IJPHT Journal
Papers Having Good Impact
International Journal of Pharmacy and Herbal Technology-ISSN NO: 2583-8962 (Online)

REVIEW ON NOVEL HERBAL DRUG DELIVERY SYSTEM

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ABSTRACT

A revolutionary approach to drug distribution, NDDS overcomes drawbacks of the conventional drug delivery methods. NHDDS come in a variety of forms, phytosomes, liposomes, niosomes, proniosomes, transfersomes, ethosomes, nanoparticles, and microspheres. When new medication delivery technology is used in herbal therapy, it may help different herbal compounds and herbs work more effectively and have fewer negative effects.This is the main concept behind adding cutting-edge drug delivery techniques to herbal remedies. To tackle more serious ailments, it is crucial to combine Indian Ayurvedic remedies with innovative drug delivery systems. In order to obtain modified delivery of herbal medications, novel drug delivery systems have become increasingly important. This has increased the therapeutic value of these drugs while lowering their toxicity. In order to improve treatment response, new drug delivery systems have been created, which are summarised in this article and used to deliver herbal medications.

KEYWORDS: *Herbal medicine, novel drug delivery system*

INTRODUCTION

Importance of NDDS in Medicine A new drug delivery system or a new method of drug administration addresses the shortcomings of modern drug delivery systems. Conventional medicine can treat certain conditions by identifying the diseased area on a patient's body and then treating that area. A drug delivery system is a way to give the patient the correct dose so that it reaches the "point of effect" and begins working immediately. In the last few years, great attention has been paid to the development of new herbal medicines (NDDS). Conventional prescriptions such as over-the-counter supplements do not meet the body's medical needs to offer herbal medicines aimed at maximum recovery and permanence at special prices throughout the treatment.

The two significant prerequisites ought to be met by the nano carriers. First, regulating the medicine at a settled rate for the term of the course of treatment. Also, it got to uncover the current substance of home grown drugs to the aiming target of activity. There may be nano carriers for herbal medications future for improvement and addressing the issues pertaining to herbal medications. For enhancement of the bioavailability of drug, the herbal product must achieve specific balance between hydrophilicity and lipophilicity. Lipophilic for lipid membrane crossing and hydrophilic for drug dissolution into the GIT.[1]

ADVANTAGES

1. Site specificity can be attained by using the innovative herbal medication delivery method.
2. The NDDS method enhances the drugs 'surface area', which facilitates faster absorption and an earlier start of action.
3. Better nanoparticle passage through the blood-brain barrier (BBB).
4. Offering great effect stability

5. Enhanced stability Lessen toxicity and unwanted effects.
6. Long-term stability by preventing the deterioration of plant activities.
7. Lessen the likelihood that herbal materials cause allergies.
8. Enhanced bioavailability and solubility.
9. Controlled drug delivery
10. Eco-friendly[2,]

DISADVANTAGES

1. More expensive than conventional dosage form.
2. There is diminished potential for dosage adjustments.
3. In case of disappointment of measurement frame, the hazard of measurements dumping is show.[3,26]

NOVEL DRUG DELIVERY SYSTEM

NDDS alludes to the approaches, details, innovations, and frameworks for transporting a pharmaceutical compound within the body as required to securely accomplish its craved restorative impacts.

TYPES OF NOVEL DRUG DELIVERY SYSTEM

- Liposomes
- Phytosomes
- Niosomes
- Ethosomes
- Transferosomes
- Microsphere
- Microemulsion
- Nanoparticles
- proniosomes
- Transdermal drug delivery system

