WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Novel Herbal Drug Delivery System

[1]Ms. Pranali Deshmukh, [2]Mr. Junghare S. L.

[1,2]College of Pharmacy Medha.

A B S T R A C T

Throughout the beginning of time, people have utilised plants as food and medicine since they are nature's remedies. The revolutionary drug delivery system, a cutting-edge approach to medication administration, addresses the drawbacks of traditional drug delivery techniques. Using herbal formulations for novel medicine delivery systems is more advantageous and useful than alternative approaches. By incorporating liposome, ethosome, phytosome, emulsion, microsphere, and solid lipid nanoparticles into herbal formulations, the therapeutic benefits of plant extracts have been enhanced. Prior until today, scientists were unable to develop novel medicine delivery techniques because to the difficulties in processing, standardising, extracting, and identifying herbal pharmaceuticals. Yet, modern technology has made it possible to construct herbal medication delivery methods thanks to new drug delivery systems (NDDS). Herbal excipients are plant and plant-based substances that are derived from diverse plant components. Herbal excipients can be utilised to avoid the problems associated with toxicity and chemical incompatibility of synthetic excipients in a variety of drug delivery methods since they are readily available, less costly, stable, and easily biodegradable. Nowadays, natural remedies are used to treat the majority of prevalent illnesses and nutritional issues. Phytosomes are freshly developed herbal formulations that have superior bioavailability and effects than traditional phyto molecules or botanical extracts because they are more readily absorbed. During the past several years, significant progress has been achieved in the creation of innovative drug delivery systems (NDDS) for anticancer medications. According to reports, the novel formulations have notable advantages over traditional anticancer formulations, including improved solubility, bioavailability, protection from toxicity, pharmacological activity, stability, improved tissue macrophage distribution, sustained delivery, and protection from physical and chemical degradation.

Keywords: herbal formulations, Herbal excipients, drug delivery methods, NDDS.

1. INTRODUCTION

1.1. Necessity of NDDS in herbal drugs

To maximise patient compliance and prevent repetitive administration, phytotherapeutics require a systematic way to administer the components over time. Designing NDDSs for herbal components can help achieve this. NDDSs serve to boost therapeutic value by lowering toxicity and raising bioavailability, which reduces the need for repeated dosing to overcome noncompliance.(1)

Herbal medications offer several benefits over conventional ones, including a decreased risk of adverse effects, wider accessibility, cheap cost, and sustained efficacy for chronic illnesses of the lifestyle. If the cutting-edge medication delivery technology is used in herbal medicine, it might improve the effectiveness and lessen the negative effects of different herbs and herbal compounds. A new method of medication delivery is called a novel drug delivery system. By integrating the medication into a carrier system or by altering the drug's molecular structure, the distribution of the drug can be controlled to act longer and more effectively.(2) Novel drug delivery system attempts to eliminate all the disadvantages associated with conventional drug delivery systems.Thus it is important to incorporate the novel drug delivery system in Indian Ayurvedic medicines to combat serious diseases. (3)

By just administering the medication to the area of the patient's body that is sick, new herbal drug carriers treat specific ailments. NDDS is useful in that it releases the herbal medication at a predefined pace and delivers the medication directly to the area of action, minimising the harmful effects while increasing the bioavailability of the medication. (4)

Table No. 1. Selection of Herbal Drug and Novel Drug Delivery System(5)

Sr. no	Herbal Drug	Biological Source	Drug Delivery system
1.	Curcumin	Root of curcuma longa	Phytosomes
2.	Silymarin	Fruits of silybum marianum	Liposome
3.	Vincristine	Catharanthus roseus	Transferosomes
4.	Podophyllotoxin	Podophyllum hexandrum	Ethosomes
5.	Ginseng	Root of genus Panax	Nanoparticles

6.	**Green Tea**	**Camellia sinensis**	**Phytosomes**

1.2. Advantages (5)

1. The novel herbal drug delivery system can be used to achieve site specificity.
2. Novel drug delivery system enhances the surface area of the drugs, therefore allows quicker absorption and rapid onset of action.
3. The enhanced penetration of nanoparticles through the Blood Brain Barrier (BBB).
4. Providing high efficacy.
5. Enhanced stability.
6. Reduce undesirable effects and toxicity.
7. Long-term stability by protecting plant activities from degradation.
8. Decrease allergic potential of herbal substances.
9. Improved solubility & bioavailability.
10. Controlled drug delivery.

1.3. Disadvantages(6)

1. Physical instability.
2. Leaking of entrapped drugs.
3. There are limits on bio acceptability.
4. Effects may be unpredictable.
5. Lack of regulation.
6. Takes longer time to show results.
7. If you are on medicine some can cause adverse effects.

1.4 Current challenges in upgrading and modernization of herbal formulations (7)

The objective evaluation of contradictory toxicological, epidemiological, and other data as well as the validation of herbal materials employed present significant challenges. These significant problems continue.

- Management within ranges of risk
- Communication of uncertainty
- Pharmacological, toxicological, and clinical documentation
- Pharmacovigilance
- Understanding why addition of harmful additives works
- Evaluating “drug” interactions
- Constraints with clinical trials and people available
- Standardization
- Safety, and efficacy assessment.

