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INTEGRATION OF NANOTECHNOLOGY IN HERBAL MEDICINE: EMERGING TRENDS, CHALLENGES, AND FUTURE PROSPECTS

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ABSTRACT

Herbal medicines have been an important source of therapeutic agents for a long time because they come from natural sources and generally have fewer side effects. Many herbal bioactives face issues such as low solubility, reduced bioavailability, instability, and limited specificity to their targets. Combining nanotechnology with herbal medicine has created new opportunities to address these issues. Different types of nanocarrier systems, including polymeric nanoparticles, solid lipid nanoparticles, liposomes, nanoemulsions, and metallic and magnetic nanoparticles, have been created to improve the solubility, stability, targeted delivery, and controlled release of plant-derived compounds. These nanostructured systems enhance the pharmacokinetics of herbal medications, lower the necessary dosage, and decrease toxicity while preserving or improving their therapeutic effectiveness. Examples include nanoformulations of curcumin, quercetin, berberine, and silymarin that demonstrate enhanced effects in cancer prevention, antioxidant activity, inflammation reduction, and liver protection. Techniques like scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), and dynamic light scattering (DLS) are used to assess particle size, shape, and surface charge. While nanotechnology presents notable benefits, there are still concerns about its scalability, safety, and regulatory issues. Nanotechnology-based delivery systems offer a promising method to convert traditional herbal medicines into scientifically validated, effective, and targeted modern treatments.

KEYWORDS: Herbal medicines, Phytoconstituents, Nanotechnology, Nanocarriers.

1. INTRODUCTION

Throughout history, medicinal plants have been a significant resource for treating illnesses and maintaining health. Herbal medicines have been essential in traditional healing practices like Ayurveda, Siddha, Unani, and Traditional Chinese Medicine.[1] These natural treatments are valued for being easy to access, compatible with the body, and having fewer side effects than synthetic medications. The World Health Organization (WHO) states that about 80% of people in developing countries rely on herbal or traditional medicines for their primary healthcare needs. Although herbal formulations have significant therapeutic potential, they often face challenges like poor solubility, instability, low bioavailability, and variable pharmacokinetic profiles, which can greatly limit their effectiveness in clinical settings.[2-4]

Recent developments in material sciences have made nanotechnology an important tool that can significantly change how herbal drugs are delivered and how they perform. Nanotechnology refers to the creation, analysis, and use of materials and systems that generally measure between 1 and 100 nanometers. At this scale, materials show distinct physical, chemical, and biological characteristics that can be used to enhance drug delivery. Combining nanoscience with herbal medicine presents a new approach to improve the solubility, stability, bioavailability, and targeted effectiveness of active compounds in plants, while also minimizing toxicity and the frequency of doses.[5]

Compounds like flavonoids, terpenoids, alkaloids, tannins, and phenolic acids contribute to the medicinal properties of various herbal medicines. Many of these molecules have limitations such as low solubility in water, instability in physiological conditions, or difficulty in crossing lipid membranes because of their large size.[6] Standard dosage forms frequently do not deliver these compounds effectively to the intended location, resulting in decreased therapeutic effectiveness. Systems that use nanocarriers, including polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLNs), nanocapsules, nanoemulsions, and magnetic nanoparticles, have been created to address these challenges.[7] These nanocarriers safeguard the active plant compounds from breaking down, improve their absorption through biological membranes, and enable sustained or targeted release at the affected area.[8]

Nanotechnology-based novel drug delivery systems (NDDS) offer various advantages for herbal formulations, such as

- Improved solubility and dissolution rate of phytoconstituents that are not easily soluble.
- Enhanced ability to pass through biological barriers, including the intestinal epithelium and the blood-brain barrier.[9]
- Maintained and regulated release of medication to ensure effective concentration for treatment.
- Delivery targeted to specific sites to reduce overall side effects.
- Improved patient adherence because of less frequent dosing.

