



Herbal Excipient and Novel Drug delivery system used in Liposome and Ethiosome

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Abstract

Drug preparation is thought to play a significant role in determining how bioavailable a drug will be. Excipients add additional characteristics including integrity, stability, solubility, and patient compliance to those fundamental to pharmaceutical formulations. the Active Pharmaceutical Ingredients' characteristics (APIs). organic excipients are already attracting attention on a global scale in contrast to the synthetic ones, biocompatible, reasonably priced, and widely accessible This review outlines the key application of a natural excipient in conventional pharmaceuticals Natural excipients have attracted a lot of attention lately because of their numerous medicinal uses. For instance, when creating and manufacturing medicinal dosage forms, natural polysaccharide polymers are used. They safeguard, encourage, or improve patient acceptance or stability and bioavailability. Plants are a key component of many pharmacological preparations and serve as a major source of medicines. In addition, they work effectively as excipients and pharmacological aids.

Keywords

Herbal excipients, Pharmaceutical aids, Herbal binders, Herbal emulsifiers, bioactive agents, Non-toxic

INTRODUCTION

Excipient

The Latin word excipients, which meaning to receive, gather, or take out, is the source of the English word excipient. The active pharmaceutical ingredient (API), the production methods, and the excipients employed all affect formulation quality. They are excipients. maintain the product's safety and efficacy while making a significant contribution to the API's performance [1]. Excipients are mostly utilised as diluents, binders, disintegrates, adhesives, glidants, and sweeteners in conventional dosage forms like tablets and capsules. [2]

Excipients are mostly utilised as diluents, binders, disintegrates, adhesives, glidants, and sweeteners in conventional dosage forms like tablets and capsules. they are frequently referred to as "bulking agents," "fillers," or "diluents" for a variety of reasons, including long-term stabilisation, bulking up solid formulations that contain potent active ingredients in small amounts, or to confer a therapeutic enhancement on the active ingredient in the final dosage form, such as facilitating drug absorption, reducing viscosity, or improving solubility. Along with promoting in vitro stability³)

Ideal point of an excipient are given as under:-

An excipient must be:-

- Chemically stable
- Non-reactive
- Less equipment and process sensitive Inert to human body
- Non toxic
- Acceptable with regards to organoleptic characteristics
- Economical
- Having efficiency in regards with the intended use.
- Excipients are considered as inert substance,
- Have the propensity to react with drug components, other excipients, and also the packaging system.

HERBAL EXCIPIENT

Advantage

- Biodegradable - Polymers that are found in nature
- Created by all living things. They don't appear to have any negative consequences on the environment or people.⁽⁶⁾
- Biocompatible and non-toxic – All of these plant components are carbohydrates and consist of repeating monosaccharide units chemically. Hence they are non-toxic.
- Economic - Compared to synthetic materials, they are less expensive and less expensive to produce.
- Secure and devoid of side effects – They are from a natural source and hence, safe and without side effects.
- Easy accessibility - They are produced in numerous nations due to their widespread use in a variety of industries.

Disadvantages

- Microbial contamination - As a result of their exposure to the outside environment during production, there is a risk for microbial
- The percentage of contamination depends on time, as well as regional, species, and climatic variations.
- Variation - While the formation of natural polymers is reliant on the environment and a number of physical conditions, synthetic manufacturing is a regulated process with fixed quantities of materials.
- Variations in the collection of natural materials at different chemical ingredients present in a specific substance may affect the unregulated pace of hydration (7)
- Slow Process - Because the production rate depends on the environment and numerous other variables, it cannot be adjusted. Natural polymers therefore produce at a sluggish rate.
- Heavy metal contamination - Possibilities With herbal excipients, heavy metal pollution is frequently related (5)

