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Review Article

Novel Herbal Drug Delivery System

Prasad Kate*1, Vilas Sawale, Rajanikant Kakade3, Runita Karale4, Teena Dubey5

Siddhi's Institute of Pharmacy, Nandgaon

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ABSTRACT

Proactive and plant selections have been used to create innovative herbal formulations, including polymeric nanoparticles, nanocapsules, liposomes, phytosomes, animations, microspheres, transfersomes, and ectosomes'. The novel formulations of plant actives and extracts are reported to have outstanding benefits over traditional formulations. These benefits include increased solubility, bioavailability, and toxicity protection; improved tissue macrophage distribution; sustained delivery; enhanced pharmacological activity; and protection against physical and chemical degradation. A well-known manufacturer of pharmaceuticals and nutraceuticals invented the patented Phytosome technique, which combines phospholipids with standardized plant extracts or water-soluble phytoconstituents to create lipid-compatible molecular complexes. Modern dose forms can incorporate natural medications with improved potency and a more upright course of treatment. Creating innovative medicine delivery methods using herbal components can help achieve this. The current study outlines the state of new herbal formulation development and provides an overview of the kinds of active ingredients, biological activity, and uses of new formulations. It is more beneficial and useful to employ herbal formulations for novel medication delivery systems than to use other strategies. Plant extracts have been shown to have more therapeutic advantages when liposome, ethosome, phytosome, emulsion, microsphere, and solid lipid nanoparticles are added to herbal preparations. The challenges associated with extracting, standardizing, processing, and identifying herbal medications prevented scientists from creating innovative methods of delivering medicine until recently. However, novel drug delivery systems (NDDS) have enabled contemporary technology to create herbal medicine delivery techniques. Plants and plant-based chemicals generated from various plant components are known as herbal excipients. Since herbal excipients are widely accessible, less expensive, stable, and quickly biodegradable, they can be used to circumvent the issues related to toxicity and chemical incompatibility of synthetic excipients in a range of drug administration techniques. Most common ailments and nutritional problems are being treated with natural therapies. Because they

*Corresponding Author: Prasad Kate

Address: Siddhi's Institute of Pharmacy, Nandgaon

Email 🔄 : kateprasad0812@gmail.com

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are more easily absorbed than conventional phyto molecules or botanical extracts, phytosomes—recently created herbal formulations—have better bioavailability and benefits. Significant advancements have been made in the development of novel drug delivery systems (NDDS) for anticancer medications over the last few years.

INTRODUCTION

Considerable attention has been focused on the evolution of a novel drug delivery system (NDDS) for herbal drugs over the past few decades. Conventional dosage forms, including prolongedrelease formulations, fail to adequately meet the dual requirements of maintaining the drug component at a specific rate as directed by the body's needs throughout the treatment period and targeting phytoconstituents to their intended site for optimal therapeutic response. In the realm of phytoformulation research, the development of nano-sized dosage forms (such as polymeric nanoparticles, nanocapsules, liposomes, solid lipid nanoparticles, phytosomes, and nanoemulsions) offers numerous advantages for herbal drugs. These advantages include the enhancement of solubility and bioavailability, protection from toxicity, augmentation of pharmacological activity, stabilization of formulations. improvement in tissue macrophage distribution, sustained delivery, and protection from physical and chemical degradation.[1] The revolutionary drug delivery system, representing a cutting-edge approach to medication administration, tackles the drawbacks of traditional drug delivery techniques. Utilizing herbal formulations for novel medicine delivery systems is deemed more advantageous and beneficial compared to alternative approaches. The therapeutic benefits of plant extracts have been enhanced by incorporating liposomes, ethosomes, phytosomes, emulsions, microspheres, solid lipid nanoparticles into herbal and formulations.[2] The novel herbal drug carriers target specific affected zones inside a patient's body, delivering the drug precisely to that area. The advantages of the novel drug delivery system

