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A scrutiny on novel herbal drug delivery system (NHDDS)

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Abstract
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, micro emulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on. The present review article was aimed to provide an overview of various novel drug delivery approaches utilized for modification of traditional herbal drugs incorporating botanical active ingredient, biological activities of specific drug, factors affecting their efficiency, methods of preparation of such formulation and their potential advantages.

Keywords: polyherbal, phytopharmaceuticals, pharmacokinetics, novel drug delivery system

Introduction

Plants are nature's remedies and have been used by human beings on earth since ancient times for food and medicine. In the past, almost all the medicines were from the plants; the plant being man's only chemist for ages. Herbal therapy is an ancient science of Indian system of medicine. Traditional formulation contains plant material as its core ingredient [1].
World Health Organization [WHO] has defined herbal medicines as finished, labeled medicinal products that contain active ingredients, aerial or underground parts of the plant or other plant material or combinations. WHO estimates that 80% of the world populations presently use herbal medicine for primary health care [2].

There are three main reasons for the popularity of herbal media [3, 4]

1. There is a growing concern over the reliance and safety of drugs.
2. Modern medicine is failing to effectively treat many of the most common health condition.
3. Many natural measures are being shown to produce better results than drugs or surgery without the side effects.

Most of the plant actives such as glycosides, tannins, flavonoids, etc., are polar molecules and are poorly absorbed due to large molecular size – which limits the absorption via passive diffusion, and poor lipid solubility – which severely limits their ability to cross the lipid-rich biological membranes. These limitations lead to reduced bioavailability and hence, low therapeutic index of plant actives [5, 6].

Novel Drug Delivery System (NDDS) [7, 8]

The new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio recognition, and efficacy of drugs were generated and are often called Novel drug delivery systems [NDDS], which are based on interdisciplinary approach that combine polymer science, pharmaceutics, bio conjugate chemistry and molecular biology. Novel drug delivery systems are designed to achieve a continuous delivery of drugs at predictable and reproducible kinetics over an extended period of time in the circulation.
A successful targeted drug delivery system comprises three elements:

- Orientation cumulation
- Control over drug release
- Non-toxic and biodegradable

Advantages of novel drug delivery system [9]

- Help to increase the efficacy and reduce the side effect of various herbal compounds.
- Quantity of component becomes less with improving quality of drug effect.
- Fewer raw materials are required to achieve the desire effect and control drug delivery to provide exact specification regarding drug dose form.
- Ready to use devices are acceptable in today's fast life style where time is important.
- Carry maximum amount of drug to the site of action by passing all barriers.Such as acidic pH of stomach increase prolong circulation of drug into blood due to their small particle size.
- Reduce repeat dose administration.

Types of NDDS for Herbal Drugs [10, 11]

Various NDDS that have been used with herbal drugs and phytochemicals may be broadly classified into the following groups

1. *Vesicular delivery systems*, which include liposomes, ethosomes, phytosomes, transferosomes, niosomes, proniosomes
2. *Particulate delivery systems*, which include nanoparticles, microspheres, micropellets

3. *Biphasic systems*, such as Micro/ Nano emulsions
4. *Other NDDS*, such as Transdermal Drug Delivery System (TDDS), Polymeric Micelle Formation (PMF), Implants, Dendrimers, Liquid Crystals, Hydrogels etc..,

Vesicular Drug Delivery System [10]

Liposomes

Liposomes are concentric bilayered vesicle in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of natural or synthetic phospholipids. They are an amphipathic molecules having bipolarity in their structure. Average size of liposome varies from 0.05 μ -5.0μ.

A cross-section of a liposome (Fig.1) depicts the hydrophilic heads of the amphiphile orienting towards the water compartment while the lipophilic tails orient away from the water towards the center of the vesicle, thus forming a bilayer. Consequently, watersoluble compounds are entrapped in the water compartment and lipid soluble compounds aggregate in the lipid section.