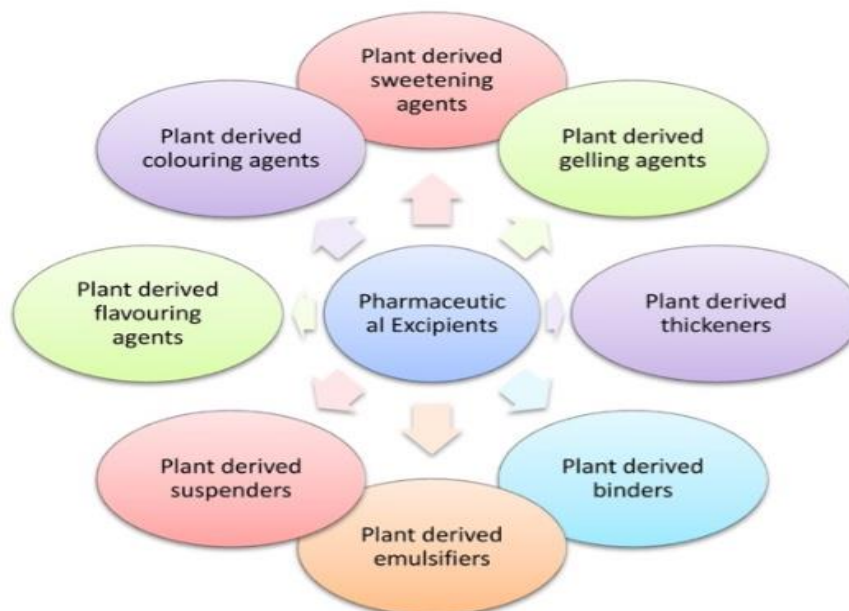
USE OF HERBAL EXCIPIENT OVER SYNTHETIC EXCIPIENT

They are non-toxic, inexpensive, and generally available, synthetic equivalents have an advantage over herbal or natural excipients. As the pharmaceutical companies become more aware of these excipients, they are beginning to use them as significant excipients in formulation development. These excipients are primarily polymers of natural origin. Many of the requirements for pharmaceutical excipients are met by the plant-derived gums and mucilages generated from natural sources, including tragacanth, carrageenan, thaumatin, lard, storax, and agar. These can be chosen over their synthetic counterparts for formulation development since they are more stable and have fewer regulatory issues. They are an effective and cost-effective way to deliver active pharmaceutical components because they can be easily modified to meet the needs of each unique patient. A global herbal renaissance is taking place as herbs make a comeback. The herbal products today symbolise safety in contrast to the synthetics that are regarded as India is home to a wide variety of ecological niches and biodiversity. India's flora and wildlife have been studied and documented for an extensive time, first in folklore and then by academics using more rigorous scientific methods (8).

Harmful to both people and the environment. More than 75 percent of people worldwide rely mostly on plants and plant extracts for their medical needs. The value of the global market for pharmaceuticals produced from plants is thought to be around 200000 crores, with India contributing less than 2000 crores. India is one of the world's top 12 biodiversity hotspots, with 426 biomes (particular species' habitats), 25 biotic provinces, and 16 different agro-climatic zones (9) Due to their numerous pharmaceutical applications as diluents, binders, disintegrants in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels, and bases in suppositories, plant-derived polymers have attracted a lot of attention recently. Due to their capacity to produce a wide range of materials and capabilities based on molecular structural modifications, protein and polysaccharides have been the focus of the majority of studies on natural excipients in drug delivery systems (10). India has always been a reliable supplier for these products among the Asian countries because of its geographic and environmental situation (11)

Classification of EXCIPIENT

Herbs have been grouped into a number of categories based on their various functions as pharmacological



aids, as seen in Fig.

1. PLANT-DERIVED THICKNER

Thickeners come in a variety of forms in nature or are derived from natural thickeners. These parts are made of polymers, which grow and become viscous when they take in water. Polyose derivatives like hydroxyethylcellulose are often utilised in goods like shampoo and body cleansers. Gum is another substance that thickens naturally. Others pick algarrobabean, gelatin, gum, and xanthan gum. Practical uses for plants and other gums include controlling water and using them to gel or thicken complicated systems. Additionally, they will act as foam stabilisers, adhesives, and impart certain properties.

2. PLANT-DERIVED BINDERS

Those used to give the granules cohesion or adherence are known as "binders." In addition to the flowing abilities provided by the creation of granules of resulting hardness and size, this guarantees that the pill stays intact when crushed [13]. It has compressional qualities since the genus *Dioscorea rotundata* is used as a binder and disintegrant in the production of pills [12].

