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Review Article

PH Dependent Herbal Nano Formulation: A Comprehensive Review

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ABSTRACT

The bioactive compounds found in herbal medicines are currently utilized in various forms, including whole plants and plant parts, for treating a range of diseases and disorders, from minor ailments to chronic conditions. This article deals into the developing area of nanomedicine as a drug delivery system aimed at enhancing the therapeutic effects of medicinal plants in herbal medicines. Using herbs is generally regarded as safer and more cost-effective than synthetic medications. In recent years, herbal drug formulations based on nanotechnology have garnered interest due to their improved effectiveness and potential to address challenges associated with herbal medicines. Phytochemicals derived from medicinal plants provide considerable therapeutic advantages, but their clinical effectiveness is frequently limited by issues like poor solubility, instability, and low bioavailability. This study emphasizes the creation of an intelligent nano-delivery system that reacts to specific pH levels in pathological conditions, such as the acidic environments of tumor tissues or inflamed areas. Herbal extracts abundant in bioactive substances were encapsulated within biocompatible and biodegradable nanocarriers, such as liposomes, polymeric nanoparticles, or solid lipid nanoparticles, designed to release their contents in response to particular pH triggers.

INTRODUCTION

The use of plants, either directly or through extracts, for medicinal purposes has been around since ancient times. Plants provide many useful chemicals called phytochemicals, which are why they have been used to help people's health. These chemicals are good because they have few side effects, are not expensive, and are widely accepted by people [1].Phytochemicals are substances made by plants, also called secondary metabolites.

These chemicals are important in traditional medicine because they have many helpful effects on the body. They can fight infections caused by

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bacteria and fungi, and they may also help with serious conditions like diabetes and cancer. A pH-dependent herbal nano formulation is a type of drug delivery system that uses nanotechnology. In this system, an herbal extract or plant-based chemical is put inside very small carriers, such as nanoparticles, liposomes, or nano emulsions. The active ingredient inside these carriers is released or works best at a certain pH level.

These kinds of formulations are helpful for delivering medicine to specific parts of the body.

For example:

- Delivering medicine to the intestines instead of the stomach,

- Targeting cancer cells, since tumour often have a slightly acidic environment,

- Using them in vaginal or skin treatments, where the pH is different from normal body tissues[1].

Plant-based products like willow bark, which contains salicin, and the opium poppy, which provides morphine, were the starting points for today's medicines[2]. In modern medicine, several drugs from plants have been very effective. For example, paclitaxel from the Pacific yew tree is used to treat cancer, artemisinin from sweet wormwood is used for malaria, and berberine from barberry helps with infections and metabolic conditions[3]. Natural and synthetic nanoparticles and microparticles, like nanovesicles, liposomes, exosome-like nanoparticles, and micelles, help improve the bioavailability, stability, specificity, and distribution of natural products.[4] Nanotechnology provides a powerful way to boost the effectiveness of phytochemicals. By putting these compounds inside tiny carriers, usually between 1 and 100 nanometres in size, scientists can greatly increase their solubility, protect them from breaking down, and make them stay in the body longer.[5] Also, when plant extracts or active ingredients are mixed with nano-formulas, they can be directed to specific areas and released at the right time, leading to better treatment results.

1. Nano Formulation of Herbal Plants.

There are usually two main types of development for nano formulations of active ingredients from medicinal plants: nano ultrafine technology and drug nanocarriers. The nano-dosage forms of these active ingredients mainly include nanoparticles and drug nanocarriers. The nanoparticles consist of forms like nanosuspensions, nano-eutectics, and similar structures. Drug nanocarriers, on the other hand, come in various forms such as liposomes, nanoparticles, nano emulsions, and colloidal polymers.[6]

3.1 Nanoliposomes

Nanoliposomes are tiny ball-shaped structures made mostly of lipids and phospholipids. They are very small, usually between 20 and 200 nanometres in size. Sometimes, they also contain other substances like carbohydrates, proteins, and sterols. The materials stored inside these nanoliposomes can be slowly released over time. This happens either through a process called double-layer diffusion or when the nanoliposomes break down because of changes in the environment, such as pH levels, pressure, salt concentration, or temperature.[6]