lie in its ability to deliver herbal drugs at predetermined rates and direct the drug to the site of action, thereby minimizing toxic effects and increasing drug bioavailability. Control over drug distribution in novel drug delivery technology is achieved either by incorporating the drug into carrier systems or by modifying the drug's molecular structure. The inclusion of herbal drugs in delivery systems enhances solubility, stability, protection from toxicity, pharmacological activity, tissue macrophage distribution, sustained delivery, and protection from degradation. For instance, liposomes serve as effective carriers for anticancer agents, increasing drug concentration in tumor areas while reducing exposure to normal cells and tissues, thereby preventing tissue toxicity. Phytosomal carriers have been investigated for delivering herbal extracts such as ginseng (Ginkgo biloba), demonstrating improved absorption compared to conventional delivery due methods to direct binding of phosphatidylcholine to herbal extract components. Other vesicular assemblies like microspheres, nanoemulsions, and polymeric nanoparticles have also proven beneficial for carrying herbal components. This review article aims to provide an overview of various types of drug delivery systems incorporating active ingredients and their potential advantages. It touches upon different aspects and applications related to novel herbal drug formulations.[3]

HERBAL DRUGS-

An herbal formulation is a dosage form that contains one or more herbs, or processed herb(s), in a prescribed amount to offer particular nutritional, cosmetic, and/or other benefits intended for use in diagnosing, treating, mitigating, or changing an animal's or human's physiology or structure. Herbal preparations are made by putting entire plants, broken up or chopped plants, or plant components through processes including fermentation, distillation,



expression, fractionation, extraction, purification, and concentration. These consist of tinctures, extracts, essential oils, expressed juices, processed exudates, and ground or powdered botanical materials. [6]

ADVANTAGES OF HERBAL DRUGS- [6]

- Low risk of side effects
- Effectiveness
- Lower cost
- Widespread availability

IMPORTANCE OF NOVEL HERBAL DRUG DELIVERY SYSTEM-

A revolutionary approach to drug distribution, the innovative drug delivery system overcomes the drawbacks of the conventional drug administration methods. The potential of the extensive Ayurvedic knowledge base in our nation has only just come to light. But because the patient is receiving the herbal medication via an antiquated and traditional drug delivery mechanism, the drug's effectiveness is diminished. The application of novel drug delivery technology in herbal medicine has the potential to enhance the effectiveness and mitigate the adverse effects of diverse herbal components and plants. This is the main concept behind adding cutting-edge medication delivery techniques to natural remedies. In order to tackle more serious ailments, it is crucial to combine Indian Ayurvedic remedies with innovative drug delivery systems. Because of their lack of scientific support and processing challenges, including standardization, extraction, identification and of specific therapeutic components in intricate polyherbal system systems, herbal medicines were long disregarded for development novel of formulations. Modern phytopharmaceutical research, however, can address the scientific requirements for herbal medicines to be included in novel drug delivery systems, such as liposomes, solid dispersions, nanoparticles, microemulsions, matrix systems, solid dispersions, solid lipid nanoparticles, and so forth. These requirements

include determining the pharmacokinetics, mechanism of action, site of action, accurate dose required, and so forth. To reduce medication loss and degradation, avoid negative side effects, and boost drug bioavailability and the percentage of the drug accumulated in the needed zone, a number of drug delivery and targeting systems are now being developed. [3]

POTENTIAL OF NOVEL DRUG DELIVERY FOR HERBAL DRUGS- [8]

Pharmaceuticals that use conventional compounds obtained from botanicals rather than chemicals are known as phytopharmaceuticals. The body metabolizes natural chemicals more rapidly and easily. As a result, they have fewer, if any, adverse effects and boost bloodstream absorption, leading to more comprehensive and successful therapies. Chemical compounds used to make pharmaceuticals can have unfavorable side effects. It is common for the human body to reject chemical substances that do not occur naturally. These rejections manifest as adverse reactions, ranging in severity from slight headaches to potentially fatal ones. Numerous research have examined lipid-based drug delivery systems and demonstrated its promise for targeted and regulated medication delivery. Pharmacosomes are drug-containing amphophilic phospholipid complexes that attach to phospholipids and contain active hydrogen. They provide the medication superior biopharmaceutical qualities, which raises its bioavailability. Phytosomes are new substances made up of lipophilic plant-derived component complexes, such as Silybum Marianum. phospholipid-containing ginseng, ginkgo biloba, and so on. Another name for them is the phytolipid delivery system. Their medicinal effects and enhanced bioavailability are accompanied by their high lipophilicity. These are sophisticated herbal extracts with enhanced pharmacokinetic and pharmacological properties, which make them useful for treating acute liver disorders of either



infectious or metabolic origin. Using a proprietary procedure, each component of the herbal extract, such as terpenoids and flavonolignans, is molecularly attached to phospholipids, such as phosphatidylcholine, via a polar end to form phytosomes. Phytosomes have several applications in cosmetology and are utilized as a medication. There are still a lot of unanswered questions about the potential medical uses of phytosomes.

