

NOVEL DRUG DELIVERY SYSTEM IN HERBAL'S

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ABSTRACT

Because of their natural origins, less side effects, and therapeutic benefits, the use of herbal medications has increased significantly. However, issues including instability, low bioavailability, and the requirement for exact dosage frequently restrict their effectiveness. By improving the transport, absorption, and therapeutic efficacy of herbal components, novel drug delivery systems (NDDS) provide creative answers to these problems. Methods that enhance the stability, bioavailability, and targeted distribution of herbal actives include solid lipid nanoparticles (SLNs), systems. For example, solid lipid nanoparticles (SLNs) offer a stable and controlled delivery method that protects the active compounds from degradation; the use of biopolymers in the creation of delivery matrices aligns with the natural essence of herbal medicines, making them biocompatible and safe for

long-term use; liposomes and phytosomes improve the solubility and stability of hydrophobic herbal extracts, which in turn enhances their cellular uptake; and nanotechnology-based delivery systems for controlled release and site-specific targeting, minimizing toxicity and optimizing therapeutic action.

KEYWORDS: Herbal drug; novel drug delivery system; natural products, solid lipid nanoparticles (SLNs), liposomes, phytosomes.

INTRODUCTION

Scientists have been deeply engaged in the study and creation of innovative methods for administering herbal medications in recent years.^[1] "Herbal drugs," which are natural materials extracted from plants, are the mainstay of traditional medical systems that have been used since antiquity.^[2] enhance drug absorption, reduce drug loss and degradation, and avoid negative side effects and the percentage of the medication that accumulated.^[3] The goal

of a novel drug delivery system is to deliver the active component at the site of action while delivering the medication at a pace determined by the body's requirements over the course of treatment. Recently, there has been a lot of interest in developing a novel drug delivery system (NDDS) for herbal medications.^[4] Over the past few decades, there has been a lot of interest in the creation of innovative drug delivery systems (NDDS) for herbal treatments. Conventional dosage forms, including those with prolonged release, are unable to hold the drug component at a specific rate as required by the body or effectively deliver phytoconstituents to the intended target site to achieve the maximum therapeutic response during the course of treatment. For the research of Phyto formulation in connection to herbal medicines, the production of nano-sized dosage forms (polymeric nanoparticles and nano capsules, liposomes, solid lipid nanoparticles, phytosomes, and Nanoemulsions) provides a number of advantages. Enhanced solubility and bioavailability, defense against toxicity, enhanced pharmacological action, enhanced stability, better tissue macrophage dispersion, prolonged administration, and defense against chemical and physical degradation are some of these advantages. In order to increase the efficacy of plant medicines and address associated problems, the nanoscale NDDSs of herbal remedies may be employed in the future.

Liposomes are carriers of hydrophilic and hydrophobic substances; they are biodegradable and generally safe.^[5] Liposome-based drug delivery systems can employ targeting techniques and improved permeability and retention effect phenomena to raise the therapeutic index of anti-cancer medicines in tumor cells and/or reduce drug exposure in healthy tissues.^[6] The effectiveness of a medication can be significantly impacted by the way it is administered. Certain medications have a range of ideal concentrations where the most therapeutic benefit is obtained; dosages outside of this range may be harmful or have no effect at all. This led to the development of fresh concepts for managing the pharmacokinetics, pharmacodynamics, nonspecific toxicity, immunogenicity, biorecognition, and effectiveness of medication.^[7]

REASONS FOR NOVEL HERBAL DRUG DELIVERY SYSTEM^[9,10]

- To prevent repetitive administration and improve patient compliance.
- to precisely transport the drug's ideal dosage to the "site of action" so that it begins to function immediately.
- To improve effectiveness and lessen adverse effects.
- Regarding "multi-drugs and multi-targets" paradigm for combination treatments for complicated illnesses like diabetes and cardiovascular disease.

A novel drug delivery system is a system that offers multiple drug delivery solutions such as.^[11]

1. Materials and Systems for Oral Drug Delivery.
2. Drug delivery systems that are parenteral and implanted.
3. Nasal and Pulmonary Drug Administration.
4. Drug Delivery Through the Transmucosal.
5. Topical and transdermal drug delivery.
6. Protein and peptide delivery.
7. Pipelines for drug delivery.
8. Deals on Drug Delivery.