3.2 Nano emulsion

Nano emulsions are great for delivering drugs, especially those that don't mix well with water. They help protect these drugs from being broken down by enzymes, the acidic environment of the stomach, and other harmful factors. Nano emulsions can also be directed to specific parts of

the body, either through natural processes or by using special targeting methods.[6]

3.3Nanoparticles

Nanoparticles are really small particles, usually between 1 and 100 nanometres in size. Because they are so tiny, they have a large surface area, which gives them special physical and chemical properties. When nanoparticles get inside the body, they first meet with bodily fluids like blood or tissue fluid. Different substances in these fluids, such as proteins, fats, and sugars, quickly stick to the surface of the nanoparticles. This creates something called a "protein corona." The type and structure of this corona depend on the properties of the nanoparticles, like their size, shape, electrical charge, and how water-friendly they are, as well as the conditions in the fluid, such as the amount of protein, the pH level, and the salt content.[6]

3.4 Nano Micelles

Nano micelles are tiny, self-made structures made from nanoscale particles that range in size from 10 to 100 nanometres. They have a part in the middle that doesn't mix with water and a part around it that does mix with water. This special structure helps dissolve and keep stable drugs that are hard to dissolve in water. This process happens naturally when the amount of the material used to make the micelles is above a certain level, called the critical micelle concentration. Nano micelles can move through the small spaces between cells that line blood vessels and go into the space around tissues through a process called passive diffusion. How well they move depends on things like their size, the surface they have, and how much of them is water-loving or water-repelling. For example, smaller nano micelles with a balanced mix of water-loving and water-repelling parts are more likely to move through the spaces between cells in blood vessel walls [6].

4. Mechanism of PH Dependent Drug Release

pH-sensitive polymers are materials that change their properties when the surrounding environment has a different pH level. These can be divided into two types: (A) polymers with groups that can gain or lose a charge; and (B) polymers that have links that break down in acidic conditions. Polymers with ionizable groups are made by adding acidic or basic groups during the process of creating the polymer. These groups can either pick up or lose a proton depending on the ph. In the case of high pH-responsive polymers, acidic groups like carboxylic acid, sulfonic acid, or methacrylic acid are part of the polymer structure. When the environment is high in pH, these groups lose their protons, leading to a higher charge on the polymer. This charge causes the polymer chains to repel each other, allowing the polymer to absorb water and swell. As a result, any material that is inside the polymer can be released. For low pH-sensitive polymers, the material includes basic groups such as pyridine derivatives, piperazines, or amino salt groups. In acidic conditions, these basic groups gain protons, increasing the charge between the polymer chains. This leads to more repulsion, making the polymer expand and release its contents.[7] The food industry uses a lot of natural polymers such as alginate, chitosan, and cellulose derivatives. These materials are good because they are safe for the body, not harmful, can break down naturally, and are found in nature. Because of these qualities, they are often used in pharmaceuticals as additives. These polymers can also be easily changed chemically, and their size and length can be adjusted, allowing scientists to make improved versions of these materials with better properties than the original ones.[8]

5. Nanotechnology-Based Drug Delivery System for Phytochemical Compounds

Using lipid-based nanotechnology to package and deliver active ingredients can be done through various methods, such as nanoliposomes, nanosuspensions, nano emulsions, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs). Among these, SLNs are the most commonly used because they offer solid and stable nanoparticles, work well as a delivery system, and can be customized with different lipid materials, emulsifiers, core substances, and production techniques. SLNs were first introduced in 1991 and are a better option compared to traditional colloid systems. SLNs have become a reliable and stable choice for encapsulating and delivering compounds found in liposomes, emulsions, and polymer nanoparticles mainly due to their ease of creating stable dispersions and high efficiency in trapping the active ingredients . [9]

5.1 Drug delivery of nano formulation

The size of the nanoparticles affects how well the drug is distributed in the body, how efficiently it works, and how much is taken up by the cells. It also plays a role in how quickly the nanoparticles break down and are removed from the body. The charge on the surface of the nanoparticles is also important. It influences how well the drug passes through the cell membrane and how stable the drug-nanoparticle mix is. A high charge helps keep the nanoparticles from clumping together by creating a repelling force. The charge also affects how well the nanoparticles are absorbed. Positive charges can stick to mucus that has a negative charge, helping the nanoparticles stay in the mucus layer longer. Many studies show how the shape and other biological traits of these nanoparticles are important for their function.[10]

6. Herbal Nano Formulation Used in Treatment of Various Disease

6. 1plant based antidiabetic nano formulations.