➢ LIPOSOMES

Liposomes are widely used in the pharmaceutical and medical industries as carriers for different types of particles. Liposomes are small, simulated vesicles with a circular form that are made of ordinary, non-poisonous phospholipids and cholesterol. The estimated liposome size ranges from 0.01 to 5 mm in diameter. Other than its biocompatibility, liposomes' size, hydrophobic, and hydrophilic characteristics make them attractive frameworks for the delivery of medications. Liposome characteristics differ greatly from lipid composition, charge on the surface, estimation, and planning strategy. The most modern delivery method used by therapeutic agents to deliver medications that function as remedial promoters to the designated bodily organs is liposomal embodiment innovation. The delivery of vital combinations to the body was the main focus of this type of conveyance framework proposition. Innovation in liposomal encapsulation may involve the production of liposomes, which are minuscule froths that represent a variety of elements.[4, 26]

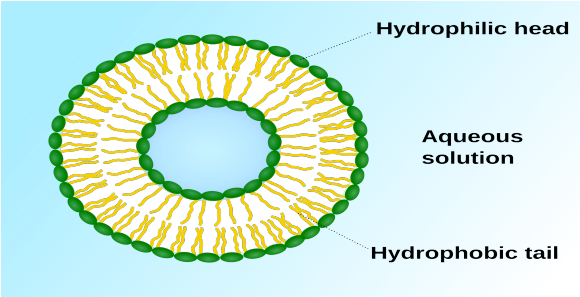


Figure:1 liposomes

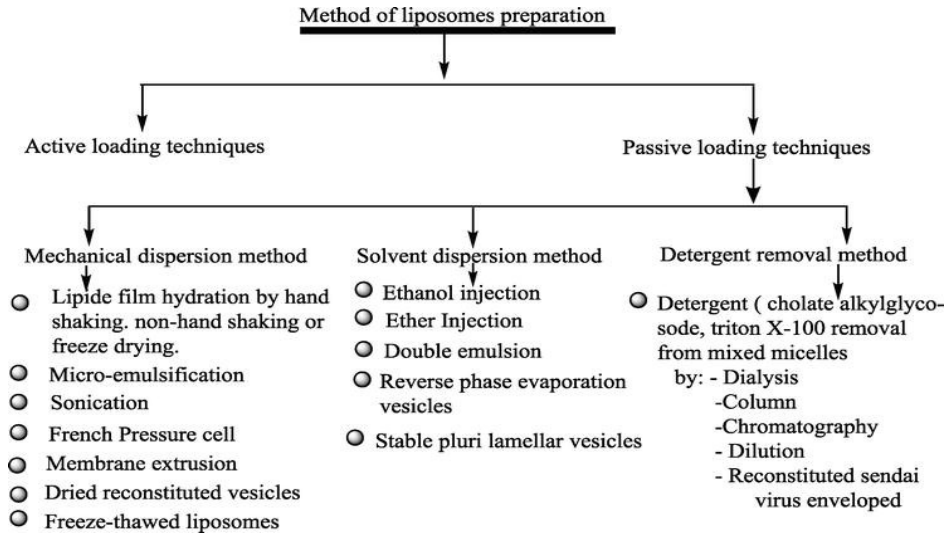
ADVANTAGES OF LIPOSOMES

1. It enables selective passive targeting of tumours.
2. Improve performance and optimise performance.
3. Induced security through packaging.
4. Biocompatible.
5. Chemically and physically well characterised entities.
6. It is used as a tool for the administration and distribution of medication.
7. It is suitable for the distribution of hydrophobic, hydrophilic and amphiphilic drugs and preparations.
8. Suitable to administer via various routes.[5]

DISADVANTAGES OF LIPOSOMES

1. Mass production and sterilisation are not easy.
2. Once applied, liposomes cannot be removed.
3. Less stability.
4. High production cost.
5. Sometimes phospholipids undergo hydrolysis and oxidation reactions.[6, 7]

METHOD OF PREPARATION OF LIPOSOME



APPLICATION OF LIPOSOME

Liposomes are a new form of drug delivery that provides better treatment and safety compared to prescription drugs. The therapeutic applications of liposomes are illustrated below:

1. Site-avoidance delivery properties of liposomes minimise passage of medicine to the old body, and improve the therapeutic efficacy of drugs against disease cells.
2. Liposomes reduce contact between drugs and normal tissues and deliver more drugs to where it is needed in the target .
3. The use of liposomal drug delivery systems can effectively transport drugs to the cytosol.
4. Liposomes used to provide sustained release of drugs.
5. Intra peritoneal administration is useful in treatment of tumour present in Intra peritoneal cavity.
6. Immune response of vaccines can be enhanced by liposomes.
7. Liposomes as artificial blood surrogates.

