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Review Article

**A REVIEW ON NOVEL DRUG DELIVERY SYSTEM OF
HERBAL FORMULATIONS.****C.Mohana¹, Dayala. Thanusha², A. Vaishnavi², M. Kishore Babu³**¹ Assistant Professor, Department of Pharmacy Practice, Krishna Teja Pharmacy College, Tirupati.² B. Pharmacy Student's, Krishna Teja Pharmacy College, Tirupati.³ Professor, Department of Pharmaceutics, Krishna Teja Pharmacy College, Tirupati.**Abstract:**

The kind of novel herbal formulations such as polymeric nanoparticles, nano capsules, liposomes, phytosomes, emulsions, microspheres, transferosomes and ethosomes has been reported using proactive and plant selections. The novel formulations are described to have remarkable over conventional formulations of plant actives and extracts which includes enhancement of solubility, bioavailability, and protection from toxicity, enhancement of pharmacological activity, enhancement of stability, improved tissues microphages distribution, sustained delivery, and protection from physical and chemical degradation. Phytosomes are cell – like small structure and advanced from herbal formulation and it is made up of active phytoconstituents of herbal extract surrounded by lipid bilayer, consisting of phosphatidylcholine. and it include high lipophilicity, enhanced bioavailability, and high stability. Liposomes are spherical vesicles made up of phospholipid bilayer used as colloidal vesicular drug delivery systems .and in this review we also summarized about nano particles, emulsions, microspheres, ethosomes, solid lipid nano practical, niosomes, proniosomes, dendrimers, liquid crystals, hydrogels.

Keywords: Herbal Formulation, Novel Formulation, Liposomes, phytomes, Nano particles

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INTRODUCTION:

Herbal formulations mean a dosage form consisting of one or more herbs or processed herbs in specified quantities to provide specific nutritional, cosmetic benefits, and / or other benefits. Herbal preparations are obtained by subjecting whole plant, fragmented, or cut plants, plants parts to treatment such as distillation, extraction, expression, fractionation, purification, concentration or fermentation. These includes comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates⁽¹⁾ Herbal drug itself is complex structure of many active constituents; as all of them provide synergistic action and enhance the therapeutic value⁽²⁾ herbal drugs have lesser side effects^(3,4)

Novel drug delivery systems can include those based on physical mechanisms and those based on biochemical mechanisms. Physical mechanisms also referred as control drug delivery systems include osmosis, diffusion, erosion, dissolution, and electro transport. Biochemical mechanisms include monoclonal antibodies, Gene therapy and vector systems, polymer drug adducts and liposomes. Targeting is the ability to direct the drug- loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release:

- i. Passive
- ii. Active targeting

Therapeutic benefits of some new drug delivery system include optimization of duration of action of drug, decreasing dosage frequency, controlling the site of release and maintaining constant drug levels^(5,6,7).

ADVANTAGES OF NOVEL DRUG DELIVERY SYSTEM⁽⁸⁾:

1. Protection from physical and chemical degradation.
2. Sustained delivery
3. Improved tissue macrophages distribution
4. Enhancement of stability
5. Enhancement of pharmacological activity
6. Protection from toxicity
7. Increased bioavailability
8. Enhancement of solubility

RECENT DEVELOPMENTS IN NOVEL DRUG DELIVERY SYSTEM OF HERBALS⁽⁹⁾

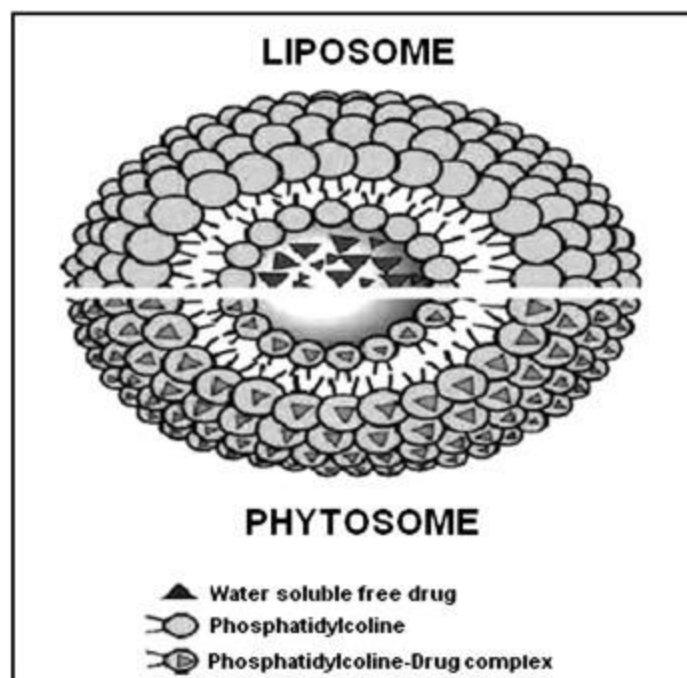
1. Phytosome
2. Liposome
3. Nanoparticles
4. Emulsions
5. Microsphere
6. Ethosome
7. Solid lipid nanoparticle
8. Niosomes
9. Proniosomes
10. Transdermal drug delivery system
11. Dendrimers
12. Liquid crystals
13. Hydrogels

