IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, January 2023
Impact Factor: 7.301

Review on Novel Herbal Drug Delivery System

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Abstract: *Ayurveda, an ancient kind of medicine practised in India, Plant products have been utilised for a variety of reasons since prehistoric times. Plants are used as natural remedies for a variety of health ailments, such as allergies, wounds, burns, gastrointestinal difficulties, and even cancer. Herbal remedies are helpful but difficult to extract, process, and distribute; as a consequence, modifications are needed to solve these problems, which is what gave rise to the Novel Drug Delivery System (NDDS).In compared to traditional and other cancer treatment modalities, NDDS is also advantageous. By using different herbal excipients and API extract the sevral novel Herbal drug delivery systems are made as like liposomes, nanosomes, microsomes, Microemulsions, Phytosomes, Transferosomes, Ethosomes, Niosomes etc. Other Herbal excipients are some time used like colourents, sweetners, binders, diluvents, viscosity builder, Disintegrants, etc. These excipients may be useful in the development of stable products. Herbal medications have been altered to have a higher therapeutic value, less toxicity, a prolonged and regulated release, improved solubility, increased bioavailability, and improved patient compliance. NDDS, which contains a variety of innovative carriers include solid-lipid nanoparticles, transferosomes, ethosomes, microspheres, microemulsions, phytosomes, and liposomes. This review's goal is to introduce readers to the many herbal NDDS for the administration of herbal medications for the treatment of various illness conditions, such as diabetes and dementia.*

Keywords: Herbal Excipients, Novel Drug Delivery System, Phytosomes, Loposomes. Transferosomes, Ethosomes, Niosomes, Lipid Bilayers, Microemulssion, Neurodistructive, Dementia, wound Healing, NHDDS (Novel Herbal Drug Delivery System)

I. INTRODUCTION

Since more recent ancient times, herbal remedies have been utilised extensively around the world. In order to cure a variety of ailments with fewer adverse effects, the usage of "herbs" has substantially expanded. The plant components that make up herbal remedies and are responsible for their biological effects are known as phytoconstituents. Desirable results are not obtained because the biological activity of the plant fluctuates from batch to batch. Additionally needed for the standardisation of herbal compounds are phytoconstituents. The age of the plant, the moment of collecting, the state of the environment, etc. all have a role. Alkaloids, flavonoids, tannins, essential oils, and other groups of phytoconstituents are a few examples. These phytoconstituents are water-soluble, but because they are large molecules, they cannot pass the lipid barrier, which results in poor absorption.Stability and absorption issues, as well as therapeutic effects, are limitations of using natural products as medicines. These issues are resolved by using Novel Drug Delivery Systems, which also includes a variety of technologies, formulations, and delivery methods to deliver a drug as required for achieving safety and the desired effects. The main focus of nanomedicine is the use of nanotechnology for the improvement of human health.[1]

Nanotechnology is the study of things at the nanoscale in science, engineering, and technology (i.e. 1-100 nm). The size of a drug carrier that can carry medication exactly to the body's sick cells is being developed by researchers. Conventional medications experience various negative side effects as a result of their generic nature and inadequate or poor dose formulations. Using nanotechnology, we can create medications that are more effective and cell-specific to reduce side effects. Polar lipids make up liposomes. Phytosomes are a more advanced sort of herbal formulation. They are tiny, cell-like structures made using a patented process that mixes lipid and active plant formulations, most often phosphatidylcholine, for enhanced medication absorption. Additional cutting-edge drug delivery systems, such as ethosomes, transferosomes, solid-lipid nanoparticles, and microspheres, improve the bioavailability, solubility, and biocompatibility of herbal formulations in addition to offering a number of other benefits. For the best utilisation of all

IJARSCT
ISSN (Online) 2581-9429
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Impact Factor: 7.301

the aforementioned advantages, we require an ideal nanoparticulate system that is small enough to reach the target cells and has increased blood availability. [1]

