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PHARMACOSOMAL DRUG DELIVERY SYSTEMS: A PHARMACEUTICS PERSPECTIVE

Parthiban S.[1], Spoorthi G. R.[2]*

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India-571422.

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***Corresponding Author**

Spoorthi G. R.

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India-571422.

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ABSTRACT

Pharmacosomes are an emerging vesicular drug delivery system formed by covalent conjugation of drugs with phospholipids, resulting in amphiphilic drug–lipid complexes. This unique structure enables Pharmacosomes to self-assemble into vesicular systems in aqueous media and significantly improves the solubility, dissolution rate, permeability, and bioavailability of poorly soluble drugs. Unlike conventional liposomes, Pharmacosomes exhibit higher drug loading, improved stability, and minimal drug leakage due to the chemical bonding between drug and lipid. Various preparation methods such as solvent evaporation, ether injection, refluxing, and hand-shaking techniques have been explored to develop Pharmacosomes for oral, nasal, and targeted drug delivery. Recent research highlights their potential in enhancing therapeutic efficacy, sustained drug release, and site-specific delivery. This review summarizes the concept, formulation approaches, characterization techniques, advantages, limitations, and pharmaceutical applications of Pharmacosomes, emphasizing their growing importance in modern drug delivery systems.

KEYWORDS: Pharmacosomes, pharmaceutical applications, targeted drug delivery, site-specific delivery.

INTRODUCTION

Topical drug administration is a localized drug delivery approach in which drugs are applied to the skin or other topical routes to produce surface, local, or systemic effects. The skin is

the most accessible and widely used route, and the effectiveness of therapy largely depends on the choice of formulation base and delivery system. Topical preparations may contain active ingredients dispersed in suitable bases that also provide emollient or protective effects. Recent advances in topical drug delivery, including novel carriers, penetration enhancers, and non-invasive technologies, have improved efficacy, patient compliance, and therapeutic outcomes in the management of skin-related diseases.[1]

Topical drug delivery systems involve the direct application of formulations containing active pharmaceutical ingredients to the skin to achieve a localized therapeutic effect. These systems offer advantages such as site-specific drug delivery, avoidance of gastrointestinal incompatibility, and elimination of first-pass metabolism, resulting in improved bioavailability and sustained drug release. In topical delivery, the drug diffuses from the formulation and is absorbed through the skin to reach the site of action. Percutaneous absorption can be enhanced by increasing the drug release rate, which is influenced by the physical and chemical properties of both the drug and the carrier. Additionally, topical systems can reduce systemic side effects and improve patient compliance due to ease of application. They are widely used in the management of dermatological conditions and localized disorders.[2]

Topical drug delivery has gained significant attention in recent years due to its ability to provide localized therapeutic effects, minimize systemic side effects and improve patient compliance. However, the stratum corneum the outermost layer of the skin poses a major barrier to effective drug permeation. To overcome this, advanced lipid-based vesicular carriers such as Pharmacosomes have been developed to enhance the skin permeability and retention of drugs.[3]

Novel drug delivery systems (NDDS) are designed to deliver drugs at a rate aligned with the body's physiological needs during the treatment period while directing the active pharmaceutical ingredient to the site of action. The biological origin of vesicular carriers was first reported by Bingham in 1965, who termed them Bingham bodies. Subsequently, several novel vesicular drug delivery systems have been developed for various routes of administration to achieve controlled and targeted drug delivery. Targeted drug delivery aims to selectively transport therapeutic agents to specific tissues, thereby enhancing therapeutic efficacy and minimizing drug exposure to non-target tissues and associated side effects. The concept of drug targeting, defined as the delivery of drugs to specific receptors, organs, or

tissues, was introduced by Paul Ehrlich in 1909, emphasizing direct delivery to diseased cells. Since then, numerous carrier systems, including immunoglobulins, serum proteins, synthetic polymers, microspheres, liposomes, niosomes, and erythrocytes, have been investigated for targeted delivery. Among these, vesicular drug delivery systems have gained considerable attention due to their ability to improve the therapeutic index, enhance solubility, increase stability, and protect drugs from rapid degradation.[4]

