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A REVIEW: NOVEL DRUG DELIVERY SYSTEM

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Abstract :

Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Our country has a vast knowledge base of Ayurveda whose potential is only being realized in the recent years. However, the drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. If the novel drug delivery technology is applied in herbal medicine, it may help in increasing the efficacy and reducing the side effects of various herbal compounds and herbs. This is the basic idea behind incorporating novel method of drug delivery in herbal medicines. Thus it is important to integrate novel drug delivery system and Indian Ayurvedic medicines to combat more serious diseases. For a long time herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction and identification of individual drug components in complex polyherbal systems. However, modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on. This article summarizes various drug delivery technologies, which can be used for herbal actives together with some examples.

Keywords:

Herbal medicines, herbs, novel drug delivery system, phytopharmaceuticals

INTRODUCTION

In the past few decades, considerable attention has been centered on the event of novel drug delivery system (NDDS) for seasoning medication. The novel carriers ought to ideally fulfill 2 stipulations. Firstly, it ought to deliver the drug at a rate directed by the requirements of the body, over the amount of treatment. Secondly, it ought to channel the active entity of seasoning drug to the location of action. typical dose forms together with prolonged-release dose forms square measure unable to fulfill none of those. In phyto-formulation analysis, developing nano dose forms (polymeric nanoparticles and nanocapsules, liposomes, solid lipoid nanoparticles, phytosomes and nanoemulsion etc.) have variety of benefits for seasoning medication, together with sweetening of solubility and bioavailability, protection from toxicity, sweetening of medicine activity, sweetening of stability, rising tissue macrophages distribution, sustained delivery,

protection from physical and chemical degradation etc. therefore the nano sized novel drug delivery systems of seasoning medication have a possible future for enhancing the activity and overcoming issues related to plant medicines. Liposomes, that square measure perishable and basically non-toxic vehicles, will encapsulate each deliquescent and hydrophobic materials [1]. vesicle based mostly drug delivery systems supply the potential to reinforce the therapeutic index of anti-cancer agents, either by increasing the drug concentration in neoplasm cells and/or by decreasing the exposure in traditional tissues exploiting increased porousness and retention impact development and by utilizing targeting methods [2]. the most benefits of victimisation liposomes include: i) the high biocompatibility, ii) the easiness of preparation, iii) the chemical skillfulness that enables the loading of deliquescent, amphiphilic, and lipotropic compounds, and iv) the easy modulation of their pharmacokinetic properties by dynamical the chemical composition of the bilayer elements [3]. Delivery of agents to the system (RES) is well achieved, since most typical liposomes square measure unfree by the RES [1]. the appliance of novel approaches may also improve the effectuality of seasoning cosmetic formulations on the anatomy [4]. equally the opposite sac systems like nanoemulsion, ethosomes and transferosomes square measure extremely helpful assemblies and notice varied benefits within the delivery of seasoning medicines; a number of them square measure summarized in gift article.

The phytosome method has conjointly been applied to several well-liked seasoning extracts together with Ginkgo biloba, grape seed, hawthorn, milk weed [5], green tea, and ginseng. The flavonoid and terpenoid elements of those seasoning extracts lend themselves quite well for the direct binding to phosphatidylcholine. Phytosome is made by binding individual elements of seasoning extracts to phosphatidyl B vitamin, leading to a dose kind that's higher absorbed and therefore, produces higher results than the standard seasoning extracts [6]. The results indicate that the absorption of silybin from silybin phytosome is or so seven times bigger compared to the absorption of silybin from regular milk weed extract [5]. medication may be embedded or dissolved in nanoparticles and may even be adsorbable or coupled on the surface [7]. Encapsulating medication among NPs will improve the solubility and pharmacology of medicine, and, in some

cases, alter additional clinical development of recent chemical entities that have stalled thanks to poor pharmacokinetic properties [8]. the main carrier materials of nanoparticles square measure artificial perishable high molecular chemical compound and natural chemical compound. the previous typically includes poly-α-cyanoacrylate alkyl radical esters, polyvinyl alcohol, polylactic acid, and polylacticco-glycolic acid, etc. The latter is typically divided into 2 classes: proteins (albumin, gelatin and vegetable protein) and polysaccharides (cellulose, starch and its derivatives, alginate, polyose and chitosan, etc.) [9].