➢ **PHYTOSOMES**

Phytosome technology emerged in 1989 and sparked revaluation in delivery of herbal phytoconstituents. It is the novel drug system in which, “Phyto" means plant and "some" means cell. It is method of indena in which herbal extract is embedded in the phospholipid complex which enhances the bioavailability of drug the size range of phytosomal particle is <100nm.It is phospholipid type of drug delivery system, Phytosomes are an innovative lipid-based delivery system that bears a striking resemblance to liposomes and can be used to entrap various phytoconstituents with polyphenolic bases to facilitate delivery and absorption. The medication itself combines with lipids to form vesicles, which enhance the effectiveness of phytosomal entrapment even more. As a result, the required dosage has been reduced while The bioavailability of the medication has greatly increased with .Phytosomes have numerous benefits, including the lipid layer encircling the constituent in the plant. [8]

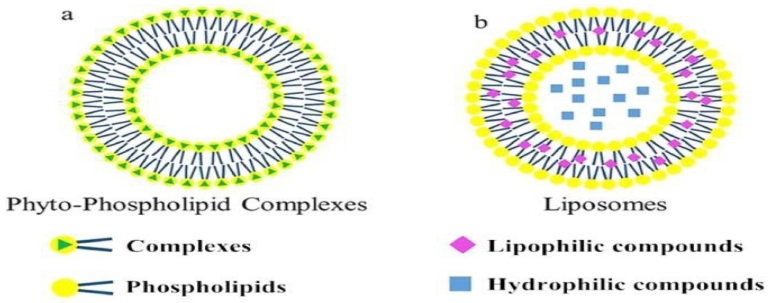


Figure:2. Difference between phytosomes and liposomes.

ADVANTAGES OF PHYTOSOMES

1. Enhanced absorption of herbal constituents.
2. It shows a better stability profile.
3. Phospho Lipomas are also preferred over liposomes in skin care products.
4. It ensures that drugs reach various tissues correctly.
5. Entrapment efficiency is high.
6. Improved bioavailability.
7. Nutritional benefit.
8. Enhanced permeation of drugs through skin.[9]

DISADVANTAGES OF PHYTOSOMES[10]

1. When administered orally or topically they limit their bioavailability.
2. Phytoconstituents are quickly eliminated from phytosome.
3. Stability problem.

METHOD OF PREPARATION

- Solvent evaporation method
- Rotary evaporation technique
- Antisolvent precipitation technique

Common stage of preparation

Phospholipids ➞Solution of phospholipids in organic solvents ➞Drug extract ➞Drying ➞Film formation ➞Hydration ➞Plant suspension formation.

- **Solvent evaporation method**

Drug, polymer and phospholipids.

↓

Take in RBF.Refluxed with specific solvent at 50-60 degrees for 2 hours.

↓

Concentrate to 5-10ml

↓

Obtain the precipitate

↓

Filter and collect

↓

Phytosomes obtained are stored in amber coloured glass bottles at room temperature.