Novel drug delivery systems (NDDS) have gained considerable importance in recent years due to their ability to enhance therapeutic efficacy. These systems are designed to maintain drug action at a predetermined rate or sustain an effective drug concentration in the body while minimizing adverse effects. NDDS can also localize drug action by controlled release near diseased tissues or by targeting specific cells using carriers or chemical modification. Various pharmaceutical carriers, including particulate, polymeric, macromolecular, and cellular systems, have been developed. Particulate carriers include lipid-based systems, microspheres, nanoparticles, polymeric micelles, and vesicular systems such as liposomes, niosomes, Pharmacosomes, and virosomes, which are formed from amphiphilic molecules in aqueous environments. Several delivery systems are under development to reduce drug degradation, improve bioavailability, and promote site-specific drug accumulation. These approaches include sustained or controlled delivery systems that provide delayed or constant release, localized delivery systems that enable spatial control, and rate-programmed systems that regulate drug release through system design and diffusion mechanisms.[5]

Vesicular drug delivery systems are structured assemblies composed of one or more concentric bilayer membranes formed through the self-assembly of amphiphilic molecules in an aqueous environment. Lipid-based vesicles of biological origin were first identified by Bingham in 1965 and were therefore termed *Bingham bodies*. These systems play a significant role in targeted drug delivery, as they can concentrate the drug at the desired site or organ of action, thereby minimizing drug distribution and associated side effects in other parts of the body.[6]

Vesicular structures are capable of prolonging drug residence time in systemic circulation and reducing toxicity through selective uptake. Their biological origin was first reported by Bingham in 1965 and termed Bingham bodies, which contributed significantly to understanding biological membranes and drug transport. Consequently, several vesicular delivery systems such as liposomes, ethosomes, niosomes, and Pharmacosomes have been

developed. At present, vesicles are recognized as promising carrier systems in immunology, membrane biology, diagnostics, and genetic engineering. They can encapsulate both hydrophilic and lipophilic drugs, making them versatile carriers in drug delivery. Lipid vesicles enhance bioavailability, particularly for poorly soluble drugs, thereby reducing the cost of therapy, delaying the elimination of rapidly metabolized drugs, and providing sustained drug release. These systems address issues related to drug insolubility, instability, and rapid degradation, while offering advantages over conventional dosage forms by minimizing drug toxicity through controlled release. Vesicles composed of natural or synthetic phospholipids, known as liposomes, possess hydrophilic, amphiphilic, and lipophilic domains, enabling the incorporation of drugs with diverse solubility profiles. Moreover, vesicular properties can be precisely controlled by modifying composition, size, lamellarity, surface charge, and concentration, allowing them to function as drug depots for controlled delivery, particularly in intracellular infections where conventional chemotherapy is limited by poor cellular drug penetration.[7]

Pharmacosomes are described as "colloidal dispersions in which drugs are covalently bound to lipids." They are stoichiometric complexes formed between polyphenolic drugs and phospholipids, predominantly phosphatidylcholine (PC). For a drug to form such a conjugate, it must contain an active hydrogen atom, such as –COOH, –OH, or $–NH_2$. In aqueous colloidal systems, Pharmacosomes organize into vesicular or micellar structures.[8]

Pharmacosomes are defined as zwitterionic, amphiphilic complexes formed by the covalent conjugation of drugs, particularly polyphenolic compounds, with phospholipids, and represent a vesicle-based novel drug delivery system. In this system, the drug (pharmakon) is chemically linked to a lipid carrier (soma), resulting in vesicular, micellar, or aggregated structures depending on the physicochemical nature of the drug–lipid conjugate. Vesicular drug delivery systems, including Pharmacosomes, enhance drug bioavailability while reducing toxicity by facilitating site-specific drug targeting. Compared with conventional vesicular carriers such as liposomes, niosomes, and transferosomes, Pharmacosomes exhibit superior biopharmaceutical properties and improved membrane permeability. Upon contact with aqueous media, Pharmacosome prodrugs self-assemble into multilayered structures, with their performance governed by both surface and bulk properties of the conjugate. Numerous Pharmacosome formulations containing non-steroidal anti-inflammatory drugs, proteins, peptides, and anticancer agents have been developed, demonstrating improved drug

absorption and reduced gastrointestinal toxicity. Their interaction with biomembranes alters membrane fluidity and thickness, enhancing drug permeation and overcoming limitations associated with polar drugs, such as poor solubility, low entrapment efficiency, and rapid efflux. As a carrier-mediated drug delivery approach, Pharmacosomes significantly improve the therapeutic index of drugs through controlled release, targeted delivery, and enhanced cellular uptake.[9]