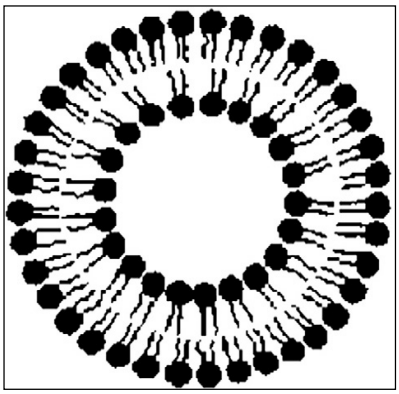

Fig 1: Cross-section of a liposome

A variety of herbal liposomal formulations have been reported for herbal drugs where liposome are able to enhance product performance by solubility enhancement, improving bioavailability, targeting at site of action and prolonged release of drug

Table 1: Liposomal herbal formulations [11]

Formulation	Active ingredients	Applications	Biological activity	Method of preparation
Quercetin liposomes	Quercetin	Reduced dose and enhanced penetration in BBB	Antioxidant and anticancer	Reverse evaporation technique
Triptolide	Diterpene triepoxide	Increase stability and reduce side effects	Anti inflammatory	Thin film depression method
Paclitaxel liposome	Paclitaxel	High entrapment efficiency and pH sensitive	Anticancer	Thin film hydration method
Capsaicin liposome	Capsaicin	Increase in skinpermeation as wellas prolongation ofduration of action	Pain reliever	Reverse evaporation technique
Curcumin Liposome	Curcumin or Diferuloylme thane	Long circulating with high entrapment	Antioxidant and anticancer	Ethanol injection method
Wogonin liposomes	Wogonin	Sustained release effect	Anticancer	Film dispersion
Colchicine liposomes	Colchicine	Enhance skin accumulation and prolong release	Antigout	Rotary evaporation sonication

Advantages

1. Liposome is used for drug delivery systems due to its unique structural properties.
2. Liposome can carry both the hydrophobic and hydrophilic drug. Therefore, liposome as a drug carrier can indiscriminately deliver drugs through the cell membrane.
3. Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as vehicle for macromolecules as gene.
4. Liposome formulation can produce sustained and controlled release of formulation and enhances the drug solubility.

Phytosomes [12]

Phytosome (also called as pharmacosome) may be defined as a neutral molecule possessing both positive and negative charge, water-loving and fat-loving properties, and an optimum ratio of polyphenol with phospholipids in a complex form. There is marked difference between phytosome and liposome; two basic differences are, in phytosome active chemical constituent molecules are anchored through chemical bonds to the polarhead of the phospholipids whereas in liposome, the active principle is dissolved in the medium of the cavity or in the layers of the membrane. No chemical bonds are formed.

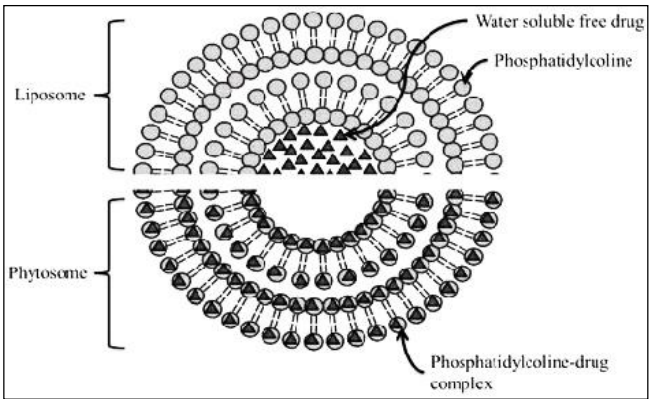

Fig 2: Difference between phytosomes and liposomes [13]

Nanophytosomes, phospholipid complex, or self-assembling bilayer vehicles of phospholipid complexes were established to encapsulate herbal extracts and phytoconstituents with lower water solubility into nano carriers to harvest lipophilic complexes.