1.PHYTOSOMES:

Phytosomes are cell like small structure and advanced form of herbal formulation. It is made up of bioactive phytoconstituents of herbal extract surrounded by the lipid bilayer, consisting of phosphatidylcholine. Phytosomes show better stability profile because phosphatidylcholine molecules and phytoconstituents are chemically bonded. Bioactive phytoconstituents possesses broad therapeutic activities and includes flavonoids(major), glycosides, Terpenoids etc. Phosphatidylcholine has gastro protective properties and hence plant extracts (drugs) are protected from destruction in GI tract, hence exhibit better pharmacokinetic and pharmacodynamic profile with improved bioavailability than conventional herbal extract. It has both lipophilic and hydrophilic drug domains so it can carry both types of drugs. Flavonoids are major and important groups of phytochemical and these are also known as nature's biological response modifier because they show the anti-inflammatory, antiallergic, antiviral, and anti-cancer properties.⁽¹⁰⁾

Advantages of phytosome

1. Phytosome increases the absorption of active constituents, so its dose size required is small.
2. There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
3. In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability⁽¹¹⁾.
4. Phytosome improves the percutaneous absorption of herbal phytoconstituents⁽¹²⁾



Ser no	Plant /constituent used	Derived from plant	Biological activity	Application of technology	Reference
1	Curcumin	Turmeric (Curcuma longa)	Anticancer and Antioxidant	Improved antioxidant activity and bioavailability	13
2	Epigallocatechin	Green tea	Anticancer and Antioxidant	Absorption enhancement	14
3	Naringenin	Orange and grape juice	Anticancer and anti-inflammatory	Prolong action and enhanced bioavailability	15
4	Procyanidins	Grape seed	Anticancer and Antioxidant	Bioavailability enhancement	16

2.LIPOSOMAL DRUG DELIVERY SYSTEMS

Liposomes are ideal drug delivery system because its morphological structure resembles with cell membrane structure. Liposomes are spherical vesicles made up of phospholipid bilayer used as colloidal vesicular drug delivery systems.⁽¹⁷⁾ Phospholipid molecules are amphipathic in nature having a hydrophilic head and hydrophobic tail, which in contact with water forms a spherical vesicle with head aligned towards the aqueous region and tails entrapped in membrane, forming an aqueous core (aqueous domain) which can accommodate

hydrophilic drugs and lipoidal domain entrapped in bilayer-membrane which accommodates hydrophobic drugs i.e. it can carry both hydrophilic and hydrophobic drugs.⁽¹⁸⁾ The average size of liposome ranges from 0.05 to 5.00 micrometer⁽¹⁹⁾.

Advantages of liposomes:

1. The high biocompatibility.
2. The easiness of preparation.
3. The chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds.



Fig. 1. Cross-section of a liposome [4].

Ser no	Plant/constituent used	Derived from plant	Biological activity	Application of technology	Ref
1	Root of <i>Atractylodes macrocephala</i>	<i>Atractylodes macrocephala</i> (sunflower family)	Digestive and anti-cancer	Enhancement of solubility and bioavailability	20
2	Curcumin	Curcumin Longa (Turmeric)	Anti-cancer long	Long systemic residence time and high entrapment efficiency	21

3.NANO PARTICLES

Nanoparticles (including nanospheres and nano capsules of size 10-200 nm) are in the solid state and are either amorphous or crystalline. They can adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in the controlled release of drugs, in targeting particular organs / tissues, as carriers of DNA in gene therapy, and in their ability

to deliver proteins, peptides and genes through the peroral route. ^(22,23).

