therapeutic efficacy

6. Components of Phytosomes

6.1 Phytoconstituents

Common herbal actives used include:

- Flavonoids
- Polyphenols
- Alkaloids
- Terpenoids

Examples:

- Curcumin
- Quercetin
- Silymarin
- Catechins

6.2 Phospholipids

Most commonly used phospholipids:

- Phosphatidylcholine
- Phosphatidylserine
- Phosphatidylethanolamine

Functions:

- Carrier
- Membrane stabilizer
- Absorption enhancer

6.3 Solvents

Used during complex preparation:

- Ethanol
- Acetone
- Dioxane
- Chloroform

7. Methods of Preparation of Phytosomes

7.1 Solvent Evaporation Method

Most widely used method.

Procedure:

1. Phospholipid and phytoconstituent dissolved in organic solvent.
2. Reaction carried out under reflux.
3. Solvent evaporated.
4. Complex precipitated and dried.

Advantages:

- Simple
- High complexation efficiency

7.2 Anti-solvent Precipitation Method

Complex precipitated using non-solvent.

7.3 Rotary Evaporation Method

Widely employed for large-scale production.

7.4 Freeze Drying Method

Improves stability of phytosomes.

8. Characterization of Phytosomes

8.1 Particle Size Analysis

Measured using:

- Dynamic light scattering
- Laser diffraction

8.2 Zeta Potential

Indicates surface charge and stability.

8.3 Entrapment Efficiency

Determines percentage of drug complexed.

8.4 Morphological Studies

Performed using:

- SEM
- TEM
- AFM

8.5 Differential Scanning Calorimetry (DSC)

Used to confirm complex formation.

8.6 Fourier Transform Infrared Spectroscopy (FTIR)

Detects hydrogen bonding interactions.

8.7 X-Ray Diffraction (XRD)

Determines crystallinity.

9. Mechanism of Bioavailability Enhancement

Phytosomes improve bioavailability through:

- Enhanced lipid solubility
- Improved membrane permeability
- Protection from degradation
- Improved gastrointestinal absorption

10. Advantages of Phytosomes

10.1 Improved Bioavailability

Enhanced absorption of poorly soluble phytoconstituents.

10.2 Enhanced Stability

Protects phytochemicals from:

- Oxidation
- Hydrolysis
- Enzymatic degradation

10.3 Better Membrane Permeability

Phospholipid compatibility enhances cellular uptake.

10.4 Reduced Toxicity

Lower doses achieve therapeutic effects.

10.5 Controlled Release

Provides sustained drug release.

10.6 Improved Patient Compliance

Reduced dosing frequency.

11. Limitations of Phytosomes

11.1 High Production Cost

Complex manufacturing processes increase cost.

11.2 Stability Issues

Phospholipids may undergo oxidation.

11.3 Scale-Up Challenges

Industrial manufacturing requires optimization.

11.4 Limited Drug Loading

Some hydrophobic compounds show poor complexation.

12. Applications of Phytosomes

12.1 Oral Drug Delivery

Phytosomes significantly improve oral absorption of phytoconstituents.

Examples:

- Curcumin phytosomes
- Silymarin phytosomes

12.2 Topical Delivery

Enhance skin penetration and retention.

Applications:

- Cosmetics
- Anti-aging formulations
- Skin antioxidants

12.3 Hepatoprotective Therapy

Silymarin phytosomes show enhanced liver targeting.

12.4 Cancer Therapy

Phytosomes improve anticancer activity of herbal compounds.

Examples:

- Curcumin
- Quercetin
- Resveratrol

12.5 Cardioprotective Applications

Improved absorption of antioxidant flavonoids.

12.6 Neuroprotective Applications

Enhanced brain delivery of phytoconstituents.

13. Examples of Herbal Drugs Formulated as Phytosomes

Herbal Drug	Source	Therapeutic Activity	Benefit of Phytosome
Curcumin	Turmeric	Anticancer, anti-inflammatory	Improved bioavailability
Silymarin	Milk thistle	Hepatoprotective	Enhanced liver targeting
Quercetin	Fruits and vegetables	Antioxidant	Improved absorption
Resveratrol	Grapes	Cardioprotective	Sustained release
Ginkgo biloba	Ginkgo leaves	Neuroprotective	Enhanced brain delivery
Green tea catechins	Camellia sinensis	Antioxidant	Improved stability
Berberine	Berberis species	Antidiabetic	Enhanced permeability

14. Curcumin Phytosomes

Curcumin possesses:

- Antioxidant
- Anti-inflammatory
- Anticancer activities

Limitations:

- Poor water solubility
- Rapid metabolism

Curcumin phytosomes improve:

- Oral bioavailability
- Stability
- Cellular uptake
- Therapeutic efficacy

15. Silymarin Phytosomes

Silymarin is one of the most successful phytosomal products.

Advantages:

- Improved hepatoprotection
- Enhanced oral absorption
- Better antioxidant activity

Commercial products are available globally.

16. Phytosomes in Cosmetic Applications

Phytosomes are increasingly used in:

- Anti-aging creams
- Sunscreens
- Skin whitening formulations
- Antioxidant products

Benefits:

- Enhanced skin penetration
- Improved hydration
- Better collagen protection

17. Recent Advances in Phytosomal Technology

17.1 Nanophytosomes

Nanosized phytosomes provide:

- Better absorption
- Improved targeting
- Enhanced stability

17.2 Targeted Phytosomes

Ligand-conjugated systems improve site-specific delivery.

17.3 Stimuli-Responsive Phytosomes

Release drugs in response to:

- pH
- Temperature
- Enzymes

17.4 Combination Therapy

Co-delivery of herbal and synthetic drugs.

18. Marketed Phytosomal Products

Product	Active Ingredient	Application
Siliphos®	Silymarin	Liver disorders
Meriva®	Curcumin	Anti-inflammatory
Greenselect®	Green tea extract	Weight management
Ginkgoselect®	Ginkgo biloba	Cognitive disorders

19. Regulatory Considerations

Phytosomal formulations require:

- Toxicity studies
- Stability studies
- Standardization

- Quality control

Major challenges:

- Herbal variability
- Reproducibility
- Regulatory harmonization

20. Future Prospects

Future research should focus on:

- Personalized herbal nanomedicine
- Large-scale production
- AI-assisted formulation design
- Smart phytosomal systems
- Clinical translation

Phytosome technology has strong potential in:

- Cancer therapy
- Nutraceuticals
- Cosmetic delivery
- Targeted herbal therapeutics

21. Conclusion

Phytosomes represent an innovative and highly promising drug delivery system for herbal active ingredients. They effectively overcome major limitations associated with phytoconstituents such as poor solubility, instability, low membrane permeability, and poor bioavailability. By forming molecular complexes with phospholipids, phytosomes significantly improve absorption, stability, pharmacokinetics, and therapeutic efficacy of herbal drugs. Numerous phytoconstituents including curcumin, silymarin, quercetin, resveratrol, and catechins have demonstrated enhanced bioavailability and pharmacological activity when formulated as phytosomes. Recent advancements in nanotechnology and targeted delivery further expand the clinical potential of phytosomal systems. Despite challenges related to stability, scale-up, and regulatory approval, phytosomes are expected to play a major role in future herbal drug delivery and pharmaceutical development[5-12].

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