3. PLANT-DERIVED EMULSIFIERS

It is feasible for the fat to be disseminated uniformly in the water as an emulsion thanks to components connected with water that are soluble in each fat. These emulsions constitute the foundation for foods like margarine, butter, salad ,mayonnaise, and frozen desserts. Emulsions remain a stable kind because to stabilisers. Margarine, salad dressings, mayonnaise, and frozen desserts are all emulsions that serve as emulsifying agents. Emulsions remain a stable kind because to stabilisers. Emulsifying chemicals are also used in roasting to help incorporate fat into the mix dough and maintain the softness of the mixture. (14)

4.PLANT-DERIVED SUSPENDERS

Gums serve as agents of suspension. They successfully stabilise the emulsion by surface absorption, which leads to the formation of a condensed film with high endurance that resists droplet coalition. They do this by producing stable multimolecular spherical films that stabilise the oil/water emulsion. Because of the liquefying barrier between the oil and water sections, every oil globe retards the coalition [15]. Gum is the dried out, glue-like exudate that *Astragalus gummifer* and other *Astragalus* species produce. The gum accumulates within the pith and medullary rays after the stem is injured. In general, water absorption causes the gum for many of the gums to enlarge and leak through the incision. The majority of gums include Ca, metal, and K-bassorin salts of bassoric acid. The majority of them purportedly serve as suspending agents for insoluble materials.

5. PLANT-DERIVED GELLING AGENTS

There are several different square measure gelling agents available. Xanthan gum, tragacanth, tree, and gum are a few of the more well-known ones. Some gelling agents are more soluble in cold water as opposed to warm water. Clay, gelatin, and sodium cellulose are all more soluble in cold water than methylcellulose and poloxamers are, although gelatin is also more soluble. Carbomers, tragacanth, and gum gels are made using lukewarm water [17]. The key gums that are used in food as gelling agents are alginate, pectin, carrageenin, gellan, gelatin, agar, modified starch, alkyl polysaccharide, and hydroxypropylmethyl polysaccharide agents [18].

6.PLANT-DERIVED FLAVOURER AGENTS

The majority of flavouring ingredients come from plants, usually in the form of flowers, leaves, stems, or bark. The ingredients are often removed from the substance to create an isolate that is only the flavour before being used in food products [19]. These flavouring chemicals play a significant role in the pharmaceutical industry, especially when it comes to masking medications with their essential flavours. As a result, they are sometimes known as "masking agents" or "bitter blockers". The primary flavours used in dental products are peppermint, spearmint, and wintergreen. These flavours may be substituted with other essential oils such as anise, clove, caraway, pimento, eucalyptus, citrus fruits, menthol, nutmeg, thyme, or cinnamon (20).

7.PLANT-DERIVED COLOURING AGENTS

In India, there are more than 450 plants that can make dye. Some of these plants can create dye, but they also offer health benefits. Mineral, plant, and animal products served as the primary sources of medicines for a very long time. The utilisation of natural products along with their medicinal capabilities dates back to the beginning of human civilization. 22)

8. PLANT-DERIVED SWEETENING AGENTS

Several very delicious diterpene glycosides known as steviol glycosides are found in stevia leaves. A variety of cucurbitane-type triterpenoid glycosides known as mogrosides are obtained from monk fruit. An oleanane-type triterpenoid chemical molecule called glycyrrhizin is obtained from the roots of the glycyrrhiza plant (21)

Excipients are frequently categorised based on how they are used and serve in the final drug products:

- Organizers and diluents
- Glidants, disintegrants, and lubricants
- Coatings and film formers for polishing
- Suspending agents; Plasticizers; Colorings Antioxidants and preservatives
- Sweeteners, flavourings, and substances that improve flavour
- Inks for printing and dispersing agents Gums [4]

1. Hina

- Synonyms include Mahendi, Mignonette, and Egyptian private.
- Biological source of Lawsonia inermis leaves that have been dried
- family: Lythraceae.
- Geographic sources include Sri Lanka, India, and North Africa.
- Chemical constituents of Lawsone (2,5-Dihydroxy-1,4-naphthoquinone), phenolic glycosides, coumarins, xanthene, flavonoids, lipids, resins, and tannins are some of its chemical components.
- Chemical test: The orange red colour in the henna decoction disappears when acid is added. Color darkens with the presence of alkali. Application: as a colourant in other cosmetics and as a hair dye.



2. TURMERIC

- Haldi and Indian saffron are synonyms.
- Biological source: Fresh and dried rhizomes of the Zingiberaceae family plant *Curcuma longa*.
- Geographical sources include China, Italy, Malaysia, Australia, and China.
- Chemical components include resin, 5% volatile oils, and a yellow colouring ingredient called curcuminoids. Other phytoconstituents include atlantone, demethoxycurcumine, tumerone, carbohydrates, minerals, etc.
- Chemical test: Sulphuric acid and curcumin produce a ruby red colour.
- Application: Used as a colourant in a range of pharmaceutical dosage forms, cosmetics, and food items.