In this article, an endeavor has been created to the touch upon totally different aspects associated with the event of novel seasoning formulations, together with technique of preparation, style of active ingredient, denial potency, and applications etc.

Types of novel drug delivery system

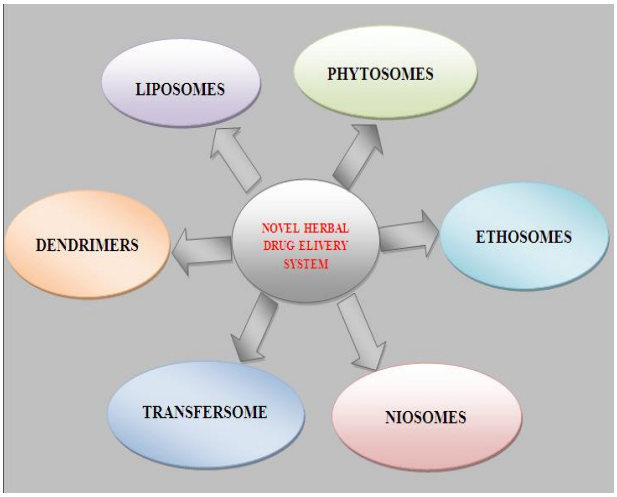


Fig. 1. Novel herbal drug delivery system

1.Liposome

The liposomes are spherical particles that encapsulate a fraction of the solvent, within which they freely diffuse (float) into their interior. they'll have one, many or multiple concentrical membranes. Liposomes are created of polar lipids that are characterised by having a lipotropic and deliquescent cluster on a similar molecules [10]. Upon interaction with water, polar lipids self-assemble and type self-

organized mixture particles. easy examples ar detergents, parts type micelles, whereas polar lipoids with bulkier hydrophobic components cannot associate into micelles with high curvature however type bilayers which might self-close into liposomes or lipid vesicles. A crosswise of a vesicle (Fig. 1) depicts the deliquescent heads of the amphiphile homing towards the water compartment whereas the lipotropic tails orient off from the water towards the middle of the sac, so forming a bilayer. Consequently, water soluble compounds are entrapped within the water compartment and lipoid soluble compounds mixture within the lipoid section. Uniquely, liposomes will encapsulate each deliquescent and lipotropic materials. Liposomes sometimes fashioned from phospholipids, are accustomed modification the pharmacology profile of, not solely medicine, but herbs, vitamins and enzymes. as a result of their distinctive properties liposomes are ready to enhance the performance of merchandise by increasing ingredient solubility, rising ingredient bioavailability, increased living thing uptake and altered pharmacology and biodistribution and in vitro and in vivo stability. Liposomes as a drug delivery system will improve the therapeutic activity and safety of medicine, primarily by delivering them to their web site of action and by maintaining therapeutic drug levels for prolonged periods of your time[11,13]