Table 2: Phytosomal herbal formulations [14, 15]

Phytosomes	Phytoconstituent complexed	Indication
Silybinphytosome	Silybin	Nutraceutical, hepatoprotective, and antioxidant for skin
Ginkgo phytosome	24% ginkgo flavonoids	Lipolytic, vasokinetic, and slowing aging process
Green Tea phytosome	Epigallocatechingallate	Provides nutrition, anticancer, and nutraceutical and prevents systemic oxidation
Olive oil	Polyphenols	Prevents oxidation, inflammation, and elevated lipid levels
Grape Seed	Procyanidins	Protects heart, provides nutrition, capillarotropic, and prevents systemic oxidation
Ginseng phytosome	Ginsenosides	Provides nutrition and improves immunity
Bilberry Phytosomes	Extract of *Bilberry* which provides anthocyanosides	Improve capillary tone, reduce abnormal permeability, and are potent antioxidants
Visnadine Phytosome	Visnadine from *Ammivisnaga*	Circulation Improver

Advantages

1. Phytosomes improve the bioavailability and stability profiles by improving drug absorption to the intestinal tract as compared to unbound phytoconstituent as well as forming a stable complex with phospholipids.
2. Phytosomes can be used for liver targeting as they increase the solubility in the bile salts.
3. There is a reduction in drug dose due to better absorption of active phytoconstituents.
4. PC gives a synergistic hepatoprotective effect with phytosomes, besides acting as a carrier.
5. Phytosomes may be used in cosmetic industry due to their improved skin penetration and high lipid profile.

Ethosomes [16]

Ethosomes are the slight modification of well-established drug carrier liposome. Ethosome are soft, malleable lipid vesicles composed mainly of phospholipids, alchol (ethanol orisopropyl) in relatively high concentration (20-45%) and water. Ethosomes were reported to improve the skin delivery of various drugs.Ethosomes have also been prepared by adding penetration enhancers such as propylene glycoland showed enhanced penetration efficacy. The presence of age-activator agents (i.e. ethanoland sodium cholate) in lipid bilayers noticeably improves carrier penetration through the stratumcorneum, allowing an efficacious local and systemic delivery of both hydrophobic andhydrophilic compounds.

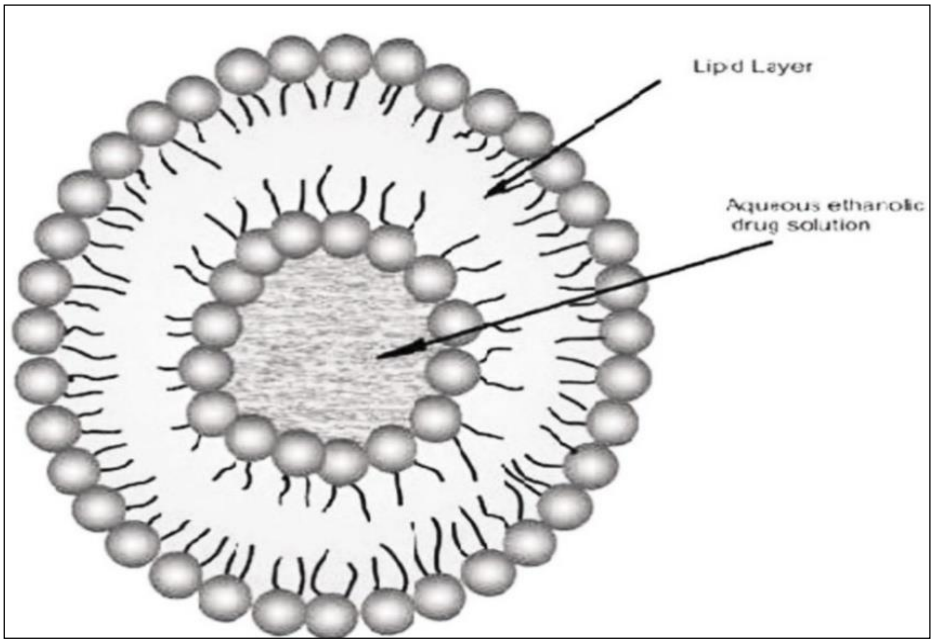

Fig 3: Structure of Ethosome [16]

Ethosome has a high deformability and entrapment efficiency and can penetrate through the skin completely and improve drug delivery through the skin. Compared to other liposomes, the physical and chemical properties of ethosomes make the delivery of the drug through the stratum corneum into a deeper skin layer efficiently or even into the bloodcirculation. The size of Ethosomes vesicles can be modulated from tens of nanometers to microns.