2. APPROACHES IN HERBAL DRUG DELIVERY SYSTEM

These systems are dominated by Cosmetochem and Indena, two businesses. Cosmetochem introduces Herbasec® technology, which are liposomal formulations of different herbal constituents such extracts of White tea, Green tea, White hibiscus, Guarana, and Aloe Vera, onto the market for the delivery of herbal drugs.(8) These extracts are used in cosmetics because of their anti-oxidant effects for prevention of aging. Indena patented the technology of phytosomes and launched many products in the market under this having diverse therapeutic benefits. Indena commercializes the plant constituents/extracts of liquorice (18ß-glycyrrhetinic acid), Ammi visnaga (visnadine), Centella asiatica (triterpenes), G. biloba (ginkgo flavone

glycosides, ginkgolides, bilobalide),Hawthorn flower (vitexin-2″-O-rhamnoside), milk thistle (silymarin and Silybin), horse chestnut (escin ß-sitosterol), Terminalia sericea (sericoside), Panax ginseng (ginsenosides), grape seed (polyphenols), Green tea (polyphenols). (9)

Table No. 2. Novel Herbal Formulations Available In Market (10,11)

Product	Daily dose	Indication
Grape Seed Phytosomes	50-100mg	Specific for the eyes ,lungs ,diabetes and protection against heart diseases.
Green Tea Phytosomes	50-100mg	Best choice for protection against cancer.
Ginkgo Biloba Phytosomes	120mg	Best choice for geriatric patient. Protects brain and vascular lining.
Siliphos	120mg	Gives antioxidant protection
Milk thistle	150mg	Good choice when the liver or skin only needs minor support.

2.1 LIPOSOMES

2.1.1 Introduction (12)

Vesicles known as liposomes can have a lot, a little, or only one phospholipid bilayer inside of them. Polar medicinal molecules can be encapsulated due to the liposomal core's polar nature. Depending on their affinity for phospholipids, amphiphilic and lipophilic compounds are solubilized inside the phospholipid bilayer. Bioactive substances contained within liposomes are shielded to varied degrees from quick dilution or degradation, proposing the use of drug carrier systems to deliver medications and other bioactive compounds to disease-affected tissues. For both hydrophilic and hydrophobic medicines, liposomes' singular capacity to entrap pharmaceuticals in both an aqueous and a lipid phase makes them desirable delivery platforms.

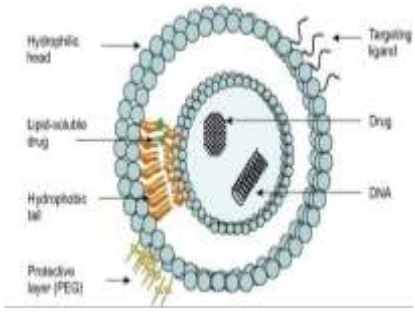


Fig 1. Liposomes

2.1.2. Methods of preparation (13)

All the methods of preparing the liposomes involve four basic stages:

- Drying down lipids from organic solvent.
- Dispersing the lipid in aqueous media.
- Purifying the resultant liposome.
- Analyzing the final product.

2.2.3. Advantages of liposome formulation (13)

- Hydrophobic and hydrophilic drugs can be delivered.
- Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as a vehicle for macromolecules as genes.
- Sustained and controlled release of formulation can be possible.
- The high biocompatibility.
- The ease of preparation.

2.2.4. Disadvantages of liposome preparation

- Low solubility
- Leakage and fusion of encapsulated drug/molecules
- Production cost is high
- Fewer stables
- Sometimes phospholipids undergoes oxidation and hydrolysis-like reaction (14)
- Short half life.(15)

2.2 PHYTOSOMES

2.2.1. Introduction (16)

A stoichiometric quantity of the phospholipid (phosphatidylcholine) reacts with a standardised extract or polyphenolic component (such as simple flavonoids) in a nonpolar solvent to form phytosomes. A bifunctional substance, phosphatidylcholine has a hydrophilic choline moiety and a lipophilic phosphatidylcholine moiety. The phosphatidylcholine molecule's choline head specifically attaches to these substances, and the lipid-soluble phosphatidyl part, which includes the body and tail, envelops the choline-bound material. As a result, the phytoconstituents generate a phyto-phospholipid complex, also known as a lipid-compatible molecular complex with phospholipids. The gastroprotective feature of phosphatidylcholine, which is produced by the phytosome technique, prevents the plant extract or its active ingredient from being destroyed by stomach secretions and gut microbes.

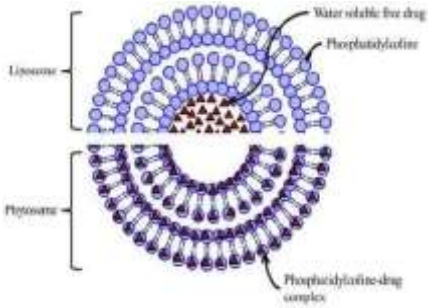
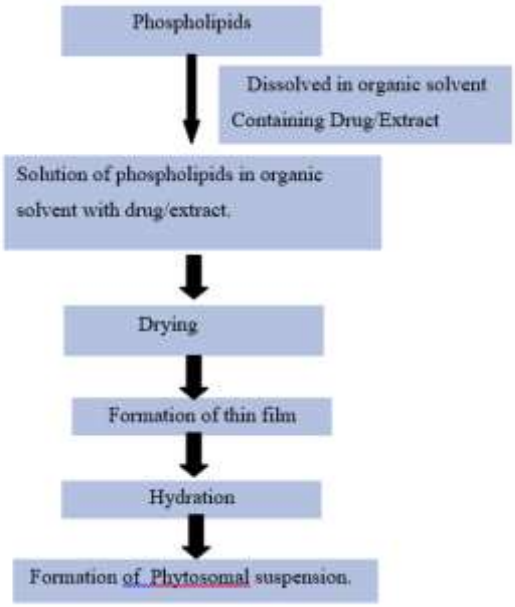


Fig 2. Phytosomes

2.2.2. Methods of preparation (17)



2.3.3 Advantages on phytosome formulation (17)

- Increased bioavailability due to phospholipid complex.
- Improved absorption in GIT.
- Increased bioavailability causes improved therapeutic effect.
- Less dose requirement due to high bioavailability.
- Higher stability.
- High lipophilicity causes high penetrability, henceforth used in cosmetics over liposomes
- Greater clinical benefits.
- Phosphatidylcholine acts as liver protective other than a carrier.