ADVANTAGES

- The drug–lipid complex is influenced by the phase transition temperature, while the drug release rate remains independent due to covalent bonding between the drug and lipid.
- Drug leakage is eliminated since the drug is covalently attached to the lipid moiety.
- Issues related to drug incorporation are avoided.
- The physicochemical stability of Pharmacosomes is governed by the inherent properties of the drug–lipid conjugate.
- Drug metabolism during absorption is affected by factors such as spacer length, lipid chain length, functional groups, and molecular size of the drug.
- Pharmacosomes are suitable for the delivery of both hydrophilic and lipophilic drugs. g. Amphiphilic drug–lipid complexes form concentration-dependent aggregates in aqueous media.
- As the drug and carrier are covalently linked, entrapment efficiency is high and can be accurately predetermined.
- Pharmacosomes significantly enhance bioavailability, particularly in the case of poorly water-soluble drugs.
- They help in minimizing adverse effects and drug-related toxicity Unlike liposomes, Pharmacosomes do not require removal of unentrapped or free drug, as the drug is covalently linked to the lipid.
- Overall, Pharmacosomes contribute to a reduction in the cost of therapy.[10]

DISADVANTAGES

- Water insoluble drugs are encapsulated relatively in a less hydrophobic region within membrane bilayer rather than relatively large surface area.
- Synthesis of a compound depends on its amphiphilic nature.
- Preffered surface and bulk interaction of lipids with drugs.
- Required covalent bonding to protect the leakage of drugs.

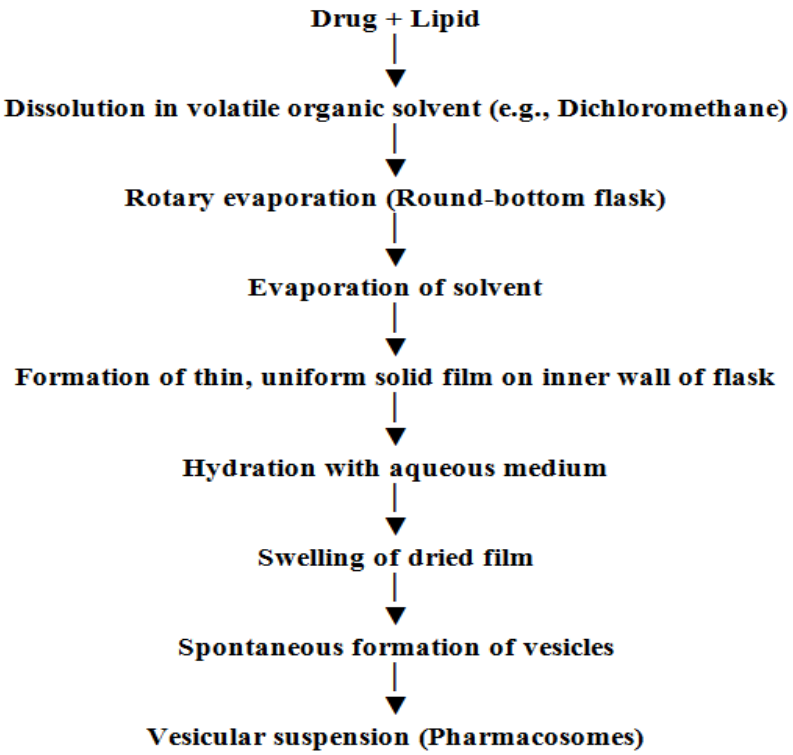
➢ The storage of Pharmacosomes undergoes fusion and aggregation and also chemical hydrolysis.[10]

Table No 1: Formulation aspects of Pharmacosome preparation.[11]

S. No.	Component	Description
1	Drug	• Drug must possess an active hydrogen atom (–COOH, –OH, $–NH_2$). • Drug salts are converted into acid form to expose the active hydrogen site. • Drug–phospholipid complex shows amphiphilic nature. • Amphiphilic property improves therapeutic efficacy. • Examples: pindolol maleate, bupranolol hydrochloride, taxol, acyclovir.
2	Lipid	• Lipids are essential components of biological cell membranes. • Common lipids used: phosphoglycerides, sphingolipids, phosphatidylcholine. • Phosphatidylcholine is most commonly used. • It is bifunctional: phosphatidyl group is lipophilic and choline group is hydrophilic. • Drug–lipid complex forms an amphiphilic system suitable for Pharmacosomes.
3	Solvent	• Highly pure and volatile solvents are required. • Solvents should have intermediate polarity. • They promote effective drug–phospholipid interaction and complex formation.

