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PHYTOSOMES NOVEL APPROACH FOR HERBAL DRUG DELIVERY SYSTEM

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Abstract:
Phytosomes represent an exciting advancement in herbal medicine, blending the age-old wisdom of plant-based therapies with the latest in drug delivery technology. These lipid-based vesicles significantly enhance the bioavailability and effectiveness of phytochemicals, addressing the common challenges of poor solubility and absorption that often hinder herbal extracts. By encasing bioactive compounds in a phospholipid matrix, phytosomes improve stability, allow for targeted delivery, and ensure a consistent release, ultimately maximizing their therapeutic benefits. While herbal medicine has been a cornerstone in many cultures for centuries, the active compounds in plants often face hurdles when it comes to absorption and utilization by our bodies. In our modern world, there's an increasing demand for innovative Drug Delivery Systems. These systems boost bioavailability, guarantee safety, and streamline the overall therapeutic process of medications in no time. Recently, many everyday ailments and nutritional concerns are being tackled with herbal remedies, thanks to their low side effects, affordability, and easy access. However, these products frequently encounter issues with stability and bioavailability. Once we isolate plant products, they can become a bit unstable and might struggle to cross biological membranes effectively. That's where the phytosome technique comes into play, helping to tackle these issues. By boosting the hydrophilicity of highly lipophilic drugs, the phytosome or Herbosome technique makes them much more suitable for drug delivery. At the same time, it enhances the lipophilicity of hydrophilic phytoconstituents, allowing them to navigate biological membranes more efficiently. These products often face challenges with stability and bioavailability, which is why these techniques are so valuable.

Key words: Bioavailability, Phytosomes, Phospholipids, Drug delivery.

Introduction:

Over the last century, many plant extracts have been thoroughly examined through chemical and pharmacological studies to uncover their chemical compositions. Most of the bioactive components found in herbal medicines are made up of water-soluble molecules. However, it's worth noting that many flavonoids and other water-soluble phytochemicals don't get absorbed very well[1]. The ideal drug delivery system would target the active ingredient right where it's needed and release the medication at a rate that aligns with the body's requirements throughoutthe treatment process[2]. Phytosomes are known for their superior bioavailability compared to regular botanical extracts. They have a knack for slipping through lipid-rich biomembranes and making their way into the bloodstream. The lipid-phase materials used to create these lipid- friendly phytoconstituents mainly come from soy, particularly phosphatidylcholine (PC)[3]. Both acute and chronic liver diseases, whether they stem from toxic metabolic issues, infections, or degenerative conditions, can see significant benefits from phytosomes thanks to their improved pharmacokinetic and pharmacological properties[4]. Phytosomes are created by combining soy phospholipids with certain botanical compounds in the right solvent. These unique complexes stand out because of their distinct spectroscopic and physical chemical properties[5].
They show promise in treating both acute and chronic liver diseases that stem from toxic metabolic

issues, infections, or degeneration, thanks to their improved pharmacokinetic and pharmacological characteristics. Plus, they have anti-inflammatory benefits and can be incorporated into pharmaceutical and cosmetic products[6]. The use of phytosomes in therapy has been investigated across various biomedical fields, and their potential health benefits are starting to catch on, particularly in the realm of cancer treatment. This innovative approach to safely delivering pharmaceutical compounds into the body targets specific areas where they can have the most impact, and it's known as a novel drug delivery system (NDDS). This idea incorporates advanced techniques, new technologies, unique formulations, and a sprinkle of creative thinking[83]. Drug carriers come in all sorts of shapes and sizes. You've got soluble polymers, microparticles made from both natural and synthetic materials that can either be insoluble or biodegradable, plus microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The method of drug administration can really make a difference in how effective it is serious illnesses highlight the urgent need for a more collaborative approach to delivering drugs exactly where they're needed in the body. This has sparked the creation of innovative strategies focused on managing the pharmacokinetics, pharmacodynamics, immunogenicity, biorecognition, and non-specific toxicity of medications. These state-of-the-art techniques, referred to as "drug delivery systems" (DDS), pull from a variety of fields, such as bioconjugate chemistry, pharmaceutics, polymer science, and molecular biology. Nowadays, a range of drug delivery and targeting systems are being developed to minimize drug loss and degradation, lessen side effects, boost medication bioavailability, and ensure that more of the drug reaches its intended destination— something that was once just a dream or a distant possibility[84]. Many herbal drugs and extracts show amazing promise in laboratory settings, but they often struggle to deliver the same results in real-world situations. This is largely because of their poor lipid solubility or the wrong molecular size, which can lead to inadequate absorption and low bioavailability. While the different components in an extract can work together in harmony, processes like purification and separation can sometimes remove key substances that are vital for the effectiveness of the main ingredients. Interestingly, the chemical complexity of the extract is often a key factor in how well the active components are absorbed. Most plant constituents, particularly phenolics, are water-soluble, which poses a significant challenge for bioavailability since they have a tough time getting through the lipid membranes of the intestines. However, we can boost bioavailability by using innovative delivery systems like liposomes, marinosomes, niosomes, and photosomes. These techniques can enhance both the release rate and the ability to traverse lipid-rich biomembranes. [85]. Phytosomes are created by combining naturally active plant compounds with phospholipids. What sets them apart from other lipid-based systems is that the bioactive components actually become a key part of the vesicular membrane. They attach to the polar head of the phospholipid through a chemical bond (specifically, a hydrogen bond), rather than just being trapped in the watery core or the phospholipid layers. This unique structure brings several benefits, such as better drug encapsulation, enhanced stability (thanks to those chemical bonds between the amphiphile's polar head and the plant compound), and improved bioavailability[89]. In this study, researchers explored the antidiabetic potential of polyherbal extracts that were incorporated into phosphatidylcholine-based phytosomes. They found that these phytosome-loaded extracts significantly boosted antidiabetic activity in rat models induced with streptozotocin and nicotinamide, showing results that were on par with the well-known hypoglycemic medication, metformin. The goal of this research was to improve the absorption and oral bioavailability of silymarin by using a phytosomal nanocarrier system. To achieve this, a two-factor, three-level full factorial design was employed to formulate and optimize the silymarin-loaded phytosomes. The resulting optimized formulation displayed porous, nearly smooth particles that fell within the nano-size range. Notably, this optimized formula significantly enhanced the aqueous solubility of the loaded silymarin compared to its pure form. Most importantly, the optimized silymarin phytosomal formulation greatly improved the oral bioavailability of silymarin and demonstrated a superior hepatoprotective effect in a rat model of CCl4-induced hepatotoxicity, outperforming plain silymarin[90]. The process might involve targeting specific sites within the body or enhancing how drugs move through the system. Typically, this is discussed in the Journal of University of Shanghai for Science and Technology, Volume 24, Issue 1, January 2022, Page