IDEAL FEATURES- [15]

- Targeted medication delivery framework-
- Biochemically inert and non-immunogenic (not harmful).
- Both in vitro and in vivo, stable both chemically and physically.
- Drug distribution need to be consistent and restricted to the target cell or organ. controlled and predictable pace of medication delivery.
- The way medications work is unaffected by their release.
- Drugs release a therapeutic amount.
- Drug leakage while travel is low.
- The carriers that are employed do not cause problems or bear mediated illness modification when they are biodegradable or easily removed from the body.
- Rapid (or comparatively simple) reproduction and economical distribution system setup.

CURRENT CHALLENGES IN UPGRADING AND MODERNIZATION OF HERBAL FORMULATIONS [2]

- Controlling within risk ranges
- Communicating uncertainty
- Pharmacological, toxicological, and clinical documentation
- Pharmacovigilance
- Comprehending the mechanisms underlying the effectiveness of harmful additive additions
- Assessing "drug" interactions

- Evaluating clinical trial participants and availability
- Standardization
- Safety and efficacy assessment.

ADVANTAGES AND DISADVANTAGES OF NHDDS: - [2]

ADVANTAGES-

- Site specificity can be achieved through the utilization of the novel herbal drug delivery system.
- The surface area of the drugs is enhanced by the novel drug delivery system, thus allowing quicker absorption and a rapid onset of action.
- The enhanced penetration of nanoparticles through the Blood Brain Barrier (BBB).
- Providing high efficacy.
- Enhanced stability.
- Long term stability by protecting plant activities from degradation.

DISADVANTAGES-

- Leaking of entrapped drugs
- Effects may be unpredictable
- Physical instability
- There are limits on bio acceptability.

TYPES OF NOVEL DRUG DELIVERY SYSTEM-

LIPOSOMES-

Liposomes are condensed bilayered vesicles containing a completely contained aqueous volume, with a lipid membrane bilayer consisting mainly of natural or synthetic phospholipids. The liposomes are spherical particles that have a portion of the solvent inside of them, where it freely diffuses or floats. They may have one, many, or numerous membranes that are concentrated. Polar lipids, which are made up of both lipophilic and hydrophilic groups on the same molecules, are what make up liposomes. Simple examples include detergents, whose constituents form micelles; conversely, polar lipids with bulkier hydrophobic parts cannot associate into



micelles with high curvature radii, but instead form bilayers that can self-close into liposomes or lipid vesicles. Polar lipids self-assemble and form self-organized colloidal particles upon interaction with water. [5] The name "liposome" comes from two Greek words: "Lipos," meaning fat, and "Soma," meaning body. Liposomes can be produced in a range of sizes as single or multilamellar structures, and their name originates from their building blocks, phospholipids, rather than their dimensions. They lack lipophobic substances, such as water, although they typically do not contain them. Liposomes are artificial vesicles consisting of bilayer lipid membranes. They can be filled with drugs and utilized for administering medicines for cancer and other diseases. Liposomes can be prepared from biological membranes through methods like sonic disruption. They serve as microparticulate or colloidal carriers, typically ranging from 0.05 to 5.0 µm in diameter, and spontaneously form in aqueous media as the lipids hydrate. Liposomes consist of relatively biocompatible, a biodegradable, and aqueous material with a certain amount of natural and/or synthetic lipids arranged in one or more bilayers. A wide variety of

medications can be encapsulated within liposomes, either within the phospholipid bilayer or at the interface of the two layers, depending on their varying lipophilicity.[15]



Fig no 1- Liposomes ADVANTAGES OF LIPOSOMES- [15]

- 1. 1.Offers liposomal doxorubicin, a specific passive target for tumor tissues.
- 2. A higher therapeutic index and effectiveness.
- 3. Encapsulation results in increased stability.
- 4. A decrease in the encapsulated compounds' toxicity.
- 5. Better pharmacokinetic outcomes (longer circulation life periods, less elimination).
- 6. Adaptability to combine with ligands unique to a given location to produce active