II. NOVEL DRUG DELIVERY APPROACHES

Which is In order to decrease medication loss and degradation, minimise and limit undesirable side effects, increase medicine bioavailability, and increase the amount of the drug accumulated in the targeted or vital zone, several drug delivery and drug targeting strategies are currently being developed. Solvable polymers, micelles, cells, cell ghosts, lipoproteins, liposomes, and microparticles comprised of insoluble or biodegradable natural and synthetic polymers are a few examples of drug carriers. targets that are even, progressively degradable, and stimuli-sensitive Getting the drug-loaded system to the desired location is called targeting. There are two types of targeting for medication release: passive and active. Passive targeting is demonstrated by the preferential accumulation of chemotherapeutic medicines in solid tumours as a result of the higher vascular permeability of tumour tissues compared to healthy tissue. One strategy that can enable active targeting is to surface and functionalize drug carriers with ligands that are easily or selectively recognised by receptors on the surface of the cells or tissues of interest. Considering that ligand-receptor interactions may be extremely selective, this might allow for more precise targeting of the area of interest. [1,2]

Successful formulation development depends on controlled drug release and subsequent biodegradation. Potential methods for release include:

1. Desorption of medications that are surface-bound or adsorbed
2. Diffusive motion inside the carrier matrix
3. Diffusion through the carrier wall (in the case of nanocapsules)
4. Carrier matrix deterioration
5. A process that combines erosion and diffusion.[1,2]

2.1 Types of Novel Herbal Drug Delivery System

Numerous formulations, including liposomes, phytosomes, pharmacosomes, niosomes, nanoparticles, microspheres, transferosomes, ethosomes, transdermal drug delivery systems, proniosomes, and others, are used in various ways when developing novel herbal drug delivery systems. These formulations are currently dominating the market. [3]

A. Liposomes

Because of how closely their morphological structure mirrors that of cell membranes, liposomes are ideal drug delivery systems. As colloidal vesicular drug delivery mechanisms, liposomes are spherical vesicles.Amphipathic phospholipid molecules create an aqueous core (aquatic domain), which can receive hydrophilic (water soluble) drugs, and a lipoidal domain imprisoned in the bilayer, resulting in a spherical vesicle with the head oriented toward the aqueous region and the tails caught in membrane. Typically, liposomes are between 0.05 to 5.00 micrometres in size. [3,4]

Since their morphological shape closely mirrors that of cell membranes, liposomes are better at delivering medications than other delivery systems. Colloidal vesicular drug delivery techniques are the spherical vesicles known as liposomes. When in contact with water, amphipathic phospholipid molecules, which have hydrophilic heads and hydrophobic tails, form a spherical vesicle An aqueous core (aquatic domain), which may house hydrophilic (water soluble) medicines, and a lipoidal domain caught in the bilayer are formed, with the heads oriented toward the aqueous area and the tails imprisoned in membrane. Liposomes typically range in size from 0.05 to 5.00 microns. [3,4]

Sr. No.	Plant constituents used	Derived from plant	Biological activity	Application of technology
1.	Nux Vomica	Strychnos nux-vomica	Anti-neoplastic, anti-inflammatory, and analgesic	Improved stability
2.	Wogonin	Scutellaria baicalensis Georgi	Anticancer	Prolonged duration of action
3.	Curcumin	Turmeric(Curcuma longa)	Anticancer	Long systemic residence time and high entrapment efficiency

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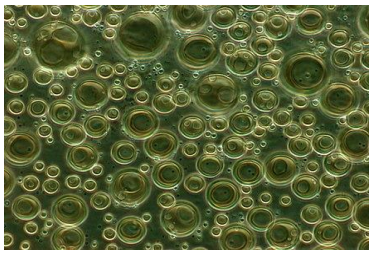
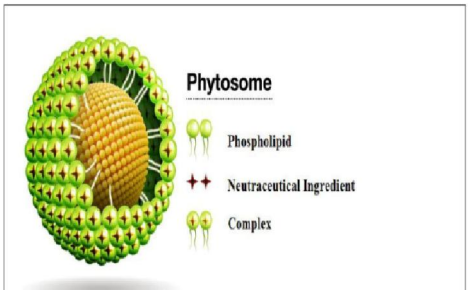


Advantages of liposomes include:

1. Improved Solubility
2. Innocuousness
3. Third, Improved Biodegradability
4. Consistent delivery
5. 5.Added Stability
6. Increased Bioavailable
7. Extreme biocompatibility [3,4,5]