2.2.4. Disadvantages of phytosome formulation

- Phytoconstituents is quickly eliminated from phytosomes.(18)
- phospholipids (lecithin) can provoke the proliferation on MCF-7 breast cancer cell line
- Phytosomes could rapidly eliminate the phytoconstituents(19)

2.3. NIOSOMES

2.3.1. Introduction (20)

A non-ionic surfactant-based liposome is known as a niosome. Cholesterol is primarily used as an excipient in the formation of niosomes. Excipients can also be used in other ways. Niosomes are more capable of penetrating than earlier emulsion formulations. While they share a bilayer with liposomes architecturally, niosomes are more stable due to the materials employed in their preparation, and as a result, they have many more benefits than liposomes. Niosome sizes are minuscule and fall into the nanometric range. The range of particle sizes is 10 nm to 100 nm.

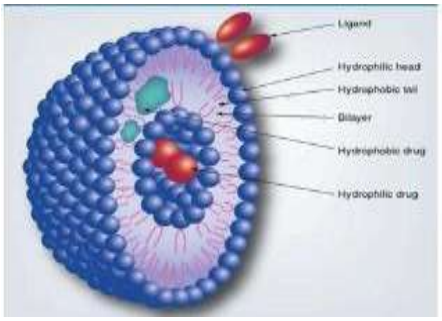


Fig 3. Niosomes

2.3.2. Methods of preparation (20) Ether injection method

By gradually adding a solution of surfactant dissolved in diethyl ether to warm water kept at 60°C, this technique offers a way to create niosomes. A 148 gauge needle is used to inject the ether-surfactant combination into the material's aqueous solution. Ether vapourization results in the creation of vesicles with only one layer. The diameter of the vesicle varies depending on the parameters utilised, from 50 to 1000 nm.

Surfactant is dissolved in diethyl ether

⬇

Then injected in warm water maintained at 60oC through a 14 gauge needle

⬇

Ether is vaporized to form single layered niosomes.

2.3.3. Advantages of niosomal formulations (20)

- They are osmotically active and stable.
- They increase the stability of the entrapped drug
- Handling and storage of surfactants do not require any special conditions
- Can increase the oral bioavailability of drugs
- Can enhance the skin penetration of drugs
- They can be used for oral, parenteral as well as topical.
- The surfactants are biodegradable, biocompatible, and Non-immunogenic.
- Improve the therapeutic performance of the drug by protecting it from thebiological environment and restricting effects to target cells, thereby reducing the clearance of the drug.

2.3.4. Disadvantages of niosomal formulations (21)

- Physical instability
- Aggregation
- Fusion
- Leaking of entrapped drug
- Hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.

2.4. ETHOSOMES

2.4.1. Introduction (22)

Alcohol (ethanol or isopropyl alcohol) is present in relatively high concentrations (20–45%) in phospholipids, water, and soft, flexible lipid vesicles called ethosomes. Touitou and her associates created ethosomes for the first time in 1997. Due to its great degree of deformability, this carrier exhibits intriguing characteristics that are connected with its capacity to pass intact through human skin. These vesicular phospholipids are the vesicle-forming part of the ethosomal system according to the physicochemical properties of ethosomes. In quantities ranging from 0.5-10%, phospholipids with different chemical structures, such as phosphatidylcholine (PC), hydrogenated PC, and phosphatidylethanolamine (PE), are utilised.

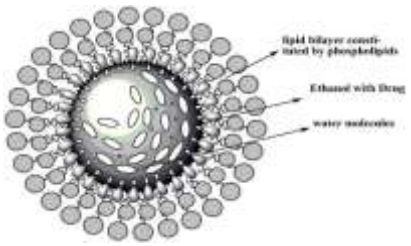


Fig .3. Ethosomes

2.4.2. Methods of preparation (22)

- Cold Method
- Hot Method
- Classic mechanical dispersion method

2.4.3. Advantages of ethosomes formulation (22)

- Enhanced permeation of drug through skin for Transdermal drug delivery.
- Delivery of large molecules (peptides, protein molecules) is possible.

- It contains nontoxic raw material in Formulation.
- High patient compliance the ethosomal drug Is administered in semisolid form (gel or Cream) hence producing high patient Compliance.
- Ethosomal drug delivery system can be Applied widely in Pharmaceutical, veterinary, cosmetic fields.

2.4.4. Disadvantages of ethosomes formulations (23)

- Poor yield .
- In case if shell locking is ineffective then the ethosomes may coalesce.
- Might not be economical.
- Loss of product during transfer from organic to water media.

2.5. MICROSPHERES

2.5.1. Introduction (24)

Small, spherical particles known as microspheres generally have diameters between one and one thousand micrometres. Microparticles are another name for microspheres. Many organic and synthetic materials can be used to make microspheres. Commercially accessible microspheres include glass, polymer, and ceramic ones. Microspheres, both solid and hollow have a wide range of densities and are employed in many applications. Since they make procedures like cell sorting and immune precipitations easier, polystyrene microspheres are often employed in biomedical applications.