APPLICATION OF PHYTOSOMES

1. Compared to silybin, silymarin phytosomes had greater therapeutic effects, which increased their bioavailability. In comparison to silymarin, silymarin phytosome demonstrated superior hepatoprotective activity. According to one study, silybin from silybin phytosomes was absorbed seven times more readily than silybin from ordinary milk thistle.
2. Green tea has polyphenols with therapeutic value, but their bioavailability is an issue. Green tea polyphenol phytosomes demonstrated enhanced antioxidant activity and increased bioavailability.
3. hytosomes containing quercetin showed enhanced hepatoprotective properties. Improved cardioprotective and antioxidant properties were demonstrated by grape seed phytosomes.
4. Cucumin phytosomes had increased antioxidant activity.
5. Compared to pure medication alone, naringin phytosomes have superior antioxidant activity and a longer duration of action because of a slower rate of rapid elimination.
6. Ginkgo phytosomes have more effective anti-asthma properties.
7. Grapes seed phytosomes showed improved antioxidant and cardio protective effects.
8. Naringin phytosomes exhibit better antioxidant activity. [25]

➢ NIOSOMES

Similar to liposomes but made of non-ionic surfactant ,which are vesicular structures of nonionic surfactants. Niosomes are currently being investigated extensively as a liposome substitute. There have been reports of surfactants of different types forming vesicles and capturing and holding onto hydrophilic and hydrophobic solute particles.

The two primary components of niosomes are additives and non-ionic surfactants.During preparation, cholesterol and fat molecules are loaded, while non-ionic surfactants form the vesicle layer. A crucial component of the cell membrane, the steroidal system increases the stiffness of the bilayer and influences the fluidity and permeability of the bilayer. This system shields the medication from undesirable pharmacological and immunological effects that could cause them to degrade and inactivate too soon.[11]

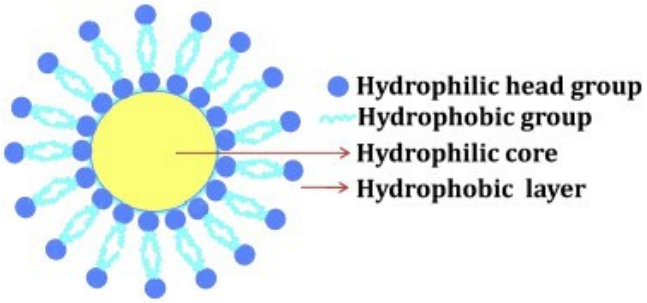


Figure-3. Niosomes

ADVANTAGES OF NIOSOMES

1. They are stable and osmotically active.
2. They make the drug that is entrapped more stable.
3. Surfactant handling and storage don't call for any particular setups.
4. May improve the medication's skin penetration.
5. May raise the drug's oral bioavailability.
6. The dose must be reduced to achieve the desired effect Niosomes are amphipathic.
7. Reduced dose is required to achieve the desired effect
8. Drugs can be released in a sustained or controlled manner.

DISADVANTAGES OF NIOSOMES

1. A few of the issues that could shorten their shelf life are vesicle fusion, agglomeration, physical and chemical instability, and leakage or hydrolysis.
2. Multilamellar vesicle preparation techniques are time taking and need special equipment.
3. drug loading that is ineffective.[12]

METHOD OF PREPARATION OF NIOSOMES

The niosomes are prepared by following methods:

- Ether Injection for LUV.
- Hand Shaking Method for MLV.
- "Bubble " Method.
- Reverse Phase Evaporation for LUV.
- Sonication for SUV.
- Multiple Membrane Extrusion Method.
- Transmembrane pH Gradient Drug Uptake Process for MLV.

- Microfluidization method for SUV.
- Formation of Niosomes from Proniosomes.

GENERAL METHOD OF PREPARATION OF NIOSOMES

Cholesterol + non-ionic surfactant

↓

Dissolve in organic solvent

↓

Dry

↓

Fine file

↓

Dispersed

↓

Niosomes suspension

APPLICATIONS OF NIOSOMES

1. Anticancer drugs are delivered via niosomes, which act as drug carriers.
2. Medicines such as doxorubicin and methotrexate Niosomal systems are applicable.
3. as tools for diagnosis. The niosomal system can be applied to the delivery of medications for the eyes as ophthalmic drug
4. The study of immune response makes use of it.
5. It is employed to deliver peptide medications.
6. Niosomes are employed as haemoglobin carriers.
7. Niosomes' prolonged release action can be used with medications that have low water solubility and low therapeutic index.
8. Niosome-based drug delivery is one method for achieving targeted drug delivery.

