International Journal of Pharmacy and Pharmaceutical Science

ISSN Print: 2664-7222
ISSN Online: 2664-7230
IJPPS 2025; 7(2): 691-700
www.pharmacyjournal.org
Received: 12-10-2025
Accepted: 15-11-2025

Bhoomika Lalchand Choudhary
BR Harne College of Pharmacy, Karav, Vangani (W), Ambernath, Thane, Maharashtra, India

Priya Ravindra Jadhav
BR Harne College of Pharmacy, Karav, Vangani (W), Ambernath, Thane, Maharashtra, India

Dr. Gita Mohire
BR Harne College of Pharmacy, Karav, Vangani (W), Ambernath, Thane, Maharashtra, India

Siddhi Sanjay Chaugule
BR Harne College of Pharmacy, Karav, Vangani (W), Ambernath, Thane, Maharashtra, India

Corresponding Author:
Bhoomika Lalchand Choudhary
BR Harne College of Pharmacy, Karav, Vangani (W), Ambernath, Thane, Maharashtra, India

Phytosomes: A novel herbal drug delivery system with emphasis on *Camellia sinensis* for enhanced topical bioavailability

Bhoomika Lalchand Choudhary, Priya Ravindra Jadhav, Gita Mohire and Siddhi Sanjay Chaugule

DOI: https://www.doi.org/10.33545/26647222.2025.v7.i2h.266

Abstract
Herbal drugs have served as valuable therapeutic sources for centuries. However, their clinical potential is often limited by poor solubility, instability, and low bioavailability. Among modern approaches, phytosomes represent a remarkable breakthrough, improving the bioavailability of polyphenolic compounds by forming stable complexes with phospholipids. This technology enhances absorption, increases stability, and prolongs therapeutic efficacy compared to conventional herbal extracts.

The current review focuses on the phytosome approach, particularly with *Camellia sinensis* (Green Tea), a plant rich in catechins such as *Epigallocatechin gallate* (EGCG), known for its strong antioxidant, anti-inflammatory, and photoprotective properties. Despite its remarkable pharmacological potential, EGCG exhibits low oral bioavailability due to its hydrophilicity and rapid metabolism. Formulating green tea extract into phytosomes provides a promising solution by improving dermal penetration, chemical stability, and controlled release when incorporated into a topical gel base. Such formulations enhance catechin stability and skin compatibility, ensuring prolonged therapeutic action through sustained release.

Phytosomal preparations show enhanced antioxidant, anti-aging, and photoprotective activities, making them an ideal candidate for dermatological and cosmetic use. It further discusses the formulation strategies, evaluation parameters, and the advantages of green tea phytosomes over conventional herbal dosage forms. Additionally, it highlights the challenges related to large-scale manufacture and regulatory approval.

Overall, phytosome-based delivery offers a scientifically validated platform to bridge ancient herbal knowledge with advanced pharmaceutical technology, enabling safer and more effective therapeutic outcomes.

Keywords: *Camellia sinensis*, Enhanced bioavailability, *Epigallocatechin gallate* (EGCG), Green tea, Herbal formulations, Novel Drug Delivery System (NDDS), Phospholipid complex, Phytosomes, Topical phytosomal gel

1. Introduction

Herbal preparations are medicinal products prepared from plant-derived substances such as leaves, roots, bark, flowers, seeds, or their extracts, either alone or in combination, to prevent or cure diseases. Despite their ancient use, plant-derived bioactives suffer from poor solubility, low permeability, rapid metabolism, and limited bioavailability. These issues necessitate modern technologies to improve delivery, targeting, and therapeutic outcomes.

Novel Drug Delivery Systems (NDDS) provide an effective solution by employing innovative drug delivery platforms that enhance the pharmacokinetic and pharmacodynamic profiles of herbal molecules. Drug delivery systems such as nanoparticles, liposomes, phytosomes, ethosomes, and nanoemulsions not only improve therapeutic efficacy, but also bridge the gap between traditional herbal therapies and modern pharmaceutical formulations.

1.1 General background on herbal drugs limitations

For several decades, medicinal plants and their bioactive constituents have been utilized to treat various diseases [1]. Numerous pharmacological studies have been conducted on different plant extracts to study their therapeutic effects [2]. Most of the plant-derived biologically active constituents are polar or water-soluble, such as flavonoids, tannins, terpenoids, and polyphenols.

However, due to their large molecular size and poor lipid solubility, these compounds exhibit low permeability across lipid-rich biological membranes, leading to poor bioavailability [3].
Consequently, Novel Drug Delivery Systems (NDDS) have gained importance for overcoming the limitations of conventional drug delivery methods [4].

1.2 Rationale of NDDS

Novel Drug Delivery System (NDDS) refers to advanced methods or formulations designed to deliver drugs in a controlled, targeted, and efficient manner. These systems enhance therapeutic efficacy, minimize side effects, and improve patient compliance compared to traditional approaches.

1.2.1 Types of NDDS: NDDS can be classified based on their mechanism and route of drug delivery into two main types: Carrier-Mediated Delivery Systems and Transdermal Delivery Systems [5].

Carrier-based Drug Delivery System

- Liposomes
- Nanoparticles
- Microspheres
- Niosomes
- Resealed erythrocytes

Transdermal Drug Delivery Systems

- Sonophoresis
- Osmotic pump
- Microencapsulation.