48, where the focus is on both the amount and the duration that a drug remains effective. The goal of Novel Drug Delivery Systems (NDDS) is to provide some level of control— whether it's about timing, location, or both—over how drugs are released in the body. These innovative delivery methods aim to either maintain a steady rate of drug action or keep a consistent, effective level of the drug in the system while minimizing unwanted side effects. Additionally, they can target drug action by placing controlled release systems near the affected tissue or organ, or by using carriers or chemical modifications to deliver the drug to specific cell types[90]. The way we attach drugs to nanocarriers and how we target them is crucial for effective therapy. A drug can either stick to the surface of the nanocarrier or be encapsulated within it. Covalent bonding is particularly beneficial because it allows us to control exactly how many drug molecules are linked to the nanocarrier, ensuring precise delivery of the therapeutic compound. When it comes to targeting specific cells with nanocarriers, we can use either active or passive methods. The active approach involves drawing the drug to the affected area by using recognition elements, like antibodies or small ligands such as folic acid and peptides, that are attached to the surface of the nanocarrier. We can also manipulate physical factors like temperature, pH, or magnetism to enhance this targeting. On the other hand, passive targeting takes advantage of the increased permeability and retention (EPR) seen in the leaky blood vessels of tumors[92].

Phytosome technology:

Plant extracts, particularly their flavonoid and terpenoid components, are really good at binding directly to phosphatidylcholine. When you mix a specific amount of this phospholipid (phosphatidylcholine) with a standardized extract or polyphenolic components (like simple flavonoids) in a nonpolar solvent, they come together to create phytosomes[7]. Just like phytosomes, liposomes come to life when you blend a water-soluble substance with phosphatidylcholine in just the right proportions. During this process, the phosphatidylcholine molecules elegantly wrap around the water-soluble material, all without any chemical reactions happening. Phosphatidylcholine is quite a fascinating molecule, featuring both a water-loving choline part and a fatloving phosphatidyl part. Specifically, the lipid-loving phosphatidyl section, which includes the body and tail, envelops the choline-bound material once the choline head latches onto these substances. This results in the formation of a phytophospholipid complex—a molecular structure that harmonizes beautifully with lipids—thanks to the combination of phytoconstituents and phospholipids. Certain spectroscopic techniques can reveal that molecules are indeed connected to the polar choline head of the phospholipids through chemical bonds [9-10]. Plant extracts, particularly their flavonoid and terpenoid components, are really good at binding directly to phosphatidylcholine. When you mix a specific amount of this phospholipid (phosphatidylcholine) with a standardized extract or polyphenolic components—like simple flavonoids—in a non-polar solvent, you end up creating phytosomes[11].