➢ ETHOSOMES

Ethosomes, a novel lipid carrier composed of ethanol, phospholipids, and water, were developed in 1997 by Touitou colleagues.They are supposed to improve the way that various drugs are applied topically. Ethanol is a potent penetration enhancer that is thought to have an impact on the stratum corneum's intercellular area. They are pliable, soft vesicles.These new vesicles,called soft vesicles.The size of ethosome vesicles varies from tens of nanometers to micrometres.[13]

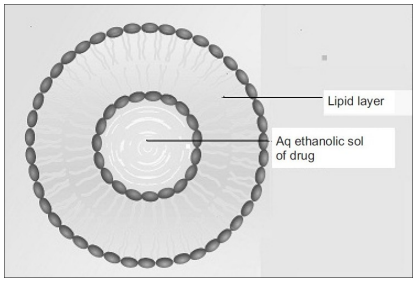


Figure 4 - Ethosomes

ADVANTAGES OF ETHOSOMES

1. Improved drug penetration for TDDS.
2. Complex drugs can be delivered.
3. High patient adherence is given in a semisolid dosage form.
4. These systems are applicable in the veterinary, cosmetic, and pharma industries.
5. Nontoxic raw materials are used in its formulation.

DISADVANTAGES OF ETHOSOMES

1. low yield.
2. The ethosomes may unite if shell locking proves to be unsuccessful.
3. Maybe not cost-effective.
4. Product loss when switching from water to organic media. [14]

METHOD OF PREPARATION OF ETHOSOMES

- Cold Method
- Hot Method
- Classic mechanical dispersion method

Cold method

In a container with vigorous agitation, dissolve medications, phospholipids, and other lipid components in ethanol at room temperature. In a water bath, warm the mixture to 30 °C. Heat the water into 30 degrees Celsius in another bowl, then add it to the mixture above and stir for five minutes. If required, sonication or extrusion can be used to decrease the vesicle size of liquid solutions in order to increase the vesicle size. The preparation needs to be put in the refrigerator the right way.

APPLICATIONS OF ETHOSOMES

1. Delivery of antiviral agents.
2. Delivery of antiparkinson agents, hormones, antiarthritic agents, NSAIDS.
3. Widely used in Cosmeceuticals

➢ TRANSFEROSOMES

The word "transferred," which has two meanings in Latin: "to carry," "to convey," and "soma," which has two meanings in Greek: "body." Interpretation is a product of manufacturing. A vesicle similar to the normal vesicle in the cell. It is therefore compatible for focused and regulated delivery. It is an elastic and dynamic aggregate that reacts rapidly to stress. It is a complex fat bilayer with a deformable vesicle bilayer of fat surrounding an aqueous core. The vesicle is dependent on both the area's composition and the bilayer's shape. Self-regulation and self-improvement together provide the user with a non-intrusive target and help them navigate a variety of effective communication barriers[15].

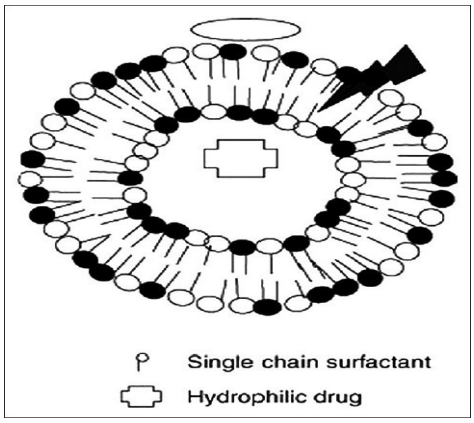


Figure -5 Transferosomes

ADVANTAGES OF TRANSFERSOMES

1. High effectiveness of entrapment.
2. Increased deformability.
3. They act as a carrier
4. Infrastructure made up of hydrophilic and hydrophobic moieties allows for the accommodation with a broad range of solubility.
5. Employed in the topical and systemic delivery of drugs.
6. Both biocompatible and biodegradable.
7. Prevent the breakdown of metabolism.
8. Scale up easily; easy process.