Advantages

1. Delivery of large molecules (peptides, protein molecules) is possible.
2. It contains non-toxic raw material in formulation.
3. Enhanced permeation of drug through skin for transdermal drug delivery.
4. Ethosomal drug delivery system can be applied widely in Pharmaceutical, Veterinary, Cosmetic fields.
5. High patient compliance: The ethosomal drug is administrated in semisolid form (gel or cream) hence producing high patient compliance.
6. Simple method for drug delivery in comparison to Iontophoresis and Phonophoresis and other complicated methods
7. The Ethosomal system is passive, non-invasive and is available for immediate commercialization.

Table 3: Ethosomal herbal formulation [17]

Formulation	Active Ingredient	Biological activity	Application
Amoniumglycyrrhizinate ethosome	Glycrrhizicacid	Antiinflammatory	Increases of invitro Percutaneouspermeation and significantlyenhanced antinflammatoryactivity
Triptolide	Diterpene triepoxide	Antiinflammatory	High entrapmentefficiency, goodpercutaneouspermeability
Podophyllotoxin	Etoposide and Teniposide	Purgative,antirheumatic,& antitumor	Higher entrapment efficiency andenhance its therapeutic effect
Sesbania ethosome	Leucocyanidin and cyanidin	Anti-miocrbial	EnhanceTrans-dermal Permeation
Sophora ethosome	Sophocarpine,matrine,oxymatrine, sophoridine,	Antiendotoxic, anticancer, and antiinflammatory	Enhance drugdeliver and Stability
Matrine ethosome	Matrine and oxymatrinealkaloid	Cardioprotective, Antiinflammatory	Improveprecutaneous Permeation

Transferosomes [18]

Transferosomes are vesicular system consisting of phospholipids as the main ingredient with 10-25% surfactant [such as sodium cholate] and 3-10% ethanol. The surfactants work as "edge activators," conferring ultra-deformability on the structure of transferosome, which helps them to squeeze through pores in the stratum corneum. Transfersome is a highly adaptable and stress-responsive, complex aggregate. Also they possess a unique ability to get accommodated with a wide range of solubility and act as an efficient carrier for both low as well as high molecular weight drugs, e.g. analgesic, corticosteroids, hormones, anticancer drugs, insulin, protein set with high entrapment efficiency and a unique advantage of protection of the encapsulated drug, from metabolicdegradation.

Transfersomes based formulations are reported crossing through a wide range of pore sizes with the diameter ranging from 50 nm to 400 nm that depends on the initial transfersomes suspension. Transferosomes are applied in a non-occluded method to the skin, which permeate through the stratum corneum lipid lamellar regions as a result of the hydration or osmotic force in the skin. It can be applicable as drug carriers for a range of small molecules, peptides, protein and herbal ingredients.

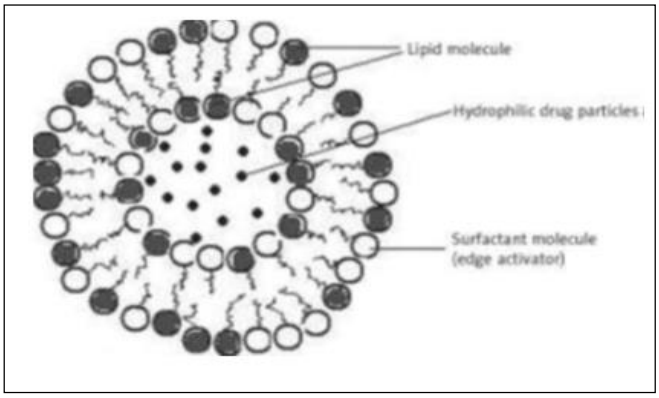

Fig 4: Structure of Transferosome

Advantages

1. Transfersomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubilities.
2. Transfersomes can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without significant loss.
3. High deformability of this system gives better penetration of intact vesicles.
4. They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anaesthetic, corticosteroids, sex hormone, anticancer, insulin and albumin.
5. They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes.
6. They have high entrapment efficiency, in case of lipophilic drug near to 90%.
7. They protect the encapsulated drug from metabolic degradation example: protein and peptides.
8. They act as depot, releasing their contents slowly and gradually.
9. Easy to scale up, as procedure is simple, and avoid unnecessary use or pharmaceutically unacceptable additives.
10. They can be used for both systemic as well as topical delivery of drug.