Diabetes mellitus is a serious and widespread condition that affects how the body processes blood sugar. It is mainly divided into two types: type 1 and type 2 diabetes. Certain compounds like curcumin, gymnemic acids, silymarin, quercetin, resveratrol, and berberine may help repair the function of pancreatic beta cells by targeting different pathways, which could be useful in treating diabetes. Both curcumin and resveratrol may help improve beta cell function by stopping harmful signals in these cells, which is done by blocking an enzyme called phosphodiesterase. Resveratrol also helps by boosting the activity of a protein called sirtuin 1 (SIRT1) [11]

Nano formulation in diabetes treatment.

1.Curcumin.

The creation of curcumin in nano-form has become a promising way to boost its solubility, stability, how well it works in the body, and its ability to treat diabetes. Studies show that curcumin mixed with zinc oxide nanoparticles at a dose of 10 mg per kg for 21 days was more effective than curcumin nanoparticles at 50 mg per kg over the same period in treating diabetes. This was seen in lower blood sugar levels, better insulin levels in the blood, and more activity of the GLUT2 and glucokinase genes in the pancreas and liver of rats with type 2 diabetes

2.Resveratrol

Resveratrol has also been studied, and putting it into nano-forms like lipid carriers, nano emulsions, micelles, polymer particles, solid mixtures, and nano-crystals has shown better results than other methods. These nano-forms improve stability, how well the body absorbs resveratrol, allow it to target specific areas, improve its effectiveness, and make it easier for patients to take.

3.Quercetin

Nanofabrication of quercetin has provided great chances to improve how well it is absorbed in the body, how precisely it targets areas, how effectively it works, and how likely people are to take it as prescribed. When quercetin is put into PLGA nanoparticles, it increases how much of the drug gets into the body through the mouth by more than five times compared to taking the drug on its own. This helps people follow their treatment better because they need smaller doses and don't have to take it as often.[11]

6.2Herbal based nano formulation for treatment of psoriasis

Psoriasis is a common skin condition that has different causes and affects about 0.5 to 1% of children and 2 to 3% of people around the world. It can have a big effect on a person's self-esteem and how they interact with others. Clinically, psoriasis is divided into five types: plaque, pustular, guttate, flexural, and erythrodermic. These types cause skin sores that are scaly, irritating, itchy, and can lead to scarring.

1.Psoralea corylifolia

Psoralea corylifolia, also known as Babchi, is a plant used in traditional Indian and Chinese medicine. It has a natural medicine called furocoumarins as its main active ingredient. This plant is part of the Fabaceae family and has properties that help fight bacteria, reduce oxidation, and lower inflammation. The main part of this plant is called psoralen. Psoralen stops DNA from copying and slows down cell growth, which means it has qualities that may help treat psoriasis. [12]

2. Nigella sativa

Nigella sativa Linn, commonly referred to as black cumin, is a member of the Ranunculaceae family. Thymoquinone (TQ), a lipid-soluble benzoquinone, is one of the primary phytoconstituents that exhibits significant anti-psoriatic effects.

3. Capsicum annum.

Capsaicin (CAP) is a powerful compound found in chili peppers and is part of the Solanaceae family. CAP is widely recognized for its effectiveness in treating inflammatory diseases like psoriasis. The initial occurrence in psoriasis development is the dilation and permeability of papillary vessels. Substance P (SP), which is a neuropeptide, initiates several processes related to psoriasis through the vanilloid receptor, including inflammatory cell activation, keratinocyte overproduction, vasodilation, and angiogenesis.[12]

6.3Plant-derived Anti-arthritic Nanomedicines for Effective Therapy in the Management of Inflammatory Diseases.