DISADVANTAGES OF TRANSFERSOMES

1. Transfersomes are chemically unstable due to their propensity for oxidative degradation.
2. The formulations and manufacturing aspects of Transferosomes are costly.

METHOD OF PREPARATION OF TRANSFERSOMES

- Thin film hydration method
- Modified hand shaking
- Lipid film hydration technique

APPLICATIONS OF TRANSFERSOMES

1. Because phospholipids are incorporated into transfersomes, they can improve stability and allow CDDS
2. Transfersomes facilitate the easy transdermal transport of large molecules and weight compounds. such as interferons and insulin.
3. Transfersomes have a bioavailability that is comparable to subcutaneous injection.
4. Applying human serum albumin transdermally and encapsulating it has been shown to be beneficial in eliciting an immunological response.
5. NSAIDS, proteins, Insulin, Interferon,transdermal,immunisation,corticosteroids,topical analgesics,anaesthetic agents,anticancer drugs,for this transfersomes system is used as a carrier.

➢ **MICROSPHERE**

Drug delivery systems that target particular body parts have a big influence on the healthcare system. Consequently, by attaching the medication to carrier particles like microspheres, nanoparticles, and liposomes,uncovers the clever strategy for innovative delivery. Throughout

the course of treatment, this system distributes the medication at a rate dictated by the body. Oral administration of medication is the most preferred mode of administration. Microspheres are tiny, diameter ranging from 1 to 100 um. These are free-flowing, naturally occurring particles composed of proteins or artificial polymers that decompose biodegradable. There are two types of microspheres.[16]

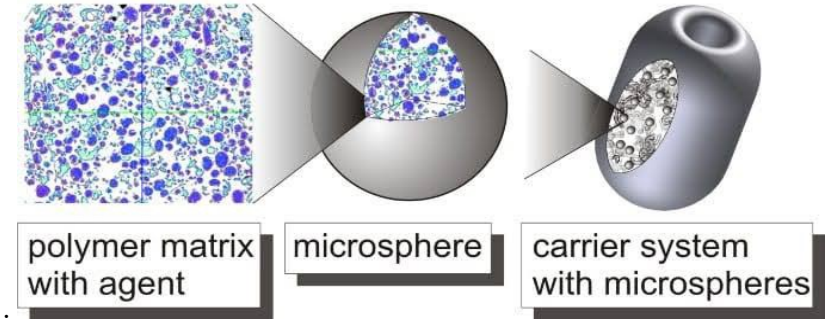


Figure 6-Microsphere

ADVANTAGES OF MICROSPHERES

1. They provide pre- and post-administration protection for unstable drugs.
2. They reduced the concentration of the drug in areas other than the tissue or the intended organ.
3. Decrease dosage and toxicity.
4. Reduction of particle size to increase the solubility .
5. Guarantee a steady and enduring therapeutic outcome. [17]

DISADVANTAGES OF MICROSPHERES

1. The effects of polymer matrix on the environment and its disposal methods.
2. Different dosage forms exhibit different patterns of release, and any deterioration in this pattern could have harmful consequences.
3. Replication is less likely.
4. Relative to parental microspheres, very little drug loading.
5. The stability of the core particles prior to encapsulation may be affected by process variables .
6. Blood components may interact or mix with microspheres that are delivered through the parent.

METHOD OF PREPARATION OF MICROSPHERES

- Solvent evaporation.
- Double emulsion technique.
- Spray drying and spray congealing.
- Solvent extraction.
- Single emulsion technique.
- Quasi emulsion solvent diffusion.
- Spray drying.
- Phase separation coacervation technique.