Table 4: Transferosomes herbal formulations [19]

Formulation	Active Ingredient	Biological activity	Application
Capsaicin transferosomes	Capsaicin	Analgesic	Increase skin penetration
Colchicines transferosomes	Colchicines	Antigout, leukocytoclastic vasculitis, psoriasis, and Sweet'ssyndrome	Increase skin Penetration
Curcumin transferosomes	Curcuminor diferuloylmethane (yellowpolyphenol)	Manage Osteoarthritis, Uveitis andchronic eyeinflammation and diabeticangiopathy	Increase in permeation
Vincristine transferosomes	Vincristine, Catharnthine, Vindolinealkaloid	Anti-cancer, Lymphoma, Leukemia	Increase entrapmentefficiency and skinpenetration byimproving the percutaneous permeation

Niosomes [20]

Niosomes are a novel drug delivery system, which entrapped the hydrophilic drug in the core cavity and hydrophobic drugs in the non-polar region present within the bilayer hence both hydrophilic and hydrophobic drugs can be incorporated into niosomes. The niosomes are ampiphillic in nature, in which the medication is encapsulated in a vesicle which is made by non-ionic surfactant and hence the name niosomes. The niosomes size is a very small and microscopic. The first niosome formulations were developed and patented by L'Oreal in 1975. Niosomes are prepared from uncharged single-chain surfactant and cholesterol whereas liposomes are prepared from double chain phospholipids [21].

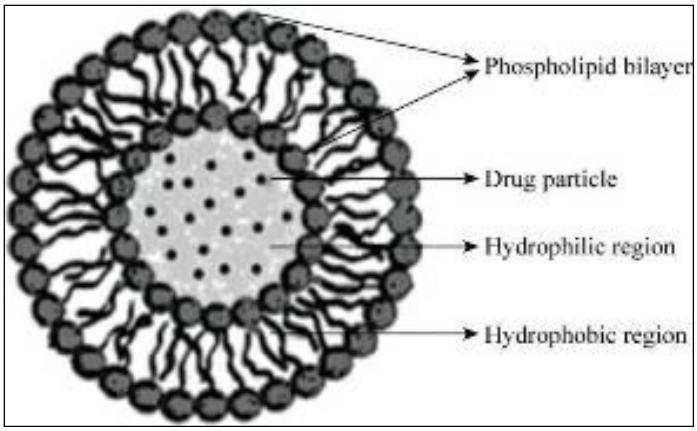

Fig 5: Structure of noisome

Example [21]

- Curcumin-based niosomal transdermal gel -Anti-inflammation therapies.
- Marigold extract loaded niosomal preparation - Employed in cell culture system.
- *Zingibercassumunar*Roxb(ZC) extract entrapped niosomal gel preparation - anti-inflammatory potential of steroid and NSAIDs
- Colchicine Prolonged release niosomes – For rheumatic complaints
- Silymarinniosomes-Treat liver and gallbladder disorders

Proniosomes [22]

Proniosome gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desired site.

Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes.

Proniosomes are water soluble carrier particles that are coated with surfactant and can be hydrated to form niosomal dispersion immediately before use on brief agitation in hot aqueous media. Few examples of proniosomal formulations are:

Table 5: Proniosomes in drug delivery systems [23]

Drug	Therapeutic category
Indomethacin Proniosomes (oral)	NSAID
Levonorgestrel Proniosomes (gel, patch)	Contraceptive agent
Estradiol Proniosomes (gel and patch)	Female hormone
Exemestane Proniosomes (oral)	Anti-hypertensive
Chlorpheniramine maleate Proniosomes (gel and patch)	Anti-histamine
Captopril Proniosomes (gel and patch)	Anticancer

Particulate Delivery System [23, 24]

Nanoparticles

Nanoparticles are nano- or sub–nano-sized structures composed of synthetic or semi-synthetic polymers. In recent times, nanoparticles of herbal medicines have attracted much attention. Nanoparticles are colloidal systems with particles varying in size from 10 nm to 1000 nm. It is an effective system as the formulation is encapsulated in it easily and can easily reach the effective site. The nano-spheres have a matrix type structure in which the active ingredient is dispersed throughout [the particles], whereas the nanocapsules have a polymeric membrane and an active ingredient core. Nanosizing led to increased solubility of components, reduction in the dose via improved absorption of active ingredient. Nanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs.