Composition:

Phospholipid:

Cell membranes are made up of phospholipids, which can serve as a fantastic delivery system for medications, enhancing their flexibility. Not only are phospholipids biocompatible, but they also come with a host of advantages, like formulation versatility and the ability to select from various innovative drug delivery systems based on specific applications. These lipids have both polar and non-polar structures and contain phosphorus, making them quite unique in their function[12]. The pharmaceutical industry often relies on both synthetic and natural phospholipids. These compounds are known for their low toxicity and can be used in various ways—topically, orally, or through injections. While synthetic polymers have their limitations, phospholipids stand out as excellent excipients. It's important to consider the quality of phospholipid content, which can differ based on how they'readministered. For oral and topical applications, natural phospholipids should contain at least 45% phosphatidylcholine (PC), but for injections, a higher concentration of around 70% PC is typically required[13].

Phosphatidylcholine:
You can draw this conclusion by looking at the NMR of the complex and comparing it to that of its earlier versions. The signals from the fatty chains have remained mostly unchanged. These results indicate that the two long aliphatic chains create a lipophilic barrier around the active ingredient, which helps protect both the catechin and the polar head of the phospholipid. By examining the NMR of the complex alongside the pure predecessors, this becomes clear. The fatty chain signals show little variation. Overall, these findings imply that the active ingredient is surrounded by two long aliphatic chains, forming a protective lipophilic envelope around the catechin and the polar head of the phospholipid[39].

Niosomes:
The primary focus of developing niosomes is to tackle challenges related to sterilization, large-scale production, and stability. Niosomes are thermodynamically stable vesicles that resemble liposomes and are tiny, typically on a nanometric scale, making them perfect for transdermal delivery. They consist of hydrated compounds like cholesterol, charge- inducing substances, and nonionic surfactants such as mono-alkyl and dialkyl polyoxyethylene ethers, which are primarily used as carriers for lipophilic and amphiphilic drugs. This method allows for targeted delivery of medication while minimizing the risk of side effects and toxicity. When surfactants interact with aqueous media, they form a lipid bilayer, enhancing the effectiveness of the delivery system [86-87].

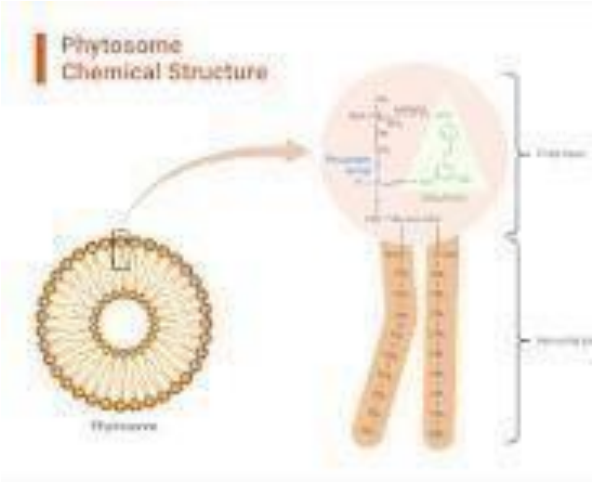
Liposomes:
Liposomes are these tiny, layered vesicles that have a remarkable knack for transporting potent drugs along with phospholipids, making them ideal for targeted drug delivery. When it comes to liposomal corneal penetration, positively charged liposomes perform the best, followed by negatively charged ones, and then neutral liposomes[88].

Phytosomes used in advanced Technology:

COVID 19
An immune response kicks off the initial stages of COVID-19, which then leads into a second phase characterized by a cytokine storm and the activation of macrophages. Quercetin has been shown to inhibit proteins involved in the COVID-19 infection cycle. To see if quercetin phytosomes could effectively prevent COVID-19, Rondanelli and colleagues conducted a pilot trial. They selected 120 participants and divided them into two groups: 60 received the supplements, while the other 60 served as the control group[14]. **Pulmonary Fibrosis**
The lung disease known as idiopathic pulmonary fibrosis is both deadly and currently without a cure. Researchers have discovered that a component from safflower, called hydroxysafflor yellow A (HSYA), can block TGF-1 from activating lung fibroblasts. In their study, Tingting and colleagues explored the effects of HSYA phytosome (HYAP) on lung fibrosis through a method called intervaginal space injection (ISI). To enhance the solubility and bioavailability of HSYA, the team developed HYAP using a thin film technique. They employed various methods, including transmission electron microscopy (TEM), dynamic light scattering (DLS), entrapment efficiency analysis, UV analysis, and FT-IR, to thoroughly investigate it [15].

Asthma
Ferrara and colleagues investigated how effective and safe Casperome® is in reducing the need for inhalational therapy. This asthma- fighting phytosome is derived from Boswellia serrata. The study included 32 participants, with 14 assigned to the control group and 18 to the Casperome® group. To evaluate the difference in treatment frequency between the two groups, patients received inhalational therapy twice a day throughout the trial[16].