A unique drug delivery system is an innovative method of delivering drugs that overcomes the drawbacks of conventional drug delivery systems. By precisely locating the afflicted spot within a patient's body and delivering the medication there, modern medicine treats a certain illness.

Pharmacokinetics, mechanism of action, site of action, necessary precise dosage, etc.

TYPES OF NOVEL HERBAL DRUG DELIVERY SYSTEM

The list of creative herbal drug delivery methods includes several formulations, including liposomes, phytosomes, pharmacosomes, nanoparticles, niosome, microspheres, transferosomes, ethosomes, transdermal drug delivery systems, and proniosomes, among others. These are discussed below.^[8]

1. A drop beneath the mouth, or sublingual.
2. A skin patch that sticks to itself.
3. A pump, such as an insulin pump.
4. Special pervious plastic, like Norplant, is injected beneath the skin.

RECENTLY DEVELOP

The ability of nanostructured carrier systems, such as polymeric nanoparticles, liposomes, SLNs, polymeric micelles, Nanoemulsions, etc., to transport anticancer medications orally has been studied in recent years. Additionally, the development of oral chemotherapy in oncology has received attention because to the significant potential for cytotoxic drug delivery via the oral route.^[12]

- Liposome's
- Phytosomes
- Niosome
- Ethosomes
- Transfersosomes
- Microspheres
- Nanoparticles
- Pharmacosomes,

1. Liposomes

The novel drug delivery technique is intended to continuously administer drugs at a steady and consistent rate during an extended period of circulation. Higher patient compliance, which helps to reduce drug-related adverse effects by maintaining stable blood levels rather than allowing them to fluctuate, may be one advantage of this idea given that doses are given less frequently and are typically smaller.^[13] Liposomes are composed of phospholipids, cholesterol, alcohols, steroids, and Springo lipids. Liposomes include active herbal ingredients such as quercetin, curcumin, paclitaxel, colchicines, capsaicin, brucine, rutin, arbutin, and others. Liposome formulations are widely utilized as drug delivery systems in the pharmaceutical industry and have been used to deliver medications via a number of channels because of their versatility and clinical effectiveness.^[14] Because liposome formulations have a higher diffusivity in the skin than the majority of other formulations, they are commonly used as topical medicine delivery methods. In addition to providing greater, more sustained drug concentrations in the skin, liposomes are added to gel to enhance medicine retention in the skin. Nevertheless, liposomes don't enhance the body's ability to absorb drugs.^[15] They act as a drug reservoir, enabling localized and regulated drug delivery. The liposomal gel approach minimizes side effects by delivering a suitable quantity of drug into the skin. Carbopol is used as a hydrogel that can enhance local drug delivery and acts as a liposome carrier. Drug release is controlled by the hydro gel matrix's degradation.^[16] The well-known antioxidant quercetin liposome shields the body from free radicals and other reactive oxidative species (ROS) linked to oxidative stress. Curcumin liposome is one of the most studied bioflavonoids at the moment, and a large body of research has demonstrated its anti-inflammatory, anti-cancer, chemoprotective, antioxidant, and gastroprotective properties. Although paclitaxel liposomes, one of the most promising paclitaxel anticancer drugs, are especially effective in treating ovarian and breast cancer, they have disadvantages such as

poor absorption and limited water solubility. Acute gout, psoriasis, and sweets syndrome can all be treated with colchicine liposomes, an alkaloid present in extracts from the plants *Colchicum autumnal* and *Gloriosa*. Bruce Liposomes: Brucine is a well-known analgesic and anti-inflammatory drug that helps with chronic and arthritic pain.^[17] A phytosomes is a mixture of organic active ingredients and phospholipids. When utilizing Phytosome, the absorption of a plant extract is improved by topically applying it or by consuming it. Phytosomes, sometimes referred to as herbosomes, contain phospholipids and herbal extract.