Arthritis is a group of serious inflammatory diseases, characterized by inflammation and degeneration in the joints and related structures like bones and cartilage. The presence of inflammation is indicated by common arthritic symptoms, such as joint swelling, stiffness, pain, and discomfort, often affecting one or multiple joints, which can lead to confusion and frustration [13]

Plant crude extracts for the treatment of arthritis

1. Benth Cleistopholis patens B.,

The ethanol and aqueous extracts of the stem of this plant was found to have anti-arthritic activity in chicken type II collagen in Complete Freund's

Adjuvant (CFA)induced Wistar albino rats with no toxicity. It was also observed that upon treatment with these plant extracts, the rats started gaining weight which they lost due to arthritis induction, which indicated the ability of this plant to reverse muscle degeneration.

2. Clerodendrum serratum (L.) Moon

Clerodendrum serratum (L.) Moon, also called Bharangi in Sanskrit and Blue glory in English, is a deciduous shrub that belongs to the Verbenaceae family. The aqueous standardized extract from the roots of this plant was found to have anti-inflammatory properties when its membrane stabilizing activity was tested. A study on CFA-induced Wistar albino rats showed that it inhibited COX-2 and TNF-α, which was determined by observing parameters such as paw edema, arthritic index, and joint diameter.

3.Withania somnifera

Withania somnifera Dunal, which is part of the Solanaceae family, is also called Ashwagandha. Its health benefits are because of certain plant compounds like Phyto steroids, Withanloids, and Withaferin A. In this study, researchers looked at the effects of a water-based extract from the roots of Ashwagandha on rats with collagen-induced arthritis. Giving the extract by mouth helped reduce swelling and the levels of harmful chemicals in the body, such as TNF-α, IL-1β, IL-6, and the protein NF-Kb that plays a role in inflammation.[13]

7. Novel Vesicular Formulation Based On A Herbal Extract Loaded with Noisome and Evaluation of Its Antimicrobial And Anticancer Potential

People have used plants for healing for many hundreds of years. A big reason why more people around the world are using these herbs, their oils, and extracts is that they usually have fewer bad side effects compared to medicines made from chemicals. They are also less expensive and easier to find.P. atlantica is a type of herb that grows naturally in many areas of Asia. It's also called Baneh locally. This herb has several helpful qualities, such as fighting free radicals, preventing genetic changes, killing harmful bacteria, reducing inflammation, and stopping the growth of cancer cells[14]

MATERIALS AND METHODS.

1.MATERIALS

poly (propylene glycol)-block-poly (ethylene glycol) diacrylate (Pluronic® F108, 99%) was obtained from Fluka Chemica, Darmstadt, Germany. 3β-Hydroxy-5-cholestene, 5-Cholesten-3β-ol (Cholesterol, 99%), Sorbitan monostearate (Span 60, 99%), PBS (phosphate buffered saline), penicillin, Trypan blue, DMSO (Dimethyl sulfoxide, 99%), MTT (3-(4,5-Dimethylt (ethylene glycol)-hiazol-2-yl)-2,5-diphenyltetrazolium bromide), streptomycin, and chloroform.

2.Plant material

The study looked at plant materials, especially fruits collected from rural areas in Kerman Province, which is in the eastern part of Iran, in August 2023. To make sure the results can be repeated, samples of the plant species P. atlantica were kept in a public university herbarium as reference specimens.

3.Extract preparation.

Ten grams of powdered dried fruit was mixed with 80% water and methanol and left to sit for 72 hours at a temperature of 25 degrees Celsius using the percolation method. To remove any plant material,

the resulting extract was filtered through a Whatman No. 3 filter. The filtered extract was then evaporated using a rotary evaporator (Heidolph, Schwabach, Germany) under a vacuum of 437 mbar at 55 degrees Celsius for 24 hours at a speed of 180 pm. The extract was then stored at minus 20 degrees Celsius until it was needed again. The temperature used to evaporate the methanol was about 64 degrees Celsius, and all organic solvents were completely removed after 24 hours under vacuum conditions.