FORMULATION OF PHARMACOSOMES[12]

1. Solvent evaporation method / Hand shaking method



2. Ether Injection Method

Drug–lipid complex
↓
Dissolved in organic solvent (e.g., Diethyl ether)
↓
Slow injection through fine/gauze needle
↓
Into hot aqueous medium (Temperature above boiling point of ether)
↓
Rapid evaporation of ether
↓
Immediate formation of vesicles
↓
Vesicular suspension (Pharmacosomes)

3. Supercritical Fluid Process (Solution-Enhanced Dispersion by Supercritical Fluid – SEDS)

Drug + Lipid
↓
Dissolution in supercritical CO_2
↓
Supercritical fluid solution
↓
Injection into nozzle mixing chamber
↓
Rapid dispersion and solvent removal
↓
Formation of fine drug–lipid complex particles
↓
Pharmacosomes

4. Anhydrous Co-solvent Lyophilisation Method

Drug powder + Phospholipid

↓

Dissolution in DMSO (containing 5% glacial acetic acid)

↓

Agitation (to obtain clear solution)

↓

Freeze drying (Lyophilisation) (overnight at condenser temperature)

↓

Dry drug–lipid complex(Pharmacosomes)

↓

Flushing with nitrogen gas

↓

Storage at 4°C

Table No: 2 Physicochemical Characteristics of Pharmacosomes.[13]

S.No	Parameter	Description
1	Shape	Pharmacosomes are generally spherical or vesicular in shape
2	Drug	Drug must contain an active hydrogen atom (–COOH, –OH, $–NH_2$) for Pharmacosome formation
3	Size	Pharmacosomes usually fall within the nanometer range
4	Solubility	Drug–phospholipid complex improves aqueous and lipid solubility of the drug
5	Drug–lipid interaction	Drug is covalently linked with phospholipid forming a stable complex
6	Structure of Pharmacosomes	Amphiphilic drug–phospholipid complex that self-assembles into vesicular structures in aqueous medium

Table No. 3: Marketed Products Related to Pharmacosomes.

S. No.	Marketed Product Name	Active Drug / Complex	Manufacturer	Status / Remarks
1	CosmoFer®	Low-molecular-weight iron dextran	Pharmacosmos A/S	Marketed injectable iron preparation; not a true Pharmacosome, but often cited historically
2	Uniferon®	Iron dextran (veterinary)	Pharmacosmos A/S	Veterinary iron preparation ; not a classical Pharmacsome
3	Ferrlecit®	Sodium ferri gluconate complex	Sanofi	Iron–carbohydrate complex; sometimes confused with Pharmacosomes, not true Pharmacosome
4	Venofer®	Iron sucrose complex	Vifor Pharma	Iron complex injection; not a Pharmacosome, but lipid-complex discussions exist in literature
5	Cosmofer Vet®	Iron dextran	Pharmacosmos A/S	Veterinary product; historical association only

Table No: 4: Summary of Published Pharmacosome Formulation Studies.[14-33]

SI.No	Author	Method	Polymers	Observation
1	Dawoud MHS *et al.*, (2023)	Refluxing method	Ethanol, Dichloromethane, Lecithin,	Vanillic acid-loaded Pharmacosomes optimized via central composite design demonstrated nanosized particles, sustained release up to 48 h, and improved bioavailability compared to free Vanillic acid. Enhanced cardioprotective effects were observed in vivo through modulation of MAPK and PI3K/NF-κB pathways and antioxidant activity.
2	Muthukumar *et al.*, (2022)	Solvent evaporation method	Soya lecithin, Chloroform, Dichloromethane	Piroxicam-loaded Pharmacosomes exhibited a markedly improved dissolution profile compared to the pure drug, attributed to the wetting and dispersion properties of amphiphilic phospholipids. While free Piroxicam showed only ~60% release at 10 h, Pharmacosomal formulations achieved 79–95% release, with the 1:1 drug–soya lecithin formulation (F1) showing the highest release (~94.7%). The enhanced dissolution was associated with improved wettability and solubility, and the optimized formulation followed near zero-order release kinetics with a non-Fickian diffusion mechanism.