NATURAL SWEETENERS

• These are the substances that are added to pharmaceutical formulations to mask the bitter taste and are also suitable for use by diabetics.

• Sweeteners with and without saccharides are both regarded as natural. Non-saccharide sweeteners come in a wide variety of forms, such as terpenoids, dihydrochalcones, dihydrocoumarins, sweet proteins, and steroidal saponins.

• Advantages:

1. Their nature is non-calorific.
2. Possess fewer potential negative effects.
3. Modern technology can help to increase both quality and quantity.
4. Financial

5. There is never increase in blood sugar 6. Reduce tooth decay.

1. STEVIA

- synonyms Names: Sugar Leaf, Honey Leaf
- biological source: derived from the Compositae plant *Stevia rebaudiana*.
- Geographic sources include Paraguay, South America, Japan, Southeast Asia, and the United States.
- Stevioside and diterpene glycoside are the chemical components.
- Application: Natural sweetener for liquid or solid foods and beverages without calories. in place of ordinary sugars. sweetener of choice for diabetic patients.



2. LIQUORICE

- Synonym: Yashtimadha, mulethi, Liquorice root.
- Biological source: dried peeled, unpeeled roots & stolons of plant *Glycyrrhiza glabra*, Family- Leguminosae.
- Geographical source: mediterranean region & china, france, italy, spain, USA, england, Asia & India.
- Chemical constituents: pentacyclic triterpenoid saponin, Glycyrrhizin. Chemical test-Description It has a rich yellow colour since it contains 80% sulfuric acid. Foam stabiliser, flavouring agent, and sweetness.



NATURAL BINDERS

- Binders are excipients that bind all of the chemicals used in formulation to create a proper dosage form.
- Natural binders are less toxic, may be naturally broken down, economical, easily obtainable, and abundant, and they improve the stability and texture of the dosage form.
- Binders Gelatin or cellulose is a type of solution binder. MC and other dry binders

1. ACACIA

- Synonym: Indian gum
- Biological source it is dried out gummy exudation from the stems & branches of *Acacia arabica*, *A. senegal*
- Family- Leguminosae.
- Description- When present, it takes the form of white, yellowish white, or yellowish-white flakes, spherical spheres, powder, or spray-dried powder.
- Chemical constituents: Arabinose, galactose, rhamnose, & glycuronic acid
- Chemical test: When acacia powder is treated with lead sub acetate, it gelatinizes the aqueous solution.
- Use: As a thickening, suspending, emulsifying, and natural tablet binder. as a basis in lozenges and pastilles.



2. TRAGACANTH

- Synonym: Gum tragacanth, Persian tragacanth.
- Biological source: dried gum obtained from plant *Astragalus gummifer*
- Family- Fabaceae.
- Geographical source: Iraq, Iran, Syria, Turkey, Afghanistan, Pakistan & Russia.
- Description: Tragacanth is made up of linear segments that might be flat, curved, spirally twisted, or twisted in a lamellated pattern. It is translucent, odourless, and ranges in colour from white to yellowish. It has a mucilagenous taste.
- Chemical test: Polysaccharides that are soluble and insoluble in water. cellulose, starch, protein, ash, and bassorin.
- Chemical test: when strong iodine solution is added to tragacanth, it develops olive green colour.
- Use: utilised to create a variety of medicinal formulations, including emulsions, gels, and creams.

NATURAL DILUENTS

- Natural fillers and diluents are the elements that increase the volume of solid dosage forms or may thin out liquid formulations.
- They provide the right structural form, guarantee the right weight for simple administration, are non-toxic, economical, and environmentally beneficial.

1. CELLULOSE

- Synonym: Arbocel, E460, Elcema, Sanacel.
- Biological source: It is a structural molecule that is present in the cells of plants, algae, and some bacteria. It is a polysaccharide..
- Description;It is described as a white, flavourless, and odourless powder with various particle sizes. Almost insoluble in water and the majority of organic solvents.
- Chemical test: Cellulose exhibits a purple colour when Schulze reagent is used..