APPLICATIONS OF MICROSPHERES

1. Microspheres for the delivery of antibodies are named using,Microparticles,Monoclonal,antibody-mediated, targeting microspheres, Chemoembolization,Imaging, Topically invasive microspheres

2. Medical application
3. Radioactive microsphere application.

➢ MICROEMULSION

Microemulsions are liquid combinations of water, oil, and surfactants that are pure, stable, and isotropic; they frequently also contain a cosurfactant. Emulsions have an aqueous phase and an oily phase, making them biphasic systems. Tiny droplets with a diameter ranging from 0.1 micrometre to 100 micrometres are formed when 1 phase is distributed throughout the other phase. Emulsion comes in three different forms. The mean droplet diameter in a micro emulsion is less than 0.22 mm. [18]

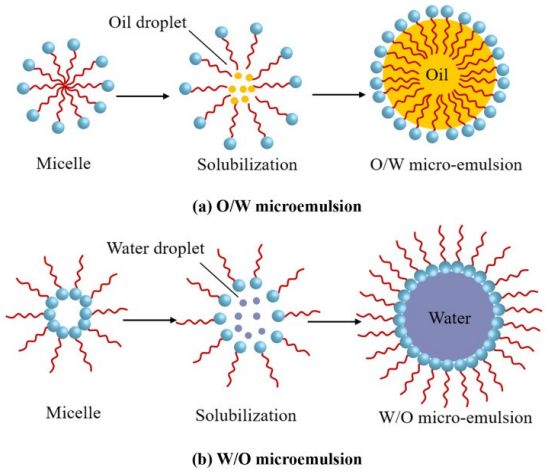


Figure 7-Microemulsion

ADVANTAGES OF MICROEMULSION

1. This system can self-emulsify because they are thermodynamically stable.
2. Micro emulsions serve as super solvents for pharmaceuticals.
3. They have the ability to solubilize drugs that are hydrophilic or lipophilic.
4. Pseudo-zero-order kinetics for drug release are achievable, contingent upon the dispersed phase volume, drug partition, and transport rate.
5. Drugs that are lipophilic or hydrophilic can be transported by the same micro emulsions.
6. Compared to primary and multiple emulsions, the viscosity of microemulsions is lower.
7. Using micro emulsion as a delivery system can minimise side effects.

DISADVANTAGES OF MICROEMULSION

1. High concentration of surfactant and cosurfactant used to stabilise the micro emulsion droplets.
2. Low capacity to dissolve materials with high melting points in systems.
3. A surfactant cannot be used in pharmaceutical applications unless it is nontoxic.
4. It is influenced by temperature and pH levels in the surrounding environment. When patients are administered micro emulsion, these parameters shift.[19]

METHOD OF PREPARATION OF MICROEMULSION

The lipophilic part of the micro emulsion, which consists of the water and oil phases mixed with a surfactant, dissolves the medication. The mixture is then continuously stirred while cosurfactant is gradually added. Repeat this process until the mixture turns translucent.Lastly,

the required size range for scattered globules is made possible by the use of an ultrasonicator. After that, it has time to stabilise. To make gel, the previously mentioned micro emulsion can be mixed with a gelling agent.

APPLICATIONS OF MICROEMULSION

Microemulsions in the development of oils, lubricants, cutting oils and corrosion inhibitors, as well as oil recovery applications such as coatings and textile finishing, are examples of microemulsion applications.

Microemulsions in detergents and cosmetics.