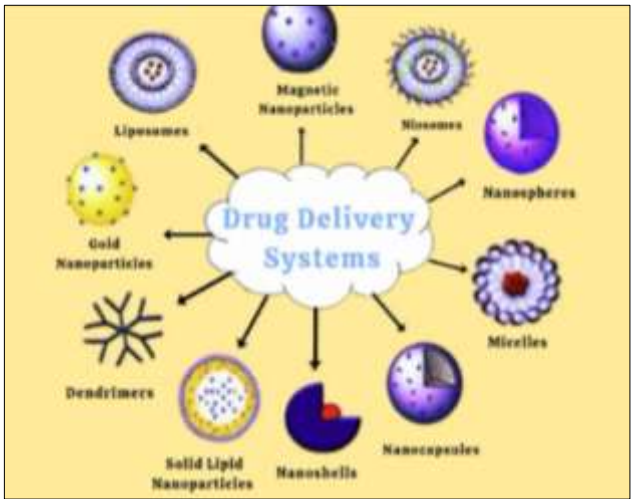

Fig 1: Recent advancements in novel herbal drug delivery systems

1.2.2 Benefits of NDDS

- Improve the curative potency of herbal medicines while reducing adverse effects.
- Uses smaller quantities of raw materials to achieve the desired therapeutic effect.
- Facilitate controlled drug delivery and accurate dosing.
- Enhances targeted delivery of drugs to the desired site of action.
- Reduces dosing frequency and improves patient compliance.
- Increases therapeutic utility by minimizing toxicity and enhancing bioavailability [7].

1.2.3 NDDS in herbal drugs

Over the last decades, significant advancements have been made in developing NDDS for many plant extracts and their active principles [2]. Nanosized dosage forms such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, phytosomes, and nanoemulsions provide multiple benefits to herbal drugs, including improved solubility, increased bioavailability, enhanced stability, and prolonged release [7].
Among the different methods, phyto-phospholipid complexes (commonly known as phytosomes) have proven highly successful in improving bioavailability [8]. Phytosomes possess superior pharmacokinetic and pharmacological profiles, making them valuable for pharmaceutical and cosmetical products [3]. NDDS in herbal drugs holds immense potential for improving therapeutic activity and overcoming challenges associated with plant-based formulations [7].
This article examines phytosome technology with special reference to green tea formulations, emphasizing evaluation parameters, enhanced bioavailability, therapeutic effects, and future perspectives.

2. Phytosomes

The word 'phyto' refers to plants, and 'some' refers to a cell-like structure [8].
Phytosomes, also known as herbosomes, were developed in the late 1980s by Indena (Milan, Italy) to enhance the bioavailability of drugs through phospholipid complexation [9]. They are formed when standardized plant extracts or polyphenolic compounds are complexed with phospholipids in a non-polar solvent [3]. These complexes display significantly higher bioavailability than standard herbal extracts because they easily permeate lipid-rich biological membranes and enter systemic circulation [10]. Phytosomes efficiently traverse lipophilic membranes such as the intestinal wall and the stratum corneum of the skin [2].

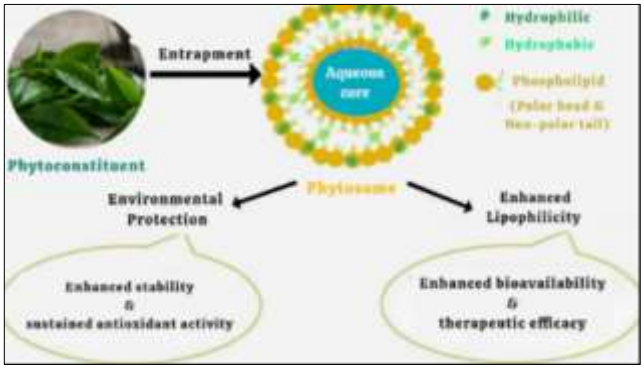

Fig 2: Structure of Phytosome

2.1 Components of Phyto-Phospholipid Complexes

Bombardelli first proposed that phyto-phospholipid complexes can be produced by reacting phospholipids with phyto-active constituents in a specific stoichiometric ratio [12]. The preparation of phytosomes generally involves 4 main components: phospholipids, phyto-active constituents, solvents, and the appropriate stoichiometric ratio between them [12].

2.1.1 Phospholipids: Phospholipids are classified into sphingomyelins and glycerophospholipids. Glycerophospholipids also include phosphatidylcholine

(PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidic acid (PA), phosphatidylinositol (PI), and phosphatidylglycerol (PG) [12].

Among these, phosphatidylcholine is most widely used for preparing phospholipid complexes because of its therapeutic effects in the management of liver disorders such as alcoholic steatosis and hepatitis [2]. Phosphatidylcho,line is a bi-functional molecule, the phosphatidyl part being lipophilic and the choline component being hydrophilic in nature.[13] The phyto-constituent binds to the choline head, while the phosphatidyl tail encapsulates the choline-bound substance, forming a lipid-compatible molecular complex known as a phyto-phospholipid complex [3].

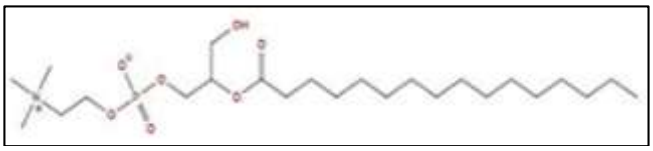

Fig 3: Molecular structure of Phosphatidylcholine

2.1.3 Phyto-constituents: The active components in herbal preparations are usually identified through in vitro pharmacological activity, although in vivo studies are equally important. Most of these belong to polyphenol class, including flavonoids, phenolic acids, lignans, etc. [12]. Flavonoids are selected from the groups that include quercetin, kaemferol, quercetin-3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoxide, vitexin, diosmine, 3-rhamnoside, (+) catechin, (-) epicatechin, apigenin-7-glucoside, luteolin, luteolin glucoside, ginkgonetine, isoginkgonetine, and bilobetine, etc. [2].

Phyto-phospholipid complexes increase the solubility of lipophilic polyphenols in aqueous medium and enhance the membrane permeability of hydrophilic polyphenols. Furthermore, such complexes formation prevents polyphenols from being degraded due to extrinsic factors such as hydrolysis, photolysis, and oxidation [1].