Uses :Uses include suspending agents for pellet production, filler for hard gelatin capsules, tablet diluent, assistance with direct compression of granules, and application in the food and cosmetics sectors.

2.LACTOSE

- Synonym: Sugar, milk, Lactin, lactosum
- Biological source: It is a naturally occurring, animal-derived disaccharide that may be found in the milk of the majority of animals and is composed of galactose and glucose.
- Description: It has a light sweetness to it and is a white, crystalline powder. At high relative humidity levels, it is hygroscopic.

VISCOSITY BUILDERS

These are the aqueous solutions that raise viscosity without changing the substance's characteristics, suppress crystal development, and enhance physical stability.

- Types:

Gums E.g. acacia, tragacanth, xanthan gum, etc.

- Cellulose derivatives E.g. Methyl cellulose, CMC
- Chitosan
- Natural Synthetic polymers E.g. carbomer, PVA
- Clays E.g. Magnesium aluminium silicates, bentonite, etc.

• XANTHAN GUM

- Synonym: corn sugar gum, Keltrol, Rhodigel.
- Biological source: *Xanthomonas compestris*, a bacterium, is used in the fermentation process to create the polysaccharide.
- Discription :It is a fine, odourless powder that flows easily and has a cream or white tint. practically insoluble in ethanol and ether, but soluble in cold or warm water On the market, it is sold as potassium and sodium salts.
- Chemical test: Xanthan gum is suspended in 0.1 N HCl, the flask is sealed with a barium hydroxide formation bulb, and it is heated. BaOH solution exhibits turbidity in white.



Use: It works well as an emulsifier, thickening, stabiliser, and viscosity enhancer for foods, cosmetics, and pharmaceutical compositions that are applied topically and orally. It can be included in dosage forms for ophthalmic liquid and sustained release matrix.

DISINTEGRATING AGENTS

These are aqueous solutions that raise viscosity without changing the substance's characteristics, suppress crystal development, and enhance physical stability.

1. CHITOSAN

- Synonym: Deacetylated chitin.
- Biological source: it's natural polysaccharide obtained from crab and shrimp shells.
- Description: White or creamy-white powder or flakes known as odorles are occasionally soluble in water and other solutions. Biological acids.
- Chemical tests: It produces intense violet colour when combined with iodine and 10% sulfuric acid.

- Use: utilised in colonic drug delivery systems, mucoadhesive dosage forms, fast release, enhanced peptide administration, and for 40

NATURAL PERFUMES & FLAVOURING AGENTS

- On people, animals, food, medications, and interior spaces, natural fragrances are a mixture of essential oils or aromatic chemicals, fixatives, and solvents.
- Flavours are taste-hiding substances that are used to improve the flavour of medications and increase patient compliance by masking the unpleasant taste or odour of dose forms.

1. ROSE OIL

- Synonym: Otto of rose, Attar of rose, Rose essence.
- Biological source: Rosa damascena, R. centifolia, and other fresh flowers are used to distil the volatile oil that makes up this product.family- Rosaceae.
- Description: Rose oil is a colourless or yellow liquid with the unmistakable rose odour that is miscible in 1ml of chloroform.
- Chemical test: Equal parts of 90% alcohol and rose oil are mixed. At 20°C, it takes five minutes to deposit crystals.
- Use: fragrance, flavouring, moisturises dry skin, treats acne, fades scars, and treats eczema.



2. LEMON OIL

- Synonym: Limbu, oleum limonis
- Biological source: produced from ripe, zesty lemon fruits that have just been peeled,
- Family- Rutaceae.
- Description: A watery, pale greenish-yellow colour with a crisp, fresh smell and unpleasant flavour.
- Chemical test: Chemical analysis reveals that the mixture of lemon oil and three volumes of alcohol is neutral to slightly acidic.
- Use; cure flu, bronchitis, asthma, constipation, dyspepsia, throat infections, and fever.

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APPLICATION OF HERBAL EXCIPIENT

- Natural excipients are employed in a range of industries to express biologically active molecules that have been hindered by synthetic components since they are harmless, low expensive (economic), and easily accessible.
- The excipients' roles in the prepared product have a direct bearing on its quality.
- Excipients are substances that aid in the function of active molecules but have no therapeutic value. (23)
- On the other hand, "natural excipients" are any ingredient originating from natural resources that is purposefully added to the formulation of a dosage form.
- Natural substances have been utilised since ancient times. Direct plant parts and extracts from a variety of medicinal flora are used in the Indian traditional medical system known as Ayurveda to treat a large range of illnesses.