Polymeric nanoparticles, constructed from biodegradable and biocompatible substances such as polylactic acid (PLA), polyglycolic acid (PGA), or their copolymer PLGA, are widely researched as carriers. These nanoparticles can enclose both water-soluble and water-insoluble plant components, safeguarding them from breakdown and allowing for controlled release. Lipid-based systems like solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) enhance solubility and compatibility with biological systems. Metallic nanoparticles, particularly those produced with plant extracts as reducing agents, have received interest due to their effective antimicrobial, antioxidant, and anticancer

properties. This is evident in the cases of silver (AgNPs), gold (AuNPs), and nickel (NiNPs) nanoparticles.[10]

In recent years, researchers have effectively included herbal bioactive compounds such as curcumin, quercetin, berberine, naringenin, ginkgo biloba, camptothecin, and silymarin in different nanosystems. Curcumin-loaded polymeric nanoparticles have demonstrated better anti-inflammatory, antimicrobial, and anticancer effects than traditional curcumin formulations because they have improved solubility and cellular absorption. Nanoemulsions and liposomal formulations of quercetin and naringenin have shown enhanced antioxidant and liver- protective properties. In addition to improving medications, nanotechnology also plays a role in the development of nutraceuticals. Nutraceuticals, which are bioactive compounds derived from food sources, frequently encounter similar bioavailability issues as herbal medications. Nanocarriers like nanoemulsions, nanocapsules, and solid lipid nanoparticles are being more frequently utilized to encapsulate vitamins, polyphenols, carotenoids, and essential oils. This helps protect these substances from degradation during processing and digestion while enhancing their absorption in the intestine.[11]

Characterizing nanoparticles is a crucial part of their development. Methods like scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), dynamic light scattering (DLS), and zeta potential analysis are used to assess particle shape, size distribution, surface charge, and stability. These characteristics directly affect how nanosystems behave in the body and their effectiveness as treatments. Nanotechnology in herbal medicine offers notable benefits, but it also faces several challenges.[12] These include high production costs, complicated processes for scaling up production, potential toxicity of nanoparticles, and the absence of standardized regulations for safety evaluation. The field of nanotoxicology is currently studying how nanoparticles interact biologically, how they distribute within the body, and their potential harmful effects on cells to ensure safety and effectiveness before they are used in clinical settings.[13]

In the near future, herbal medicines that utilize nanotechnology are anticipated to be important in personalized and precision medicine. Nanotechnology has the potential to improve drug delivery, reduce side effects, and increase treatment effectiveness, thereby connecting traditional practices with contemporary advancements in pharmaceuticals. The integration of traditional plant-based medicine with advanced nanoscience marks a significant change in creating safer, more effective, and targeted natural treatments.[14]

1.1. Nanotechnology in Herbal Drug

Nanotechnology can improve the delivery of herbal drugs that are not easily soluble in water, allow for targeted delivery to specific cells or tissues, facilitate crossing tight epithelial and endothelial barriers, enable the release of larger herbal molecules, support the simultaneous delivery of multiple drugs, and help visualize drug delivery sites by combining herbal drugs with imaging techniques.[15-17]

Researchers in herbal and nanomedicine have found that therapeutic nanoparticles (NPs) can serve as a more effective drug delivery system compared to traditional drug forms. A transdermal gel called nanocarriers transdermal gel (NCTG) was developed using optimized nano transfer somes containing diclofenac diethylamine (DDEA) and curcumin (CRM) to deliver a prolonged and targeted effect. The small size of NCTG nanoparticles leads to better drug absorption. Additionally, when lecithin is used alongside it, it creates a hydration gradient for the vesicles, which enhances permeability and reduces degradation and clearance by surfactants compared to the marketed gel and regular curcumin gel. Nanotransfersomes of DDEA and CRM were developed and improved to offer a large surface area with

significant penetration capability, resulting in high bioavailability.[18] pH-sensitive nanoparticles containing a combination of curcumin and celecoxib were developed as a potential treatment for ulcerative colitis. Curcumin solid lipid nanoparticles (CRM-SLN) were developed to have a high loading capacity and chemical stability for treating oral mucosal infections. Hydrogel nanoparticles containing curcumin, made from hydroxyl propyl methyl cellulose (HPMC) and polyvinyl pyrrolidone (PVP), were successfully created and showed a notable enhancement in anti-malarial effectiveness. The leaf extract of Mukia scabrella was shown to produce silver nanoparticles (AgNPs) and exhibited notable antimicrobial effects against multidrug-resistant Gram-negative bacterial pathogens associated with healthcare settings.[19]

1.2. Challenges

Most complications related to the use of herbal medicines have been found to stem primarily from some governments categorizing these products as foods or dietary supplements. Herbal products generally do not need to provide proof of quality, strength, or safety before they can be sold. As a result, the quality testing and manufacturing standards for herbal medicines are often less rigorous or structured. Additionally, in some instances, practitioners of traditional medicine may not be registered or licensed. Consequently, the safety of traditional and herbal remedies became a major concern for both national medical professionals and the general public.[20]