8. Modern Herbal Nanogels

In recent years, nanogels have become a good choice for delivering and releasing medicine to patients. They are one of the many areas in nanomedicine, which combines nanotechnology, medicine, and pharmaceuticals. Nanogels are crosslinked polymer networks that are very small, on the nanoscale, and can absorb a lot of water. They are a type of hydrogel that is smaller than a nanometre. A hydrogel is a gel made from polymers, where the polymer chains are connected to form a large network. Hydrogels can be made in different ways [15]

8.1 PH stimulated or responsive nanogels

pH-sensitive or pH-responsive nanogels with a slightly acidic or basic chain of charged molecules may have parts that either pull electrons away or give electrons. These nanogels can become active when the pH level changes in the environment due to their structure. Positively charged particles tend to stick to blood serum, leading to clumping and quick removal from the body, which reduces their effectiveness. The way these nanogels work depends on how they take in protons and how their ion groups react, which happens in two main steps: first, ions either positive or negative attach to the surface of the gel, and then they move into the gel's network. The pH value at which the nanogel starts to change its shape, called pHc, is important because it helps determine where and when the medicine inside the nanogel will be released. This pHc is usually calculated using the pKa of acidic parts or the pKb of basic parts of the charged chain. Anionic nanogels tend to expand when the pH is higher than the pKa of their acidic parts, while cationic ones expand when the pH is lower than the pKb of their basic parts. The polymer used in this system does not dissolve in neutral pH conditions. When the pH goes down, the polymer starts to swell, and the drug begins to come out of the system. Glucose is turned into gluconic acid by the enzyme glucose oxidase, which lowers the body's ph. Because of the swelling effect of the pH-sensitive polyacrylic acid chains, temozolodine has controlled release over time.[15]

8.2 Temperature stimulated response

Thermo-responsive nanogels are tiny materials made up of structures that change when the temperature around them changes. These nanogels are often used in drug delivery systems that respond to temperature. They can be made from natural substances like alginate, chitosan, hyaluronic acid, ovalbumin, pullulan, and chondroitin sulphate, or from man-made materials like branched PEG, poly- (N-isopropylacrylamide-co-acrylic acid), poly- (N-isopropyl acrylamide) (PNIPAM), poly (N-vinyl caprolactam), poly(N-isopropylacrylamide-co-acrylamide), poly (ethylene oxide) (PEO), and elastin-like polypeptides (ELP). Sometimes, mixtures of natural and synthetic materials are used to create nanogels that are safe for the body and can break down on their own. These properties make them very useful in medical treatments. [16]

9. Formulation Technique For Nano formulation

Complex coacervation method

This is a process where two liquid layers form naturally in a colloid system. It happens when two types of charged polymer molecules mix in water, and they attract each other, causing them to separate into two different liquid phases.[17]

Co-precipitation method

This is a modified version of the complex coacervation method used to make tiny particles with a core and a shell. This approach helps keep drugs that don't dissolve well in water from clumping together.[17]

Nanoprecipitation.

Nanoprecipitation is a straightforward, easy, fast, and reliable one-step process. This method doesn't require a lot of energy and can be easily scaled up. It is time-saving, affordable, and doesn't need a pre-made emulsion like some other techniques. By adjusting certain factors, you can change the size of the nanoparticles produced, and they tend to be small with a narrow size range. The process works by using interfacial deposition, where a solvent moves into a non-solvent, causing the polymer to dissolve, which then leads to the formation of nuclei, crystal growth, and nanoprecipitation. [18]

Homogenization Method.

The high-pressure homogenization (HPH) technique depends on intense shear forces and potential cavitation, achieved by forcing a suspension through small openings or crevices and applying it to the drug crystals to disperse them. The two principles of homogenization utilized, along with the type of homogenizer that corresponds to these principles, are micro fluidization and piston-gap homogenization. Micro fluidization operates on a jet-stream principle, where the coarse suspension accelerates through the homogenizing chamber, particularly influenced by high-speed collisions, shear, and cavitation forces, leading to a reduction in particle size due to these forces. The pressures used in these processes can range from 500 bar to 350 MPa. Generally, increasing both the pressure and the number of cycles facilitates the creation of nanoparticles with smaller sizes.[19]