Metal Nanoparticles based drug delivery

Various metal nanoparticles (MNPs) based herbal formulations are reported to be better and efficacious. Biologically prepared metal nanoparticles known as *—Bhasma"* are used for the treatment of various diseases/ disorders in Ayurveda (Pal *et al*., 2014). Nano forms of seven metals are generally utilized in Ayurveda: gold (Au), silver (Ag), copper (Cu), iron (Fe), lead (Pb), tin (Sn) and zinc (Zn). Tremendous applications of such nanomaterials based herbal preparations in the field of biomedicine have led to an innovative concept of 'Herbo-nanoceuticals'

Nanoshells

Nanoshells are popularly known as core–shells which are few nanometer (1-20 nm) in size. These have sphere-shaped cores (concentric particles) made up of a specific compound which is surrounded by an outer coating or shell made up of a different compound. Nanoshells have immense applications in the biomedical field especially in drug delivery and *in vivo* imaging-based diagnostic approaches because of their unique optical and chemical properties.

Table 6: Nanoparticle herbal formulations

Biological source	Active Ingredient	Biological activity	Application
Nanoparticles of Cuscuta chinensis	Ethanolic extract	Anticancer, immunostimulatory and antihepatotoxic	Improve water solubility
Glycyrrhizic acid-loaded nanoparticles	Glycyrrhizic acid	Anti-inflammatory, antiviral and antihepatotoxic	Improve bioavailability
Triptolide-loaded solid lipid nanoparticle	Triptolide	Anticancer and anti-inflammatory	Increase solubility and decrease toxicity
Ginkgo biloba nanoparticles	Extract of ginkgo biloba	Brain function activation	Increase cerebral blood flow
Artemisininnanocapsules	Paclitaxel	Anticancer	Increase therapeutic index
CPT-encapsulated nanoparticles	Camptothecin	Anticancer	Prolonged blood circulation and high accumulation in tumors
Tetrandrine-loaded nanoparticles	Tetrandrine	Anti-inflammatory, antiplatelet action, immunosuppressive and calcium channel blocker	Sustained drug release
Breviscapine-loaded nanoparticles	Breviscapine	Cardiovascularand cerebrovascular	Prolong the half-life and decrease RES uptake

Advantages

1. Nanoparticulate system delivers the herbal formulationdirectly to the site of action.
2. Encapsulating drugs within nanoparticles can improve the solubility and pharmacokinetics of drugs.
3. Nanoparticles can also reach the choice of formulations, promote the drugs through the biological barriers and increase the bioavailability of drugs.
4. It can take the drug directly to the site of action without destroying surrounding environment.

Microspheres [25]

Microsphere comprises of small spherical particles, withdiameters in the micrometer range, typically 1 μm to1000 μm (1 mm). Microspheres are sometimes referredto as micro-particles in which drug is uniformly dispersed in polymeric matrix. Microspheres can be manufactured from various natural and synthetic materials.

It mainly consists of protein and polymer (Poly Lactic Acid (PLA), Polylactic-co-glycolic acid (PLGA), gelatine, albumin, polylactic etc. are some of the approved of polymers). Polymers may be natural or synthetic.

Three main factors are there which influence the released amount as well as its rate. They are:

1. Size- Smaller the size more will be the surface area, lesser will be the path length to diffuse or lesser layers required to erode for drug release.
2. Type of matrix – It depends on way in which matrix show its release
3. Polymer concentration- It is inversely proportional to the amount of drug released.