2.1.3 Solvents: Earlier, aprotic solvents such as aromatic hydrocarbons, halogen derivatives, and cyclic ethers were used to prepare phyto-phospholipid complexes. However, these have been largely replaced by safer protic solvents like ethanol and methanol [14]. If the yield of phospholipid complexes is sufficiently high, ethanol proves to be a good solvent because it leaves minimal residue and cause less degradation. Some liposomal drug complexes act in the presence of a buffer solution or water, while phytosomes act in solvents of lower dielectric constant [15].

Recent studies have utilized the supercritical fluid (SCF) process to control the particle size and morphology of the final product. Of these, the supercritical anti-solvent (SAS) method has proven to be a viable option for manufacturing micronic and submicronic particles with accurate size and distribution control [14].

2.1.4 Stoichiometric Ratio of Phyto-Constituents and Phospholipids: Typically, the active constituents and synthetic or natural phospholipids are combined in molar ratios ranging from 0.5:1 to 2:1, with 1:1 ratio yielding the most effective results [16]. This ratio is experimentally optimized for each compound to achieve the desired outcomes, such as maximum drug loading, bioavailability, and stability [14].

2.2 Properties of Phytosomes

2.2.1 Chemical Properties

Phytosomes are active compound-phospholipid complexes formed by reacting stoichiometric concentrations of phospholipid with polyphenols in an appropriate solvent [3]. Spectroscopic analyses reveal that the major interaction between phospholipids and polyphenols is through hydrogen bonding between the polar head groups of phospholipids (phosphate and ammonium) and the polar functional groups of the polyphenols [2]. In aqueous environment, phytosomes form micelle-like structures similar to liposomes [3]. However, in liposomes, the active compound is dissolved in the inner cavity or dispersed throughout the membrane layer; while in phytosomes, the active compound is chemically bonded to the polar head of phospholipids, making it an integral part of the membrane [3]. The size of phytosomes typically ranges from 50 nm to several hundred micrometers [2].

2.2.2 Biological Properties

Phytosomes provide better absorption and utilization compared to traditional herbal extracts. Pharmacokinetic and pharmacodynamic studies in both animals and humans confirm their superior bioavailability and improved therapeutic performance [3].

2.3 Comparison between Phytosomes and Liposomes

Table 1: Difference between Phytosome and Liposome [3, 17]

No.	Properties	Phytosome	Liposome
1.	Composition	Complex of polyphenolic constituents with phospholipids in a non-polar solvent.	Water-soluble substances encapsulated by multiple phosphatidylcholine molecules (hundreds or thousands).
2.	Chemical Bonds	Hydrogen bond between the polar head of the phospholipid and the phytoconstituent.	No chemical bonds present.
3.	Mechanism	Phyto-constituents attach to the polar head of phospholipids via chemical bonds, while the non-polar body surrounds the choline-bound complex.	Phyto-constituents enclosed within the phospholipid cavity with minimal or no interaction with the surrounding lipid core.
4.	Ratio	Typically, 1:1 or 2:1 stoichiometric ratio (phosphatidylcholine: phytoconstituent)	No fixed ratio.
5.	Pharmacokinetic profile	Superior pharmacokinetic profile.	Relatively weaker pharmacokinetic profile.
6.	Bioavailability	It possesses higher bioavailability.	It exhibits lower bioavailability.
7.	Applications	More effective in topical and skincare applications.	General drug delivery.

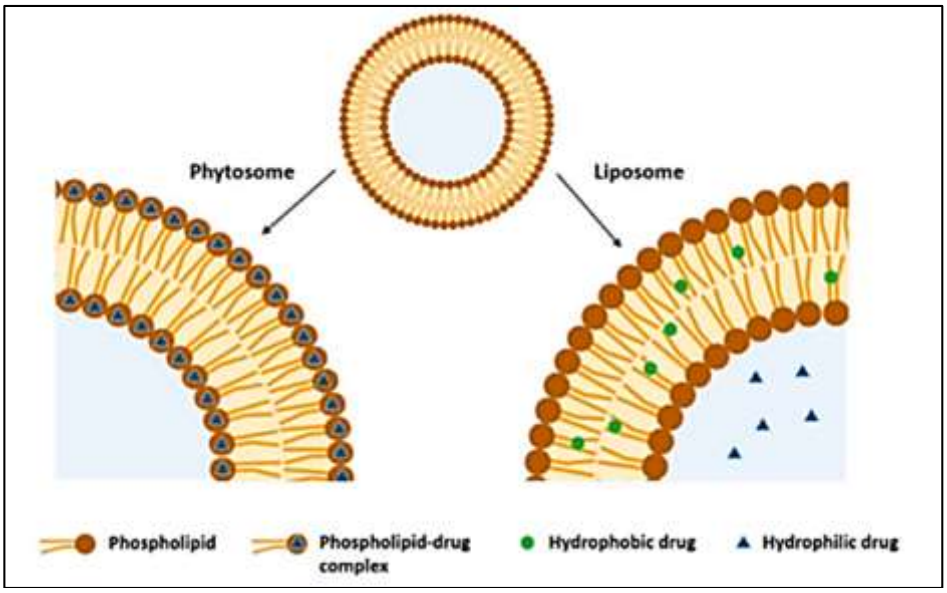

Fig 4: Structural difference between Phytosome and Liposome [18]

2.4 Advantages of Phytosomes

- Phosphatidylcholine, a key phospholipid component of phytosomes, serves dual role by functioning as a carrier and providing hepatoprotective properties, thereby producing a synergistic effect [3].
- Enhances the absorption of lipid-insoluble phytoconstituents through both oral and topical routes, resulting in higher bioavailability [3].
- With improved absorption of the phyto-constituents, the required dose is consequently reduced [3].
- The chemical bonding between phosphatidylcholine and phytoconstituents imparts superior stability profile [2].
- Phytosomes exhibits high drug entrapment efficiency [2].
- Provides prolonged therapeutic action of herbal drugs [17].
- Phytosomes can penetrate the skin owing to the lipid layer surrounding the phytoconstituent, making it suitable for cosmetics applications [17].