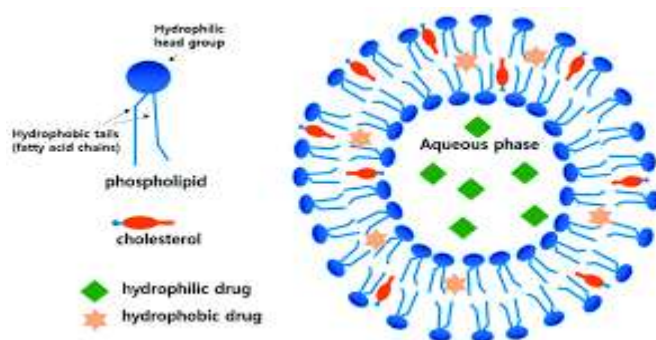


Fig: structure of liposomes,

2. Phytosomes

It is a vesicular drug delivery system based on lipids and phytoconstituents.^[18] The bioavailability of phytoconstituents is increased by phytosomes, which promote their absorption via the GIT. Phytosomes are composed of plant extracts, phospholipids, and phytochemicals. Among the botanical elements included in phytosomes are *ammivisanga*, *citrus aurentium*, *cucurbitapepo*, *fraximusornus*, *gingko biloba*, *glycine max*, and *oleaeuropaea*. Phytosomes, an advanced herbal medicinal technology, give plant medicines a specified bioavailability as compared to herbal extracts. decreased particle size, accelerated absorption rate, and claims of improved in vivo performance for the herbal extracts. By forming hydrogen bonds between the polar side front of phospholipids and the polar functional group of the secondary metabolites, a specific pattern is produced during the chemical interaction between phospholipids and the herbal substrate, according to structural elucidation. Phytosomes show up in solvents such as acetone, dioxane, methylene chloride, hexane, and ethyl acetate.^[19] Their cellular structure is similar to that of liposomes, and in water they assume the form of micelles. Phospholipids' active polar moiety serves as an essential component of the cell membrane. Numerous factors influence the particular distinctiveness of phytosomes, including their physical size, membrane permeability, entrapment ratio, chemical composition, quantity, and purity of the precursor beginning

chemical components.^[20] To make phytosomes, phosphatidycholine and phytoconstituents can be mixed 1:1 in an aprotic solvent. In the complex of Phyto-phospholipids, the ratio of phytoconstituents to phospholipids falls between 0.5-2 moles. Phospholipids and phytoconstituents should be in a 1:1 ratio. Usually, phospholipids with the soy lecithin phosphatidycholine, phosphatidylserine, and phosphatidylethanolamine groups selected. Phospholipid molecules are chemically connected to phytoconstituents, as shown by spectroscopic research. Due to their complexation with phospholipids and improved intestinal absorption, herbal extracts' bioavailability has unexpectedly boosted. They have been utilized to supply liver-protective flavonoids and can make them accessible.^[21] This approach offers cost-effective distribution of phytoconstituents together with synergistic benefits. Additionally, they can be used to improve the absorption of medications delivered topically and transdermally via the skin. The vesicular system is instantly marketable, passive, and non-intrusive. There is no risk of drug entrapment during formulation production. Because of the improved absorption of the primary ingredient, the dosage needed is reduced. They can even contribute in smaller amounts to achieve the intended results.^[22]

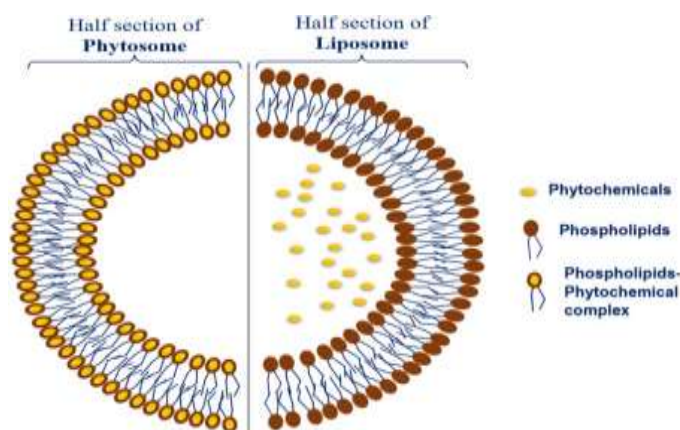


Fig: structure of phytosomes.

3. Niosomes

These tiny structures, known as lamellar ones, are produced by combining a charges-inducer, cholesterol, and a nonionic surfactant with watery medium, then hydrating the mixture. Because of its hydrophobic and hydrophilic moiety design, niosomes may accept drug molecules with a broad spectrum of solubilities. Numerous therapeutic uses for niosomes have been investigated.