Table 7: Microsphere herbal formulations

Formulation	Active Ingredient	Biological Activity	Applications	Method of preparation
Curcumin floating microspheres	Curcumin or diferuloylme thane (yellow polyphenol)	Antioxidant, anti-arthritic and anti-cancer	Sustained drug release	Emulsion solvent diffusion method
Quercetin	Quercetin, 3,3′,4′,5′-7-pentahydroxy flavones	Antioxidant and antiinflammatory and anti-cancer	Significantly decrease the dose size	Solvent evaporation
Rutin alginate chitosanmicerocapsules	Flavonoid	Useful for Cadriovascular And cerebrovascular diseases	Targeting into cardiovascular and cerebrovascular region	Complex coacervation method
CPT loaded microsphere	Camptothecin (CPT) is acytotoxic Quinolone alkaloid	Anti-cancer	Prolonged release of camptothecin	Oil in water evaporation method
Cynarascolymus microspheres	Cynarascolymus extract	Nutritional supplement	Controlled release of nutraceuticals	Spray-drying technique
Zeodoary oil microsphere	Curcumin or diferuloylme Thane (yellow Polyphenol)	Hepatoprotective, anti-arthritic and anti-cancer	Sustained release and Higher bioavailability	Quasi-emulsionsolvent Diffusion method

Advantage

1. Administration of medication via micro-particulate system is advantageous because microspheres can be ingested or injected, and they can be tailored for desired release profiles and used for site-specific delivery of drugs and in some cases can even provide organ targeted release.
2. Drug can be easily released from the formulation.
3. It can protect the specific function of drugs, and can release the drugs into an outer phase for a long period.

Micropellets [25]

Micro pellets is an agglomeration process that converts fine powder or granules of bulk drugs and excipients into small, free flowing semi spherical units. These are the solid particles with size range of 1-1000 μm. In micropellets, the drug could be either dissolved or dispersed in the polymeric solutions and spray-dried. Controlled release pellets are used for the delivery of drugs to specific sites and for the extended period of time.

These are also used for the delivery of the two incompatible drugs simultaneously at same or different sites. The main advantage of the pellets is that it prevents dose dumping which occurs with the conventional dosage forms. Pellets are also used for the coating and taste masking of the formulations.

Example

1. Pectin-hydroxypropyl methylcellulose (HPMC) coated curcumin pellets were prepared for delivery of the curcumin in the colon to treat the inflammatory disease. The drug release from the pellets is induced by the pectinolytic enzymes present in the colon.
2. The bitter alginate micro pellets loaded with alcoholic extract of *Andrographis penniculata* were successfully inhibit the paracetamolinduced hepatotoxicity by decreasing ASL, ALT, and liver weight.
3. The extract of Piper sarmentosumn was entrapped into calcium alginate microbeads. It was found that the encapsulation efficiency of drug is independent of the encapsulation method.

Biphasic System

Emulsion [26]

Emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets ranging in diameter from 0.1 μm to 100 μm[4].Its appearance is translucent to transparent liquid.

Emulsion can be classified into ordinary emulsion (0.1–100 μm), micro-emulsion (10–100 nm), sub-micro-emulsion (100–600 nm), etc. Among them, the micro-emulsion is also called Nano-emulsions and the sub-micro-emulsion is also called lipid emulsion.

Advantages

- It can release the drug for a long time because it is packed in the inner phase and makes direct contact with the body and other tissues.
- As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosised by macrophages and increase its concentration in liver, spleen and kidney.
- As the emulsion contains herbal formulation, it will increase the stability of hydrolyzed formulated material and improve the penetrability of drug into skin and mucous. The new type, *viz*., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver

Table 8: Emulsion based herbal formulations

Formulation	Active Ingredient	Biological Activity	Application
Self-nanoemulsifying Zedoary essential oil	Zedoary turmeric oil	Improved aqueous dispersibility, stability and oral bioavailability	Hepatoprotection anticancer and anti-bacterial
Triptolidemicroemulsion	Triptolide	Antiinflammatory	Enhance the penetration of drugs through the stratum corneumby increased hydration
Docetaxel submicron emulsion	Docetaxel	Anticancer	Improve residence time
Berberine nanoemulsion	Berberine	Anticancer	Improve residence time and absorption
Silybinnanoemulsion	Silybin	Hepatoprotective	Sustained release formulation
Quercetinmicroemulsion	Quercetin	Antioxidant	Enhance penetration into stratum corneum and epidermis

Other Novel Herbal Drug Delivery Systems

Transdermal drug delivery system [27, 28]