2.5 Preparation Methods of Phytosomes

Fig 5: Preparation Methods of Phytosomes

2.5.1 Solvent Evaporation Method: In this process, the phytoconstituents and phosphatidylcholine (PC) are mixed in a round-bottom flask containing an organic solvent such as acetone, methanol, or chloroform. The mixture is stirred at approximately 40 °C for about one hour to ensure high drug entrapment in the phytosomes. The solvent is then removed using a rotary evaporator to obtain a thin film, which is passed through a 100-mesh sieve and kept in a desiccator overnight. Lastly, the dried phytosomes are stored in amber glass bottles to prevent light-induced degradation [19].

2.5.2 Anti-solvent Precipitation Method: Measured quantities of phytochemical and phospholipid are refluxed with a suitable organic solvent such as acetone under controlled conditions at temperatures not exceeding 50 °C for around 2-3 hours. The solution is then concentrated to approximately 10 mL, and an anti-solvent (n-hexane) is added with constant stirring to induce precipitation. The precipitate is filtered, dried in a desiccator, finely powdered, and stored in dark amber glass bottle [10].

2.5.3 Rotary Evaporation Method: A specific amount of the phospholipid and phytochemical are dissolved in a suitable solvent in a rotary round-bottom flask and stirred continuously for three hours at a temperature below 40 °C. A thin film forms, to which n-hexane is added and stirred using a magnetic stirrer. The resulting phytosome precipitate is collected and stored in an amber-coloured glass container [20].

2.5.4 Salting Out Technique: In this method, phytosomes are prepared by dissolving the phosphatidylcholine (PC) and phytoconstituents in an appropriate organic solvent and then adding n-hexane slowly so that the precipitate of phyto-phospholipid complex forms [10].

2.6 Characterization and evaluation of phytosomes

2.6.1 Visualization: Phospholipid complexes are probed with transmission electron microscopy (TEM) and scanning electron microscopy (SEM), which employ electron beams to generate high-resolution images. Secondary electrons in SEM provide surface topography, backscattered electrons give atomic number, and X-rays offer elemental composition. TEM, on the other hand, employs transmitted

electrons to display detailed internal structures and crystallographic data [19].

2.6.2 Entrapment efficiency (EE): Entrapment efficiency of drug is determined by ultracentrifugation method. A known quantity of the phyto-phospholipid complex, equivalent to the content of the herbal drug, is dispersed in phosphate buffer (pH 6.8) and magnetically stirred. After one hour, the solution is centrifuged at 5000 rpm for 15 minutes. The supernatant is filtered through a 0.45 µm Whatman filter paper, and absorbance is measured by UV spectrophotometry or HPLC [19].

Drug entrapment efficiency (%) is calculated using the formula:

EE (%)=[(Total drug − Free drug) / Total drug] × 100 [21]

2.6.3 Particle size and zeta potential: Dynamic light scattering (DLS) with Photon correlation spectroscopy (PCS) are used to determine zeta potential and particle size.[10] Typically, phytosomes have a particle size range of 50 nm to 100 µm.[14] A uniform size distribution ensures better stability and drug release profile.

2.6.4 Drug Content: The drug content is determined using High-performance liquid chromatography (HPLC) or an appropriate spectrophotometric method [10].

% Drug content=(Amount of drug loaded/ amount claimed) × 100 [22]

2.7 Commercially available phytosomal product

Indena is the company that developed and licenses many Phytosome® ingredients and publishes the most complete catalogue of commercial phytosome ingredients.

Table 2: Commercially available phytosomal products [23]

Sr. No.	Brand Name	Botanical Origin	Health Benefits
1.	**Anthocran®** Indena phytosome®	*Vaccinium macrocarpon* Ait.-fruit	Urinary tract health
2.	**Berbevis®** Berberin Indena Phytosome®	*Berberis aristata* L.-Root	Healthy Metabolism
3.	**Casperome®** Boswellia Indena Phytosome®	*Boswellia serrata* Roxb. ex Colebr.-Resin	Healthy inflammatory response, Joint health, Gut health
4.	**CUBO™** Curcumin + Boswellia Indena Phytosome®	*Curcuma longa* L. Rhizome *Boswellia serrata* Roxb. ex Colebr.-Resin	Gut health
5.	**Ginkgoselect® Plus Indena Phytosome®** Ginkgo Biloba Indena Phytosome®	*Ginkgo biloba* L.-Leaf	Cognition & Circulation health, Antioxidant activity, Vasokinetic
6.	**Greenselect® Indena Phytosome®** Green Tea Indena Phytosome®	*Camellia Sinensis* (L.) O. Kuntze-Leaf	Body weight balance, Antioxidant activity
7.	**Leucoselect® Indena Phytosome®** Grape Seed Indena Phytosome®	*Vitis vinifera* L.-Seed	Cardiovascular health, UV Protectant, Antioxidant activity
8.	**Silymarin Indena Phytosome®**	*Silybum marianum* (L.) Gaertn.-Fruit	Healthy Liver, Antioxidant activity, UV Protectant
9.	**Siliphos®** Silybin Indena Phytosome®	*Silybum marianum* (L.) Gaertn.-Fruit	Healthy Liver, Retinoic acid-like activity
10.	**Meriva®** Curcumin Indena Phytosome®	*Curcuma longa* L. Rhizome	Joint health, Healthy Inflammatory response
11.	**Ubiqsome®** CoQ10 Indena Phytosome®	-	Cells Bio-energetics Support, Sports Nutrition, Cardiovascular health, Brain health
12.	**Vazguard®** Bergamot Indena Phytosome®	*Citrus bergamia* Risso & Poit. Fruit juice	Healthy Blood Levels, Visceral Fat Optimizer
13.	**Quercefit®** Quercetin Indena Phytosome® SF/MD	*Sophora japonica* L. Flowering head	Sports Nutrition, Antioxidant activity
14.	**Relissa™** Melissa Indena Phytosome®	*Melissa officinalis* L.-Leaf	Brain Health, Healthy Mood, Quality Sleep
15.	**Cronilief™** Palmitoylethanolamide Indena Phytosome®	-	Chronic Ache Relief

3. *Camellia sinensis*

Camellia sinensis (Green tea) is one of the most widely consumed beverages in the world [24]. Green tea leaves are rich in flavonoid-based polyphenols, primarily in the form of catechins [25]. The major catechins found in green tea include *Epigallocatechin-3-gallate* (EGCG), *Epigallocatechin* (EGC), *Epicatechin-3-gallate* (ECG), and *Epicatechin* (EC) [22].