In many countries, herbal remedies and related products are introduced without mandatory safety or toxicology evaluations because there are insufficient tools to ensure quality control and proper manufacturing processes. These products often reach consumers without the need for a prescription and without awareness of the possible risks related to herbal medicines. Depending on definitions and regulations in various countries, a medical herb may be categorized as food, therapeutic food, nutraceutical, or herbal remedy.[21] Introducing herbal medicines into national drug regulation poses significant challenges and creates confusion for both patients and consumers. For instance, in the United States, the Dietary Supplement Health and Education Act (DSHEA) of 1994 regulates natural remedies. A dietary supplement is a substance that includes a "dietary element" intended for consumption. This may consist of vitamins, minerals, herbal products, and other phytochemicals, provided that the herb was available on the market prior to 1994 and has undergone additional toxicity studies. In many countries, the regulatory information regarding herbal products is frequently not shared among regulatory experts and pharmacovigilance centers. In India, traditional and alternative medicines were incorporated into the Drug and Cosmetic Act of 1940 and its amended rules from 1959, which include traditional Indian medicine systems as recognized by the government. The original committee was established in 1962, as various specialized panels for different Indian Systems of Medicine (ISM) were recognized periodically. In 1969, Unani, Ayurveda, and Siddha were established as distinct categories under Act 13 of 1964, which was revised in 1983, 1987, 1994, and 2002 with some changes. In 2006 and 2008, several guidelines for the assessment and research of ISM drugs were issued according to the Drug and Cosmetic Rule of 1945. In 1970, the Central Council of Indian Medicine (CCIM) was formed to develop and enforce specific standards in Indian Systems of Medicine (ISM), including curriculum and syllabi.[22] The Sowa Rigpa medical system was incorporated into the Central Council of Indian Medicine (CCIM) in 2012, along with Unani, Siddha, and Ayurveda. In 2013, the Indian Medicine and Homeopathy Department (ISM & H) was established with the aim of creating the ISM. Additionally, the Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) was renamed to reflect this change. In 2014, a separate ministry for AYUSH was created.[23]

2. TYPES OF NANOCARRIERS USED FOR HERBAL DRUGS

2.1. Polymeric Nanoparticles

Researchers are currently focusing on nanotechnological methods that utilize medicinal plants. They have created various new delivery systems, including polymeric nanoparticles. These materials, which are composed of biodegradable and biocompatible polymers, offer a method for controlled drug delivery.[24] Polymeric nanoparticles are a potential option for drug delivery systems due to their ability to be directed toward specific areas. These nanoparticles are colloidal systems that serve as carriers to regulate the release of drugs and target them effectively. Polymeric nanoparticles can enhance the solubility of ingredients, lower the required therapeutic dose, and improve the absorption of active components when compared to traditional formulations. Additionally, nanoparticles offer benefits when utilized in blood due to their stability and safety. They are non-toxic, do not promote blood clotting, do not trigger immune responses or inflammation, do not activate neutrophils, and can evade the reticuloendothelial system. Polymeric nanoparticles are occasionally utilized to target specific tissues or function as cell surfaces.[25] These nanoparticles can be produced through different methods based on their intended use and the substances they carry. These particles are composed of biodegradable polymers that can be either natural or synthetic. Natural materials are favored due to their various benefits, including the capacity to deliver multiple active components with a single carrier, extend the duration of action in the body, offer a sustained release mechanism, and minimize side effects. Nanoscale systems are also referred to as submicrometer, as their particle diameters are less than 1 micrometer. They offer multiple therapeutic benefits in different areas, such as methods of delivery, targeted action, and enhanced effectiveness, making them appealing to researchers. Taking some traditional formulations by mouth can result in side effects, and the acidic pH of the stomach may cause the active ingredients to break down.[26,27]

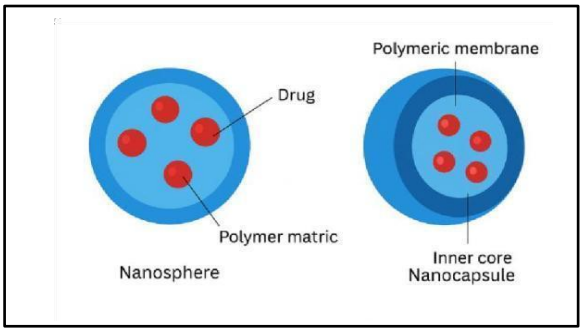

Fig.1: Polymeric Nanoparticles.