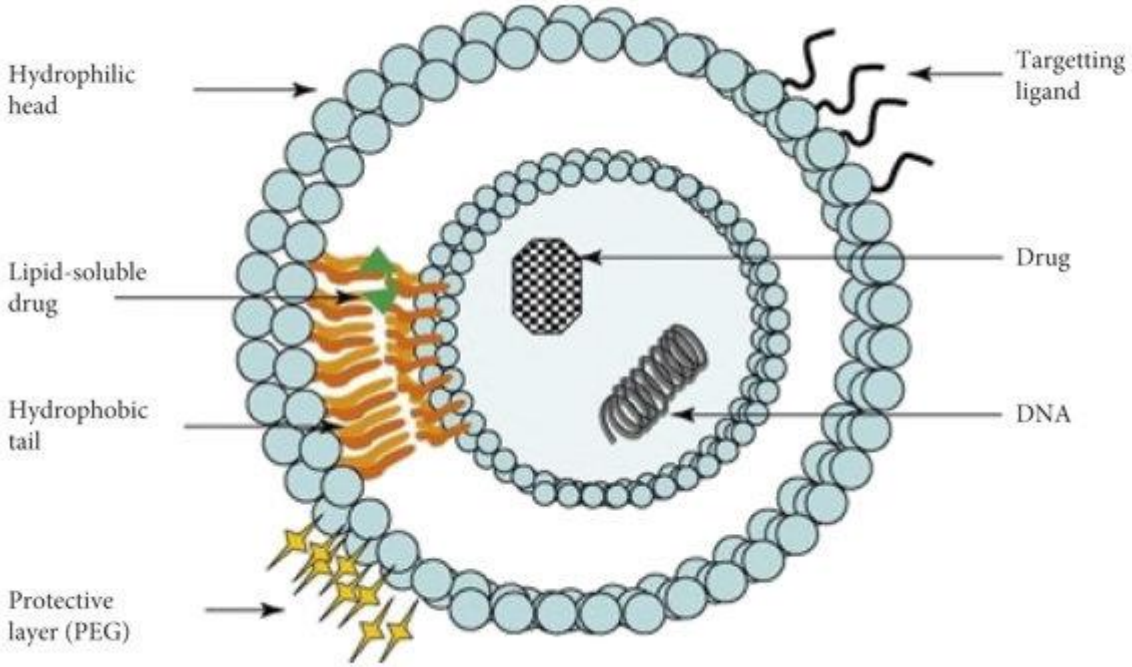


Fig. 2. Liposomes

Table no 1. Liposomal herbal formulations.

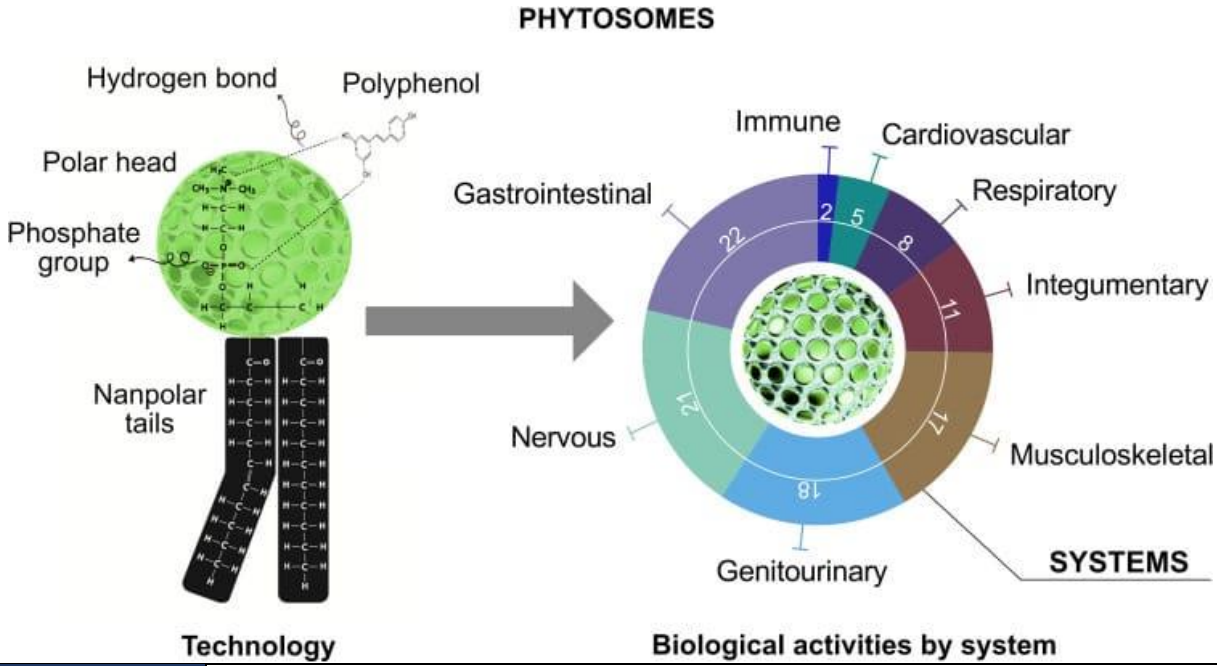
Formulations	Active ingredients	Applications of liposome formulations	Biological activity	Method of preparation	% Entrapment efficiency	Route of administration
Quercetin liposomes	Quercetin	Reduced dose, enhance penetration in blood brain barrier	Antioxidant Anticancer	Reverse evaporation technique	60%	Intranasal
Liposomes encapsulated silymarin	Silymarin	Improve bioavailability	Hepatoprotective	Reverse evaporation technique	69.22 ± 0.6%	Buccal
Liposoma artemisia arborescens	Artemisia arborescens essential oil	Targeting of essential oils to cells, enhance penetration into, cytoplasmatic barrier	Antiviral	Film method and sonication	60–74%	In vitro
Ampelopsin liposome	Ampelopsin	Increase efficiency	Anticancer	Film-ultrasound method	62.30%	In vitro
Paclitaxel liposome	Paclitaxel	High entrapment efficiency and PH sensitive	Anticancer	Thin film hydration method	94%	In vitro
Curcumin liposome	Curcumin	Long-circulating with high entrapment efficiency	Anticancer	Ethanol injection method	88.27 ± 2.16%	In vitro
Garlicin liposome	Garlicin	Increase efficiency	Lungs	Reverse-phase evaporation method	90.77 %	–
Flavonoids liposomes	Quercetin and rutin	Binding of flavonoids with Hb is enhanced	Hemoglobin	Solvent evaporation	–	In vitro
Usnea acid liposome with β-CD	Usnea acid	Incrase solubility and localization with prolonged-release profile	Antimycobacterial	Hydration of a thin lipid film method with sonication	99.5%	In vitro
Wogonin liposome	Wogonin	Sustained release effect	Anticancer	Film dispersion method	81.20 ± 4.20%	In vivo
Colchicine Liposome	Colchicine	Enhance skin accumulation, prolong drug release and improve site specificity	Antigout	Rotary evaporation sonication method	66.3 ± 2.2%	Topical
Catechins liposomes	Catechins	Increased permeation through skin	Antioxidant and chemopreventive	Rotary evaporation sonication method	93.0 ± 0.1	Transdermal
Breviscapine liposomes	Breviscapin	Sustained delivery of breviscapine	Cardiovascular diseases	Double emulsification process	87.9 ± 3.1%	Intramuscular