B. Phytosomes

A complex form of herbal preparation known as phytosomes is made up of microscopic, cellular-like components. It is contained in a lipoidal bilayer made of phosphotydicholine and is made up of bioactive phytoconstituents from a herbal extract. Phytosomes always have greater stability profiles due to their chemical connections to phytoconstituents and phosphatidylcholine molecules. Bioactive phytoconstituents, which include terpenoids, alkaloids, glycosides, and flavonoids (the primary one), among others, have a variety of therapeutic benefits. Plant extracts (drugs) are protected from digestive system breakdown by the gastroprotective properties of phosphotydylcholine, and they exhibit an effective pharmacokinetic and pharmacodynamic profile with increased bioavailability compared to ordinary herbal extract. Since it has both of these drug domain types, it can transport both hydrophilic and lipophilic medications. One of the most important and significant families of phytochemicals is flavonoids, which have anti-inflammatory, anti-allergic, antiviral, and anti-cancer properties. They are frequently described as the biological response modifiers of nature. [6]



Sr. No.	Plant constituents used	Derived from plant	Biological activity	Application of technology
1.	Procyanidins	Grape seed	Anticancer and Anti-oxidant	Bioavailability enhancement
2.	Naringenin	Orange and grape juice	Anticancer and Anti-inflammatory	Prolong action and enhanced bioavailability
3	Curcumin	Turmeric (Curcuma longa	Anticancer and Anti-oxidant	Improved antioxidant activity and bioavailability

Table No. 2

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Advantages of Phytosome include:

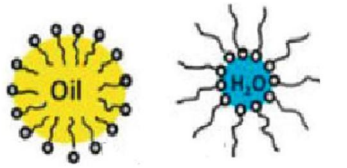
- Good lipophilicity
- Increasing bioavailability
- Superior stability[6]

C. Microemulsions

Surfactants and subsurfactants stabilise transparent, thermodynamically stable mixes of water and oil known as microemulsions. Small-scale emulsions of oil in water (O/W) and water in oil (W/O), such as droplet-type dispersions, are both possible. Sizes of micro emulsions range from 5 to 100 nm. Salt and other components are present in the aqueous phase, whereas hydrocarbons and olefins are present in the oil phase. While W/O or W/O/W emulsion is manufactured for water-soluble pharmaceuticals, O/W or O/W/O emulsion is generated for oily or lipophilic substances. [7]

Sr.no.	Plant constituents used	Derived form plan	Biological activity	Application of technology
1.	Berberine	Berberis vulgaris	Anticancer	More residence time in the body
2.	Docetaxel	European yew tree Taxus baccata	Anticancer	More residence time in body
3.	Curcumin	Turmeric (Curcuma longa)	Anti-tumour, anti-oxidant and antiplatelet aggregation	Enhance anti-inflammatory activity

Table 3



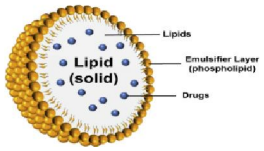
W/O microemulsion W/O microemulsion

Advantages of micro-emulsion:

- Easily soluble
- Release that continues
- Highly stability
- Simplicity for the production
- Increased bioavailability[7]

D. Transferosomes and Ethosomes

In order to deliver drugs transdermally by improving skin permeability, new and adaptable vesicular drug delivery systems built of phospholipid are called ethosomes and transfersomes. Both phospholipid vesicles have a different mode of action: ethosomes, which contain a significant amount of ethanol, destroy the membrane barrier whereas tranferosomes employ the skin's moisture and osmotic qualities to increase solubility and permeability. While transfersomes are utilised to transport pharmaceuticals to the surface layers of skin, ethosomes are noninvasive delivery systems that allow drugs to reach the deep skin layers and/or the systemic circulation. Ethosome vesicles can range in size from a few nanometers to many microns. [8]