- Before introducing synthetic substances, herbal remedies like churn, baati, and bhasma are used.
- Because of their high toxicity or unfavourable effects, synthetic compounds are only used in specific situations and according to specific rules.
- Scientists today prefer to use natural excipients or semi-synthetic compounds whenever possible to boost the efficiency of drugs.
- • The bulk of chemicals that are used as medicines can be found in nature or are created as derivatives from naturally occurring active substances.
- Because they are less or non-toxic, people are also using more natural or herbal products. [24,25]

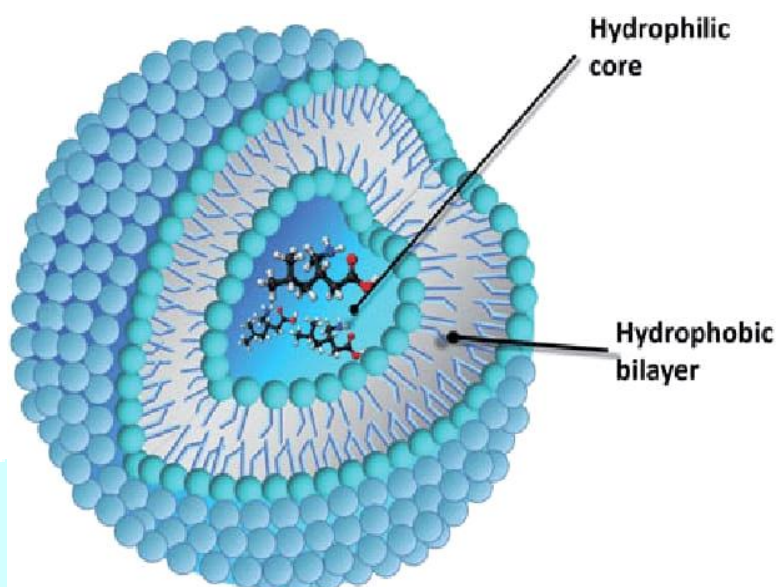
Different types of new herbal formulation currently available in market :

It has been claimed that employing proactive and plant selections, unique herbal formulations such as ethosomes, nanocapsules, polymeric nanoparticles, liposomes, emulsions, and microspheres have been created. The new plant active formulas and extracts are said to possess notable advantages over traditional formulations, including improved solubility, bioavailability, and toxicity protection; increased pharmacological activity; increased stability; improved tissue macrophage distribution; sustained delivery; and protection from physical and chemical deterioration. By adding standardised plant extracts or water-soluble phytoconstituents to phospholipids, a major manufacturer of pharmaceuticals and nutraceuticals can create lipid-compatible molecular complexes. This process is known as "phytosomal encapsulation.". By combining the herbal medications into contemporary dose forms, they can be utilised in a more ethical manner with increased effectiveness. Designing new medicine delivery mechanisms for natural components can help achieve this. The current review highlights the state of innovative herbal formulation development and provides an overview of the types of active ingredients, biological activities, and novel formulations' uses. Mouth-dissolving tablets, liposomes, phytosomes, pharmacosomes, emulsions, nanoparticles, microspheres, transfersomes, ethosomes, transdermal drug delivery system (TDDS), and proniosomes are just a few of the various approaches that can be used for new pharmaceutical herbal drug delivery systems.

▪ LIPOsome

The aqueous content of liposomes, which are concentric bi-layered vesicles, is completely encased by a membranous lipid layer bi-layer made primarily of phospholipids (natural or manufactured). The solvents are enclosed inside the liposomes, which are spherical particles with free-floating solvents inside. Because they have a hydrophobic tail and a hydrophilic polar head, phospholipids, the building blocks of liposomes, are amphipathic molecules.