Active	Biological Activity	Application of Liposomal
Ingredient		Formulation
Magnolol	Preventing the growth of vascular smooth	Accelerate the effectiveness of
	muscle cells (VSMCs)	treatment
Nux vomica	Anti-tumor, analgesic and anti-	Increase stability of formulations
	inflammatory activities	
Puerarin	Anti-arrhythmia activity	Their membrane integrity and surface
		charge are modified by these
		compositions.
Myrtus communis	Anti-oxidant and Anti-Microbial Activity	Increase in its activity

HERBAL	LIPOSOMAL	FORMUL	ATION-	[7]
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PHYTOSOME-

The majority of phytomedicines' bioactive ingredients are flavonoids, which have a low oral bioavailability. Phytosomes are lipid-compatible molecular complexes that are created from watersoluble phytoconstituent molecules, mostly polyphenoles. Because phytosomes have a greater ability to pass through lipid-rich biomembranes than basic herbal extracts, they are more accessible. and arriving to the blood at last.



Phospholipids from soy, namely phosphatidylcholine, are the lipid-phase molecules used to render phytoconstituents lipid compatible. studied for cosmetic Originally purposes, phytosomal complexes have shown promise in recent years for drug delivery, with positive results in the areas of cardiovascular, anti-inflammatory, hepatoprotective, and anticancer applications. Compared to their non-complexed herbal extract counterpart, phytosome complexes have superior pharmacokinetic and therapeutic profiles. Some bioavailability phytochemicals' has been significantly increased via the Phytosome technique. [20]



ADVANTAGES OF PHYTOSOME [15]

- 1. Enhanced bioavailability of phospholipid complexes.
- 2. Better absorption in the GIT.
- 3. Higher bioavailability is thought to contribute to better treatment outcomes.
- 4. Low dose is necessary due to high bioavailability.
- 5. More steadiness. More steadiness.
- 6. great lipophilicity is preferred over liposomes in cosmetics due to its great penetrating properties.
- 7. Notable therapeutic benefits.
- 8. Phosphatidylcholine protects the liver rather than acting as a carrier.

HERBAL PHYTOSOMAL FORMULATION-[7]

Active	Biological Activity	Application of Liposomal
Ingredient		Formulation
Quercetin	Antioxidant	Improves effectiveness of treatment
Oxymatrine	Anti-viral	Enhancement of bioavailability
Ginkgo biloba	Cardioprotective, anti-asthmatic	Induced therapeutic effect
Embelin	Antibacterial and anti-fertility	Increase in solubility

ETHOSOME-

Ethosomes are pliable, soft lipid vesicles that are mostly made up of water, ethanol (or isopropyl alcohol) in relatively high concentrations (20– 45%), and phospholipids. Touitou and her associates created ethosomes for the first time in 1997 Because of its great deformability, this carrier exhibits intriguing properties that are associated with its capacity to pass through human skin intact. These vesicular phospholipids can function as the vesicle-forming element of the ethosomal system due to the physicochemical properties of ethosomes. Phospholipids are employed in concentrations ranging from 0.5 to 10%. Examples of phospholipids with different chemical structures include phosphatidyl choline (PC), hydrogenated PC, and phosphatidyl ethanolamine (PE). Phospholipids can come from eggs, soybeans, semi-synthetics, and synthetic materials. Soy phospholipids like Lipoid S100 and Phospholipon 90 (PL-90) are among the phospholipids that are recommended. The formulation's high alcohol content (20–45%) gives the vesicles their soft, flexible qualities and stability while also upsetting the skin's lipid bilayer structure, which increases membrane permeability.Examples of acceptable alcohols are isopropyl alcohol and ethanol, which are both



often used. Moreover, preparations can employ glycols as a penetration booster. Propylene glycol and transcutol are often used among glycols. Cholesterol can also be added to ethosome vesicles in quantities of between 0.1 and 1% to provide them additional stability. [4]



HERBAL ETHOSOMAL PREPARATION- [7]

ADVANTAGES- [4]

- 1. Improved medication penetration via skin for transdermal administration.
- 2. It is feasible to deliver big molecules, such as peptides and protein molecules.
- 3. The formulation uses harmless raw materials.
- 4. High patient compliance is a result of the semisolid form (gel or cream) in which the ethosomal medication is delivered.
- 5. The ethosomal system is immediately commercializable, passive, and non-invasive.
- 6. The ethosomal drug delivery technology has several applications in the veterinary, cosmetic, and pharmaceutical industries.