3	Kotha *et al.*, (2020)	Solvent evaporation method	Phospholipid , Tetrahydrofuran	Levodopa-loaded Pharmacosomes for intranasal delivery were successfully developed and characterized to enhance brain targeting and therapeutic efficacy in Parkinson's disease. The formulations exhibited nanosized globules (123–237 nm) with narrow polydispersity (PDI 0.1–0.4), high drug content (>98%), and excellent entrapment efficiency (>98%). Chitosan-based mucoadhesive Pharmacosomes showed positive zeta potential (+28.6 to +33.5 mV), improving nasal retention and permeation. The optimized formulation (F7) demonstrated superior in vitro drug release (~75.3% in 8 h), significantly enhanced ex vivo nasal flux (302.13 μg/cm²/h; 3.12-fold increase over drug solution), and confirmed drug–lipid conjugation by FTIR, with spherical morphology observed by SEM. Stability and nasal toxicity studies confirmed formulation safety. Pharmacodynamic and biochemical evaluations in a rotenone-induced Parkinson's model revealed marked improvement in behavioral parameters, oxidative stress markers, and histopathology with F7 compared to nasal and oral drug solutions, highlighting the potential of intranasal Pharmacosomes as an effective brain-targeted delivery system for Levodopa.
4	Sheoran *et al.*, (2024)	Ether Injection Method	Soya Lecithin, Diethyl ether	Glibenclamide Pharmacosomes were prepared using the ether injection method with varying drug–soya lecithin molar ratios and demonstrated high drug loading (≈89.6–97.8%), a notable advantage over conventional liposomes. The optimized formulation (F1; 1:1 drug–lipid ratio) showed the highest drug content and significantly enhanced solubility compared to pure Glibenclamide, attributed to phospholipid-mediated wetting, dispersion, and partial conversion of the drug to an amorphous form. FTIR studies confirmed drug–lipid compatibility and stability during complexation, while XRD analysis indicated reduced crystallinity in the Pharmacosomal system. In vitro release studies revealed markedly improved dissolution, with Pharmacosomes achieving ~79–95% drug release within 10 h compared to ~60% for the pure drug, and SEM analysis showed disc-shaped particles with rough surfaces.

5	Patil *et al.*, (2014)	Solvent evaporation method	Soya phosphatidyl choline, Methyl alcohol.	Furosemide–phospholipid complexes were prepared at different drug–lipid ratios (1:1 and 1:2), with the optimized formulation (PMC2, 1:2) showing higher yield and drug content. Pharmacosomes markedly enhanced the solubility of furosemide in water and buffers, achieving up to a 5.4-fold increase, attributed to phospholipid-mediated wetting, dispersion, and micellar solubilization. Partition coefficient studies indicated increased lipophilicity due to masking of polar groups by phospholipids. In vitro dissolution revealed significantly improved drug release (~88–95%) compared to free Furosemide (~63%), while ex vivo permeation studies demonstrated higher and faster drug permeation from Pharmacosomes, confirming enhanced permeability and potential improvement in oral bioavailability.
6	Nachikethana *et al.*, (2024)	Solvent evaporation method	Chloroform, Soya lecithin, Dichloromet hane	Telmisartan was identified as a white, odourless powder with poor aqueous solubility but good solubility in organic solvents. UV spectrophotometric analysis showed a λmax at 296 nm, and the drug obeyed Beer–Lambert's law with good linearity (R^2 = 0.9988). FT-IR, DSC, and XRD studies confirmed the absence of chemical interaction between Telmisartan and soya lecithin, while indicating reduced crystallinity and partial amorphization of the drug in Pharmacosomes. Micromeritic evaluation demonstrated acceptable flow properties for all formulations. Drug content ranged from 88.60% to 96.83%, with formulation F1 showing the highest loading. Solubility and in-vitro dissolution studies revealed a marked improvement in drug solubility and release from Pharmacosomes compared to the pure drug, with F1 exhibiting the highest cumulative drug release (94.69% at 10 h). SEM analysis showed roughly disc-shaped particles, confirming successful Pharmacosome formation and enhanced biopharmaceutical performance.
7	Mujeeb *et al.*, (2025)	Solvent evaporation method	Soya lecithin, Dichloromet hane	Indomethacin–phospholipid Pharmacosomes were prepared using varying lecithin concentrations and rotary evaporator speeds,with the optimized formulation (F9) showing high desirability (0.994), optimal particle size, and maximum entrapment efficiency. FT-IR and DSC studies confirmed compatibility between indomethacin and excipients, with no significant chemical interactions and closely related melting points. Response surface analysis revealed that increasing lecithin concentration significantly enhanced entrapment efficiency, while higher rotation speeds provided additional improvement. The optimized formulation exhibited sustained in-vitro drug release, achieving ~94.3% release over 20 hours, demonstrating the potential of Indomethacin Pharmacosomes for prolonged drug delivery and improved biopharmaceutical performance.