(Fig.1: Chemical structure of phytosome)



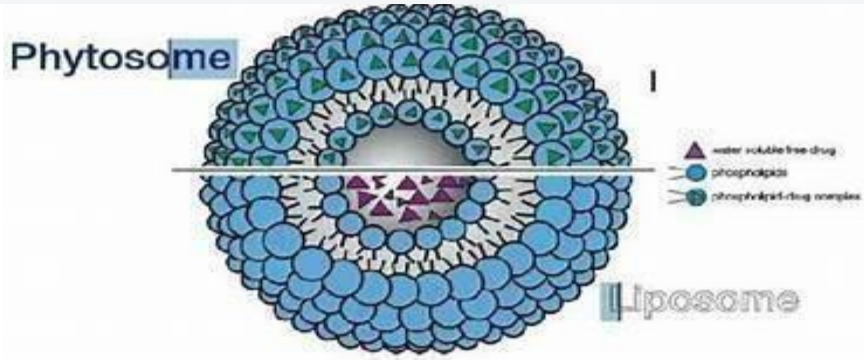
Preparation of phytosome:

Phytosomes are an exciting blend of lipids and plant extracts. The process of making phytosomes involves attaching a standardized extract of the herb's active ingredients to a phospholipid, like phosphatidylcholine (PC), phosphatidylethanolamine, or phosphatidylserine, using a polar end[18]. Phytosomes are fascinating complexes formed by combining 3-2 moles, ideally one mole of a synthetic or natural phospholipid—like phosphatidylcholine, phosphatidylethanolamine, or phosphatidylserine—with one mole of a component such as flavolignanans. This can be done either on its own or as part of a natural mixture in a nonpolar solvent like acetone or dioxane. Once created, the complex can be isolated through methods like lyophilization, precipitation using n on- solvents like aliphatic hydrocarbons, or spray drying. The ideal ratio for developing phytosomes typically falls between
0.5 to 2.0 moles, with a perfect 1:1 ratio of phospholipid to flavonoids being the sweet spot[19]. Phytosomes are innovative complexes formed by combining one mole of a natural or synthetic phospholipid— such as phosphatidylcholine, phosphatidylethanolamine, or phosphatidylserine—with one mole of another component, like flavolignanans. This reaction typically occurs in an aprotic solvent, such as dioxane or acetone, and can involve either a single component or a natural mixture [20].

(Table 1:- Difference between phytosomes and liposome)

PHYTOSOMES	**LIPOSOME**
A phytosome refers to a cluster of molecules that are bundled together.	A liposome is essentially a cluster of phospholipid molecules that can encase other phytoactive compounds without actually bonding with them.
When it comes to the substances involved, phosphatidylcholine and plant components form a molecular complex in a 1:1 or 2:1 ratio during the phytosome process, thanks to their molecular bonds. This results in better bioavailability and improved absorption.	Liposomes don't have any chemical bonding going on. Instead, they're made up of phosphatidylcholine molecules that encase the water-soluble material. In fact, this water- soluble substance can be surrounded by hundreds or even thousands of these phosphatidylcholine molecules.

Acetone, dioxane, methylene chloride, hexane, ethyl acetate, and other solvents that have a lower dielectric constant can interact with phytosomes.	Liposomes don't have any chemical bonding going on. Instead, they're made up of phosphatidylcholine molecules that encase the water-soluble material. In fact, this water- soluble substance can be surrounded by hundreds or even thousands of these phosphatidylcholine molecules.