By delaying the release of the agent, encapsulating medicinal substances can reduce systemic toxicity and drug clearance from the body. These are only a handful of the many noteworthy

advantages of this strategy in medical contexts.^[23] Niosomes typically share traits with liposomes that make them appropriate drug carriers, according to earlier study done in partnership with L'Oreal.^[24] None of these problems have an impact on niosomes.^[25] Multilamellar vesicles called niosomes are made of cholesterol and non-ionic surfactants belonging to the alkyl or dialkyl polyglycerol ether family. Previous research conducted in collaboration with L'Oreal has demonstrated that niosomes often share characteristics with liposomes as possible medication carriers. One way that niosomes vary from liposomes is that they have some benefits over them.^[26] Niosomes may be used in two different methods for specific drug organization as they have been shown to significantly enhance transdermal medicine conveyance over the stratum corneum, which serves as the main barrier against drug transport through the skin.^[27] Recently, extensive study has focused on niosomes' potential as a drug delivery system. Numerous nonionic surfactant types have been shown to create niosomes, which enable the trapping of a wide range of medications with different solubilities. Drug delivery efficiency can be increased by modifying and improving the size, content, number of lamellae, and surface charge of niosomes. With an emphasis on more recent research, this review aims to describe the principles of niosome synthesis and characterization as well as their use in drug administration.

Niosomes contain lipids, fatty acids, and non-ionic surfactants. Tyloxapol, span 60, and tween 20 are among the botanical components of Niosomes.^[28] Multilamellar vesicles called niosomes are made of cholesterol and nonionic surfactants belonging to the alkyl or dialkyl polyglycerol ether family. Previous research conducted in collaboration with L'Oreal has demonstrated that niosomes often share characteristics with liposomes as possible medication carriers. The way that niosomes vary from liposomes is that they have some benefits. Problems with liposomes include their high cost, the chemical instability of their constituents (phospholipids) due to oxidative destruction, the need for particular handling and memory, and the varying purity of natural phospholipids. None of these issues affect niosomes.^[29]

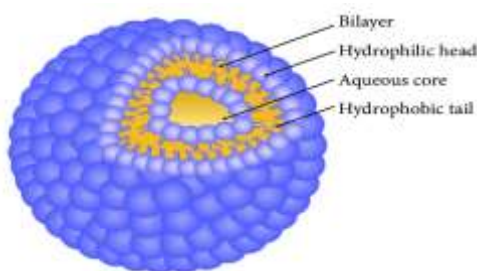


Fig: structure of Niosomes.

4. Ethosomes

Ethosomes are elastic nanovesicles based on phospholipids that contain a high percentage of ethanol (20–45%). Ethosomes were created as innovative lipid carriers made of water, phospholipids, and ethanol to enhance the skin's absorption of several medications. It makes it possible for medications to enter the systemic circulation and/or deep skin layers.^[30] Since ethanol may fluidize different intercellular lipids found in the stratum corneum of the skin, ethanolosomes have a greater potential for skin penetration than liposomes. It has been shown that while the phospholipid concentration remains constant, the ethosomes' size decreases as the ethanol content rises. Additionally, the presence of ethanol causes the surface of ethosomes to become negatively charged, enhancing their colloidal security.^[31] Ethosomes systems are distinct from liposomes in that they have a comparatively high ethanol content in addition to water and phospholipids. New generations of ethosome systems are produced by supplementing basic classical ethosomes with additional chemicals to enhance vesicular characteristics and skin penetration. However, a clear distinction between traditional and modern ethosomes has not been made.^[32] Ethosomes' ethanol makes cell membrane lipids more fluid, which raises skin permeability. Because of this, the ethosomes easily penetrate the thick epidermal layers, where they react with lipids to liberate the medications. Ethosomal cells are a more innocuous technique of delivering drugs. Among other things, ethosomal formulation is well known for delivering large and varied groups of proteins, peptides, and medications. Because ethosomes have safe compositions, they are authorized for use in both medications and cosmetics. Because non-toxic ingredients are included in their composition, ethosomes are a safe way to distribute medications. The Ethosomal formulations should be produced in a semisolid form, such gel or cream, to facilitate simple administration.^[33] More recent developments in patch technology led to the creation of the ethosomal patch, which contains medicine in ethosomes. Ethosomal systems are made up of water, ethanol, and soy phosphatidylcholine. Elastic vesicles and transferosomes have also been used as drug delivery systems for a range of small molecules, proteins, peptides, and vaccines.^[34]