8	Kaur *et al.*, (2021)	Solvent evaporation method	Soya Lecithin, Diethyl ether	Mefenamic acid Pharmacosomes were evaluated for organoleptic, physicochemical, and micromeritic properties in accordance with the Indian Pharmacopoeia. The prepared Pharmacosomes were non-sticky in appearance and showed melting behavior (230.2°C) comparable to the standard drug (230–231°C), confirming drug stability. Flow property analysis indicated passable flow characteristics. In-vitro dissolution studies demonstrated sustained drug release, indicating prolonged therapeutic action. The Pharmacosomes showed enhanced skin permeation potential, suggesting their suitability as a topical or transdermal alternative to oral Mefenamic acid for the management of gynecological disorders, with reduced risk of gastrointestinal side effects.
9	Semalty *et al.*, (2009)	Solvent evaporation method	Chloroform, Dichloromethane	Diclofenac Pharmacosomes were prepared using an equimolar (1:1) ratio of Diclofenac and phosphatidylcholine by the solvent evaporation method, showing a high drug content of 96.2 ± 1.1%, significantly higher than Diclofenac liposomes (59%). The enhanced loading and stability were attributed to reversible chemical bonding between the drug and phospholipids. Pharmacosomes exhibited improved water solubility and amphiphilic character, contributing to enhanced bioavailability. DSC and XRPD studies confirmed complex formation with loss of crystallinity and amorphous dispersion of Diclofenac. SEM revealed irregular, disc-shaped particles with rough surfaces. The Pharmacosomes showed superior dissolution behavior (87.8% release at 10 h) compared to Diclofenac acid (60.4%), attributed to improved wettability and dispersion properties of phospholipids.
10	Bhusari *et al.*, (2023)	Solvent evaporation method	Chloroform, Dichloromethane	Metformin HCl Pharmacosomes were successfully developed and characterized, exhibiting a nanoscale particle size (120.5 ± 8.3 nm), narrow size distribution (PDI 0.21 ± 0.03), and adequate zeta potential (−25.7 ± 2.1 mV), indicating good stability. The formulation showed sustained drug release with nearly complete release (~99% at 24 h) and remained physically stable over 12 months with minimal changes in size and surface charge. The UV spectroscopic method demonstrated excellent linearity (2–20 µg/mL, $R^2 = 0.9992$), high accuracy, robustness, and sensitivity (LOD 0.05 µg/mL, LOQ 0.15 µg/mL). FT-IR, XRD, and SEM analyses confirmed successful drug–lipid interaction, reduced crystallinity, and uniform disc-shaped morphology, supporting the suitability of Pharmacosomes for controlled oral delivery of Metformin HCl.

11	Harikumar *et al.*, (2013)	Solvent evaporation method	Soya lecithin, Dichloromethane	Ketoprofen–phospholipid Pharmacosomes were successfully prepared by a simple and reproducible method, showing uniform drug content (98–99%), high drug loading, and significantly improved solubility compared to pure Ketoprofen due to their amphiphilic nature and micellar solubilization. Vesicle size increased with higher soya lecithin concentration, consistent with lipid bilayer composition effects, and SEM confirmed disc-shaped, free-flowing particles with improved morphology at higher phospholipid purity. DSC, XRPD, and FT-IR studies confirmed drug–phospholipid complexation with reduced crystallinity and amorphous drug dispersion. In vitro dissolution studies demonstrated sustained drug release (87.9% at 24 h), following mixed-order kinetics best described by the Higuchi model with non-Fickian diffusion. Overall, the Pharmacosomal system enhanced solubility, dissolution, and sustained release of Ketoprofen, indicating its potential to improve bioavailability and reduce gastrointestinal toxicity.
12	Naveentaj *et al.*, (2023)	Solvent evaporation method	Soya lecithin, Dichloromethane	Fluconazole-loaded Pharmacosomes were optimized using a Box–Behnken design by evaluating the effects of lecithin, solvent (DCM), and DMSO on particle size, entrapment efficiency, and in vitro drug release. The optimized formulation (F2) exhibited nanosized particles, high entrapment efficiency, and enhanced drug release, confirmed by statistically significant quadratic models. Characterization studies (SEM, FT-IR, and DSC) indicated spherical morphology and good compatibility between drug and excipients. The optimized Pharmacosome gel showed acceptable pH, good spreadability, sustained drug release following Higuchi kinetics with anomalous diffusion, and superior antifungal activity compared to pure drug and marketed gels, demonstrating its potential for effective topical delivery of fluconazole.