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For Formulation of Transferosomal Drug delivery system				
Sr. no.	Plant constituents used	Derived from plant	Biological activity	Application of technology
1.	Colchicine	Genus colchicum	Anticancer, Antigut	Reduction in GIT side effects.
2.	Vincristine	Catharanthus roseus	Anti-cancer	Increase in permeability
For Formulation of Ethosomal Drug delivery system				
1.	Matrine	Sophora flavescens	Anti-inflammatory, anti-cancer, anti-rheumatism and anti-bacterial	Permeation enhancement and improved efficacy
2.	Podophyllotoxin	Podophyllum hexandrum	Purgative, anti-rheumatic, antiviral and antitumor	Higher entrapment efficiency

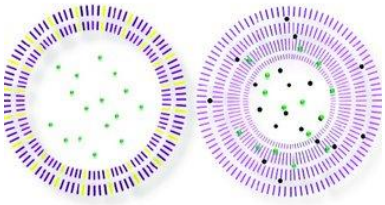
Table 4

Advantages of Transferosomes and Ethosomes

- Delivery of a number of prescription drugs
- Permeation improves the skin
- Distribution of semisolid medications[8]

E. Solid-Lipid Nanoparticle

Solid-lipid nanoparticles have a size range of 50–100 nm and are a sub-micron colloidal system. It is created by dispersing biologically relevant solid lipid particles at the nanoscale in water or an aqueous surfactant solution. Because of their potent hydrophobic core, these monolayer phospholipid carrier systems are more likely to carry lipophilic than hydrophilic medications. SLNPs are non-toxic, biocompatible, and degradable. The benefits of SLNPs include enhanced control over the release kinetics of the encapsulated component and long-term stability. [9]



F. Niosomes

Solid-lipid nanoparticles have a size range of 50–100 nm and are a sub-micron colloidal system. It is created by dispersing biologically relevant solid lipid particles at the nanoscale in water or an aqueous surfactant solution. Because of their potent hydrophobic core, these monolayer phospholipid carrier systems are more likely to carry lipophilic than hydrophilic medications. SLNPs are non-toxic, biocompatible, and degradable. Two benefits of SLNPs are enhanced control over the release kinetics of the encapsulated component and long-term stability. [10]

Types of Niosomes

1. The size and number of bilayers used to classify niosomes.
2. and the preparation technique.
3. Multilamellar, with a diameter of 0.5 to 10 mm.
4. Larger unilamellar, with a diameter of 0.1 to 1 mm
5. Small unilamellar, with a diameter of 25–500 nm[10]

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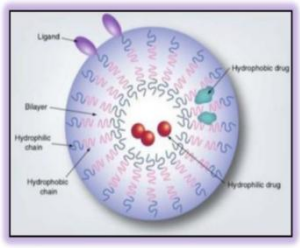

Structure of Niosome

III. HERBAL EXCIPIENTS

As they are non-toxic, less costly, and readily available, herbal or natural excipients offer a significant benefit over their synthetic equivalents. The pharmaceutical industries are becoming more attracted towards using these herbal excipients, which are mainly polymers produced from natural origin, as part of the creation of efficient and cost-effective formulations as knowledge of these excipients grows.To suit the needs of the pharmaceutical excipients, the plant generated a variety of mucilages and gums from natural sources, including carrageenan, thaumatin, lard, storax, agar, gum acacia, tragacanth, and many more. These are preferable for the creation of formulations since they are stable and involve less regulatory difficulties than their synthetic counterparts.[12,13]

3.1 Classification of Excipients

- Excipients are commonly classified based on how they are used and serve in the creation of the product
- Lubricants, gliders, disintegrants,
- Polishing film formers,
- Coating agents, binder and diluent,
- Suspending Agent, Colorants, Plasticizers, and Preservatives,
- Printing ink, a dispersing agent, and flavouring, sweeteners, and gum [12,13]

A. Colorants

To affect the colour of a substance or surface, colourant additives are substances that are added to or applied to the formulation.

Classification:

- Plant-based natural dyes derived from berries, flowers, bark, leaves, seeds, etc (e.g. Catechu, Indigofera, Myrobalan and Pomegranate).
- Cochineal and lac, two naturally occurring insect-derived colours.
- Animal-based natural dyes such as mollusk, murex snail, cuttlefish, and shellfish. •Mineral-based natural colours such as malachite, ochre, and clay. [13,14]

B. Sweeteners

Foods and additives that taste sweet like sugar but contain far less food energy than sugar-based sweeteners are known as sugar replacements. This makes them zero-calorie or low-calorie sweeteners. [12]
Sativa example: Since stevia has no effect on blood sugar levels, it is safe for diabetics.