2.Phytosomes

Phytosomes are complicated of phospholipids and natural active phytochemicals, certain in their structures, obtained by the reaction between phosphatidylcholine (or Associate in Nursingy deliquescent polar head groups)

Fig. 3. Phytosomes

and plant extracts in an aprotic solvent. Phytosomes are originated from the reaction of a ratio amount of the lipide (phosphatidylcholine) with polyphenolic constituents or standardized extracts (flavonoids, tannins, terpenoids, xanthones) among a non-polar solvent.Different solvents are employed in numerous studies as a reaction medium to formulate phyto-phospholipid complexes. In aprotic solvents, no chemical element atoms exist directly connected to Associate in Nursing negative atom and don't have any capability at chemical element bonding. historically, these solvents like aromatic hydrocarbons, chloride, grouping derivatives, cyclic ethers, and ester are used for making ready phyto-phospholipid complexes. However,



these are largely substituted by protic solvents, like ethyl alcohol.38,39 In protic solvents, like wood alcohol and ethyl alcohol, a minimum of one atom is directly connected to Associate in Nursing negative atom. due to the upper yield of complexes, ethyl alcohol is a good solvent additionally because of the low presence of residues. Some liposomal drug complexes act within the existence of solution or water, wherever the interaction of the phytosomes with a solvent happens with a shriveled material constant. yet, the employment of one solvent is enclosed in most preparation strategies, mixed solvent systems are employed in many studies whereby the phospholipids are dissolved in an exceedingly completely different solvent from that of the drug/extract. The mixed solvent systems embrace chloride and methanol, water and diethyl ether, as well as ethanol and dichloromethane.[14,15]

Table no. 2 Phytosomes Herbal Formulations

Formulations	Active ingredients	Applications of phytosomal formulations	Biological activity	Method of preparation	Dose	Route of administration
Ginkgo biloba phytosomes	Flavonoids	Flavonoids of GBP stabilize the ROS	Cardio-protective, antioxidant activity	Phospholipids complexation	100 mg and 200 mg/kg	Subcutaneous
Ginkgoselect phytosome	Flavonoids	Inhibits lipid peroxidation (LPO), stabilize the ROS	Hepatoprotective, antioxidant	Phospholipids complexation	25 and 50 mg/kg	Oral
Silybin phytosome	Flavonoids	Absorption of silybin phytosome from silybin is approximately seven times greater	Hepatoprotective, antioxidant for liver and skin	Silybin-phospholipid complexation	120 mg	Oral
Ginseng phytosome	Ginsenosides	Increase absorption	Nutraceutical, immunomodulator	Phospholipids complexation	150 mg	Oral
Green tea phytosome	Epigallocatechin	Increase absorption	Nutraceutical, systemic antioxidant, anti-cancer	Phospholipids complexation	50–100 mg	Oral
Grape seed phytosome	Procyanidins	The blood TRAP nTotal Radical-trapping Antioxidant Parameter) were significantly elevated over the control	Systemic antioxidant, cardio-protective	Phospholipids complexation	50–100 mg	Oral
Hawthorn Phytosome	Flavonoids	Increase therapeutic efficacy and absorption	Cardio-protective and antihypertensive	Phospholipids Complexation	100 mg	Oral
Quercetin phytosome	Quercetin	Exerted better therapeutic efficacy	Antioxidant, anticancer	Quercetin–phospholipid complexation	–	Oral
Curcumin phytosomes	Curcumin	Increase antioxidant activity and Increase bioavailability	Antioxidant, anticancer	Curcumin–phospholipid complexation	360 mg/kg	Oral
Naringenin phytosomes	Naringenin	Prolonged duration of action	Antioxidant activity	Naringenin–phospholipid complex	100 mg/kg	Oral