13	Kusuma *et al.*, (2018)	Ether injection method	Soya Lecithin, Diethyl ether	Naproxen sodium Pharmacosomes were prepared using soya lecithin and evaluated for physicochemical characteristics, drug loading, and release behavior. The formulations exhibited good drug entrapment efficiency (≈72.4–83.2%) and drug content (≈65.5–92.4%), with formulation NF2 showing optimal performance. FT-IR analysis confirmed the absence of drug–excipient interactions, indicating compatibility and stability of the Pharmacosomal complex. The optimized formulation demonstrated enhanced in-vitro dissolution (~86.1%) compared to other formulations and followed Higuchi release kinetics, suggesting diffusion-controlled drug release. Characterization studies revealed discrete, nearly spherical vesicles with a mean particle size of 1.4 nm and a zeta potential of −9.5 mV. The Pharmacosomal gel prepared from NF2 showed good physicochemical properties and sustained drug diffusion (~84.5% in 7 h), highlighting the potential of Naproxen Pharmacosomes for improved topical drug delivery.
14	Kumar *et al.*, (2016)	Solvent evaporation method	Soya lecithin, Dichloromethane	Rosuvastatin calcium Pharmacosomes were successfully developed using the hand-shaking method with soya lecithin, showing superior drug content (≈90.4–94.4%) and drug loading (≈25.1–26.2%) compared to conventional liposomes. UV spectroscopic analysis confirmed λmax at 242 nm with excellent linearity (2–18 µg/ml, R^2 = 0.999) in both water and pH 6.8 buffer. FT-IR and XRD studies verified drug–phospholipid complex formation, compatibility, and partial conversion of the drug into an amorphous form, contributing to improved aqueous solubility and reduced log P values (−0.25 to −0.34). SEM analysis revealed disc-shaped particles with rough morphology. In-vitro dissolution and diffusion studies demonstrated sustained drug release from Pharmacosomes over 24 h, unlike the immediate release of pure Rosuvastatin calcium. In vivo studies showed significant lipid-lowering efficacy with reduced dosing frequency, improved bioavailability and favorable histopathological outcomes. Stability studies confirmed the physicochemical stability of Pharmacosomes under accelerated conditions, highlighting their potential as an efficient sustained-release delivery system for Rosuvastatin.
15	Al-kaf *et al.*,(2017)	Solvent evaporation method	Soya lecithin, Dichloromethane	Pharmacosomes are novel lipid-based vesicular drug delivery systems formed by amphiphilic complexes of drugs with phospholipids, offering an effective alternative to conventional vesicles.They enhance bioavailability of poorly soluble drugs, reduce toxicity, drug leakage, and cost of therapy, while enabling controlled and targeted drug release at the site of action. Prepared mainly by hand-shaking and ether injection methods, Pharmacosomes are evaluated for size, surface morphology, and in-vitro drug release performance.