Advantages of herbal nano particles delivery system

1. Nanoparticulate system delivers the herbal formulation directly to the site of action.
2. Increased efficacy and therapeutic index.
3. Increased stability via encapsulation.
4. Improved pharmacokinetic effect.
5. Producing with various sizes, compound sur



4. MICRO-EMULSIONS ⁽²⁴⁾

Microemulsions are clear, thermodynamically stable, an isotropic mixture of oil and water, stabilized by surfactants and sub-surfactants. Small-scale emulsions, such as droplet-type dispersions, either oil in a water type (O/W) or water in oil type (W/O). Micro emulsion's size ranges from 5-100 nm. The aqueous phase contains salt and other ingredients and the oil phase contains a mixture of hydrocarbons and olefins. O/W or O/W/O emulsion are made for oily or lipophilic drugs while W/O or W/O/W emulsion are prepared for water-soluble drug

Advantages of emulsion-based formulations

1. It can release the drug for a long time because it is packed in the inner phase and makes direct.
2. Contact with the body and other tissues.
3. As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosis by macrophages and increase its concentration in liver, spleen and kidney.
4. 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.
5. The new type, viz., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to heart and liver ⁽²⁵⁾.

Serial no	Plant /constituent used	Derived from plant	Biological activity	Application of technology	Ref
1	Curcumin	Turmeric (Curcuma longa)	Anti-tumour, antioxidant and antiplatelet aggregation	Enhance anti-inflammatory activity	26, 27
2	Triptolide	Diterpenoid triepoxide obtained from Chinese medicine Tripterygium Wilfondil hook F	Used in the treatment of autoimmune disease especially leukaemia and antineoplastic activity	Reduce the toxicity	28
3	Berberine	Berberis vulgaris	Anticancer	More residence time in the body	29,30
4	Docetaxel	European yew tree Taxus baccat	Anticancer	More residence time in the body	31,32

5.MICROSPHERES

Microspheres are used as a vehicle for the controlled release drug delivery system. It is a matrix-based drug encapsulating device in which drugs are uniformly dispersed in the polymer matrix and can encapsulate a variety of drugs. ⁽³³⁾ 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. The release of drug dispersed in polymer occur by first order process. Polymeric concentration is inversely proportional to the amount of drug release. ⁽³⁴⁾ Size of microspheres ranges from 1 μ to 300 μ . They can be tailored for

desired release profiles and used for site specific delivery of drugs. Microspheres are ideal vehicles due to their high bioavailability, biocompatibility, and sustained release characteristics.

Advantages of microsphere

1. Facilitate accurate delivery of small amount of potential drug
2. Controlled release of drug
3. Protect unstable drug
4. Enhanced bioavailability

Serial no	Plant/ constituent used	Derived from plant	Biological activity	Application of technology	Ref
1	camptothecin	Bark and stem of camptothecin acuminata	Anti-cancer	Dose reduction	[35]
2	Quercetin	Citrus fruits, apples, onions	Anti-cancer	Permeation enhanced	[36]

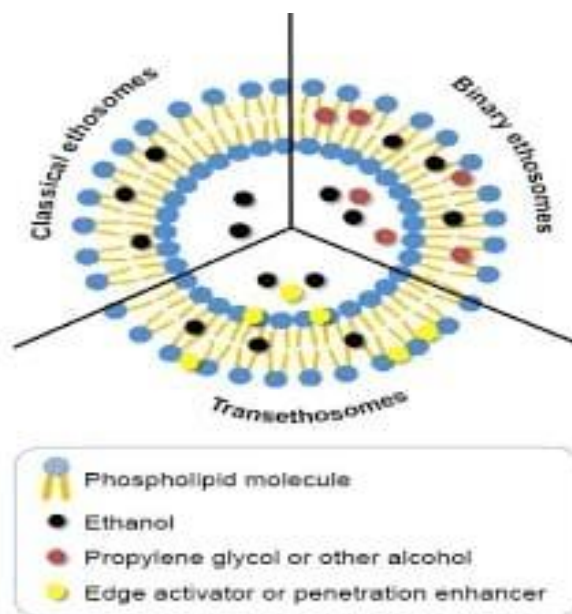
6.ETHOSOMES

Ethosomes are novel and flexible vesicular drug delivery systems made up of phospholipid for transdermal delivery, by enhancing the skin permeation. Mode of action of both the phospholipid vesicles differs, Ethosomes are non-invasive delivery carriers that enable drugs to reach the deep skin layers and/or the systemic circulation while transferosomes are used for delivering the drug in upper layers of skin.