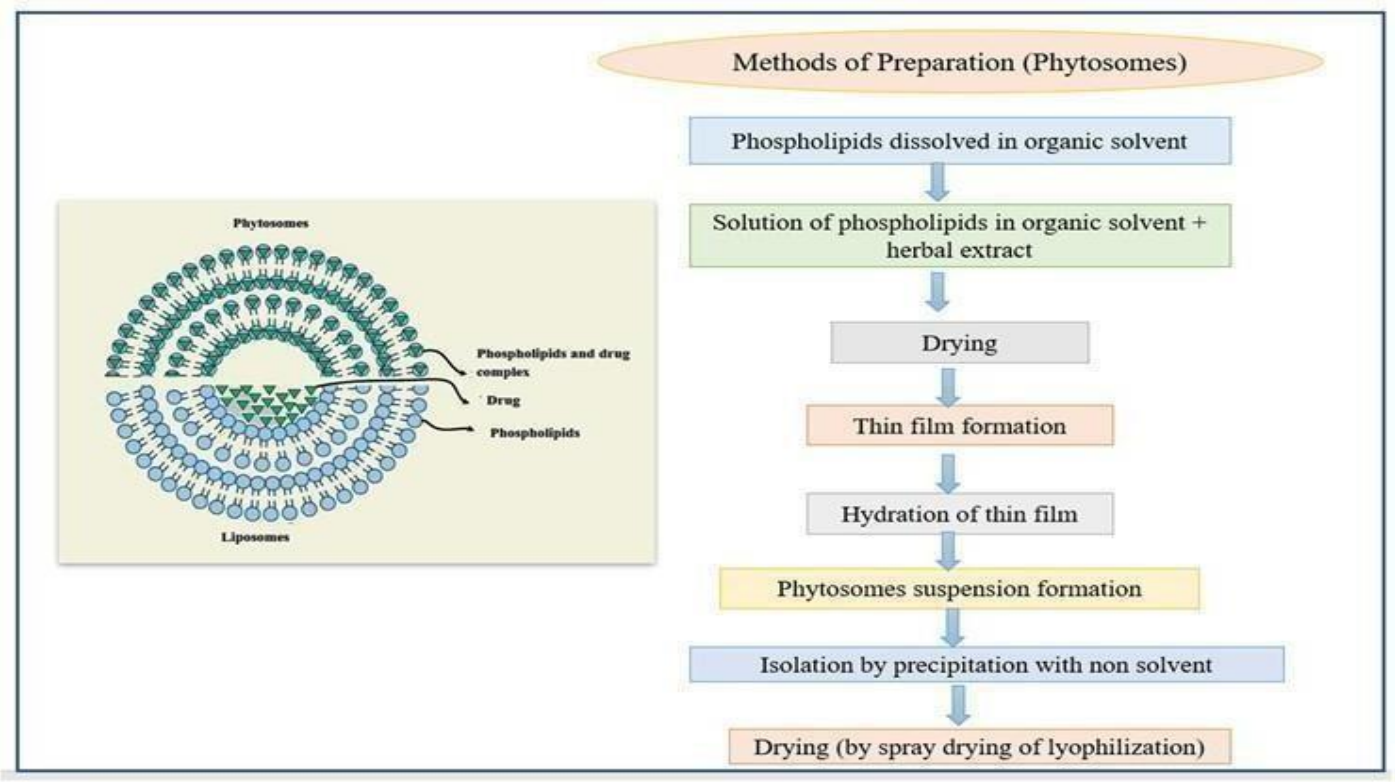


(Fig 2:- Comparison between phytosome and liposome)

Properties of phytosome: Chemical properties :
Phytosomes are created when natural substances, including phospholipids like those found in soy, come together. This happens when
specific amounts of phospholipid interact with a selected polyphenol, such as simple flavonoids, in a nonpolar solvent, resulting in a complex formation [21]. These compounds have a distinct melting point, are lipophilic, and dissolve easily in nonpolar solvents (though they don't mix well with the hydrophilic part), while showing moderate solubility in lipids. When exposed to water, phytosomes adopt a micellar shape and create structures that look like liposomes. In phytosomes, the active ingredient is linked to the polar head of phospholipids, making it a crucial part of the membrane. In contrast, in liposomes, it either dissolves in an intracellular pocket or floats within the membrane layer [22-23-24]. The complexes tend to dissolve quite easily in aprotic solvents, show moderate solubility in lipids, are not soluble in water, and can be a bit unstable in alcohol[25].

Biological properties:
Pharmacokinetic studies and pharmacodynamic tests conducted on both experimental animals and human subjects have revealed that phytosomes are innovative complexes. They offer improved absorption and utilization, leading to enhanced bioavailability and more effective results compared to traditional herbal extracts or non-complexed versions [26]. Pharmacokinetic studies and pharmacodynamic tests conducted on both experimental animals and human subjects have shown that phytosomes are innovative complexes that enhance absorption. This improvement helps tackle the bioavailability issue and leads to better outcomes compared to traditional formulations. [27]. Phytosomes are advanced herbal medicines that outperform traditional herbal extracts due to their superior absorption and utilization in the body. Research, including pharmacokinetics studies and pharmacodynamic tests conducted on both experimental animals and humans, has demonstrated that phytosomes offer greater bioavailability compared to non- complexed botanical derivatives [28].

Fig.3: General preparation of Phytosomes



Characterization of phospholipid :

There are several factors that affect how phytosomes function in both physical and biological systems. These include their physical size, how easily substances can pass through their membranes, the percentage of solutes trapped inside, their chemical makeup, and the quality and quantity of the starting materials[43]. To understand phytosomes better, we look at their physical traits like shape, size, distribution, the percentage of drug captured, the volume of the drug that's entrapped, the percentage of drug released, and their chemical composition. Essentially, the physical characteristics of phytosomes encompass their size, shape, distribution drug capture percentage, entrapped volume, drug release percentage, and overall chemical structure[49].

Enhanced bioavailability:

A wealth of studies has shown that phytosomes can significantly enhance absorption and bioavailability compared to traditional methods. Recent research highlights that most of the work on phytosomes focuses on Silybum marianum, commonly known as milk thistle, which is known for offering some of the best flavonoids for liver protection. These flavonoids, which have hepatoprotective properties, are found in the fruit of the milk thistle plant [37].

The star player in silymarin, which is the flavonoid complex found in milk thistle, is silybin. This plant, known scientifically as

Silybum marianum, has an extract that doesn't absorb well when taken by mouth, but it's recognized as a solid protector for the liver[38].