Fig 6: *Camellia sinensis* (Green Tea) leaves

3.1 Monograph of *Camellia sinensis*

- **Botanical name:** *Camellia sinensis* Linn. Kuntze.
- **Family:** Theaceae.
- **Synonyms:** *Thea sinensis* Linn, *Camellia thea* Link; C. *theifera* Griff.
- **Common names:** *Hindi*: Chai; *English*: Tea; *French*: Thé vert imperial; *German*: Chinesischer Thee.
- **Description:** An evergreen shrub with alternate branches. Leaves are elliptic-lanceolate or obovate-lanceolate, short petioled, and acuminate, with serrated margins, smooth on both sides, occasionally pubescent beneath, green, shiny, pinnately veined, with a prominent midrib. Flowers are white and axillary; sepals orbicular, glabrous with membranous ciliate edges; petals obovate, obtuse, glabrous or pubescent on back; stamens numerous, ovary villous; styles 3, glabrous, connate for two-thirds of their length. Capsule depressed, leathery, three-cornered, one to rarely two-seeded. Seed about 1.8 cm in diameter, nearly globose or obtusely angled, smooth, and pale brown.
- **Part used:** Green leaf
- **Macroscopical:** Leaves 5 to 10 cm long, usually broadly lanceolate, firm in texture, rather thick, each tapering to a short petiole. Upper surface glossy, under surface pubescent in young leaves but nearly glabrous in older leaves. The serrated margin is slightly inrolled and bears characteristic shrunken, glandular teeth which readily break off. Odour-agreeable aromatic; taste-bitter and astringent.
- **Distribution:** Cultivated in Assam, Sikkim, and Darjeeling (Himalayas) and in the Nilgiris.
- **History and Authority:** Proved and introduced by Roth, *Mat. Med.* I, 510; Allen: *Encyclop. Mat. Med.* Vol. IX, 583; Clarke: *A Dictionary of Pract. Mat. Med.* Vol. III, 1406.[26]

3.2 Major Constituents in *Camellia sinensis*

EGCG is the most abundant and active polyphenol, making up about 50-75% of total catechins [25]. It offers benefits in disease management and safeguarding against excessive ultraviolet (UV) radiation, while also exhibiting strong anti-inflammatory and antioxidant properties [27]. EGCG helps in managing diabetes, cardiovascular diseases, Parkinson's disease, Alzheimer's disease, stroke, and obesity [24].

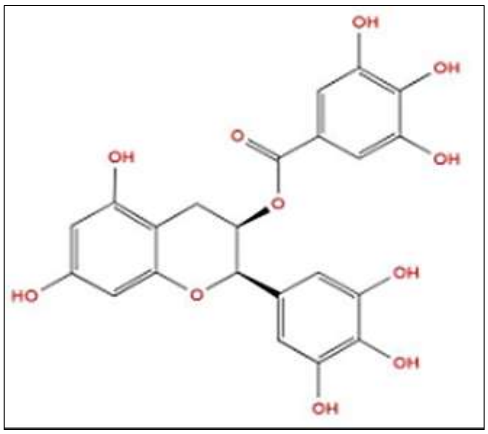

Fig 7: EGCG (*Epigallocatechin-3-gallate*)-Active Catechin (a type of flavonoid) found in *Camellia sinensis*

3.3 Limitations of EGCG on oral administration:

Orally administered EGCG shows very low absorption (< 5%), due to its polyphenolic structure, which contains multiple hydroxyl groups, making it highly polar and unable to readily cross the intestinal lipid membrane.[28] Several pharmacokinetic factors significantly contribute to the poor bioavailability of EGCG, some of which are:

- Low chemical stability under gastrointestinal conditions,
- Extensive metabolic transformation along the GI tract, and
- Limited intestinal permeability [29].

Formulating green-tea extract in lipid-based carriers such as phytosomes overcomes these issues [28]. These are innovative delivery systems designed to enhance the absorption and bioavailability of phytoconstituents, based on the amphiphilic nature and emulsifying properties of phospholipids.[25] Several studies on the topical application of catechins has demonstrated notable benefits, indicating that this route of administration is more effective than oral or intravenous delivery [30].

3.4 Applications of *Camellia sinensis*

3.4.1 Antiproliferative effects on skin cancer cells: Depletion of the ozone layer has increased exposure to ultraviolet radiation (UVR), a major factor responsible for skin damage and carcinogenesis [31]. Green-tea catechins (GTCs) exhibit tumor-preventive efficacy, particularly against skin cancers. Among them, EGCG exhibits the most potent effects by inhibiting cancer cell proliferation, metastasis, angiogenesis, and other pathways involved in tumor progression [32].

3.4.2 Anti-Inflammation and Wound Healing: In vitro studies has shown the anti-inflammatory and wound-healing activities of GTCs, which were strengthened by in vivo tests that proved that they could reduce inflammation and enhance tissue healing [32]. Application of ECG (200 µM) promotes wound healing without causing local irritation or inflammation [33]. Topical application of nano-EGCG show more than 20-fold higher wound-healing activity than free EGCG [34].