C. Binders

Powders, granules, and other dry components are physically "bonded to gether" by binder excipients, which function as an adhesive, giving the product the required mechanical strength.
Some solution binders that can dissolve in a solvent include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose, and polyethylene glycol. [12,13,14]

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D. Diluents

To promote weight and composition homogeneity, diluents are fillers used in pharmaceutical tablets. Starches, hydrolyzed starches, and starches that have undergone some pre-gelatinization are all examples of natural diluents. [13]

E. Viscosity Builders

Pharmaceuticals' consistency and thickness can be altered by adding viscosity modifiers. Thickeners, texturizers, gelation agents, and stiffening agents are examples of substances that can be used as viscosity modifiers. In order to turn liquids into pastes, gels, or powders, a variety of viscosity modifiers can be used, aiding formulators in creating the ideal product for consumers. A viscosity modifier can thin a liquid out to make it easier to pour and eventually improve flavour. [13,14]

Various thickeners can be discovered in nature or be produced using natural thickeners.

F. Disintegrants

The oral solid dose forms have disintegrants added to them to help with their de-aggregation. When in contact with moisture, disintegrants are designed to trigger the fast disintegration of solid dosage forms..

Example are:

Isapghula Husk (Plantago ovata)

Plantago ovata seeds were cooked for a short period of time after being steeped in distilled water for 48 hours to completely release the mucilage into the water.

Rosa sinesis hibiscus Linn.

Chinese hibiscus, China roses, and shoe flower plant are all common names for the Malvaceae family member Mucilage Hibisicus rosa-sinensis Linn.

Ligustrum sativum Lepidium sativum (family-Cruciferae), also known as asaliyo, is a plant that is easily accessible in India and whose mucilage has been identified to function as a super disintegrant. It is commonly used as a herbal treatment and pharmaceutical excipient as a disintegrating agent. [11,12,13]

3.2 Advantage of Herbal Excipients

1. Biodegradable – Polymer that is naturally created by all living things. They don't appear to have any negative consequences on people or the environment.
2. Biocompatible & Nontoxic - Chemically speaking, practically all of these plant components are mostly constituted of monosaccharides, which repeat. They are therefore not poisonous.
3. They are more affordable since they are readily available and their production costs are substantially lower than those of synthetic materials.
4. Safe and free of side effects - Because they come from a natural source, they are risk-free and free of side effects.
5. Easy accessibility - Because they are used by people, they are created in numerous nations.[13,14]

3.3 Disadvantages of Herbal Excipients

1. Microbial contamination – While producing, they are exposed to the outside environment, which increases the likelihood of significant microbial contamination.
2. Variation: In contrast to the manufacture of naturally derived polymers, which is influenced by a variety of environmental and physical conditions, synthetic manufacturing is regulated by technique and set amounts of the component.
3. The uncontrolled rate of hydration - Changes in the area, species, and climate conditions, as well as variations in the collection of natural materials at different times of the day, are all responsible for variations in the quantity of chemical components present in a given material.
4. Slow Process - The manufacturing speed cannot be changed because it depends on the environment and a number of other factors. Natural polymers are created in enormous quantities but slowly.

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3.4 Application of Herbal Excipient