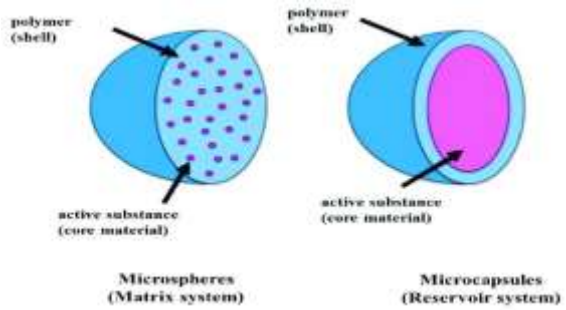


Fig 5. Microspheres

2.5.2. Methods of preparation (24)

- Spray Drying
- Solvent Evaporation
- Single emulsion technique
- Phase separation coacervation technique.
- Spray drying and spray congealing.
- Solvent extraction.

2.5.3. Advantages of microspheres (25)

- Microspheres provide constant and prolonged Therapeutic effects.
- Reduces the dosing frequency and thereby improves patient compliance.
- They could be injected into the body due to the Spherical shape and smaller size.
- Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects.

2.5.4. Disadvantages of microspheres (25)

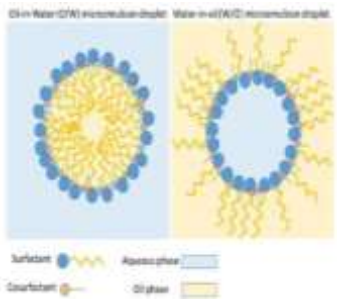
- The modified release from the formulations.

- The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit through the gut.
- Differences in the release rate from one dose to another.
- Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the Release characteristics of the dosage form may lead to potential toxicity.

2.6. MICROEMULSION

2.6.1. Introduction (26)

If the surfactant with balanced hydrophilic and lipophilic qualities is used at the proper concentration, an unique oil and water system will be generated. The system is still an emulsion, but it has characteristics that set it apart from the milk emulsions mentioned before. "Micro-emulsions" are what these are.



2.6.2. Advantages of microemulsion (26)

- Microemulsions are ready and require no energy during preparation due to the improvement of thermodynamics stability.
- Microemulsion creation can be reversed. At low or high temperatures, they can be unstable, but the microemulsion reforms when the temperature returns to stability.
- The thermodynamically stable system of microemulsions allow the system to self emulsify.
- Compared to emulsions, microemulsions have low viscosity.
- The capacity to take lipophilic and hydrophilic medicinal products.

2.6.3. Disadvantages of microemulsion systems (27)

- Having limited solubilizing capacity for high- melting substances.
- Require a large amount of Surfactants for stabilizing droplets.
- Microemulsion stability is influenced by environmental parameters such as temperature and PH.

3. HERBAL EXCIPIENTS

3.1. Introduction to excipients (28)

The material utilised as a vehicle for administering a medication is referred to as an excipient. Natural polysaccharide polymers are specifically used in pharmaceutical formulations to support or protect stability, bioavailability, or patient acceptability during manufacturing, support product identification, or improve any other aspect of the overall safety, effectiveness, or delivery of the drug during storage or use. The pharmaceutical industry uses a variety of plant-based excipients such as starch, agar, alginates, carrageenan, guar gum, xanthan gum, gelatin, pectin, acacia, tragacanth, and cellulose as colloids, thickening agents, gelling agents, bases in suppositories, stabilisers, and coating materials as well as binding, disintegrating, sustaining, and protective agents. Plant sources can provide continuous availability of raw materials since they are renewable and can be grown or collected in a sustainable way.

3.2. Classification of herbal excipients (29)

Excipients are commonly classified according to their application and function in the drug products:

- Binders .

- Diluents, Fillers .
- Lubricants, Glidants , Disintegrants .
- Plasticizers, Colouring agents.
- Suspending agents, Preservatives, antioxidants.
- Flavorings, Sweeteners, Taste improving agents.
- Printing inks, Dispersing agents ,Gums.

3.2.1. BINDER (30)

Binder excipients are designed to function as an adhesive, holding powders, granules, and other dry components together in order to give the completed product extra mechanical strength. Granule formulations that are more reliable and efficient are produced using binders. They can also provide low active dose tablets, which are commonly employed in wet granulation, more volume. Solvents such gelatin cellulose derivatives are used to dissolve solution binders, which are categorised according to their intended purpose. Sucrose and polyethylene glycol are added to polyvinyl pyrrolidone starch. Natural binders include Acacia, Alginic acid, Corn starch, and others.

Fig 7. Binder

3.2.2. DILUENTS AND FILLERS

- **Diluents (30)**

A diluting agent is a diluent (also known as a filler, diluent, or thinner). Certain liquids can't simply be pumped because they are either too thick to move from one area to another or too viscous. As it might not be advantageous to transmit these fluids in this form, this might be troublesome. Diluents are used to aid with the reduced movement. As a result, both the price of pumping and shipping and the viscosity of the fluids are reduced. Some examples of natural diluents include: cellulose, lactose, mannitol, starch, etc.

Fig 8. Diluents

- **Fillers (30)**

Filler excipients are used to expand the material and make it simpler to process so that it may be created in a size that is acceptable for consumption. They can help with both product stabilisation and production. Filler and diluent are used in a variety of dosage forms, including tablets, pills, pellets, paste, solutions, suspensions, and emulsions.

Examples of natural fillers are – Plant cellulose, Gelatin, Lactose, Sucrose, Glucose etc .

3.2.3. LUBRICANTS, GLIDANTS AND DISINTEGRANTS

- **Lubricants (31)**

By adding certain compounds, lubrication serves the objective of facilitating a smooth procedure. Lubricants are used to keep materials from clumping together while the formulation process is being carried out. They keep the formulation's stickiness while reducing friction between the particles and the processing machinery. Like solid dosage forms, they are included into formulations in minute amounts. Since they lessen particle-to-particle friction, lubricants improve product flow.