3.4.3 Reducing Oxidative Stress: UV radiation damages vital macromolecules in the skin, such as proteins and lipids, leading to sunburn, inflammation, premature aging, and even skin cancer. This damage occurs due to oxidative stress initiated by reactive oxygen species (ROS) [35]. GTCs, rich in hydroxyl groups, act as potent antioxidants that protect cells from oxidative damage. EGCG in particular exhibits exceptional photoprotective and anti-aging activities by reducing UV-induced skin damage [36].

3.4.3 DNA Protection: Prolonged UV exposure can cause DNA damage and mutagenesis. GTCs protect DNA integrity by preventing strand breaks and inducing repair pathways, thus showing dose-dependent photoprotective effects [32].

3.4.4 Antimicrobial Activity: GTCs possess antibacterial and antiviral properties [37]. Several in vitro studies have confirmed the antibacterial activity against a broad variety of microorganisms, such as gram-positive and gram-negative bacteria. Their mechanism is either direct or indirect and involves alteration of bacterial gene expression, inhibition of essential enzymes, and interaction with bacterial cell membranes. This membrane binding enhances permeability, induces hydrogen peroxide formation, and destroys membrane integrity, thus inhibiting bacterial adhesion to host tissues [29].

4. Benefits of Phytosomes in Topical Applications

Due to their strong antioxidant and anti-aging properties, green tea catechins such as EGCG are incorporated into modern drug-delivery and cosmetic formulations for topical applications [27]. Lambert, *et al*. observed that transdermal delivery of EGCG achieves higher plasma concentrations compared to oral tea consumption [38].

EGCG has photoprotective effect because it has UVB-absorbing capacity, although it results in its photodegradation. As catechins degrade extensively under UV light, various stabilizers like benzophenone-4, vitamins C and E, butylated hydroxytoluene, and α-lipoic acid are added to prevent degradation [40].

Several investigations have focused on the incorporation of EGCG in liposomes and liposome-like vehicles, such as phytosomes and niosomes. Anwar *et al*. formulated nano-vesicular phytosomes containing green-tea extract and phospholipid containing 30% phosphatidylcholine, which were evaluated to improve the stability and efficacy of EGCG.[28] Phytosomes increases dermal penetration and bioavailability, enhancing the delivery of herbal active components to target tissues.[41] Additionally, phytosomes enhance skin functions by improving hydration, maintaining enzyme balance, and stimulating collagen synthesis [9].

5. Composition of Green tea phytosomal gel

Green tea phytosomal gel is prepared by incorporating *Camellia sinensis* phytosomes into a suitable gel base to improve skin penetration, stability, and sustained therapeutic effects [42].

Selection of Active Ingredient

(Green tea extract, rich in catechins such as EGCG, is selected for its potent antioxidant, anti-aging, and anti-inflammatory actions)

⬇

Phospholipid Complexation

(Green tea extract is complexed with phosphatidylcholine by solvent evaporation or anti-solvent precipitation technique to form phytosomes)

⬇

Selection of Gel Base

(A suitable gel base is chosen to provide desirable texture, spreadability, and stability)

- **Carbopol 940 (0.5-1%) / HPMC:** Provides smooth, transparent, and elegant appearance.
- **Xanthan Gum:** Acts as a natural stabilizer to prevent phase separation

⬇

Incorporation of Phytosomes into Gel

(Prepared green tea phytosomes are uniformly dispersed into the selected gel base by gentle stirring)

⬇

Homogenization

(A high-shear homogenizer or mechanical stirrer is used to ensure even distribution of the phytosomes within the gel matrix)

⬇

pH Adjustment

(By using Triethanolamine, the pH of the formulation is adjusted to 5.0-5.5 to match skin pH, ensuring optimal compatibility and reduced irritation)

⬇

Addition of Preservatives and Stabilizers

(Preservatives such as methylparaben are added to extend shelf life, while stabilizers such as vitamin E and ascorbyl palmitate prevents EGCG oxidation and degradation).

6. Evaluation parameters of green tea phytosomal gel

Table 3: Evaluation parameters of phytosomal gel [43, 42]

Sr. No.	Parameters	Method	Formula / Condition	Acceptance Criteria
1.	Organoleptic test	Visual inspection for colour, odour, clarity, and homogeneity.	—	Uniform greenish colour, characteristic odour, smooth texture, and no phase separation.
2.	pH	1% w/v dispersion in distilled water, measured by calibrated digital pH meter.	pH buffers-4.0, 7.0, 10.0	pH 5.0-5.5 (skin compatible).
3.	Viscosity	Measurement using Brookfield viscometer at various rpm.	(Spindle LV-2/LV-4), 25 ± 0.5 °C.	20,000-120,000 mPa·s (depends on gel base).
4.	Spreadability	Two-glass-slide weight method to determine ease of spreading.	S=(M × L) / T Where, M=Weight (g) L=Length moved (cm) T=Time (s)	4-8 g·cm/s (good spreadability).
5.	Drug Content	Dissolve 1 g gel in ethanol, filter, and measure absorbance using UV-Visible spectrophotometer	% Drug Content=(Measured drug / Theoretical drug) × 100	90-110% of label claim.
6.	In-vitro Drug Release	Franz diffusion cell or dialysis bag using phosphate buffer (pH 6.8) over 6-8 hrs.	32±0.5 °C, 600 rpm.	Sustained release (50-80% in 8-12 h).
7.	Stability Study	Store gel at temp of 40°C for 1-2 weeks and re-evaluate	pH variation, viscosity change	No color change; pH variation ≤ 0.5; viscosity change ≤ 15%.