Research by Tedesco et al. shows that silymarin phytosomes are much more effective at combating liver toxicity than silymarin on its own. Additionally, silymarin phytosomes help reduce the negative impact of aflatoxin B1 on the performance of broiler chicks. Busby et al. also discovered that these phytosomes provide better protection against behavioral issues caused by ethanol compared to regular silymarin. [40].

Silymarin phytosomes were introduced by Bombardelli and his team, where they combined phospholipids with silymarin, a carefully crafted blend of isolated flavanolignans. When compared to individual ingredients, these phytosomes showed significantly better effectiveness and a longer-lasting impact on reducing edema, inhibiting myeloperoxidase activity, and enhancing antioxidant and free radical scavenging abilities[41] . In contrast to the control groups that received a similar dose of standard grape seed extract, the phytosomes resulted in noticeably less aortic plaque. In a randomized human study involving young, healthy participants, they took grape seed phytosome once daily for five days. Blood samples were taken multiple times on the first and fifth days to measure the TRAP (Total Radical-trapping Antioxidant Parameter) [42].

Natural phospholipids, like those found in soy, primarily made up of phosphatidylcholine, come together with natural plant compounds to create phytosomes. In this process, specific amounts of phospholipids interact with the plant constituents in a nonpolar solvent to form this unique complex [44].

Table No.2 :- Innovations of Phytosome in drug formulation

Topics	**Innovation**	**Patent No**	**Reference**
Discover how phospholipid complexes derived from olive fruit or leaf extracts can enhance bioavailability. Just remember, when you’re looking for results, our AI Content Detector can help you get accurate, human-like feedback in just seconds	Extracts or blends that include phospholipid complexes from olive fruits or leaves are known to have improved bioavailability.	EP/1844785	[50]
Discover the fascinating world of saponin complexes with phospholipids, along with the pharmaceutical and cosmetic formulations that incorporate them.	Saponin complexes, thanks to their high lipophilicity and improved bioavailability, are great candidates for active ingredients in pharmacological, dermatological, and cosmetic products, whether they're made from natural or synthetic phospholipids.	EP0283713	[52]
Looking for a natural way to tackle circulation and weight issues? Check out this antioxidant blend made from plant extracts, designed specifically to help with those problems	This preparation, made from plant extracts, boasts antioxidant properties and is particularly effective for addressing circulation-related issues like varicose veins, phlebitis, arteriosclerosis, hemorrhoids, and high blood pressure.	EP1214084	[53]

Discover the benefits of fatty acid monoesters derived from sorbity furfural, along with their unique compositions designed for cosmetic and dermatological applications.	From two unique series of compounds, we selected fatty acid monoesters of sorbityl furfural. The side chains of these compounds consist of linear or branched C3-C19 alkyl radicals, which might have at least one ethylenic unsaturation, or they might not. Just a quick reminder: when crafting responses the specified language and avoid using any others	EP1690862	[54]

Discover how thymosin β4 can aid in skin	Discover the latest formulations and techniques	US/2007/	[55]
treatment and wound healing. Just paste your text into our AI Content Detector, and you'll receive quick, accurate, and human-like results in no time	for skin care that harness the power of thymosin β4.	0015698	
Looking for a solution to combat aging or sundamaged skin? Check out our cosmetic and dermatological formulation designed specifically for these concerns	The formula for topical skin therapy includes a chemical that boosts collagen production and another that helps strengthen the connection between fibroblasts and the extracellular matrix. These are key dermatological or cosmetic ingredients designed for topical use.	EP1640041	[56]

Advantages:

Phytosomes have the following advantages

1. When it comes to hepatoprotective compounds, phosphatidylcholine plays a dual role as both a protective agent for the liver and a carrier for phytosomes, creating a powerful synergy.
2. These compounds enhance the absorption of lipid-insoluble polar phytoconstituents, whether taken orally or applied topically, leading to better bioavailability and a significantly improved therapeutic effect[29].
3. Phosphatidylcholine molecules and phytoconstituents create chemical connections that enhance the stability of phytosomes.
4. This process boosts the absorption of lipid-insoluble polar phytoconstituents, both orally and topically, leading to better bioavailability and a significantly greater therapeutic effect. [31].
5. Phosphatidylcholine, which is used to create phytosomes, not only acts as a carrier but also boasts hepatoprotective properties that enhance the effectiveness of other liver-protective compounds[32].
6. Phytosomes, being more bioavailable plant extracts that bond with phospholipids, greatly improve bioavailability and allow for faster, more efficient absorption in the digestive tract.
7. They enhance the absorption of lipid-insoluble polar phytoconstituents, both orally and topically, leading to better bioavailability and significantly improved therapeutic effects.
8. Thanks to their rich lipid profile and superior skin penetration, phytosomes are often used in cosmetic products. [33].