Transdermal drug delivery devices are the polymeric formulations which are applied over the skin and deliver the drug at predetermined rate and for predetermined time. TDDS has been an increased stake in the drug administration via the skin for both local therapeutic effects on diseased skin (topical delivery) as comfortably as for systemic delivery of drugs.Transdermal delivery system provides the advantage of controlled drug delivery, enhanced bioavailability, reduction in side effects, and easy application. Formulation of transdermal films incorporating herbal drug components such as boswellic acid (*Boswelliaserrata*) and curcumin (*Curcuma longa*) is one of the first few attempts to utilize herbal drugs through TDDS, which utilizes skin as a site for continuous drug administration into the systemic circulation.

Polymeric Micelle formulation [29]

Polymeric micelles consist of hydrophobic core stabilized by the hydrophilic polymer chains exposed to the aqueous environment. The size of the polymeric micelles ranges from 10-100 nm.

Polymeric micelles have been reported for the delivery of the poorly soluble herbal drugs.

Examples

- Artemisinin from *Artemisiaannua L*. and Curcumin from the roots of *Curcuma longa L*. are used as antimalarial drugs, but these are poorly soluble drugs. Micelles formulations of these drugs with sodium dodecyl sulphate led to 25 fold increase in solubility of these drugs.
- The polymeric micellar formulation of paclitaxel led to increase in the solubility of the drug. The micellar formulation of paclitaxel has been used for the treatment of LNcap prostate tumours.

Implants

These are the polymeric devices which are used for the controlled and sustained delivery of the drugs. These are directly placed in the body fluids/cavities and are fabricated by using biodegradable polymers.

A microsurgery is always required for the insertion of these devices.

Example

Implants of the extract of danshen (*Radix SalviaeMiltiorrhizae*) were developed using the chitosan and gelatin. This drug is used for healing of muscles and tissues in the abdominal cavities [30].

Liquid crystals [31]

Liquid Crystals combine the properties of both liquid and solid states. Liquid crystal nanoparticles (LCNPs) are made through the mini-emulsion method which is giving droplet size from 180 to 630 nm.

LCNPs can be used as effective method for targeted drug delivery, better bioavailability and drug stability. Curcumin-loaded lipid cubic liquid crystalline nanoparticles were prepared and their physicochemical properties and oral

absorption were evaluated and reported to be better for oral administration of curcumin as compared to only crude curcumin. However, due to high cost and energy needs required for development of LCNPs based preparation cause hindrances to their extensive usage in the pharmaceutical industry.

Hydrogels [31]

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. They are used to regulate drug release in reservoir-based, controlled release systems or as carriers in swellable and swelling-controlled release devices.

Conclusion

This review gives information about Novel drug delivery system in herbals, their types, formulation and herbal drugs used. This information would be useful in the form of base for the further research work, isolation of chemical entities from Novel drug delivery system in herbals, formulation of Novel drug delivery system in herbals.

Herbal drugs have enormous therapeutic potential which should be explored through some value added drug delivery systems. Several plant extracts and phytomolecules, despite having excellent bio-activity *in vitro* demonstrate less or no *in vivo* actions due to their poor lipid solubility or improper molecular size or both, resulting in poor absorption and poor bioavailability. Standardized plant extracts or mainly polar phytoconstituents like flavonoids, terpenoids, tannins, xanthones when administered through novel drug delivery system show much better absorption profile which enables them to cross the biological membrane, resulting enhanced bioavailability. Hence more amount of active constituent becomes present at the site of action (liver, brain, heart, kidney, etc.) at similar or less dose as compared to the conventional plant extract or phytomolecule. Hence, the therapeutic action becomes enhanced, more detectable and prolonged.

Several excellent phytoconstituents have been successfully delivered using NDDS. Hence there is a great potential in the development of novel drug delivery systems for the plant actives and extracts.

The drugs of herbal origin can be utilized in a better form with enhanced efficacy by incorporating in modern dosage forms. However, phytotherapeutics need a scientific approach to deliver the components in a novel manner to increase patient compliance and avoid repeated administration. This can be achieved by designing novel drug delivery systems for herbal constituents.

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