7. Challenges and Limitations

Despite their promising potential, green tea phytosomal gels faces several challenges that hinder large-scale commercialization. Here's an overview of major challenges:

- **Stability Issues:** Catechins such as EGCG are sensitive to temperature, pH, and light, leading to oxidation and degradation during formulation and storage. For increasing their stability and efficacy, the use of antioxidants and airtight, opaque packaging is important.
- **Scalability:** Solvent evaporation and anti-solvent precipitation techniques used for laboratory-scale preparation need complex optimization for large-scale industrial production. Implementation of solvent-free or continuous techniques such as spray-drying makes industrial production easier.
- **Cost Limitations:** High-purity phospholipids, organic solvents, and specialized equipment increase manufacturing cost, impacting large-scale production and affordability. Using cost-effective natural phospholipids and optimized formulation ratios can reduce expenses**.**
- **Regulatory Barriers:** Standardized guidelines for quality control, stability testing, and toxicity evaluation of phytosomal formulations are still evolving, posing regulatory challenges.

Overcoming these obstacles through novel formulation methods, cost-reduction measures, and clinical evaluation is vital for successful commercialization of green tea phytosomal products.

8. Future Prospects

Integration of nanotechnology with phytosome science opens new opportunities for the targeted delivery of herbal actives.

Future research should emphasize:-

- Nano-phytosomes and lipid-based hybrids to enhance dermal penetration, stability, and sustained drug release.
- Green extraction and solvent-free production techniques such as supercritical fluid technology for sustainability.
- Smart delivery systems, like stimuli-responsive or temperature-sensitive phytosomal gels for personalized skin therapy.
- Clinical and pharmacokinetic studies validating enhanced bioavailability and safety.
- Expansion into cosmeceutical and dermatological products for anti-aging, UV protection, and wound healing.

With increasing consumer demand for natural, safe, and effective skincare formulations, phytosome-based green tea products hold immense potential across pharmaceutical, nutraceutical, and cosmetic industries.

9. Conclusion

Phytosomes provide a scientifically validated strategy to overcome the bioavailability limitations of herbal actives. Green tea (*Camellia sinensis*) phytosomal gels combine antioxidant and photoprotective effects with improved dermal delivery, creating a promising platform for dermatological and cosmeceutical applications.

Catechins such as EGCG, EGC, and ECG exhibit potent antioxidant, anti-inflammatory, and anti-aging actions, but their hydrophilic nature limits topical penetration. The phytosomal approach enhances lipid compatibility, dermal retention and stability, resulting in prolonged therapeutic action.

Research demonstrates that green tea phytosomal gels improve skin hydration, UV protection, and collagen integrity, thereby enhancing skin texture and elasticity. Although formulation and scale-up challenges persist, advancements in nano-formulation design, natural stabilizers, and process optimization are expected to overcome these barriers. Moreover, comprehensive toxicological and clinical evaluations are essential for safety and regulatory acceptance.

In summary, green tea phytosomal gels bridge traditional herbal wisdom with modern nano-pharmaceutical innovation, providing a safe, effective, and sustainable platform for enhanced bioavailability, prolonged action, and better patient compliance. With the growing trend towards green and eco-friendly skincare, phytosome technology is

set to redefine herbal formulation development in both pharmaceutical and cosmetic sectors.