Examples: stearic acid, sodium stearyl fumarate,castor oils, sodium chloride, and paraffin oil.

- **Glidants (31)**

To enhance the flow of the tablet-core mix material, glideants are used into the formulation. During the initial phases of compression, glideants are added to the particle configuration of the tablet powder mix to improve flowability and uniformity inside the die cavity of tablet presses. Talc has a concentration restriction because of its retardant influence on the dissolution-disintegration profile, despite the fact that it is regarded to be a superior glidant than starch. Glidants make it easier for tablet granulation to flow by reducing friction between particles.

- **Disintegrant (32)**

Disintegrants are added to oral solid dosage forms to help in deaggregation. Disintegrants are substances that are intended to swiftly dissolve solid dosage forms when they come into contact with moisture.

Fig 9. Disintegrant

3.2.4. PLASTISIZERS AND COLOURING AGENTS

- **Plasticizers (32)**

Plasticizers are chemicals that are applied to materials to make them softer and more flexible; certain plasticizers are better than others at this.

- **Colouring agents (32)**

• Natural dyes derived from plants, such as berries, flowers, bark, leaves, seeds, and so on (e.g. Catechu, Indigofera , Myrobalan and Pomegranate).

• Insect-derived natural colours such as cochineal and lac.

• Animal-derived natural dyes, such as mollusk, murex snail, cuttlefish, and shellfish.

• Mineral-based natural colours such as clay, ochre, and malachite**.**

3.2.5. SUSPENDING AGENT, PRESERVATIVES AND ANTIOXIDANTS

- **Aqueous suspending agents (33)**

Gums serve as agents of suspension. They successfully stabilise the emulsion by surface absorption, which leads to the formation of a condensed film with a high durability and resistance to 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 slows the coalition.

- **Preservatives (32)**

Chemical substances known as preservatives can be found in the food, cosmetics, and pharmaceutical industries. They are included into formulation to prevent microbial growth from causing product deterioration. Also, they stop the harmful chemical changes from happening. The two types of preservatives that are most frequently utilised are antioxidants and antimicrobial preservatives.

- **Antioxidants (32)**

A substrate known as an antioxidant prevents molecules within a cell from oxidising. It is a well-known chemical process that enables the removal of electrons or hydrogen from a substance. Antioxidants are frequently used as food supplements, and researchers have looked at how well they help shield against illnesses like cancer and heart disease.

3.3. Advantages and disadvantages of herbal excipients

3.3.1. Advantages (28)

1. Biodegradable – Naturally occurring polymers produced by all living organisms. They show no adverse effects on the environment or human beings.
2. Biocompatible and non-toxic – Chemically, nearly all of these plant materials are carbohydrates in nature and composed of repeating monosaccharide units. Hence they are non-toxic.
3. Economic - They are cheaper and their production cost is less than synthetic material. Safe and devoid of side effects – They are from a natural source and hence, safe and without side effects.

4. Easy availability – In many countries, they are produced due to their application in many industries.

3.3.2. Disadvantages (28)

1. Microbial contamination – During production, they are exposed to the external environment and hence, there are chances of microbial contamination.
2. Variation – Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on the environment and various physical factors.
3. The uncontrolled rate of hydration—Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary.
4. Slow Process – As the production rate depends upon the environment and many other factors, it can't be changed. So natural polymers have a slow rate of production.
5. Heavy metal contamination – There are chances of Heavy metal contamination often associated with herbal excipients.

3.5. Applications of herbal excipients (34)

The biological active agent that has been impeded by synthetic materials is expressed through the use of natural excipients in a variety of industries. Natural excipients have the advantages of being non-toxic, economically priced, and readily available. The excipients' functions are intimately correlated with the finished product's quality. Excipients are chemicals that are internal in nature, distinct from therapeutically active compounds, and which improve the way in which active compounds work. Similarly, natural excipients are any ingredient derived from natural resources that is purposefully included with a dosage form's formulation in addition to the active ingredients. An overview of natural excipients utilised in both conventional dosage forms and cutting-edge drug delivery methods is provided in this article. From ancient times, natural substances have been utilised. Ayurveda is the traditional medical method utilised in India, where a variety of medicinal plants' direct plant parts and extracts are used to cure a wide range of illnesses. In order to increase the effectiveness of substances, modern scientists also favour using natural excipients wherever feasible or semi-synthetic molecules.

4. ANALYTICAL ASPECTS OF NOVEL HERBAL FORMULATION

4.1. Visualization-Visualization of phytosomes can be achieved using transmission electron microscopy and by scanning electron microscopy.

4.2. Particle size and zeta potential- The particle size and zeta potential can be determined by dynamic light scattering using a computerized inspection system and photon correlation spectroscopy.

4.3. Equipment efficiency -The entrapment efficiency of a drug by phytosomes can be measured by the ultracentrifugation technique.

4.4. Transition temperature- The transition temperature of the vesicular lipid systems can be determined by differential scanning calorimetry.

4.5. Surface tension activity measurement-The surface tension activity of the drug in aqueous solution can be measured by the ring method in a Du Nouy ring tensiometer .

4.6. Vehicle stability- The stability of vesicles can be determined by assessing the size and structure of the vesicles over time .The mean size is measured by dynamic light scattering and structural changes are monitored by transmission electron.

4.7. Drug content - The amount of drug can be quantified by a modified high performance liquid chromatographic method or by a suitable spectroscopic method.