- **Tamarind Gum:** The 21 type enduring families include the tamarind tree (Tamarindus indica). The Tamarind Kernel Powder (TKP), also known as Tamarind xyloglucani, is obtained from the endosperm of the tamarind seed whose microspheres were generated and ranged in size from 230 to 460 m. [14]
- **Guar Gum:** Guar gum is made from the endosperm of Cyamopsis tetragonolobus, a legume plant. When the thin covering of fibrous material that makes up the husk is removed and split from the endosperm halves with polishing, refined guar splits are obtained. Alkalies at high concentrations also have a tendency to reduce viscosity, while strong acids tend to hydrolyze substances and cause them to lose some of their viscosity. Most hydrocarbon solvents cannot dissolve it.[14]
- **Locust Bean Gum:** Carob gum, commonly known as locust bean gum (LBG), is made from the refined endosperm of seeds from the Ceretonia siliqua L. carob tree. It is a tree in the family of legumes that is evergreen. The endosperm from carob tree seeds must be separated and processed in order to produce carob bean gum.[14]
- **Honey Locust Gum:** It is known to us by its scientific name, Gleditsia triacanthos, and it is a member of the Leguminosea order (suborder Mimoseae). You may get gum from the seeds.[14]
- **Aloe Mucilage:** Aloe barbadensis It is taken from miller leaf extract. It has been shown that, in addition to the various carbohydrates, aloe parenchyma tissue/pulp also contains proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds, and other minute organic molecules. The bulk of the gel's polysaccharides are discovered to be composed of partly acetylated mannan and pectic material, according to several studies. [14]
- **Pectin:** Pectins are linear polysaccharides that aren't starches that are taken out of plant cell walls. In order to increase the stability of the folic acid, combinations of alginate and pectin polymers were used in the creation of folic acid-containing microcapsules. [14]
- **Alginates:** Brown seaweed was used to make the polymers and natural polysaccharides known as alginates (Phaeophyceae). Alginate may be transformed into its salt form, of which sodium alginate is the one that is used the most frequently in modern times. Liposomes, matrix-type alginate gel beads, gastrointestinal transit time management, local applications, and biomolecule delivery in tissue engineering applications are just a few of the choices for drug administration that alginates provide. [14]

IV. USE OF NOVEL HERBAL DRUG DELIVERY SYSTEM (Patches) IN TREATMENT OF DIABETES

Motherwort charantia Linn Diabetes is typically treated with it using drugs. The goal of the current experiment was to create and assess Momordica charantia Linn transdermal patches. Using hydroxypropyl methyl cellulose as a polymer, transdermal films that are separated from M and include the herbal medicine component An ethanolic extract of Charantia fruits was produced. We looked at the films' stability research, rat skin irritancy, biochemical studies, acute and subacute antihyperglycemic activity in diabetic rats, folding durability, thickness, weight variation, drug content, and in vitro diffusion investigations. [16]

Transdermal patches containing M. charantia 10 mg/patch were reported to weigh 0.03 gm. M. charantia patches were determined to be good in terms of patch thickness at 10 mg/patch. Transdermal patches containing 10 mg of M. charantia were shown to release 47.59% of their active ingredients after 6 hours in a 10% hydroalcoholic phosphate buffer with a pH of 7.4. [16]

The transdermal method is demonstrated by the minimal skin irritation, in vivo findings, and the effective reduction of blood glucose levels by the patches. According to the findings, the well-known herbal medication made from M. charantia Linn. has been discovered to be helpful for treating diabetes when made using contemporary pharmaceutical formulation processes, such as NHDDS. [16]

The rat where used in the experiment shows the following Drug release rate as per graph after application:

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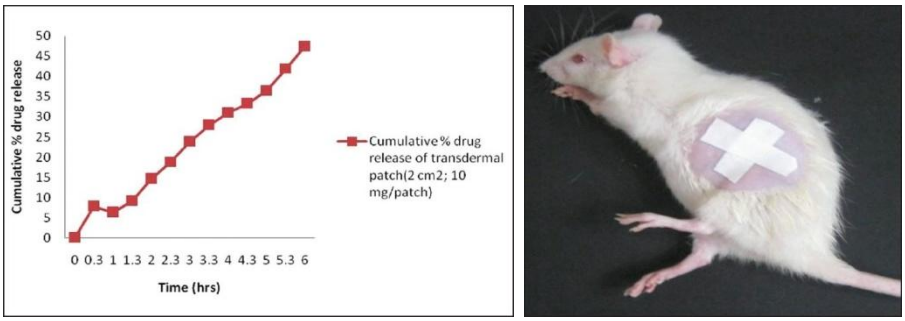

Figure: Rat with Transdermal patch of M. Charantia

V. USE OF NOVEL HERBAL DRUG DELIVERY SYSTEM (LIPOSOMES) IN TREATMENT OF DEMENTIA

Dementia is mostly caused by neurodegenerative disorders (such as Alzheimer's, Parkinson's, and others) that destroy brain cells. Blood-brain barrier is the main obstruction to drugs reaching the central nervous system (BBB). This study's goal was to create a liposomal drug delivery system with leaf extract from Aphanamixis polystachya that would be utilised to treat neurodegenerative illnesses like Alzheimer's and Parkinson's disease. [17]