3.Ethosome

Ethosomes are ethanolic liposomes". Ethosomes will be outlined as noninvasive delivery carriers that modify medication to succeed in deep into the skin layers and/or the circulation. These are soft, malleable vesicles tailored for increased delivery of active agents. The vesicles are documented for his or her importance in cellular communication and particle transportation for several years. Vesicles would conjointly permit dominant the discharge rate of drug over AN extended time, keeping the drug secure from immunologic response or different removal systems and so be able to unharness simply the proper quantity of drug and keep that concentration constant for longer periods of your time. one in all the main advances in cyst analysis was the finding of a cyst spinoff, referred to as AN Ethosomes[9].Ethosomes are the slight modification of well established drug carrier cyst. Ethosomes are lipide vesicles containing phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water. Ethosomes are soft vesicles product of phospholipids and fermentation alcohol (in higher quantity) and water. the scale vary of ethosomes might vary from tens of nanometers (nm) to microns (μ) ethosomes permeate through the skin layers quicker and possess considerably higher percutaneous flux.[16]

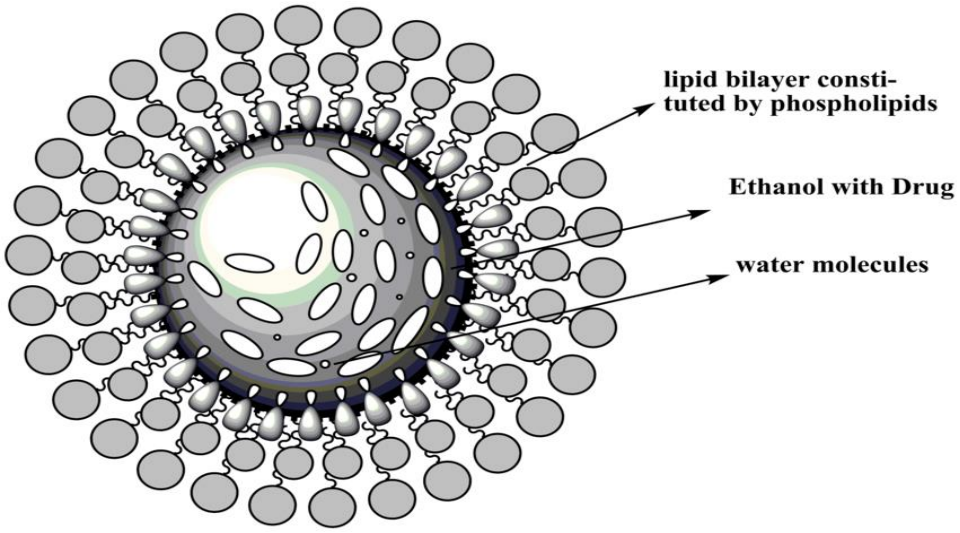


Fig.5. Ethosomes

4.Niosomes

A typical niosome cyst would comprises a cyst forming amphiphilic i.e. a non ionic wetter such as Span-60, that is sometimes stabilised by the addition of cholesterin and a little quantity of anionic wetter like dicetyl phosphate, that additionally helps in helpful the cyst.Compositions of niosomes: [17] he two major elements used for the preparation of niosomes are,

1). cholesterin
2).Nonionicsurfactants

1) cholesterin
Cholesterol could be a steroid by-product, that is employed to produce rigidity and correct form, conformation to the niosomes preparations.