Polymeric nanoparticles could help decrease these issues. In eye treatment, nanoparticles manage the release of active ingredients, which enhances their availability in the eye and minimizes side effects. Polymeric nanoparticles can have diameters between 10 and 1,000 nanometers, effectively protecting drugs. They can take the form of nanocapsules (NCs) or nanospheres (NSs), with variations in their composition and structural arrangement. Nanocapsules consist of an oily center encased in a polymer membrane. The active ingredient may either adhere to the polymer membrane or be dissolved within the oily center. Nanospheres are composed solely of a polymer structure that holds or adsorbs the active ingredient. There is a growing interest in discovering new types of polymers, some of which have already been widely used to create polymeric nanoparticles. Examples include poly-L-lactic acid (PLA) and its copolymers with glycolic acid (PLGA). The primary methods for producing polymeric nanoparticles can be categorized into two main types: in situ polymerization, which involves dispersed monomers like alkyl cyanoacrylate, and the precipitation method, which uses preformed polymers such as PLA, PLGA, poly(ε-caprolactone) (PCL), methacrylic acid copolymers, and acrylic or

methacrylic esters. No matter the method used, the products are produced as aqueous colloidal suspensions. Some issues can hinder industrial use, such as nanoparticle precipitation and stability concerns. These problems can be minimized through drying methods, like sublimation (freeze drying), which facilitate dehydration while preventing the aggregation of particles.[28]

2.2. Metallic Nanoparticles

Metal nanoparticles refer to metal particles that have dimensions, including length, width, and thickness, ranging from 1 to 100 nanometers. There are several liquid phase techniques for producing metallic nanoparticles, including chemical reduction, sol-gel processes, and reversed micelle methods. Spherical nanoparticles made of noble metals were continuously produced using chemical reduction methods.[29] This diagram illustrates the various methods used to synthesize metallic nanoparticles, as shown in Figure No. 2. Metal nanoparticles are commonly utilized because of their distinct properties, which include a large surface area, a specific electronic structure that lies between molecular and metallic states, and a significant number of low coordination sites. These are utilized in the magnetic separation of labeled cells and other biological substances, as well as for delivering therapeutic drugs, genes, and radionuclides. They are also used in radio frequency techniques for tumor breakdown through hyperthermia and as contrast agents for magnetic resonance imaging.[30]

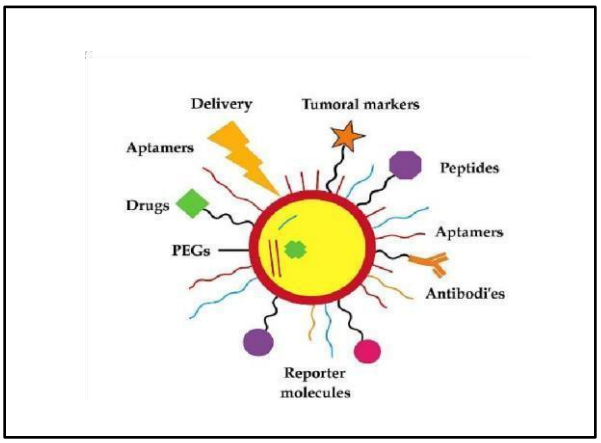

Fig.2: Metallic Nanoparticles.

2.3. Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles (SLNs) are colloidal carrier systems created in the early 1990s. They integrate the benefits of various colloidal systems, including emulsions, liposomes, and polymeric nanoparticles, for drug delivery while reducing some of their disadvantages.[31] SLNs exhibit greater physicochemical stability and provide improved protection for sensitive drugs against degradation. Additionally, they can be produced easily on a large scale. SLNs consist of colloidal particles made from highly purified triglycerides, primarily composed of lipids that remain solid at room temperature. These structures are made from solid lipids or combinations of them and are stabilized by surfactants.[32,33] The lipid particle has a solid matrix that can safeguard drug molecules from chemical breakdown. When the system is created, crystallization takes place, leading to low efficiency in encapsulating and releasing the drug. Introducing a liquid lipid (oil) into an oil/water emulsion that contains a solid lipid or a blend of solid lipids enhances the development of solid lipid nanoparticles (SLNs). Because of their small size (50–1,000 nm) and compatibility with biological systems, SLNs can be utilized in pharmaceuticals for different methods of administration, including oral, parenteral, and transdermal routes.