Aphanamixis polystachya (Wall) R. Parker is a medicinal plant that contains chemical elements that probably have therapeutic properties. It is a member of the Meliaceae family. This plant has the same phytochemicals that have antioxidant, antibacterial, antidiarrheal, thrombolytic, diabetes-lowering, and cytotoxic properties. To the best of our knowledge, no drug delivery mechanism has been used to improve the performance of the A. polystachya plant extracts and their efficacy against dementia. CNS depressive and analgesic effects were reported for the methanol extract of A. polystachya leaf. [17]

The fundamental issue with herbal medications is that they have relatively poor water solubility, which results in decreased bioavailability and increased systemic clearance. The stability of the phytochemicals on a physical and chemical level is still another issue. To increase the bioavailability of several phytoconstituents, liposomes have been used. One of the main reasons the liposome was chosen over other nano drug delivery methods was due to its exceptional ability to interact with the body's membrane. Studies have determined that the liposome does not penetrate the blood-brain barrier; rather, it adheres to the membrane and, after the liposome opens, permits the medication to enter through the other side. [17]

Liposomal preparation process for Aphanamixis polystachya leaf extract:

In order to create the liposomal preparation, the solvent injection approach was applied in two separate ways (drugs that dissolved in ethanol and drugs that dissolved in water). Here, the medication was extracted, combined with an extract of phospholipids and cholesterol, and then further dissolved in ethanol. Then, using the magnetic stirrer at a predetermined speed, the mixture was injected/instilled into the water that it was being swirled at two distinct rates. The leftover surplus ethanol that was in the finished product was heated vigorously to evaporate it. To allow the mixture to cool, it was left unattended for some time. In a similar way, when this procedure first started, medication extract was added to the water. The additions of cholesterol and phospholipid were then dissolved using ethanol. The ethanolic solution containing phospho-lipid and cholesterol was then injected into the aqueous drug solution at two different rates of injection, and it was being stirred at a predetermined rate of 10 mL of the ethanolic solution that was injected into 100 mL of distilled water during the preparation of the liposomal batches containing A. polystachya leaf. [17]

A. polystachya leaf extract delivered by liposomes significantly and convincingly improved the behavioural traits of dementia-induced rats even when compared to the extract group, which is perhaps likely connected to the extract's increased permeability through the BBB.[17]

VI. USE OF NOVEL HERBAL DRUG DELIVERY SYSTEM (NIOSOMES) IN TREATMENT OF WOUND HEALING

Traditional medicine has offered a variety of natural remedies for skin damage, including wound healing that mostly uses medicinal herbs, one of which is Psidium guajava. It is necessary to create herbal formulations of cutting-edge

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drug delivery systems, such as niosomal formulation, in order to lessen the adverse effects connected with allopathic therapy. [18]

6.1 Psidium Guajava and its Medicinal Uses

Psidium guajava, often known as the guava, is a member of the Myrtaceae family and is referred to as the poor man's apple of the tropics. Guava leaves have long been used medicinally, and various nations have employed preparations of the leaves in traditional medicine. Many ailments, including inflammation, diabetes, hypertension, wounds, aches, and fever, have historically been treated with this herb. Natural guava leaf, root, and bark extracts have been used traditionally to treat wounds, ulcers, toothaches, coughs, swollen gums, gastroenteritis, vomiting, diarrhoea, and dysentery. The guava leaves have powerful anti-microbial effects on gram-positive and gram-negative organisms, as well as antibacterial and antiseptic characteristics. The leaves of the guava are anti-inflammatory. Guava tree leaves are processed to make a decoction that is used to treat brain diseases including epilepsy and spasms (CNS activity). The young leaves and shoots are employed in the treatment of malaria as well as for renal inflammation and other kidney-related issues. [18]

A wound is when the skin's epithelial integrity is compromised, or when the cellular, anatomical, or functional continuity of live tissue is lost or broken. Physical injuries cause wounds, which result in an opening or break in the skin and alter the normal architecture and function of the skin. [18]