References

1. Kidd PM. Bioavailability and activity of phytosome complexes from botanical polyphenols: the silymarin, curcumin, green tea, and grape seed extracts. Altern Med Rev. 2009;14(3):226-246.
2. Khanzode MB, Kajale AD, Channawar MA, Gawande SR. Review on phytosomes: A novel drug delivery system. GSC Biol Pharm Sci. 2020;13(1):203-11.
3. Kumar AB, Habbu P, Thimmasetty L, Hullatti P, Kumar SR. Phytosomes as novel drug delivery system for herbal medicine-a review. Syst Rev Pharm. 2016;8(1):5-7.
4. Soman S. Phytosomes-a novel approach for herbal drug delivery. J Anim Res. 2020;10(4).
5. Dhiman J. Novel drug delivery system: Brief review. J Drug Deliv Ther. 2023;13(11):188-96.
6. Rao Khadam VK, Singh RP, Prajapati D, Yunus M, Prajapat B, Rai KS, *et al*. An updated comprehensive review on novel drug delivery systems (NDDS) in the pharmaceuticals. Asian J Pharm Res Dev. 2024;12(1):55-64.
7. Sarangi M, Padhi S. Novel herbal drug delivery system: An overview. Arch Med Heal Sci. 2018;6(1):171.
8. Barani M, Sangiovanni E, Angarano M, Rajizadeh MA, Mehrabani M, Piazza S, *et al*. Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of literature. Int J Nanomedicine. 2021;16:6983-7022.
9. Alharbi WS, Almughem FA, Almehmady AM, Jarallah SJ, Alsharif WK, Alzahrani NM, *et al*. Phytosomes as an emerging nanotechnology platform for the topical delivery of bioactive phytochemicals. Pharmaceutics. 2021;13(9):1-20.
10. Anusha G, Sunayana R, Ponnam M, Kumar BA. Asian Journal of Pharmaceutical Research and Development. Asian J Pharm Res Dev. 2020;8(6):77-80.
11. Singh A, Srivastav S, Singh MP, Singh R, Kumar P, Kush P. Recent advances in phytosomes for the safe management of cancer. Phytomedicine Plus [Internet]. 2024;4(2):100540. Available from: https://doi.org/10.1016/j.phyplu.2024.100540
12. Lu M, Qiu Q, Luo X, Liu X, Sun J, Wang C, *et al*. Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents. Asian J Pharm Sci [Internet]. 2019;14(3):265-74. Available from: https://doi.org/10.1016/j.ajps.2018.05.011
13. Kareparamban JA, Nikam PH, Jadhav AP, Kadam VJ. Phytosome: A novel revolution in herbal drugs. Int J Res Pharm Chem. 2012;2(2):299-310.
14. Gaikwad AR, Ahire KD, Gosavi AA, Salunkhe KS, Khalkar A. Phytosome as a novel drug delivery system for bioavailability enhancement of phytoconstituents and its applications: A review. J Drug Deliv Ther. 2021;11(3):138-52.
15. Patel J, Patel R, Khambholja K, Patel N. An overview of phytosomes as an advanced herbal drug delivery system. Asian J Pharm Sci. 2009;4(6):363-71.
16. Tripathy S, Patel DK, Baro L, Nair SK. A review on phytosomes, their characterization, advancement & potential for transdermal application. J Drug Deliv Ther [Internet]. 2013;3:147-52. Available from: http://jddtonline.info
17. Edulakanti A. Phytosomes: An emerging trend for herbal drug delivery. Int J Pharmacogn Pharm Sci. 2023;5(1):08-12.
18. Fernandes F, Teixeira DM, Matos DC, Grosso C. Critical review of lipid-based nanoparticles as carriers of neuroprotective drugs and extracts. Nanomaterials. 2021;11(3):1-51.
19. Gnananath K, Nataraj KS, Rao BG. Phospholipid complex technique for superior bioavailability of phytoconstituents. Adv Pharm Bull. 2017;7(1):35-42.
20. Singh RP, Gangadharappa HV, Mruthunjaya K. Phytosome loaded novel herbal drug delivery system: A review. Int Res J Pharm. 2016;7(6):15-21.
21. P K, R K. Phytosome technology: A novel breakthrough for the health challenges. Cureus. 2024;16(8).
22. Ray P, Kalita B. Formulation and evaluation of phospholipid complex of green tea polyphenol. Int J Res Dev Pharm Life Sci. 2017;6(6):2813-9.
23. Dixon P. Our mission. Early Years Educ. 2007;9(7):58-58.
24. Prasanth MI, Sivamaruthi BS, Chaiyasut C, Tencomnao T. A review of the role of green tea (*Camellia sinensis*) in antiphotoaging, stress resistance, neuroprotection, and autophagy. Nutrients. 2019;11(2).
25. Shariare MH, Afnan K, Iqbal F, Altamimi MA, Ahamad SR, Aldughaim MS, *et al*. Development and optimization of epigallocatechin-3-gallate (EGCG) nano phytosome using design of experiment (DoE) and their in vivo anti-inflammatory studies. Molecules. 2020;25(22):1-16.
26. Homoeopathic Pharmacopoeia of India (HPI). Vol. V. Government of India, Ministry of Health and Family Welfare; 1986.
27. Koczorowska CM, Nowaczyk WM, Bakun P, Goslinski T, Koczorowski T. Current view on green tea catechins formulations, their interactions with selected drugs, and prospective applications for various health conditions. Appl Sci. 2021;11(11).
28. Anwar E, Farhana N. Formulation and evaluation of phytosome-loaded maltodextrin-gum Arabic microsphere system for delivery of *Camellia sinensis* extract. J Young Pharm. 2018;10(2):S56-62.
29. Ilieva RM, Stoeva S, Hvarchanova N, Georgiev KD. Green tea: Current knowledge and issues. Foods. 2025;14(5).
30. Menaa F, Menaa A, Menaa B. Polyphenols nano-formulations for topical delivery and skin tissue engineering. Polyphenols Hum Heal Dis. 2013;1:839-48.
31. Zzaman W. Tea polyphenols and their preventive measures against cancer: Current trends and directions. 2022;1-20.
32. Zheng XQ, Zhang XH, Gao HQ, Huang LY, Ye JJ, Ye JH. Green tea catechins and skin health; 2024.
33. Orlowski P, Tomaszewska E, Ranoszek K, Slonska A, Cymerys J. Polyphenol-conjugated bimetallic Au@AgNPs for improved wound healing. 2020;4969-90.
34. Siddiqui IA, Vaqar M, Adame S, Massey RJ, Wood GS, Longley BJ, *et al*. Epigallocatechin-3-gallate (EGCG) modulates human keratinocyte-induced

responses and alleviates imiquimod-induced murine psoriasiform dermatitis. 2018;4189-206.
35. Bosch R, Philips N, Pérez SJA, Juarranz A, Devmurari A, Khaosaat CJ, *et al*. Mechanisms of photoaging and cutaneous photocarcinogenesis, and photoprotective strategies with phytochemicals. 2015;2:248-68.
36. Bernatoniene J, Kopustinskiene DM. The role of catechins in cellular responses to oxidative stress. Molecules. 2018;23(4):1-11.
37. Wu M, Brown AC. Applications of catechins in the treatment of bacterial infections. Pathogens. 2021;10(5).
38. Lambert JD, Kim DH, Zheng R, Yang CS. Transdermal delivery of (-)-epigallocatechin-3-gallate, a green tea polyphenol, in mice. J Pharm Pharmacol. 2006;58(5):599-604.
39. Mittal A, Piyathilake C, Hara Y, Katiyar SK. Exceptionally high protection of photocarcinogenesis by topical application of (-)-epigallocatechin-3-gallate in hydrophilic cream in SKH-1 hairless mouse model. Neoplasia [Internet]. 2003;5(6):555-65. Available from: http://dx.doi.org/10.1016/S1476-5586(03)80039-8
40. Bianchi A, Marchetti N, Scalia S. Photodegradation of (-)-epigallocatechin-3-gallate in topical cream formulations and its photostabilization. J Pharm Biomed Anal [Internet]. 2011;56(4):692-7. Available from: http://dx.doi.org/10.1016/j.jpba.2011.07.007
41. Dini I, Laneri S. The new challenge of green cosmetics: natural food ingredients for cosmetic formulations. Molecules. 2021;26(13).
42. Meti V, Mohare A, Guddad A, Harish KH, Dasankoppa F. Herbal phytosomal gels: Benefits, challenges, and future directions: A review. IP Int J Compr Adv Pharmacol. 2025;10(1):3-15.
43. Joshua JM, Anilkumar A, Verjina CU, Vasudevan DT, Surendran SA. Formulation and evaluation of antiaging phytosomal gel. Asian J Pharm Clin Res. 2018;11(3):409-22.