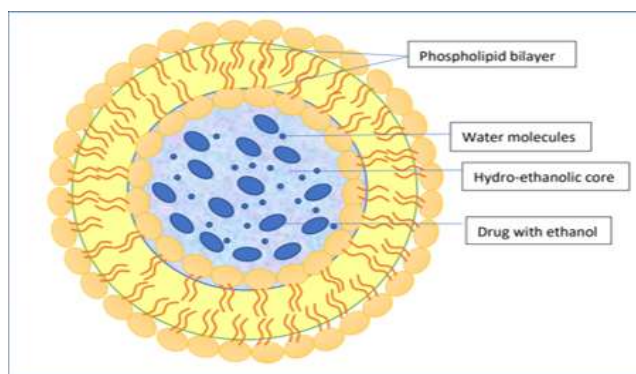


Fig: structure of Ethosomes.

5. Transfersosomes

Phospholipid vehicles called transfersomes and ethersomes are designed to deliver medications transdermally. Although their modes of action differ, both have the goal of improving penetration through the stratum corneum barrier.^[35] Transfersome delivery of colchicine offers local, site-specific, sustained distribution while shielding it from the gastrointestinal adverse effects associated with oral dosing.^[36] Transfersomes are specially designed particles, or vesicles, that can swiftly and affordably alter their form in reaction to outside stimuli.^[37] Although the basic structure of transfersosomes is similar to that of conventional liposomes, its softness, extreme deformability, and more readily adjustable system membrane set them apart from liposomes in several respects.^[38] One essential property of transfersosomes is their ability to attach to and retain water from the epidermis. Transfersosomes contain a large number of hydrophilic molecules to keep you hydrated. Phospholipid-and edge-activator-based vesicles comprise the initial generation of Transfersosomes. The second generation of Transfersomes is made up of many amphipathic membrane destabilizing components and a bilayer component (like phosphatidylcholine). When injected to the epidermis, the Transfersomes go deeper toward the water-containing strata to hydrate themselves. Reversible, ultra-thin bilayer deformation that preserves the integrity of the bilayer is what allows transfersomes to penetrate the epidermal barrier. Transfersomes are made up of water, phospholipids (lipid bilayers), and edge activator.^[39] Compared to allopathic medications, they are less costly. They are effective for many different conditions. They are associated with fewer adverse effects. They can be used in a variety of ways. There is no need to test them. Highly deformable vesicles called transfersomes address issues related to transportation, including as Because of the skin's barrier qualities, high molecular weight medications cannot be applied transdermally. Drugs are transported by transfersosomes, which are deformable particles that may penetrate

biological permeability barriers like the skin. Through pores in the tissue, these pliable vesicles alter their form. They do a great job of distributing peptides and proteins. To maximize transdermal flow, these Transfersosomes may adjust to environmental stress by squeezing through skin pores that are far smaller than usual.^[40]

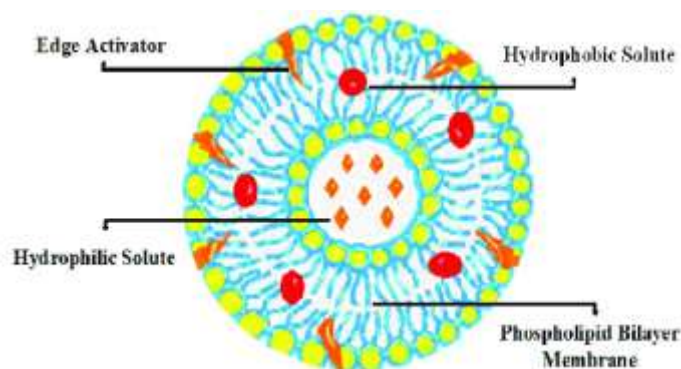


Fig: structure of Transfersosomes.