Materials that are both hydrophilic and lipophilic can be contained by liposomes..(27)



Advantages of Liposome

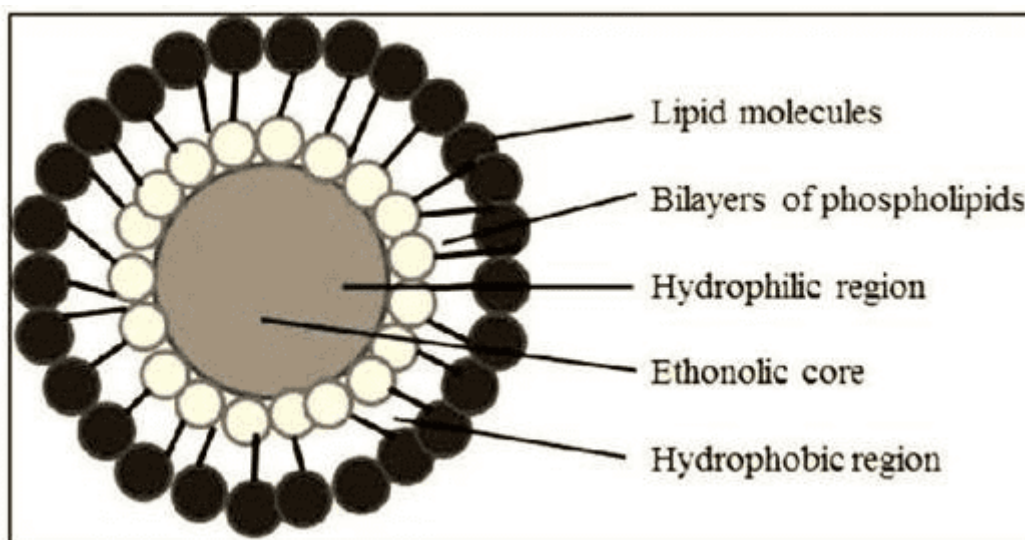
- Liposomal doxorubicin (which offers specific passive targeting to malignant tissues) has amplified efficacy and beneficial index.
- More stability thanks to encapsulation.
- Site avoidance effect; reduction in the toxicity of the encapsulated drugs. 6. Increased effects of pharmacokinetics (reduced elimination, increased circulation life times)
- Flexible pairing with site-specific ligands for active targeting 8. Flexible and biodegradable
- Micro and macro molecules can be included, and medications that are lipid- and water-soluble can be carried (28)

Table 2: Liposome Herbal Formulations(29)

Sr no	Herbal medicine	Chemical classification	Pharmacological activity	Benefit of formulation
1	curcumin	Curcuma longa's root has been separated for its natural polyphenol.	Anti-inflammatory, anti-platelet aggregation, anti-amyloidin, anti-tumor	Improved intravenous delivery of curcumin to tissue macrophages
2	catechins	Polyphenolic plant metabolites abundant in teas resulting from the tea plant Camellia sinensis	Polyphenolic plant metabolites abundant in teas obtained from the tea plant Camellia sinensis	Improved loading and in vivo deposition of catechins

▪ Ethosomes

Phospholipids and highly concentrated ethanol are combined to form ethanosomes. Because it can penetrate the skin deeply, this carrier can increase drug delivery to the skin's deeper layers and blood circulation. These formulations are helpful for topical alkaloids distribution in cream and gel form for patient comfort. They do this by fluidizing the skin's lipid domain, increasing their permeability through the skin. Tropic administration of ethanosomes is constrained by their unstable nature and low skin penetration. The Ethosomes were created and tested for their capacity to deliver tetrandrine topically via skin absorption. The relationship between formulations and the pharmacological activity of tetrandrine loaded in the formulation was also investigated. The results of the drug levels in rat plasma showed that when Tetrandrine loaded Ethosomes were administered topically to rats, the drug level was too low to be detected in rat plasma. Topical treatment may offer positive efficacy with fewer adverse effects by delivering less Tetrandrine into the bloodstream, which could enhance patient compliance. Ethosomes were shown to be a suitable carrier for enhancing topical administration of tetrandrine via the skin [30].