4.8. In vitro drug release study by dissolution apparatus- In vitro drug release of the sample was carried out using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was placed into the dissolution flask maintaining the temperature of 37±0.50c and rpm of 50.Equivalent to 100 mg of phytosomes was placed in each bowl of dissolution apparatus. The apparatus was allowed to run for 10 hours. Sample measuring 5 ml were withdrawn after every 1 hour up to 10 hours using 10 ml pipette. The fresh dissolution medium (370C) was replaced every time with the same quantity of the sample. From this take 0.5 ml and dilute up to 10 ml and take the absorbance at 420.0 nm using spectroscopy. (35)

4.9. Excipients compatibility study - The physicochemical compatibility between mixture of extract and polymer used in the research were carried out by infrared spectral studies using Fourier Transform Infrared Spectrophotometer by using KBr dispersion method. The resultant spectrum was compared for any spectrum changes. (36)

4.10. Spectroscopic and chromatographic analysis- The following spectroscopic techniques are employed to verify the development of a complex or investigate the reciprocal interaction between the phytoconstituents and the phospholipid. a) H1 NMR: In nonpolar liquids, the 1H-NMR signal from the atoms involved in the complex's creation changes significantly without any accumulation of the signal specific to each individual molecule. In order to prevent the proton from being released, the signals coming from the flavonoids' protons must be widened. All of the signals in phospholipids expand, but the singlet corresponding to the choline N-(CH3)3 undergoes an upward shift. When the sample is heated to 60°C, some new broad bands arise. These

bands mostly correspond to the resonance of the flavonoids' moietylavonoids, which have to be expanded in order to prevent the proton from being alleviated.. (35)

5. APPLICATIONS OF NOVEL HERBAL DRUG DELIVERY –

Table No 3. Applications of novel herbal drug delivery system (37)

Natural sources	Phytoconstituents complexed	Phytosomal products	Dose and dosage form	Mechanism of action	Utilization
Silybum maranium (Milk Thistle)	Silybin, Silycristin, Isosilbin, silydianin.	Silybin PhytosomeTM (Siliphos®)	120-200 mg Emulsion, gel, lotion and cream.	Prevents the destruction of glutathione in liver	Hepatoprotective, hepatitis, cirrhosis and inflammation.
Panax ginseng (Ginseng)	Ginsenosides	Ginseng PhytosomeTM	150mg	Increases catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase activities and prevents depletion of these antioxidant enzymes.	Nutraceutical, Immunomodulator.
Camellia sinensis (Tea)	Epigallocatechin, catechin, epicatechin-3-O-gallate, Epigallo catechin-3-O- gallate	Green tea PhytosomeTM	400 mg	Inhibits urokinase enzyme which is responsible for increase in tumour size. Enhances the antioxidant mechanisms by increasing the activity of enzymes such as glutathione peroxidase and catalase.	Nutraceutical, Anticancer, Antioxidant, Hepatoprotective, Atherosclerosis, Anticancer, Reduces weight, Antidiabetic, Antiinflammatory.
Gingko biloba (Maiden hair tree)	Gingko flavonoids, Gingoic acids of ginkgoflavon glucosides ginkgolides and bilobalide	Gingko biloba terpene PhytosomeTM	120mg	Ginkgolides inhibits the binding of platelet activating factor to its platelet membrane receptor. Gingko flavonoids inhibit cAMP phosphodiesterase enzymes thus improving lipolysis in fat cells and capillary blood flow.	Antidepressant,cardio protective, dermatitis, soothing, antiinflammatory
Vitis vinifera (Grapes)	Resveratrol, quercitin, catechin, procyanidins, epicatechin.	Biovin and leucoselect PhytosomeTM Masquilier's PhytosomeTM	50-100mg	Reduce the oxidant level and increase antioxidant level and enhance the resistance of LDLs and as a result causes oxidative modification.	Cardioprotective, systemic antioxidant, nutraceutical.
Citrus aurantium (Bitter orange)	Naringenin	Naringenin PhytosomeTM	100 mg/kg	Increase the activity of glutathione peroxidase, superoxide dismutase, catalase.	Antioxidant

6. TARGETED HERBAL DRUG DELIVERY SYSTEM SPECIFICALLY FOR CANCER TREATMENT-PHYTOSOMES DRUG DELIVERY SYSTEM (38)

Many anti-cancer properties of compounds produced from plants have been demonstrated through studies. Herbal extracts' low bioavailability is mostly due to their large molecular size and/or poor lipid solubility, which severely limits their capacity to traverse phospholipid-based cellular membranes. Recent preclinical and clinical investigations have shown that an anti-cancer plant derived molecule, parcelled in an appropriate herbal delivery vehicle, such as nano-phytosomes, might overcome these obstacles. Nevertheless the poor absorption of herbal extracts hinders their clinical applicability in cancer therapy.

6.1. Silibinin phytosome -

Glycyrrhizic acid and silibinin, two plant-based anti-cancer drugs, were encapsulated in nano-phytosomes by Ochi et al. to increase their low bioavailability, and their effects on hepatocellular carcinoma (HCC) cell lines were assessed (HepG2). A naturally occurring substance derived from silymarin, silibinin, has been shown to have anti-cancer properties by lowering N-nitrosodiethylamine in hepatocellular carcinomas. A herbal remedy called glycyrrhizic acid, which is derived from the plant Glycyrrhiza glabra (L.), has been shown to have anti-cancer properties due to its potent MMP inhibitory properties and ability to protect DNA in malignant cells. The use of phytosomes increased the bioavailability of silibinin, and the co-encapsulated systems they might produce—made possible by glycyrrhizic acid's synergistic actions—improved the therapeutic benefits of silibinin. Current research has shown that combining silibinin with other anticancer medications increased its effectiveness against prostate cancer (e.g. Doxorubicin , Mitoxantrone and Cisplatin,, Carboplatin etc.)