6. Microspheres

Microspheres, which are usually free-flowing powders made of biodegradable proteins or synthetic polymers and have a particle size of less than 200 m, are novel because, unlike drug delivery systems, they are looking for something out of necessity. For chronic patients, the medication must be taken over an extended period of time, and multiple medications must be taken simultaneously.^[41] Frequent drug administration is necessary when a medication's half-life is shortened and patient compliance suffers as a result. To address the aforementioned problems, many kinds of controlled release dosage forms are developed and altered, decreasing peak plasma concentration to decrease unwanted effects and improving patient compliance through delayed effects.^[42] Over a long period of time, the controlled release dosage form administers the medicine at a predefined rate in order to maintain a typically constant medication level in the plasma. Microspheres are composed of native iron, aluminosilicate ferrous, and iron oxides. Microspheres include naturally occurring chemicals called curcumin and berberinenanoemulsion. Polystyrene (PS), silica, poly (methyl methacrylate) (PMMA), rutin, and turmeric oil are common microsphere constituents. The different physical and optical properties of these materials may be beneficial or detrimental, depending on the use. The robust protein binding capabilities of polymer beads are a result of their frequent hydrophobicity. To guarantee ease of handling, they usually need some surfactant in the storage buffer (such as 0.01-0.1% Tween® 20 or SDS). Styrene or methyl may co-polymerize with functional monomers during the production process.^[43] Functional

monomers may co-polymerize with methyl methacrylate or styrene during the synthesis process to create beads with reactive groups on their surface. Functional groups are sometimes used in covalent binding processes, and they also aid in suspension stabilization. Silica microspheres are hydrophilic and inherently negatively charged. As a result, aqueous silica solutions seldom ever utilize stabilizers like surfactants. Using a range of silanes and coating procedures, silica spheres functionalized with carboxyl and amine can be used in conventional covalent processes. Alternatively, plain silica microspheres can be modified to add functional groups or alter their surface properties. Microspheres have a long-lasting and persistent therapeutic effect. helps the patient by reducing the need for frequent dosage. The therapeutic effects of microspheres are long-lasting and ongoing.^[44]

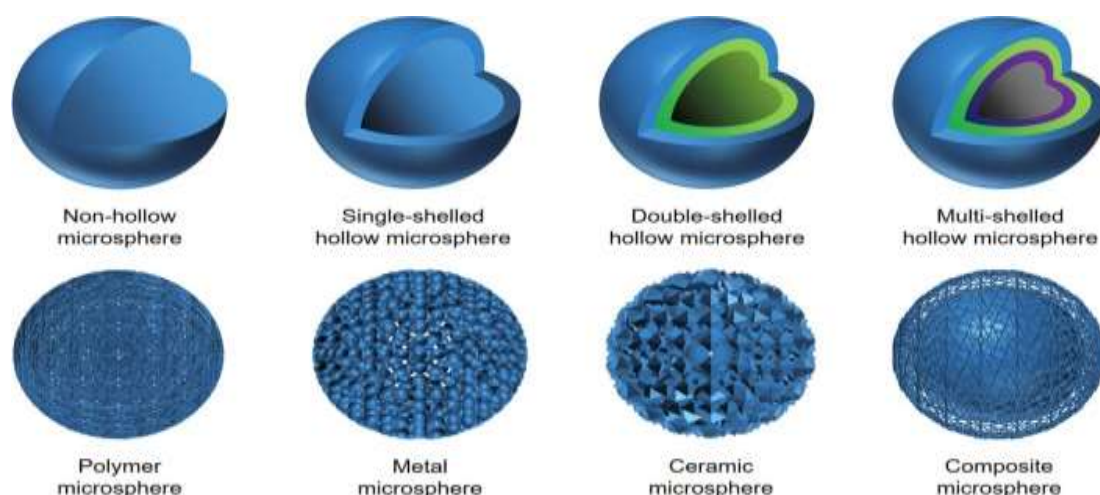


Fig: structure of Microspheres.