Nanostructured lipid carriers (NLCs) enhance the effectiveness of encapsulating active substances and reduce their loss during the process. As second-generation systems, NLCs are gaining interest as alternative options for delivering colloidal drugs. These systems consist of a combination of lipid and solid phases that create a disordered liquid lipid matrix, which holds active substances. Some examples of lipids used in the solid phase include stearic acid, glyceryl dilaurate, hydrine, glyceryl monostearate, and cetyl alcohol. Examples of substances in the liquid phase are oleic acid, glyceryl monodicaprylate, and caprylic/capric acid. Typically, about 5% of the drug (by weight) is included in the initial precursor mixture for nanoparticle lipid carriers (NLCs), leading to a drug loading efficiency of around 3% to 4%, while the usual encapsulation efficiency is about 70%. These formulations can be administered through various methods, including oral, pulmonary, intravenous, and dermal routes. The latter option is beneficial because the films create barriers, provide a controlled release of substances, and the formulation is biodegradable and relatively non-toxic. Additionally, the small size of the two particles allows for better contact with the outer layer of the skin, which helps enhance the penetration of the drug.[34]

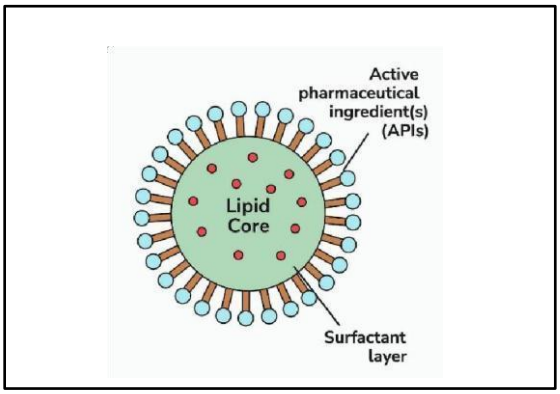

Fig.3: Solid Lipid Nanoparticles.

2.4. Liposome

Liposomes are tiny vesicles made up of one or more layers of lipids, with a water-based solution between the layers. Hydrophilic substances are contained within the water-based area, while lipophilic substances that have been adsorbed are integrated into the membrane. Another option is to encapsulate both types of substances. These vesicles are mainly made up of phospholipids (either synthetic or natural), sterols, and an antioxidant. Liposomes are categorized based on their size, the number of layers they have, and their surface charge.[35]

Liposomes are categorized based on their surface charge as anionic, cationic, or neutral. Liposomes can be categorized based on their shape, size, and the number of lamellae into oligo-, uni-, or multilamellar types, as well as small, large, or giant. Unilamellar liposomes (ULs) consist of a single bilayer and are categorized by size. They include small unilamellar liposomes (SUVs), which have diameters of about 25–100 nm; large unilamellar liposomes, with diameters ranging from 100 nm to 1 μm; and giant unilamellar liposomes, which have diameters larger than 1 μm and can reach sizes in the tens of microns, similar to the size of eukaryotic cells. Multilamellar liposomes (MLVs) are made up of multiple layers arranged concentrically, resembling the structure of an onion. ULs are typically present in dilute solutions of surfactants, while MLVs occur in more concentrated systems. Andrade et al. developed, characterized, and studied the antitumor effects of liposomes containing Cratylia mollis lectin (Cra), which was purified from the seeds of Cratylia mollis Mart (Camaratu bean), against Sarcoma-180 in Swiss mice. Cra, known for its immune-boosting effects, was included in the protein supplementation of the animals' diet. This action supports the production of

immunoglobulins in cultures of human B lymphocytes and promotes antibacterial activity in laboratory conditions. Systems with positively charged surfaces were created using a mixture of soybean-phosphatidylcholine, cholesterol, and stearylamine in a molar ratio of 7:2:1. This involved using 36 micromoles of lipids per 10 microliters of a 0.2 M phosphate buffer solution at pH 7.4.[36]

Table 1: Herbal Drugs in Nanoparticles

Sr. No.	Name of Active Ingredient	Formulation (Nanoparticle Type)	Activity / Therapeutic Use
1	Curcumin (from Turmeric)	Polymeric nanoparticles, SLNs	Anti-inflammatory, Anticancer, Antioxidant
2	Quercetin (from plants like onion, apple)	Liposomes, Solid Lipid Nanoparticles	Antioxidant, Antiinflammatory, Anticancer
3	Resveratrol (from grapes)	Polymeric nanoparticles, Liposomes	Cardioprotective, Anticancer, Antioxidant
4	Epigallocatechin gallate (EGCG) (from green tea)	Liposomes, SLNs	Antioxidant, Anticancer, Antiobesity
5	Berberine (from Berberis species)	Metallic nanoparticles (gold, silver)	Antimicrobial, Antidiabetic, Anticancer
6	Silymarin (from Milk Thistle)	Solid Lipid Nanoparticles, Polymeric NPs	Hepatoprotective, Antioxidant
7	Curcumin + Piperine	Polymeric nanoparticles	Enhanced bioavailability, Antiinflammatory, Anticancer
8	Aloe vera extract	Liposomes, SLNs	Wound healing, Antimicrobial, Anti-inflammatory
9	Ginsenosides (from Ginseng)	Polymeric nanoparticles, Liposomes	Immunomodulatory, Anticancer, Neuroprotective
10	Andrographolide (from Andrographis paniculata)	Solid Lipid Nanoparticles	Anti-inflammatory, Anticancer, Hepatoprotective