6.2. Sinigrin phytosome

The care of malignant wounds, particularly those caused by skin malignancies, is crucial for maintaining human health. We value medicines for treating wounds that also have cytotoxic effects on cancer cells. Sinigrin, a naturally occurring substance and one of the main glucosinolates, is derived from the Brassicaceae family and has been shown to have anticancer properties. In a ground-breaking work, Mazumder et al. investigated Sinigrin's phytosome formulation anti-cancer activities on A-375 melanoma cells while also studying the wound healing benefits of Sinigrin on the normal human keratinocytes cells (HaCaT). This study demonstrated that phytosomes that were sinigrin-loaded might effectively enhance the therapeutic benefits of phytosomes in the treatment of cancer and cancerous wounds.

6.3. T.arjuna phytosomes-

T. arjuna (TA), a Combretaceae family member, possesses antimutagenic and anti-cancer properties in its bark. The primary issue limiting the therapeutic use of TA bark extract is poor bioavailability. Shalini et al. produced nano phytosome complex of methanolic extract of TA bark (its size range between 30 and 80 nm) and studied its antiproliferative activity on human breast cancer cell lines in order to overcome the low bioavailability of TA (MCF-7).

6.4. Mitomycin phytosomes-

Natural substance mitomycin C (MMC), which has an aziridine ring and a carbamoyl chain, has powerful anticancer properties and is thus used to treat many malignancies. The primary barrier preventing MMC from being used clinically is its quick absorption into systemic circulation, which lowers the plasma concentration of medicines at the effect-relevant sites and, as a result, lessens MMC's therapeutic benefits. Hou et al. created a delivery strategy of mitomycin C-soybean loaded phytosomes PC (MMC SPC) complex with a mean particle size of 210 nm to get over this issue.

6.5. Luteolin phytosomes-

Due to its ability to potently inhibit the Nrf2 (Nuclear factor erythroid 2 related factor 2) signalling pathway selectively and sensitise non-small lung cancer cell lines to anti-cancer agents, luteolin (Lut), a natural component, has been found to have anti-cancer activities by acting on multiple molecular targets to kill cancer cells. The high level of Nrf2 expression in cancer cells and its established function in the development of drug resistance in the fight against the disease. By blocking Nrf2 mediated signalling, Sabzichi et al. made human breast cancer cells more sensitive to the drug doxorubicin (dox). In a nutshell, phytosomes might increase the therapeutic efficacy of dox by strengthening the action of luteolin on the inhibition of Nrf2 by increasing its bioavailability.

6.6. Curcumin phytosomes-

Turmeric is another name for the ancient traditional herb curcuma longa. Curcumin, demethoxycurcumin, and bisdemethoxycurcumin are three naturally occurring hydrophobic polyphenol chemical compounds in turmeric known as curcuminoids having a wide range of pharmacological activity, including beneficial effects on the treatment of various malignancies. Studies have also shown that curcumin has beneficial effects on myeloma cell lines and that it inhibits TNF-.

CONCLUSION -

Several therapeutic potentials are there in plant-based substances or herbal medications, which should be examined using cutting-edge drug delivery technology. This study provides information on the varieties, formulations, applications, and innovative drug delivery systems of herbal medicines as well as on the state of the market at the time of writing. Yet, in order to promote patient compliance and prevent recurrent administration, phytotherapeutics require a scientific methodology to provide the components in a novel way. Designing NDDS for natural compounds can do this. For the delivery of herbal drugs, two businesses, Cosmetochem and Indena, introduce liposomes and phytosomes preparations with a range of therapeutic advantages. Compared to their synthetic cousin, herbal excipients are less costly, easily accessible, and non-toxic. In order to have better materials for drug delivery systems, there will continue to be interest in natural excipients in the near future. There are several obstacles to updating and modernising the delivery

system for herbal drugs, including the destruction of forests, a lack of scientific validation and standardisation, a lack of quality and regulatory considerations, and a lack of pharmacokinetic investigations of bioactive compounds. Although there are many different phytosome products on the market, many more phytoconstituents that have a great potential to heal serious illnesses have not been included into phytosome technology. To create phytosomes that are very target-specific, more research may be done**.**

References

1.Vani Mamillapalli, Amukta Malyada Atmakuri, Padmalatha Kantamneni, Nanoparticles of herbal extracts, Asian Journal of Pharmaceutics, 10(2), Apr-Jun 2016,page no.55

2. Shaktipal Patil , Amrapali Mhaiskar,et al, A Review On Novel Drug Delivery System: A Recent Trend, International Journal of Current Pharmaceutical & Clinical Research,6(2),2016,Page no.89

3. V. Kusum Devi, Nimisha Jain, Kusum S. Valli, Importance of novel drug delivery systems in herbal medicines, Pharmacognosy Reviews, 4(7), January-June 2010, Page no.28-29

4. Kharat A, Pawar P, Novel drug delivery system in herbal's, International journal of pharmaceutical, chemical and biological sciences,4(4),2014, page no.911.

5.Sanjida Afrin, Ishrat Jahan, et al, Novel approaches of herbal drug delivery, Journal of pharmaceutical research international, 21(5), 2018, page no 3-7.

6. Bahuguna S. Joshi D., Singh B. and Semwal N.: A review on novel pharmaceutical approaches of herbal drugs in derma care, Dermatol and Cosmet JOJ,4(2),2021,Page no.1.

7. Thillaivanan.S, Samraj.K,Challenges, Constraints and Opportunities in Herbal Medicines – A Review,International Journal of Herbal Medicine , 2 (1),2014,Page no.21-24

8. Shyam Baboo Prasad et.al,International Journal of Current Pharmaceutical Review and Research,4(3),Page no.96

9. Manoj kumar sarangi, Sasmita padhi, Novel herbal drug delivery system: An overview ,Arch med health science,6(1),2018,page no.171-179.