2) Nonionic surfactants
The following non-ionic surfactants are typically used for the preparation of niosomes.
e.g. Spans (span sixty, 40, 20, 85, 80)
Tweens (tween twenty, 40, 60, 80)
Brijs (brij thirty, 35, 52, 58, 72, 76)
The non ionic surfactants possess a hydrophilic head and a hydrophobic tail.

PREPARATION METHODS OF NIOSOMES

Etherinjection methodology
The ether injection methodology is basically supported slowly introducing an answer of wetter dissolved in ether into heat water maintained at 60°C. The wetter mixture in ether is injected through 14-gauge needle into associate solution of fabric. Vaporization of ether ends up in formation of single stratified vesicles. The particle size of the niosomes fashioned rely on the conditions used the diameter of the cyst vary from fifty to a thousand nm.

Hand shaking methodology (thin film association technique): [20]

In this methodology the wetter and cholesterin are dissolved during a volatile organic solvent (such as diethyl either, chloroform or methanol) during a spherical bottom flask. The organic solvent is removed at temperature (20°C) mistreatment rotary evaporator deed a skinny layer of solid mixture deposited on the wall of the flask. The dried wetter film will be rehydrated with binary compound section at 0-60°C with light agitation to yield multilamellar niosomes.

Sonication methodology
In this methodology associate aliquot of drug answer in buffer is else to the surfactant/cholesterol mixture during a 10- cc glass ampoule. The mixture is probe sonicated at 60°C for three minutes employing a sonicator with a metal probe to yield niosomes.

Micro fluidization methodology [22]

Micro fluidization could be a recent technique won't to prepare unilamellar vesicles of outlined size

distribution. This methodology relies on submerged jet principle during which 2 fluidized streams move at immoderate high velocities, in only outlined small channels at intervals the interaction chamber. The impingement of skinny liquid sheet on a typical front is organized such the energy equipped to the system remains at intervals the realm of niosomes formation. The result's a bigger uniformity, smaller size and higher reliableness of niosomes fashioned.

Multiple membrane extrusion methodology

Mixture of wetter, cholesterin and dicetyl phosphate in chloroform is created into skinny film by evaporation. The film is hydrous with binary compound drug polycarbonate membranes, answer and also the resultant suspension extruded through that are placed serial for upto eight passages. it's an honest method for dominant noisome size.

Reverse section Evaporation Technique (REV) [23]

In this methodology, cholesterin and wetter (1:1) ar dissolved during a mixture of ether and chloroform. associate binary compound section containing drug is else to the current and also the ensuing 2 phases are sonicated at 4-5°C. a transparent gel is made that is more sonicated when the addition of phosphate buffered saline (PBS). The organic section is removed at 40°C underneath air mass. The ensuing viscous noisome suspension is diluted with PBS and heated on a water bathtub at 60°C for ten min to yield niosomes.

Transmembranes pH gradient (inside acidic) Drug

Uptake Process: or Remote Loading Technique [23]

A solution of wetter and cholesterin are dissolved in chloroform. The solvent is then

evaporated underneath reduced pressure to induce a skinny film on the wall of the spherical bottom flask. This film is hydrous with 300mm acid (PH four.00) by vertex combination. The ensuing multilamellar vesicles are frozen and shared 3 times and later sonicated. to the current niosomal suspension, solution containing ten mg/ml of drug is else and vortexes. The pH of the sample is then raised to seven.0-7.2 with 1M disodium phosphate. This mixture is later heated at 60°c for ten minutes to present niosomes.

The Bubble methodology [24]

The effervescent unit consists of round-bottom flask with 3 necks, and this is often positioned during a water bathtub to regulate the temperature. cool reflux and measuring system is positioned within the 1st and second neck and atomic number 7 provide through the third neck. cholesterin and wetter are spread along during this buffer (PH seven.4) at 70°C, the dispersion mixed for fifteen seconds with high shear homogenizer and straight off later on “bubbled” at 70°C mistreatment atomic number 7 gas [17]