Disadvantages:

1. Sometimes, folks turn to herbal remedies without realizing that their symptoms might actually be linked to a different health issue. Unlike conventional medications that require a prescription and regular health check-ups, herbal medicines are often used on a trial-and- error basis. This can lead some people to navigate their health journey without proper guidance [45].
2. People often turn to herbal medicines without realizing that their symptoms might actually be tied to a different health issue. Unlike conventional medications that require a
3. prescription and regular health check-ups, herbal remedies are often used on a trial-and- error basis. This can lead some individuals to navigate their treatment without proper guidance [46].
4. In some cases, herbal medications can trigger allergic reactions. It's important to check if you're allergic to the specific herb you intend to use before diving into herbal remedies. On the other hand, conventional medications, especially those that are usually prescribed, tend to have a lower risk of causing allergic responses, although they can still lead to them [47].
5. Herbal medicines, in any form, aren't officially approved by the government. People often use them at their own risk, and there's no assurance of quality when it comes to branded herbal supplements [48].

Evaluation:-

India stands out as a key player in the pharmaceutical market, attracting the attention of many multinational companies eager to invest and expand in this sector. The emergence of new and advanced techniques in Novel Drug Delivery Systems (NDDS) is set to drive a significant demand for a variety of excipients, both in usage and development. India has a reputation for quickly adapting to new excipients and related technologies. As a result, the market for excipients in India is poised to grow in two main ways: first, through the export of innovative organic excipients, and second, by incorporating these new excipients into various advanced delivery technologies. Many pharmaceutical companies in the country are actively applying for and obtaining new patents in the realm of NDDS. This trend is likely to create a substantial demand for the products and services provided by pharmaceutical and related businesses in the near future. Additionally, nanotechnology presents a range of modern applications in novel drug delivery systems, potentially enhancing diagnosis, treatment, and monitoring of drug composition changes within the body after administration. Another significant development worth mentioning is Computer-Aided Drug Design, which opens up numerous opportunities for creating these advanced systems. This approach allows for the design and development of drugs and delivery systems in a more efficient manner, using less time and resources while achieving greater accuracy and quality compared to traditional methods[94-95].

Applications :

Silybum marianum, commonly known as milk thistle, is at the forefront of phytosomal research thanks to its impressive liverprotective flavonoids. These beneficial compounds are primarily found in the fruit of the milk thistle plant, which belongs to the Asteraceae family. Research has shown that silymarin, a key component of milk thistle, can aid in the treatment of various liver conditions, including hepatitis, cirrhosis, and fatty liver disease caused by chemicals or alcohol, as well as inflammation of the bile ducts. One of the standout features of silymarin is its antioxidant properties, which significantly bolster the liver's ability to withstand harmful stressors. In recent studies, Maiti et al[57]. (2006) also developed phytosomes containing curcumin and naringenin, showcasing the ongoing exploration in this field[58-59].

Silybin takes the spotlight as the main ingredient, with silydianin and silychristin following closely behind. Essentially, silybin is a flavonolignan that likely forms in the plant through the combination of coniferyl alcohol and a flavonol[60]. It's now established that silybin is the most powerful of the trio. The antioxidant properties of silymarin significantly boost the liver's ability to withstand harmful attacks[61]. The majority of silymarin consists of three flavonoids from the flavonol subclass, with silybin being the most prevalent, followed by silydianin and silychristin. Silybin, a flavonolignan, is probably produced by

the plant when a flavonol merges with coniferyl alcohol. Today, silybin is recognized as the most effective among the three[62].

The flavonoids and terpenoids found in these herbal extracts are particularly good at binding directly to phosphatidylcholine. A literature review suggests that phytosomes might help ease the pain and symptoms associated with various conditions, including rheumatism, asthma, arthritis, ulcers, phlebitis, edema, varicose veins, premenstrual syndrome, diabetic retinopathy, and hemorrhoids. Phytosomes have a wide array of potential uses in both cosmetics and medicine[63]. As research continues, we can expect to uncover even more about the possible pharmacological applications of phytosomes. The first phytosome studies focused on Silybummarianum [Family Steraceae], as its fruit is rich in flavonoids known for their liver- protective benefits. This research has shown promising results for treating liver issues like cirrhosis, hepatitis, fatty liver, and bile duct inflammation. Among the flavonoids in silymarin, silybin is the most prevalent and effective, as it helps protect the liver by maintaining glutathione levels in the liver cells. In its natural form within the milk thistle fruit, silybin primarily forms complexes with sugars, such as flavonolignan or flavonyl glycoside[64-65- 66].

To explore the effects of a hypocaloric diet on overweight individuals [n=100] of both sexes, Francesco and colleagues examined an oral formulation of coated tablets called Monoselect Camellia® [MonCam], which contains a highly bioavailable green tea extract known as GreenSelect® Phytosome. This formulation has shown no adverse effects, making it a promising and safe option for weight loss[67-68].