3. METHODS OF PREPARATION

3.1. Solvent emulsification–diffusion method

The emulsification–solvent diffusion method is a commonly used and efficient technique for creating polymeric nanoparticles and nanocarriers, especially for encapsulating herbal bioactive compounds. This method involves the mixing of an organic solvent that contains both the polymer and the drug into a water-based phase that includes a stabilizer, while maintaining continuous stirring. At first, an organic solvent that mixes well with water, like ethyl acetate, acetone, or ethanol, is used to dissolve the polymer (such as PLGA, PCL, or chitosan) together with the herbal drug or extract. The organic phase is then mixed with an aqueous phase that includes a stabilizer or surfactant such as polyvinyl alcohol (PVA), Tween 80, or Span 60. This process is done using high-speed homogenization or ultrasonication to create a fine oil-in-water (O/W) emulsion.

After the emulsion is created, the organic solvent starts to spread into the outer water phase because of the concentration difference. This leads to the polymer precipitating around the drug molecules and the development of solid nanoparticles. The diffusion process can be sped up by keeping the temperature at a moderate level and stirring consistently. Once diffusion is finished, the solvent is evaporated using reduced pressure or gentle heating to eliminate any remaining solvent, resulting in a stable colloidal suspension of nanoparticles. The nanoparticles are collected using centrifugation, washed multiple times with distilled water to eliminate any unencapsulated drug and stabilizer residues, and then freeze-dried to produce a dry nanoparticle powder.

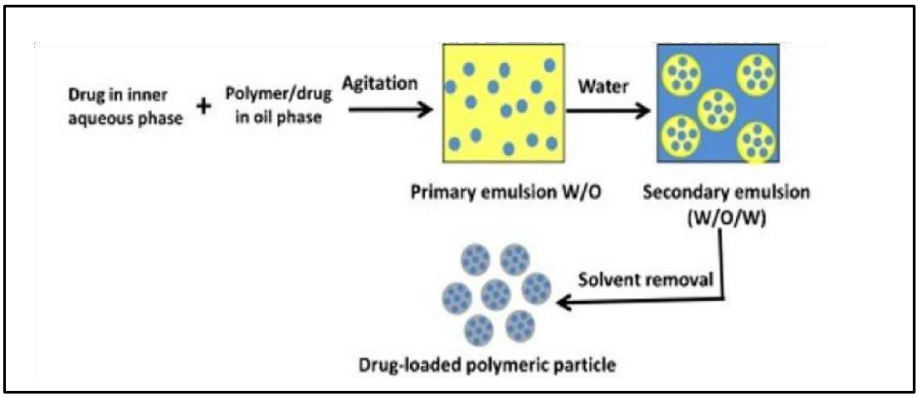

Fig. 4: Emulsion Solvent Diffusion Technique.

This approach provides multiple benefits, including a narrow range of particle sizes, high efficiency in encapsulation, and consistent results. Additionally, it does not use highly toxic organic solvents, making it appropriate for encapsulating heat- and light-sensitive herbal substances. Some limitations involve the requirement for accurate control of process parameters, including the type of solvent, concentration of polymer, amount of emulsifier, stirring speed, and diffusion rate. These factors significantly affect the size, shape, and stability of the nanoparticles. The emulsification-solvent diffusion method is an easy, dependable, and scalable approach for producing herbal nanoparticles that enhance solubility, bioavailability, and therapeutic effectiveness.[37]

3.2. Salting Out Method

The salting out method is a straightforward and commonly utilized technique for creating polymeric nanoparticles, especially for encapsulating herbal medications that are sensitive to heat or organic solvents. This method relies on the principle of decreasing a polymer's solubility in water by introducing a high concentration of electrolytes or salts, leading to the formation of nanoparticles from the polymer.