Active Ingredient	Biological Activity	Application of Liposomal Formulation
Sophora	Anti-endotoxic, anti-cancer	Ethosome enhances delivery of drugs
Alopecuroides		through the stratum corneum barrier into the
		deep layer of the skin.
Matrine	Antibacterial, anti-inflammatory	Increase the per cutaneous permeation and
		improve anti-inflammatory effect

NANOPARTICLES-

Nanoparticles, which can be either amorphous or crystalline, are in the solid form and include nanospheres and nano capsules with sizes ranging from 10 to 200 nm. They possess the ability to encapsulate and/or adsorb the drug, shielding it from enzymatic and chemical breakdown. Biodegradable polymeric nanoparticles have garnered significant interest as possible drug delivery agents in recent times due to their potential uses in controlled drug release, targeting specific organs or tissues, acting as DNA carriers in gene therapy, and delivering proteins, peptides, and genes via the peroral route.[9] The benefits of the nanoparticles include better absorption of the integrated medication, longer term storage, higher solubility of components, decreased dosage, and fewer negative effects associated with dosage.Curcuma longa's rhizomes contain

curcumin, which has anticancer properties. However, the action is restricted because to its low bioavailability and poor water solubility. Improved bioavailability was obtained by using crosslinked random copolymers of nisopropylacrylamide with N-vinyl-2-pyrrolidone and polyethylene glycol monoacrylate to create curcumin nanoparticles. [10]



ADVANTAGES- [7]



- 1. The herbal formulation is delivered straight to the site of action using the nanoparticulate technology.
- 2. Drug solubility and pharmacokinetics can be enhanced by encasing pharmaceuticals in nanoparticles.
- 3. In addition, nanoparticles can penetrate various formulations, help medications cross biological barriers, and raise the medications' bioavailability.
- 4. It can deliver the medication directly to the affected area without causing environmental damage.

Active	Biological Activity	Application of Liposomal Formulation	
Ingredient			
Berberine	Anti-neoplastic activity	H. pylori growth inhibition	
Hypocrellins	Antiviral activity	Improved performance in both stability and hydrophilicity	
Silybin	Anti-hepatotoxic activity	Shows sustained release and targeting system	
Ginseng	Antioxidant activity	Improvement in stability and improvement in its action	

HERBAL NANOPARTICULATE FORMULATION- [7]

NIOSOME-

These are lamellar microscopic structures that are created in watery conditions by a nonionic surfactant, a cholesterol admixture, and a chargesinducer. Because of the hydrophobic and hydrophilic moiety architecture of niosomes, a wide variety of pharmacological compounds may be included. Niosomes have been evaluated for a number of medicinal uses. Decreased clearance from the body by limiting medication release of such agents is one of the significant benefits in clinical use, such as the capacity to lessen systemic toxicity by encapsulating therapy medicines. [15] Niosomes vary from liposomes in that they have a few benefits over the latter. Liposomes have a number of drawbacks, including high cost, constituents chemical instability of its (phospholipids) due to oxidative destruction, need for particular handling and storage, and inconsistent purity of natural phospholipids. Niosomes are not affected by any of these issues. [20]



ADVAN TAGES- [2]

- 1. They are stable and osmotically active.
- 2. They improve the stability of the drug that is entrapped.
- 3. There is no need for special handling or storage of surfactants.
- 4. They can boost the skin penetration and oral, parenteral, and topical administration of drugs.
- 5. The surfactants are biodegradable, biocompatible, and non-immunogenic.

MICROSPHERE-

"Monolithic spheres or therapeutic agents disseminated throughout the matrix, either as a molecular structure composed of a continuous phase of one or more miscible polymers, whereby medication particles are distributed on a macroscopic or molecular scale," is the



fundamental definition of microspheres. Microspheres are small, spherical particles with size generally ranging from 1 to 1000 µm. Microspheres can also be referred to as "micro particles." As they require fewer doses to be administered, microspheres increase patient compliance. Because of the uniform and persistent therapeutic benefits of microspheres, as well as their morphology, which allows for regulated flexibility in medication release and degradation, effective drug usage will result in a decrease in side effects and an increase in bioavailability. [16] Microsphere Cross Section



ADVANTAGES OF MICROSPHERE – [18]

The use of microspheres for pharmaceutical administration is useful since they may be injected or swallowed, customized for desired release profiles, employed for site-specific drug delivery, and in certain situations, even for organ-targeted release. The drug is readily released from the mixture.