10.Recent Advances in Drug Delivery of Curcumin, Quercetin, Bergenin

Many studies have looked into creating and testing nano-curcumin, which is designed to deliver curcumin to specific areas in the body. This form of curcumin is more effective because it can pass through tissues more easily, stays in the body longer, and spreads better, leading to better treatment results. To make this even more effective, different nanoparticle methods have been explored, like putting curcumin inside liposomes, chitosan and solid-lipid microparticles made with bovine serum albumin. These methods help overcome problems like poor absorption, low levels in the body, and difficulty reaching the right tissues, which have limited how well curcumin can be used as a therapy.[20] Several studies have shown that QUE has many different medicine-like effects, such as acting as an antioxidant, reducing inflammation, fighting cancer, helping with diabetes, and killing harmful microbes . Out of these, the antioxidant and anti-inflammatory effects are especially important because they help prevent and treat many diseases, like cancer, heart problems, and conditions that happen as people get older.[21] Bergenin is a substance made from gallic acid and is known for its ability to fight oxidation and protect the liver. When given to bladder cancer cells, Bergenin greatly reduced their ability to survive and caused them to stop at an earlier stage of growth called the G1 phase. HCT116 cancer cells were treated with different amounts of Bergenin for 24 and 48 hours.

Bergenin strongly slowed down the survival of these cells. It also made the cells pile up in the G1 phase and caused damage to their DNA. Bergenin has shown great effectiveness against various long-term health conditions.[22]

11. Characterisation Technique For Nano Formulation

1.Particle size and Polydispersity

The most important characteristics of nanocarriers are particle size, shape, and dispersity, which refers to the heterogeneity of particles in terms of size, expressed by the polydispersity index (PDI). The particle size and shape influence the biodistribution and elimination of nanocarriers. They also impact their attachment, firm adhesion, phagocytosis, circulation half-life, cellular distribution, cellular uptake, and endocytosis. [23]

2.Surface charge and Hydrophobicity

The surface properties of nanocarriers play a crucial role in determining their bioavailability, stability, cellular uptake, and biodistribution. The zeta (ζ) potential, which reflects the surface charge, indicates potential electrostatic interactions between nanocarrier units, influences their tendency to aggregate, and aids in selecting appropriate coating materials. It can be measured by applying an electric current to the sample while recording the movement of the nanocarriers using laser Doppler velocimetry. The hydrophobicity of nanocarriers can be assessed through methods such as the adsorption probe method, hydrophobic interaction chromatography, contact angle measurements, and biphasic partitioning. Additionally, X-ray photon correlation spectroscopy helps identify specific chemical groups on the surface of nanocarriers and ultimately predicts their hydrophobicity.[23]

3.Transmission Electron Microscopy

Transmission electron microscopy can be used to easily examine the structure, surface, and shape of carriers along with their formulation. First, the samples should be diluted with distilled water, then a drop should be placed on a copper grid that has a 200-mesh carbon film. After that, the sample should be stained with an appropriate staining solution. Once the sample is dried, the shape can be analysed.

4.Zeta Potential

Zeta potential measures the effective electrical charge on the surface of a nanoparticle and shows how much charge is present. When a nanoparticle has a charged surface, this charge is hidden by a layer of ions that have opposite charges and are close to the nanoparticle. These layers of opposite ions move along with the nanoparticle and are part of the overall charge layer.[24]

12.Challenges And Opportunities in Herbal Nano Formulation

Herbal nanotechnology needs more research to make the most of its benefits and ensure it works as intended. Creating and bringing herbal nanotechnology products to market has several challenges, like dealing with rules, considering ethical concerns, and setting up proper ways to make the products consistently.