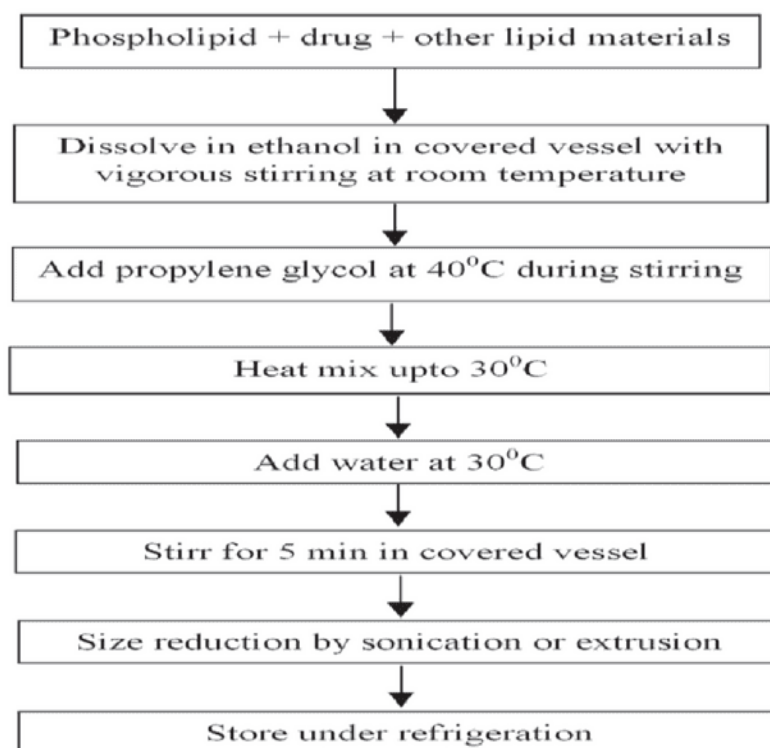
Advantages of Ethosomes[31]

- ❖ Delivery of big molecules, such as protein molecules and peptides, is feasible.
- ❖ The formulation of this product uses non-toxic raw materials.
- ❖ Greater drug absorption through the skin for transdermal medicine delivery.
- ❖ The pharmaceutical, veterinary, and cosmetic industries can all benefit from ethosomal drug delivery systems.
- ❖ Since the ethosomal drug is supplied in semisolid form, high patient compliance is attained (gel or cream).
- ❖ A comparison of a simple drug delivery method with more advanced methods like phonophoresis and iontophoresis
- ❖ The passive and non-invasive Ethosomal system is immediately commercialisable.

Method of preparation

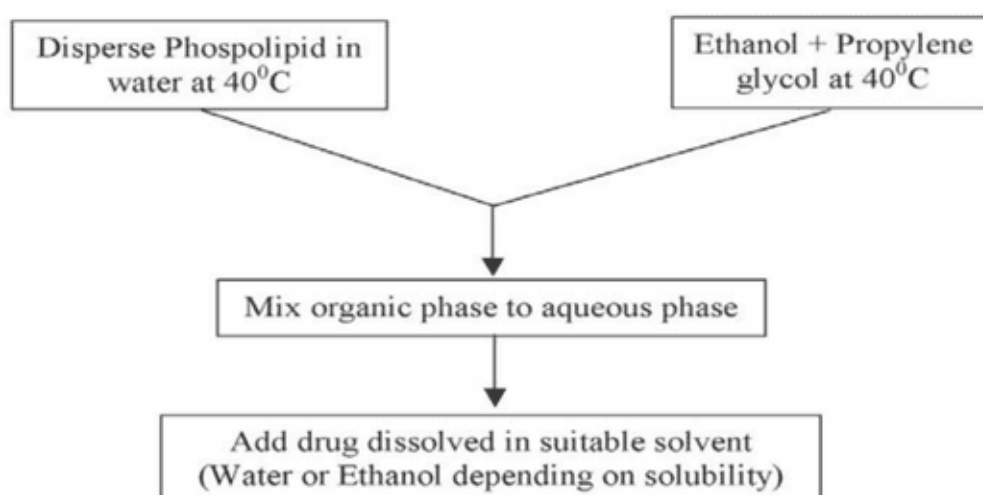
1. Cold Method

This approach is the most well-liked and widely employed one. At room temperature, the ethanol was forcefully swirled in with the phospholipid, medication, and other lipid components. The mixture was cooked to 300 c in a water bath. After adding the mixture, water that had already reached 300 c in another jar was swirled for 5 minutes. The ethosomal formulation's vesicle size was reduced to the desired level by sonication. After that, the formulation was accurately kept.



3. Hot Method

This process involved heating phospholipid in a H₂O bath at 400 degrees until a colloidal solution was produced. The medication and ethanol were combined in a different jar that had been heated to 400 c. The organic phase and aqueous phase were mixed, and five minutes of stirring followed. The ethosomal formulation's vesicle size was sonicated down to the ideal size. Last but not least, the formulation was stored in a safe place. [32, 33].



AUTHORS' CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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