Two phases are prepared in this process: one that is aqueous and another that is organic. The organic phase typically includes the biodegradable polymer, such as poly(lactic-co-glycolic acid) (PLGA) or polycaprolactone (PCL), along with the herbal drug dissolved in a water- soluble organic solvent like acetone or ethanol. The water phase has a significant amount of salts like magnesium chloride, calcium chloride, or magnesium acetate, which serve as salting- out agents. Surfactants such as polyvinyl alcohol (PVA) or Tween 80 can be included to stabilize the nanoparticles and reduce clustering.

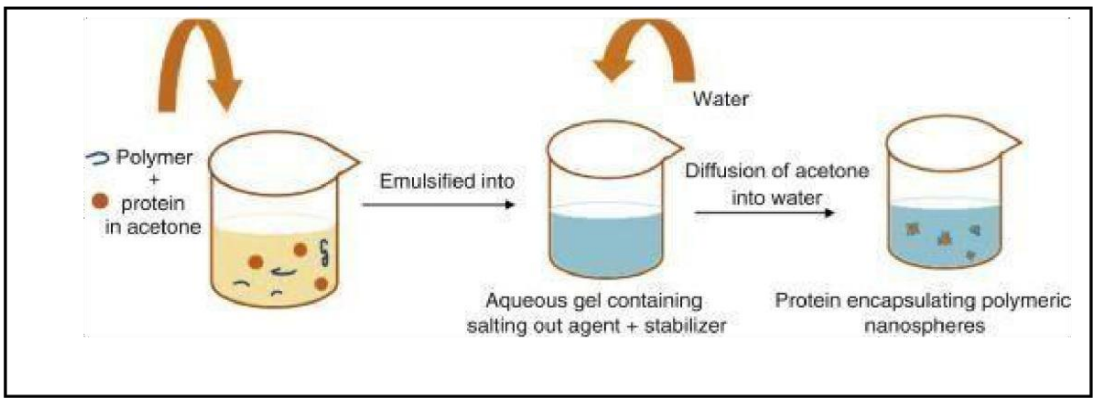

Fig. 5: Salting-Out Method.

The organic phase is gradually added to the aqueous phase while stirring continuously. The addition of the salting-out agent reduces the ability of the organic solvent to mix with water, resulting in the creation of an emulsion. When water is added, the concentration of salt decreases, which enables the organic solvent to move into the water phase. This diffusion process leads to the formation of uniform nanoparticles by precipitating the polymer together with the enclosed herbal drug. The nanoparticles are collected through centrifugation and washed multiple times to eliminate any remaining salts and solvents. They are then dried using either a vacuum or freeze-drying process. The salting-out method has several benefits, such as operating under gentle conditions, not requiring high shear or heat, and having lower toxicity because it does not use harmful organic solvents. It is particularly appropriate for herbal bioactives that are sensitive to heat, including curcumin, quercetin, and silymarin. One drawback of this method is the requirement for complete purification to eliminate salts, as any remaining electrolytes can impact particle stability and biological activity. Nonetheless, the salting-out method continues to be a favored technique for encapsulating herbal compounds in biocompatible nanoparticles to enhance drug delivery, stability, and bioavailability.[38]

3.3. Nanoprecipitation Method

The nanoprecipitation method, also referred to as the solvent displacement method, is a straightforward and commonly used technique for creating polymeric nanoparticles that include herbal bioactive compounds. This method includes the natural creation of nanoparticles by dissolving a polymer and a herbal drug in a water-compatible organic solvent, like acetone, ethanol, or acetonitrile. This solution is then combined with an aqueous phase that has a stabilizer or surfactant while being stirred gently. The quick spread of the organic solvent into the water phase results in the polymer becoming supersaturated, which causes the immediate creation of small, evenly sized nanoparticles. The method relies on the principle of interfacial deposition, which occurs when variations in solvent polarity lead to the precipitation of the polymer and the drug, resulting in the formation of nano meter-sized particles.

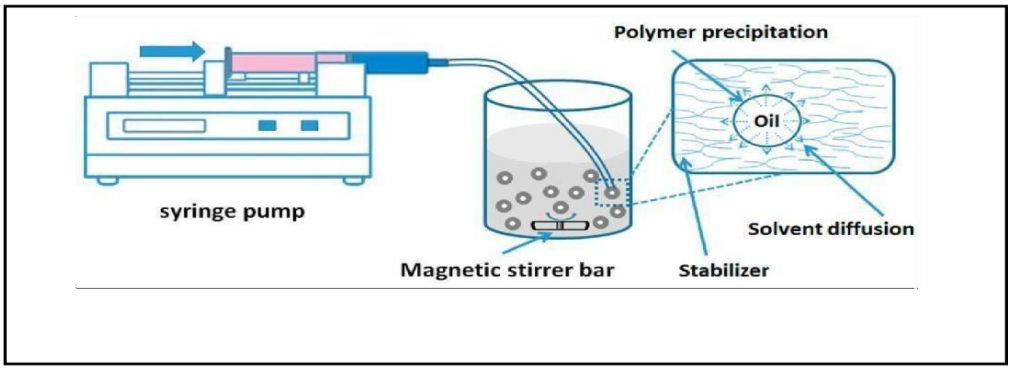

Fig. 6: Nanoprecipitation Method.