The complex chemical nature of herbal extracts is characterized by a wide range of phytoconstituents that vary in molecular weight, solubility, therapeutic potential, and chemical classes. Some compounds, such as monoterpene, sesquiterpene, diterpene, and triterpenoids, are non-polar and lipid-soluble, while others, like polyphenolics and glycosides, are polar and water-soluble. These variations complicate the development and

characterization of a nano formulation strategy. However, by fractionating the extracts using bioassays, these challenges can be addressed. The resulting fractions would contain phytoconstituents with similar chemical classes and solubility profiles, thereby enhancing their synergistic effects.[25]

Physical Stability of Nano formulation: The nano formulations are meant to be used in the lungs, eyes, through injection, and on the skin. It's very important that each drug delivery system stays stable to make sure it works well and is safe. For example, if nanoparticles in a nasal spray start to clump together or get bigger than 5 microns, it could block blood vessels in the nose, cause the drug to leak out of the nanoparticles, or break down the nano emulsion, which might reduce how much drug is delivered and how well it works. However, these issues can be handled well by using the right way to make the formulation and by keeping the zeta potential as high as possible.[25]

Because of their fragile composition, many herbal extracts are susceptible to deterioration when in contact with moisture, light, air, heat, metal ions, and fluctuations in ph. Consequently, they are unable to preserve their efficacy over their designated shelf life. Their vulnerability to light, heat, and oxygen results in the rapid oxidation and degradation of bioactive compounds, causing a decline in their active properties.[26] Nanocarriers loaded with drugs encounter various obstacles for both researchers and regulatory bodies. To address these issues, it is essential to implement reliable characterization techniques, scalable optimization strategies, safety protocols, and measures to ensure stability.[27]

13. Advantages Of Nanoformulation of Herbal Extract

Herbal treatments and plant-based ingredients are thought to be safer and work better than traditional medicines. Around the world, more people are using natural medicines. Scientists have used ideas from nanoscience and technology to make these natural drugs work better in the body and deliver medicine exactly where it's needed. Across the globe, herbal remedies are commonly used and trusted by both doctors and patients because they often have fewer side effects compared to modern medicines.[28]

14.Applications

Plant-derived nanoparticles (PDNPs) are gaining traction in drug delivery systems thanks to their capability to encapsulate and transport bioactive compounds, which enhances their solubility, bioavailability, and targeted effects. In the realm of cancer treatment, PDNPs present numerous advantages, particularly in targeted drug delivery, gene therapy, and photothermal therapy. These nanoparticles can be customized to transport chemotherapeutic drugs, therapeutic genes, or proteins directly to cancerous cells, thereby reducing harm to healthy tissues. For instance, nanoparticles derived from turmeric that are loaded with curcumin have demonstrated high efficiency in drug encapsulation and stability, leading to improved therapeutic outcomes against ovarian cancer. Regenerative medicine aims to repair or replace damaged tissues and organs, and PDNPs are being explored for their potential application in tissue regeneration. Given their robust antimicrobial properties, PDNPs have shown considerable promise in combating microbial infections. These nanoparticles can act as both antimicrobial agents and carriers for antimicrobial medications, thus enhancing drug effectiveness and diminishing the likelihood of resistance.[29]

15. New Approaches and Future Prospect

Currently, a growing number of individuals are opting for herbal medicine due to its lower cost and easier accessibility. Therefore, enhancements in the production and delivery methods of these medicines are needed. In a particular study, nano curcumin was combined with unique nanoparticles known as rare-earth-doped up conversion nanoparticles (UCNPs). They utilized a substance called poly (lactic-co-glycolic acid) (PLGA) to facilitate the gradual release of the medication over time. [30] This approach ensures that the drug targets the appropriate area in the body, minimizes its interaction with unintended tissues, and improves its solubility in water. Nanotechnology has resulted in substantial advancements in pharmacology over the last thirty years. Engineered nanomaterials, which are a key application of nanotechnology, have already integrated into everyday human life, serving as food packaging materials, drug delivery systems, therapeutics, biosensors, and more. The goal of targeted drug delivery is to minimize drug side effects while simultaneously reducing consumption and overall treatment costs.[31]

16. CONCLUSION

PH dependent herbal nano formulations are a new and promising way to deliver drugs more effectively. These systems use the changes in PH levels in different parts of the body and during diseases to release herbal active ingredients exactly where they are needed. This helps make the ingredients more stable, easier to dissolve, and more effective in treating illnesses. Forms like liposomes, polymeric nanoparticles, and nanogels have been found to help protect the drugs from breaking down too early and improve how well they are absorbed by the body. Overall, these PH responsive nano formulations provide a better, more convenient, and eco-friendly way to use plant-based medicines.

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