7. Nanoparticles

Nanoparticles are sub-Nanoscale colloidal structures made of natural or manmade polymers that range in size from 1 to 1000 nm. The drug is separated, confined, imprisoned, or linked to a network of nanoparticles. Depending on the method employed for organization, nanoparticles may take the shape of nanospheres or nanocases. Nano spheres are network frameworks where the medication is actually and evenly distributed, whereas nano containers are constructions where the drug is kept to a hole confined by a particular polymer film. The nanocarrier is made from safe ingredients including lipids, polysaccharides, and specially formulated biodegradable polymers. Nanoparticles are composed of inorganic particles and phospholipids. Herbal components of nanoparticles include doxorubicin, quercetin, paclitaxel, curcumin, and zedoary-turmeric oil.^[45] However, the use of herbal medications is constrained by a number of issues, such as low solubility, poor bioavailability, limited oral

absorption, instability, and unanticipated toxicity. In order to address the problems caused by herbal drugs, nanotechnology has created promising treatments for the pharmaceutical sector. It is expected that the value and importance of integrating herbal remedies and natural goods with the nanocarrier would improve the existing approach to drug delivery. Because liposomes and microspheres are smaller than other systems with longer circulation periods, they can more easily pass through the sinusoidal gaps in the bone marrow and spleen. Nanoparticles improve the resistance of proteins and medications to enzymatic breakdown.^[46] Recent years have seen a notable increase in interest in potential biodegradable drug delivery systems.^[47] Nanoparticles are an effective way to deliver both hydrophilic and hydrophobic drugs. Nanoparticles are submicron particles with sizes between 10 and 1000 nm.^[48] One of the main goals of creating nanoparticles as a delivery system is controlling the release of pharmacologically active compounds, surface properties, and particle size. This enables the medication to function at the ideal dosage and tempo for treatment on a particular location.^[49]

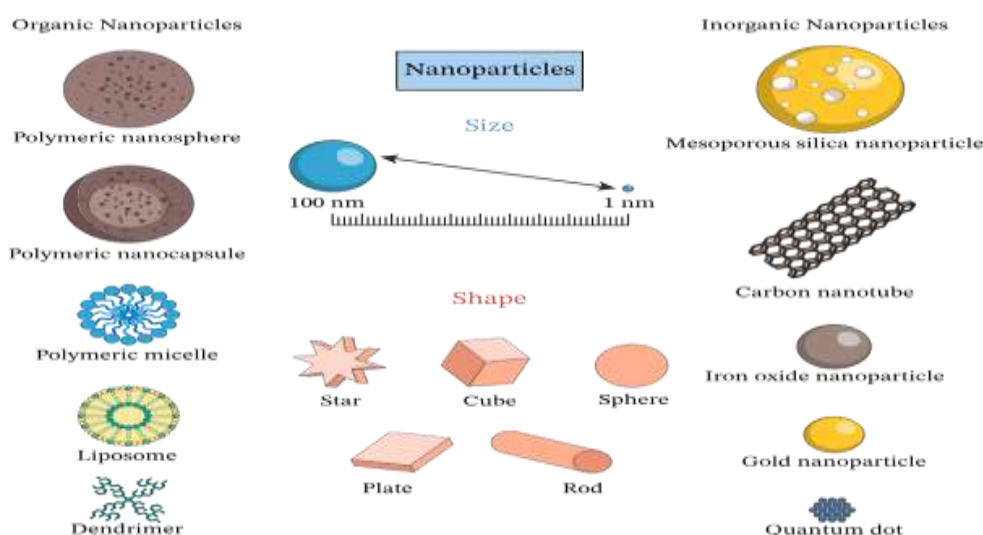


Fig: structure of Nanoparticles.

8. Pharmacosomes

Pharmacosomes are particularly defined as zwitterionic complexes of amphiphilic, polyphenol stoichiometric compounds with phospholipids. These lipid-based drug delivery systems are accurately defined as colloidal pharmaceutical dispersions that improve drug transfer across an organism's cell walls, tissues, or membranes.^[50] They work well to accomplish therapeutic objectives like controlled release and medication targeting. For vesicular pharmacosomes to form, they must interact with drugs both inside and outside of their bulk. Any medication with an active hydrogen atom (-COOH, -OH, -NH₂, etc.) can be