ICROSPIERE HERDAL FORMULATION-[/]		
Active	Biological Activity	Application of Liposomal Formulation
Ingredient		
Ginsenoside	Anti-cancer activity	To enhance solubility and stability
Quercetin	Antioxidant and anti-inflammatory	Enhancing its bioavailability and sustain release the formulation
Zedoary oil	Hepatoprotective	Sustained-release and higher bioavailability

Cardiovascular and cerebrovascular

HEDDAL FORMULATION [7]

MICROEMULSION-

Rutin

Microemulsions are thermodynamically stable, optically isotropic liquid solutions of oil, water, and amphiphile that allow for the transdermal, topical, ocular, percutaneous, oral, and parenteral delivery systems with regulated or prolonged release [16] It is possible to create microemulsions using the phase titration technique. This technique is also known as spontaneous emulsification. The phase diagram provides a characterization for microemulsions. A four compartment system takes a lot of time to process and is challenging to intercept. Therefore, the pseudoternary phase diagram is used in the creation of microemulsions. These have distinct zones well as as microemulsion zones. These displaying all of the specific components at 100%. [17]



cerebrovascular regions

into



cardiovascular

and

W/O microemulsion

Targeting

W/O

microemulsion

ADVANTAGES OF MICROEMULSION- [17]

- 1. The absorption process should eliminate variability;
- 2. Lipophilic drugs will be solubilized;
- 3. Solution forms are provided for waterinsoluble drugs;
- 4. Bioavailability increases;



- 5. The product can be delivered by a variety of routes, including oral, intravenous, and tropical;
- 6. The drug moiety penetrate quickly and effectively

PHARMACEUTICAL EXCIPIENTS-

A material utilized as a delivery system for a medication is known as an excipient; that is, it serves just as an inert means of supporting the active principle or principles. The Latin term excipients, which means to accept something together and out, is the source of the English word excipient. The production methods, active pharmaceutical ingredient (API), and excipients utilized in the formulation all affect the product's standard. These excipients significantly improve the API's performance, enhancing the product's safety and effectiveness. [12]

Idea features of excipients-[11]

- Protect, support and enhance stability of the formulation.
- When formulating a strong medication, add more bulk to the formulation to help in the creation of an exact dosage form.
- Improve patient acceptance
- Helps to improve bioavailability of active drugs
- Enhance overall safety and effectiveness of the formulation during its storage and use.

PHARMACEUTICAL HERBAL EXCIPIENTS-

Pharmaceutical excipients can be defined as nonactive ingredients that are mixed with therapeutically active compounds to form medicines. Agar, Alginate, Starch, Carrageenan, Guar Gum, Xanthan Gum, Gelatin, Pectin, Acacia, Tragacanth, & Cellulose are among the numerous plant-based pharmaceutical excipients used in the pharmaceutical industry as binders, disintegrants, protectives, thickening agents, bases for suppositories, gelling agents, stabilizers, and coating agents.[12]

ADVANTAGES OF HERBAL EXCIPIENTS-[12]

- Biodegradable
- Biocompatible and non-toxic
- Economic
- Safe and devoid of side effects
- Easy availability

CONCLUSION-

Plant-based compounds and herbal remedies have several therapeutic potentials that should be investigated with state-of-the-art drug delivery technologies. This research offers details on the many types, compositions, uses, and creative medication delivery methods of herbal remedies in addition to market conditions at the time of writing. However, a scientific technique is needed to supply the components of phytotherapeutics in a unique fashion, which will encourage patient compliance and prevent repeated administration. This can be achieved by designing NDDS for natural substances. The effectiveness of herbal remedies can be increased by using a variety of new advanced drug delivery techniques. Since the sublingual mucosa has a strong blood supply, medications can be administered sublingually dissolving tablets for a speedy start of action. This avoids the primary issue with herbal drugs, which is first-pass metabolism. as integrated into novel drug delivery methods, certain plant ingredients have demonstrated improved therapeutic impact at comparable or lower doses as compared to traditional extracts. Hence, there is a lot of opportunity for creating novel drug delivery systems for expensive herbal medicines.

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