➢ NANOPARTICLES

The study of extremely small objects is known as nanotechnology. It entails working with and modifying matter. Atoms and molecules operate differently at this scale and have a plethora of fascinating and unexpected uses. Over the past few years, research on nanotechnology and nanoscience has surged in many different product domains. In areas where more conventional techniques might have their limitations.It is erroneous to consider nanotechnology as a singular method applicable solely to specific domains. Nanotechnology is often referred to as the "tiny science," but it involves more than just incredibly small material and object.Pharmaceutical nanoparticles are submicron-sized, solid drug delivery systems that have a diameter of less than 100 nm and can either be biodegradable or not. All together, nanospheres and nanocapsules are called nanoparticles.[20, 21]

ADVANTAGES OF NANOPARTICLES

1. They are site-specific, non-toxic, and biodegradable.
2. By using magnetic guidance or attaching specific ligands to particle surfaces, they can direct a medication to a particular site within the body.
3. A key element in maintaining drug activity is the ability of drugs to be integrated into systems without causing a chemical reaction.
4. They provide superior pharmacological activity.
5. Oral, nasal, parenteral, intraocular, and other routes for administration.
6. Attain drug targeting that is both passive and active following parenteral infusion.

DISADVANTAGES OF NANOPARTICLES

1. Presents limitations on bio acceptability.
2. Difficult to produce on a large scale.
3. Physically handling nanoparticles in liquid and dry forms can be challenging due to particle-particle aggregation caused by their large surface area and small particle size.
4. Prior to the clinical application or commercial release of nanoparticles, these pragmatic issues must be resolved.

METHOD OF PREPARATION OF NANOPARTICLES

- **Methods based on evaporation**
  •Physical vapour deposition.
  •Laser ablation.
- **Chemical methods**
  •Colloids synthesis.
  •Synthesis of metal nanoparticles by colloidal method.
  •Sol-Gel method.
- **Biological methods**
  •Synthesis using plant extracts.
  •Synthesis using DNA.

APPLICATIONS OF NANOPARTICLES

In the field of pharmaceuticals.

1. Nanoparticle particles are an effective way to target and deliver cytotoxic drugs to tumours. the drug dosage to the tumour site and thereby stop the drugs from being exposed to normal tissue.
2. Additionally, nanoparticles are anti-tubercular drugs that are applied (e.g., as an ex-somatic agent).The nanoparticles are delivered to the target cell as the casatives are found inside the cell's microorganismes. The brain-blood barrier This has shown to be a success because the BBB has a tight junction, efflux transport, and other active properties that make it difficult for drugs to pass through.
3. Pilocarpine and other miotic drugs have also been delivered using suspensions of nanoparticles to the eye.
4. These are efficient ways to formulate a pourny soluble medication.
5. These have demonstrated a positive impact on the oral delivery of proteins and peptides

➢ PRONIOSOMES [22, 23]

Proniosome is a dry formulation made from a suitable vehicle coated with a nonionic surfactant.They can be hydrated right before use to transform into niosomes.Compared to conventional niosomes, these proniosome-derived niosomes perform equally well or better.

ADVANTAGES OF PRONIOSOMES

1. Proniosomes are dehydrated versions of surfactant-coated carriers that are quickly rehydrated in water.
2. Reduces niosome physical stability issues like drug entrapment leakage, fusion, and aggregation.
3. More ease of distribution, storage, dosing, and transportation.
4. Able to transport both hydrophilic and hydrophobic medications.[24]

METHOD OF PREPARATION OF PRONIOSOMES

- Hand shaking method
- Slurry method
- Slow spray coating method

APPLICATIONS OF PRONIOSOMES

1. Applications in cardiology
2. Application in diabetes treatment
3. Applied in Hormonal therapy
4. It used to study the nature of the immune system elicited by antigens

CONCLUSION

Herbs used have fewer side effects than contemporary pharmaceuticals because of their superior therapeutic value. Ayurvedic medicines can be used more ethically and more effectively if they are incorporated into modern dosage forms through a number of mechanisms, including increased bioavailability and decreased toxicity. Scientists studying pharmaceuticals have recently focused on creating a drug delivery system for herbal remedies that is supported by science. New research has the potential to support market penetration as well as market retention.Many challenges remain with herbal drugs, though, such as the difficulty of performing clinical research on them.NDDS not only reduces the frequency of drug use and overcomes non-compliance, but also helps in increasing the cost of treatment by reducing toxicity and improving bioavailability.

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