The size of Ethosomes vesicles can be modulated from tens of nanometres to microns. ^(37,38)

Advantages of Ethosomes

1. Ethosomes enhance transdermal permeation of drug through skin.
2. Ethosomes are a platform for the delivery of large amounts of diverse groups of drugs.
3. Ethosomal drug is administered in semisolid form resulting in improvement in patient's compliance



7.SOLID LIPID NANO PARTICLES

Solid-lipid nanoparticles are sub-micron colloidal system and its size ranges from 50-100 nm. It is prepared by dispersing the physiological solid lipids particles in nanometre range in having a solid hydrophobic core i.e., they tend to carry lipophilic or hydrophilic drugs. SLNPs are biocompatible, non-toxic, biodegradable etc. SLNPs have long-term

stability and better control over the release kinetics of encapsulated compound. ⁽³⁹⁾

8.NIOSOMES

Niosomes are multilamellar vesicles formed from non-ionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies, in association with L'Oréal have shown that, in general, niosomes have properties as potential drug carriers

similar to liposomes. Niosomes are different from liposomes in that they offer certain advantages over liposomes⁽⁴⁰⁾.

9.PRONIOSOMES

Proniosomes gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desire site. Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes⁽⁴¹⁾.

10.DENDRIMERS

Dendrimers are precisely defined, synthetic nanoparticles that are approximately 5–10 nm in diameter. They are made up of layers of polymer surrounding a control core. The dendrimers surface contains many different sites to which drugs may be attach and also attachment sites for materials such as PEG which can be used to modify the way of dendrimer which interacts with body. PEG can be attached to dendrimer to ‘disguise’ it and prevent the body’s defense mechanism for detecting it, there by slowing the process of break down. This fascinating particle holds significant promise for cancer treatment. Its many branches allow other molecules to easily attach to its surface. Researchers have fashioned dendrimers into sophisticated anticancer machines carrying five chemical tools – a molecule designed to bind to cancer cells, a second that fluorescence upon locating genetic mutations, a third to assist in imaging tumor shape using x – rays, a fourth carrying drugs released on demand, and a fifth that would send a signal when cancerous cells are finally dead. The creators of these dendrimers had successful tests with cancer cells in culture and plan to try them in living animals soon^(42,43)

11.LIQUID CRYSTALS

Liquid Crystals combine the properties of both liquid and solid states. They can be made to from different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueous drug solutions can be included⁽⁴⁴⁾

12.HYDROGELS

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 (45).

FUTURE PROSPECTS

Nowadays, people are opting for herbal medicines for their better therapeutic values and lesser adverse

effects, so there is a need to develop a novel drug delivery system and a targeting system for herbal drugs.⁽⁴⁶⁾ Novel drug delivery system, not only provides a safe and effective delivery, enabling people to regain faith over herbal drug delivery systems but also increases the market for herbal drugs. Several other novel drug delivery systems can be used for enhancing the efficacy of drugs.^(47,48)

- Sublingual delivery of phytoconstituents, for rapid action of the drug as it bypasses the first pass metabolism which is the main problem of herbal drugs
- Muco-adhesive Drug delivery can also be used for targeted delivery of drugs which increases the bioavailability of drug locally.
- Floating Drug delivery of drugs which are stable at gastric pH for their absorption in upper GI tract
- Niosomes can also be used in place of liposomes and are less toxic than liposomes since they have non-ionic carrier system. Unlike liposomes, they don't undergo any free radical oxidation.

CONCLUSION:

Novel drug delivery system not only reduces the repeated administration to overcome noncompliance, but also helps to increase the therapeutic value by reducing toxicity and increasing the bioavailability, and so on. Extensive research is going on for herbal drugs to incorporate them in novel drug delivery systems. Application of these novel techniques to natural medicines will led to enhanced bioavailability, reduced toxicity, sustained release action, protection from GI degradation which cannot be obtained through conventional drug delivery system due to large molecular size, poor solubility, degradation of herbal medicines in Gastrointestinal media.

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