esterified to the lipid, with or without the spacer chain strongly forming an amphiphilic molecule. The three primary components of pharmacosomes are drugs, lipids, and solvents. Pharmacosomes have proven to be useful in the administration of several drug types to cure a variety of illnesses. NSAIDs (aceclofenac, aspirin, diclofenac, etodolac, ibuprofen, ketoprofen, and naproxen, among others), anti-cancer drugs (camptothecin, cytarabine, gemcitabine, paclitaxel, etc.), and antiviral drugs (acyclovir, adefovir, didanosine (isoniazid), etc.) are among the many drugs that are administered via Pharmacosomes.^[52] Compared to liposomes, they take less time and effort. Instead of bilayer diffusion, surface desorption, or degradation as in the case of liposomes, drug release happens during hydrolysis. The effectiveness of trapping in Pharmacosomes remains unaltered, in contrast to liposomes. by the amount of inclusion. Since the drug and lipid are covalently linked to one another, the temperature at which the conjugate phase shift occurs influences the fluidity of the Pharmacosomes' membrane.^[53] However, in the case of liposomes, membrane fluidity—which is reliant on lipid composition—controls drug release and system stability. Because the medication and carrier are covalently linked, there is neither drug leakage nor sedimentation.^[54]

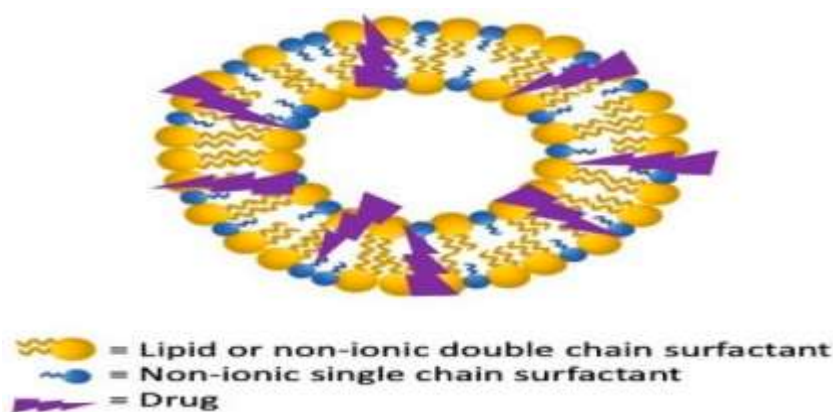


Fig: srtucture of Pharmacosomes.

CONCLUSION

A conclusion of this review, promising strategy for boosting the therapeutic potential of herbal medicines is the development of innovative herbal drug delivery systems. Despite being widely used and reliable, traditional herbal treatments can have drawbacks such poor stability, fluctuating absorption rates, and low bioavailability. By enhancing the targeted distribution, sustained release, and bioavailability of herbal substances, advanced delivery technologies such as liposomes, nanoparticles, phytosomes, and transdermal patches can help

solve these problems. These systems may improve the effectiveness, safety, and patient compliance of herbal medicines by fusing contemporary technology with traditional herbal expertise. This method helps create more standardized, consistent, and scientifically verified herbal products while also bridging the gap between traditional and modern treatment. The development of alternative medicines for a variety of illnesses might be greatly aided by the improvement of these systems as research progresses, opening the door for herbal medicine to play a larger part in conventional healthcare. It is clear that a new benchmark for therapeutic applications is being set by the combination of contemporary delivery technology with traditional herbal therapy. In addition to addressing some of the herbal remedies' long-standing drawbacks, such as irregular dosage and poor solubility, this integration creates opportunities for their use in the treatment of chronic and complicated illnesses including cancer, diabetes, and neurological conditions. Hydrogels, microspheres, and nanoemulsions are examples of advanced drug delivery systems that enable the exact administration of active herbal constituents to specific tissues or organs. This accuracy reduces possible adverse effects and optimizes the medicinal benefits of herbal ingredients, which is especially helpful for therapies that call for controlled release and sustained medication activity. Additionally, by shielding delicate phytochemicals from deterioration, these systems improve their stability and shelf life—a major benefit in medicinal and commercial applications. Innovative herbal medication delivery methods fit in nicely with the worldwide movement toward sustainable and natural healthcare. Because they employ fewer synthetic compounds and more plant-based resources, they provide a more sustainable approach to medicine development. The commercial and regulatory environments may be significantly impacted by these systems as they continue to be researched and developed, which might result in the implementation of strict quality control guidelines for herbal medications. In addition to meeting clinical and therapeutic objectives, the creation of innovative herbal drug delivery systems also satisfies the growing desire for patient-centered, natural, and holistic healthcare solutions.

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