Once the nanoparticles are created, the organic solvent is typically eliminated by evaporation under reduced pressure or through continuous stirring, resulting in a stable nanosuspension. The size of the particles and the stability of the formulation are influenced by various factors, including the concentration of the polymer, the ratio of drug to polymer, the type and amount of surfactant, the speed of solvent addition, and the stirring rate. Nanoprecipitation has several benefits, such as being simple to perform, producing consistent results, and not requiring high energy. These features make it especially appropriate for heat-sensitive herbal compounds. Additionally, it does not need complicated equipment and can be easily scaled for large-scale manufacturing. This method is primarily suitable for hydrophobic drugs and polymers because it depends on the ability of the organic and aqueous phases to mix. Nanoprecipitation has

been effectively used in the delivery of herbal drugs to create nanoparticles from different plant compounds, including curcumin, quercetin, and resveratrol. These nano formulations have shown better solubility, increased bioavailability, and longer duration in the bloodstream compared to traditional formulations. Nanoprecipitation is an efficient and cost-effective method for creating herbal nanocarriers that enhance therapeutic effectiveness and patient adherence [39].

4. TOXICITY OF NANOPARTICLES

Nano-toxicology is a specialized area within the field of particle toxicology. It discusses the toxicology of nanoparticles, which seem to have toxicity effects that are different from those observed with larger particles. Smaller particles have a larger surface area relative to their volume, which increases their chemical reactivity and biological activity [40]. Due to their large surface area, nanoparticles will quickly adsorb some of the macromolecules they come into contact with when exposed to tissues and fluids. This could impact the regulatory processes of enzymes and other proteins. Consumer concerns about toxicity are significant, and given that nanoparticles tend to be more reactive, mobile, and potentially more harmful, it is important to address these issues. There is a significant chance that nanoparticles in the body may cause increased oxidative stress, which can produce free radicals. This process could lead to DNA mutations, cancer, and potentially death. It is not completely clear if increasing the bioavailability of specific nutrients or food additives could have adverse effects on human health.[41]

5. FUTURE PROSPECTIVE

Research on herbal remedies and natural products is being conducted globally. Several institutes are working on the development of herbal remedies within drug delivery systems at both basic research and clinical trial stages. The main requirement is to create improved systems for the effective delivery of these drugs to specific areas in the body and throughout the entire body, ensuring that the doses do not interfere with current treatments. A solution that can alleviate side effects such as toxicity and hypersensitivity, while also enhancing the patient's internal strength, is highly desirable. In the future, the idea of using herbal nanoparticles for delivering cancer treatments may interest certain research groups and lead to noteworthy findings.

Therefore, incorporating "herbal remedy" into the nanocarriers will enhance its effectiveness in treating various chronic diseases and provide health benefits. There are numerous successful examples and experienced evidence in the field of nano research. Herbal remedies are valuable sources of beneficial compounds that contain antioxidants and can be used in functional foods. Collaborative research combining traditional herbal remedies with modern drug delivery systems, such as nanotechnology, has the potential to create effective therapies for the pharmaceutical industry in the near future, improving public health. It is expected that the effective use of natural products and herbal remedies with nanocarriers will improve the importance of current drug delivery systems.[42- 47]

CONCLUSION

Nanotechnology has transformed herbal medicine by providing new solutions to persistent issues, including low solubility, instability, low bioavailability, and limited specificity of herbal bioactive compounds. Herbal drugs can now be delivered in a more controlled, stable, and effective way using different nano systems such as polymeric nanoparticles, solid lipid nanoparticles, liposomes, nano emulsions, and metallic nanoparticles. These nanosystems improve treatment effectiveness and lower toxicity and dosing frequency, which helps increase patient adherence to their medication regimen. Although there have been notable improvements, issues like toxicity concerns, large-scale production, standardization, and regulatory approval continue to pose significant obstacles to clinical application.

Conducting thorough toxicological studies and establishing internationally standardized regulations will be crucial for ensuring the safe use of herbal nanomedicines.

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