10. Sharma D, Bhujbale AA; Phytosomes is a Novel Drug Delivery System based herbal formulation: An Review; Pharma Tutor , 6(3) ,2018, page no.23-26.

11. Kulkarni Giriraj T, Herbal Drug Delivery System:An Emerging Area In Herbal Drug Research ,Journal of Chronotherapy and Drug Delivery, 2(3),2011,Page no.115

12. Kulkarni et al. Liposomes: A Novel Drug Delivery System,Int J Curr Pharm Res, 3(2), 2018,Page no.10

13. Prajakta N. Dongare, Anuja S. Motule,et al, Recent development in novel drug delivery system for delivery of herbal drugs ..and updates, GSC Advanced Research and Reviews,08(02),2021, Page no.11.

14. Sharma D,Ali AAE,et al,An Updated Review on :Liposomes as drug delivery system,PharmaTutor,6(2),2018,Page no .50-62

15. Kant Shashi et al.A Complete Review on: LIPOSOMES , IRJP 2012, 3 (7), Page no.10

16. Jain et al.,Phytosome: A Novel Drug Delivery System For Herbal Medicine ,IJPSDR , 2010, 2(4), Page no.225

17. Suvarna G. Bhokare, Surekha V. Lahane, et al, Herbal Novel Drug Delivery A Review, World Journal of Pharmacy and Pharmaceutical Sciences,5(8), 2016,Page no.596-597.

18. V, A., Reddy, P.D. and S, R. 2019. Phytosomes : A Promising Technology in Novel Herbal Drug Delivery System. PharmaTutor. 7, 6 (Jun. 2019), 18-25

19. Sharma S et al., Review On Phytosomes: As A Emerging Strategy To Improve The Bioavailability Of Phytoconstituents. American Journal of PharmTech Research 2020.10(5),Page no.124

20. V. Pola chandu, A. Arunachalam, et al, Niosomes : A novel drug delivery system, International journal of novel trends in pharmaceutical sciences, 2(1),2012, Page no.25-28.

21. Sharma D, Ali AAE, Aate JR; Niosomes as Novel Drug Delivery System ,PharmaTutor, 6(3),2018 ,Page no.58

22. Hiraman P. Nandure, Dr. Prashant Puranik, et al, ethosome: A Novel Drug Carrier ,International Journal of Pharmaceutical Research and Allied Sciences,2(3),2013, Page no.20-23.

23. Siddiqua et al.,A Review on Novel Approach of Drug Delivery Ethosomes, World Journal of Pharmaceutical Research,9(5), 2020,Page no.2194.

24. Mahesh Mangnale et al. A Review on Microspheres: Method of Preparation and Evaluation.Ijppr, 20 (3),2021 Page no.486.

25. Sahil Kataria et al. Microsphere: A Review ,IJRPC , 1(4),2011 ,Page no.1186.

26. Vaibhav D Mane, Vipul M. patil, Manisha V. Mane, Sachintumar V. patil. A Review on Microemulsion- A Recent approach for topical drug delivery system, International Journal Of creative Research Thought, 9(7), 2021, page No. 64-65.

27. Verma et al. A Review on Microemulsion for Antifungal Activity, European Journal of Biomedical and Pharmaceutical Sciences,8(1), 2021, Page no.195.

28. Prashant singh, Tarique Mahmood, Arshiya shameem et al, A review on Herbal ExcipientS & their pharmaceutical applications, Sch. Acad. J. Pharm, 5(3) ,2016, page No. No. 53-54.

29. Kaur et al. A Review - Types of Natural Excipients, World Journal of Pharmacy and Pharmaceutical Sciences, 10(3), 2021, Page no.394

30. Nida Mulla, Sanjay Bais,et al,Review On: Herbal Excipients, IJCSPUB, Volume 13(1), 2023, Page no.771-772

31. Alwossabi A, et al. Natural Excipients Applications in Conventional Pharmaceutical Formulations –Part I,Med Aromat Plants (Los Angeles), 10(7), Page No: 3

32. Diksha D. Dherange, et al, Review on: Excipients Used in Herbal Drug Technology, International Journal of research publication & Reviews , 3(2),2022,page no. 466-474.

33. Pal et al.Current Review on Plant based Pharmaceutical Excipients, Open Medicine Journal,6, 2019, Page no.3

34. Verma Poonam, Gupta Sagar,et al,Remarkable Contribution of Natural Excipients in Finished Pharmaceutical Products ,Int. J. Pharm. Sci. Rev. Res., 52(1), 2018, Page no. 7-14

35.Arpita Singh, Anil Pratap Singh, et al, Phytosome: A Revolution in Herbal Drug Delivery system, Asian Journal of Chemistry, 23 (12), 2011, Page no.5190-5191

36. Sarita karole, Girendra kumar Gautam, et al,Preparation and evaluation of Phytosomes containing ethanolic extract of leaves of Bombax ceiba for hepatoprotective activity,The pharma Innovation Journal, 8(2) ,2019 page No. 24.

37. Anupama Singh, Vikas and Saharan, et al, Phytosome: Drug Delivery system for polyphenolic phytoconstituents, Iranian Journal of pharmaceutical sciences, 7(4), 2011, Page No. 209-219.

38. Afshin Babazadeh, Mahdi Zeinali and Hamed Hamishehkar, Nano-Phytosome: A Developing Platform for Herbal Anti-Cancer Agents in Cancer Therapy, Current Drug Targets,19(2),2018, page no.175