6.2 Why Niosomes

In order to encapsulate both hydrophilic and hydrophobic molecules, niosomes, which self-assemble from non-ionic surfactants with or without cholesterol, are utilised. One of the numerous Method Expanded used nowadays is the use of novel drug delivery technologies, such as niosomal formulations, to improve the transport and effectiveness of several materials through the stratum corneum. Niosomes have been demonstrated to significantly improve transdermal drug delivery across the stratum corneum, which serves as the principal barrier to drug absorption via the skin. As a result, niosomes can be employed for targeted drug administration via two different methods. By hydrating it and altering its characteristics by lowering transepidermal water loss, niosomes enhance stratum corneum. As its matrix delays the release of the medicine in cases of skin injury, niosomes boost drug transfer across the stratum corneum, lowering the necessity for changing clothes throughout the day. [18]

VII. MATERIALS AND METHODS

7.1 Preparation of Leaf Powder

The fresh guava plant leaves were gathered and dried. After 4 to 5 weeks of drying, the dried leaves were ground into a powder using an electric blender or blander. The powdered mixture was then put through sieve number 44 and should be kept in an airtight container. [18]

7.2 Extraction

Following the creation of the powder, ethanol is used to remove the leaves from the powder. In this procedure, ethanol is heated during the extraction of 10 grammes of powder, and the process is maintained until a clear extract is achieved. A rotating vacuum evaporator operating at 50–55 oC and 85 rpm was used to evaporate the extract to dryness under decreased pressure after each extraction solvent. This extract was put onto a porcelain dish, placed on a hot plate for one hour, let to air dry for two days, and then triturated into a fine powder. The extracted powder is shown in the next image; the extract is further purified using a soxhalet device. [18]

7.3 Preliminary Phytochemical Analysis

To examine several chemical groups found in extracts, preliminary phytochemical assays were conducted. The phytochemical tests for alkaloids, flavonoids, carbohydrates, proteins, tannins, steroids, terpenoids, phenols, quinones, starch, fat, and oil were conducted after the ethanolic extract of guava leaves was dissolved in a variety of solvents. Psidium guajava's physio-chemical composition was investigated using methods that are often used to determine if phytochemicals are present or not. [18]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, January 2023
Impact Factor: 7.301

7.4 Anti Microbial Activity

Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli were the species employed in the test. The agar diffusion technique was used to conduct the anti-microbial investigation. After chilling and drying the produced nutrient broth in sterile petri plates, each bacterial culture was distributed using a micron wire loop. A sterile cork borer was used to create holes that were 4 mm deep. The extract was then injected into the hole to a volume of 0.5 gm. 48 hours are spent incubating plates at 37 °C. The zone of inhibition that had formed for that specific chemical at each microorganism strength was then assessed. [18]

7.5 Preparation of Formulations

Method of Reverse Phase Evaporation: Supplies Used: The formulation includes Span 60, cholesterol, diethyl ether, chloroform, and phosphate buffer. Twelve different formulations were created by adjusting the cholesterol ratio and the medication to surfactant ratio. Diethyl ether and chloroform are used to dissolve the surfactant and cholesterol in a 1:1 ratio. To this, the drug's aqueous phase is introduced. The two phases that arise are sonicated at 4-5 °C. After a modest amount of phosphate buffer is added, the clear gel that has formed is further sonicated. Low pressure is used to eliminate the organic phase. Niosomes are produced by diluting the niosomal solution with phosphate buffer and heating it for 10 minutes at 60°C in a water bath. After that, a projection microscope is used to see the resulting niosomes. [18]

VIII. CONCLUSION

Because it contains wound-healing qualities including anti-inflammatory, antioxidant, and anti-microbial activity, Psidium guajava is used to treat wound healing. In the current research, ethanol was used as a hot extraction solvent to extract 10gms of powdered material using the Soxhlet equipment.

According to antimicrobial studies, P. guajava L's ethanolic extract had inhibitory effects on E. coli, with respective zones of inhibition of 25 mm. This demonstrates that the plant may be effective in treating illnesses resulting from these bacteria, including skin infections. [17]

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IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, January 2023
Impact Factor: 7.301

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