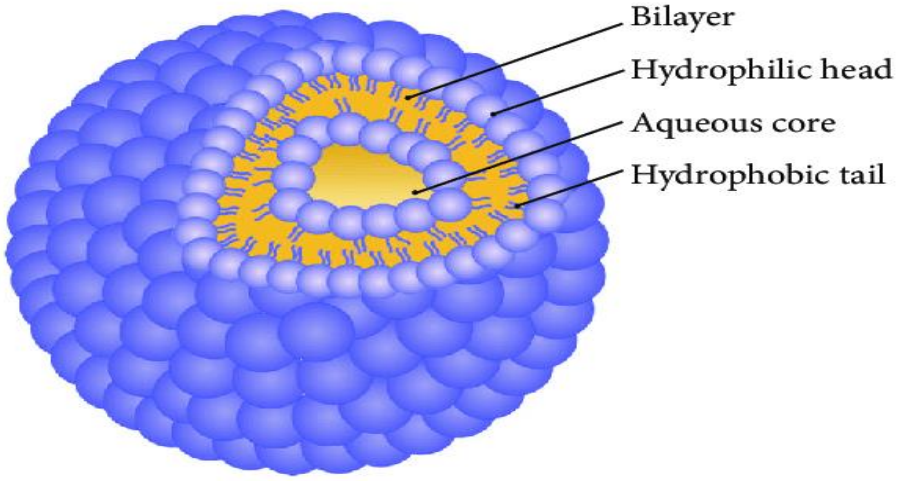


Fig.6. Niosomes

4.Transferosomes

Transfersome may be a term registered as a trademark by the German company plan silver, and employed by it to discuss with its brand-name drug delivery technology. The name means "carrying body", and comes from the Latin word 'transferre', that means "to carry across", and the Greek word "soma", for a "body". A transfersome carrier is a synthetic sac designed to be sort of a cell vesicle or a cell engaged in exocytosis, and therefore appropriate for controlled and, probably targeted, drug delivery. Transferosomes are promising nanocarriers for non invasive stratum delivery. Transferosomes ar ultradeformable vesicles possessing Associate in Nursing binary compound core surrounded by the complicated macromolecule bilayer .Interdependency of native composition and form of the bilayer makes the sac each self-moving and self optimizing one Transferosomes ar capable of stratum delivery of low furthermore as high mass medication two Transferosomes are specially optimized, immoderate versatile lipid above molecular aggregates, that are able to penetrate the class skin intact then act as a drug carrier for non-invasive targeted drug delivery and sustained unleash of therapeutic agents three Transferosomes are mixture carriers that are simply accumulated into the leaky secretion tissue that results in Peripheral targeting. Transferosomes conjointly act as depot leading to controlled drug delivery system. higher drug delivery by transferosomes is because of the drive provided by the diffusion gradient between outer and inner layer of corneum four, thus, they will go through| meet up with| submit to|suffer|taste| tolerate| withstand} the intact skin ad lib under the influence of the naturally occurring in vivo transdermic association gradient. because of their deformability, transferosomes are sensible candidates for the non-invasive delivery of tiny, medium, and huge sized medication.[29,30,31,32]