16	Tyagi *et al.*,(2024)	Ether injection method	Soya Lecithin, Diethyl ether	Pharmacosomes are an advanced lipid-based drug delivery system in which drug molecules are conjugated with phospholipids to enhance solubility, stability,and bioavailability.This review highlights recent advancements in formulation strategies, characterization methods, and applications of Pharmacosomes, emphasizing their role in targeted delivery, improved therapeutic efficacy, and reduced toxicity. By addressing challenges associated with poorly water-soluble drugs, Pharmacosomes offer promising future prospects for optimizing drug performance and therapeutic outcomes.
17	Sharma *et al.*,(2023)	Solvent evaporation method	Soya lecithin, Dichloromethane	Pharmacosomes are lipid-based drug delivery systems formed by complexation of drugs with phospholipids, enhancing bioavailability, stability, and therapeutic efficacy. They facilitate efficient transport across biological membranes and controlled drug release at target sites, showing improved performance for antihypertensive, anti-inflammatory, and anticancer drugs.Due to their simplicity, high drug-loading capacity, and stability, Pharmacosomes hold strong promise for future advancements in drug delivery systems.
18	Naveentaj *et al.*,(2022)	Solvent evaporation method	Soya lecithin, Dichloromethane	Simvastatin-loaded Pharmacosomes were developed as a transdermal drug delivery system to overcome the drug's poor oral bioavailability (~5%), extensive first-pass metabolism (CYP3A4), high protein binding, and short half-life. Pharmacosomes were incorporated into transdermal patches prepared by the solvent evaporation method using HPMC, ethyl cellulose, dibutyl phthalate, and DMSO as a permeation enhancer. The optimized formulation (F3/S3) exhibited acceptable physicochemical properties, including suitable surface pH, uniform thickness, weight uniformity, and swelling behavior. In-vitro release studies demonstrated significantly enhanced and sustained drug release from Pharmacosomes and Pharmacosome-loaded patches compared to pure Simvastatin, with ~86.9% release from Pharmacosomes and ~92.6% from the transdermal patch over 24 h. SEM analysis confirmed uniform patch morphology. Overall, the results indicate that Simvastatin Pharmacosomes and their transdermal patches are promising controlled-release carriers capable of improving percutaneous drug delivery and therapeutic efficacy compared to the pure drug.

19	Patel *et al.*,(2021)	Solvent evaporation method	Dichloromethane, Soya lecithin	Valsartan is an orally active angiotensin II type 1 (AT_1) receptor antagonist widely used in the management of hypertension, myocardial infarction, and heart failure by inhibiting the vasoconstrictive effects of angiotensin II. Developed by Novartis, it is a lipophilic drug with a moderate onset of action and is commonly marketed alone or in combination with other antihypertensive agents. This review highlights the physicochemical properties, pharmacokinetics, therapeutic indications, storage conditions and formulation challenges of Valsartan, with particular emphasis on Pharmacosomal drug delivery systems. The primary objective is to demonstrate that Pharmacosomes represent an effective strategy for enhancing the solubility and bioavailability of Valsartan.
20	Khudhur *et al.*,(2020)	Solvent evaporation method	Lipoid S 100, Dichloromethane	Mefenamic acid–phosphatidylcholine (MA–PC) Pharmacosomes were prepared by solvent evaporation using different drug–lipid molar ratios, with a 1:1 ratio identified as optimal for maximum conjugation. Comprehensive characterization (DSC, XRD, FT-IR, and NMR) confirmed successful drug–lipid interaction mainly through hydrogen bonding between the COOH group of Mefenamic acid and the phosphate moiety of phosphatidylcholine, resulting in reduced crystallinity and drug amorphization. The MA–PC conjugate exhibited significantly enhanced solubility and lipophilicity compared to pure Mefenamic acid, attributed to the amphiphilic nature of phosphatidylcholine and masking of hydrophilic groups. Pharmacosomal vesicles showed higher entrapment efficiency, uniform spherical morphology, suitable zeta potential, and larger particle size compared to conventional liposomes. In-vitro dissolution studies demonstrated markedly improved dissolution of Pharmacosomes over pure drug, conventional liposomes, and marketed suspension, highlighting the superiority of Pharmacosomes in enhancing solubility and dissolution performance of poorly soluble drugs.

CONCLUSION

Pharmacosomes represent a promising vesicular drug delivery system based on the formation of stable drug–phospholipid complexes. By imparting amphiphilic properties to drug molecules, Pharmacosomes significantly enhance solubility, dissolution rate, permeability and bioavailability of poorly soluble drugs. Compared to conventional liposomes, they offer higher drug loading, better stability, and reduced drug leakage. Various preparation methods have been successfully employed to develop Pharmacosomes for oral, nasal, and targeted delivery applications. Overall, Pharmacosomes hold considerable potential for improving

therapeutic efficacy and patient outcomes, with further research needed to support large-scale production and clinical translation.

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