Recent studies have shown that phytosomes offer superior absorption and bioavailability compared to traditional methods. These phytosomes are made up of oligomeric polyphenols, specifically grape proanthocyanidins or procyanidins derived from grape seed extract (Vitis vinifera), which are complexed with phospholipids. The key benefits of procyanidin flavonoids from grape seeds include boosting overall antioxidant capacity and enhancing the body's natural antioxidant defenses in plasma. They also provide protection against ischemia/reperfusion damage in the heart and help guard against atherosclerosis, thereby offering significant protection for the heart and other organs through various mechanisms that extend beyond their impressive antioxidant properties[69]. When it comes to reducing oedema, inhibiting myeloperoxidase activity, and showcasing antioxidant and free radical scavenging abilities, phytosomes really stand out with their impressive specific activity and longer-lasting effects compared to their individual components[70]. The scopolamine-amnesia test is a well-recognized method for screening antialzheimer medications, and the way Ginkgo biloba phytosomes extended the transfer latency (the time it took for mice to enter the dark chamber) in this test clearly highlights their memory-boosting potential. This supports their use in treating Alzheimer's disease[71].

A wealth of research on grape seed phytosomes has revealed some impressive benefits, including a boost in overall antioxidant capacity, enhanced physiological defenses in the plasma, and protection against heart damage from ischemia/reperfusion. They also show promising effects against atherosclerosis, offering significant protection for the cardiovascular system. In one study, rabbits that received grape seed phytosomes had noticeably less plaque buildup in their aortas and carotid arteries compared to a control group that was given a similar dose of traditional standardized grape seed extract[72]. Additionally, research indicates that phytosomes exhibit stronger anti-inflammatory properties than pure herbal extracts. For instance, a study on the skin absorption of rutin phytosomes found that they are more effective than free rutin at penetrating the tough outer layer of the skin, allowing for a greater retention of rutin that gradually passes through the viable dermis, resulting in a longer-lasting anti-inflammatory effect [73]. Another study showed that when compared to plant lawson gel after four hours in a rat model of paw edema induced by carrageenan, the lawsone phytosome gel therapy demonstrated a significant anti-inflammatory effect[74].

According to various studies, phytosomes show a more effective antihepatotoxic action compared to standardized herbal plant extracts. For instance, research on silymarin phytosomes revealed that they were not only more targeted but also had a longerlasting impact than pure silymarin when it came to reducing edema, inhibiting myeloperoxidase activity, and scavenging free radicals and antioxidants[72].

In a study involving 100 overweight participants of both genders on a hypocaloric diet, Francesco et al. examined an oral formulation of coated tablets (Monoselect Camellia®) (MonCam) that contained a highly bioavailable green tea extract (GreenSelect® Phytosome). This formulation appears to be a safe and effective weight loss option, especially since it has no negative side effects[75-76].

By merging hesperetin with hydrogenated phosphatidylcholine, Mukerjee and colleagues developed a novel hesperetin phytosome. They then evaluated the antioxidant activity of this complex, revealing that the phytosome had a higher relative bioavailability compared to the active pharmacological compound [77-78-79].

When comparing the phytosomal extract to the nonphytosomal one, we found that the plasma concentration of total flavonoids more than doubled over the 6-hour testing period. To assess antioxidant capability, we used the Total Radical-trapping Antioxidant Parameter, or TRAP. The results showed that the phytosome formulation had about twice the overall antioxidant effect, with a 20% boost at its peak[80-81].

Recent advances:

Recent years have seen a growing interest in how nanostructured carrier systems—like polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLNs), polymeric micelles, and nanoemulsions—can effectively deliver anticancer medications through oral administration. The field of oral chemotherapy in oncology is particularly exciting, given its remarkable potential for delivering cytotoxic drugs via this route.

Conclusion:

When you compare phytosomes to traditional herbal extracts, you'll find that phytosomes are a more sophisticated type that gets absorbed much better. They can really help with acute liver disorders, whether they're caused by metabolic issues or infections, thanks to their improved pharmacokinetic and pharmacological properties. The flavonoids and terpenoids in these herbal extracts are particularly good at binding directly to phosphatidylcholine. A literature review suggests that phytosomes might ease the pain and symptoms of various conditions, including rheumatism, asthma, arthritis, ulcers, phlebitis, edema, varicose veins, premenstrual syndrome, diabetic retinopathy, and hemorrhoids. Plus, phytosomes have a wide array of uses in both cosmetics and medicine. There's still so much to discover about phytosomes and their potential pharmacological applications in the future. The ratios for component and phospholipid complex formation are 1:1 and 2:1, respectively. Phytosomes act as a bridge between cutting- edge delivery systems and traditional ones. Many popular herbal extracts, like ginseng, milk thistle, hawthorn, grape seed, ginkgo biloba, and green tea, have gone through the Phytosome process.

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