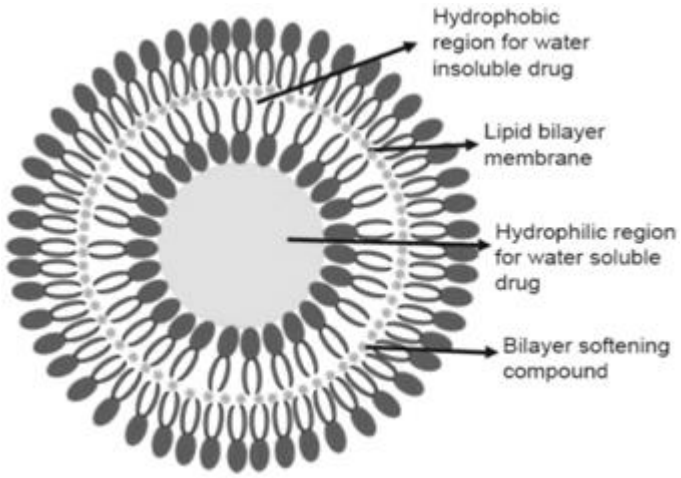


Fig.7. Transferosome

6.Dendrimers

Dendrimers are nano-sized, radially isobilateral molecules with well-defined, uniform, and monodisperse structure consisting of tree-like arms or branches [33]. These hyperbranched molecules were 1st discovered by Fritz Vogtle in 1978, by Donald Tomalia and colleagues within the early Nineteen Eighties, and at an equivalent time, however severally by St. George R. Newkome. The second cluster known as synthesized macromolecules 'arborols' suggests that, in Latin, 'trees'. Dendrimers may additionally be known as 'cascade molecules', however this term isn't the maximum amount established as 'dendrimers' [34-36]. Dendrimers are nearly monodisperse macromolecules that contain isobilateral branching units engineered around a tiny low molecule or a linear compound core [37-39]. 'Dendrimer' is merely associate subject motif and not a compound. Polyionic dendrimers don't have a persistent form and should bear changes in size, shape, and suppleness as a operate of skyrocketing generations [40-42]. Dendrimers are hyperbranched macromolecules with a fastidiously tailored design, the end-groups (i.e., the teams reaching the outer periphery), which might be functionalized, so modifying their chemistry or biological properties [43-48]. Dendrimers have gained a broad vary of applications in supramolecular chemistry, significantly in host-guest reactions and self-assembly processes. Dendrimers are characterised by special options that build them promising candidates for heaps of applications. Dendrimers are extremely outlined artificial macromolecules, that are characterised by a mixture of a high range of practical teams and a compact molecular structure [49]. The rising role of nerve fiber macromolecules for antitumour therapies and diagnostic imaging is exceptional. the benefits of those well-defined materials build them the most recent category of molecule nanoscale delivery devices [50]. nerve fiber macromolecules tend to linearly increase in diameter and adopt a additional globose form with increasing dendrimer generation

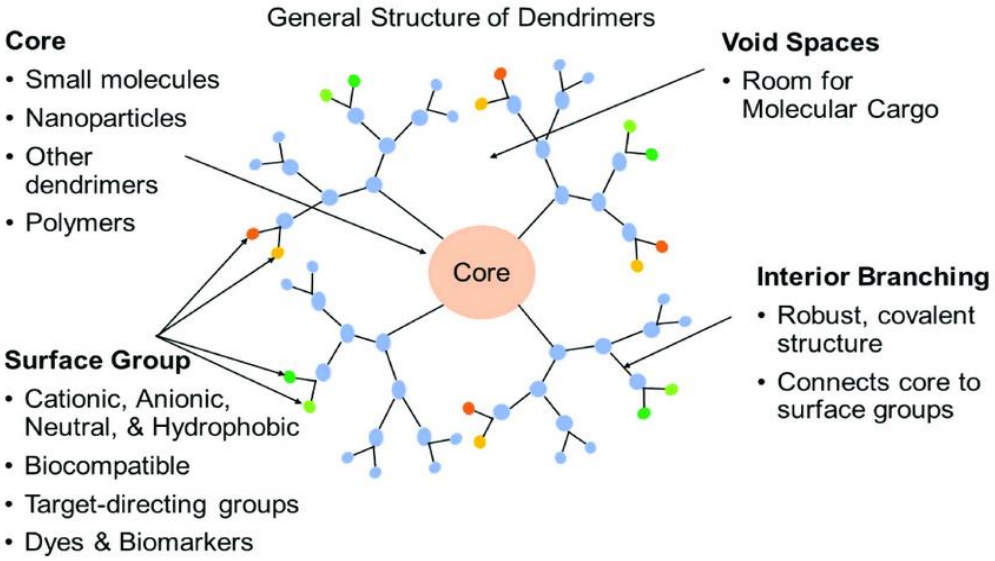


Fig.7. Dendrimers

CONCLUSION

Herbal medication have huge therapeutic potential that ought to be explored through some worth more drug delivery systems. supermolecule solubility and molecular size square measure the main limiting factors for drug molecules to pass the biological membrane to be absorbed consistently following oral or topical administration. many plant extracts and phytomolecules, despite having glorious bio-activity in vitro demonstrate less or no in vivo actions because of their poor supermolecule solubility or improper molecular size or each, ensuing poor absorption and poor bioavailability. Standardized plant extracts or primarily polar phytoconstituents like flavonoids, terpenoids, tannins, xanthones once administered through novel drug delivery system show far better absorption profile that allows them to cross the biological membrane, ensuing increased bioavailability. therefore additional quantity of active constituent becomes gift at the positioning of action (liver, brain, heart, kidney, etc.) at similar or less dose as compared to the traditional plant extract or phytomolecule. Hence, the therapeutic action becomes increased, additional detectable and prolonged. many glorious phytoconstituents are with success delivered exploitation NDDS. therefore there's a good potential within the development of novel drug delivery systems for the plant actives and extracts

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