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Review Article

Herbal Nanoparticles: A Commitment towards Contemporary Approach

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ABSTRACT

Herbal medicines have been used extensively since ancient times in almost every region of the world and are regarded by patients and doctors as having the best therapeutic value or effect because they have very few or lesser side effects than synthetic medications. In order to deliver the components over time, avoid the need for repeated dose administration, and improve patient compliance, phytotherapeutics requires some scientific approaches. The current article discusses the various kinds of nanoparticles, nano drug delivery methods, agricultural applications, advantages, properties, disadvantages, and methods of preparing nano herbal medicines. Nanoparticle applications in a variety of fields, including cosmetics, plant protection, crop enhancement, wastewater treatment, and treatment of several chronic diseases, are also discussed. The review utilizes papers obtained from various databases like Google scholar, PubMed, Science Direct and the articles from 1976 to 2022 are incorporated. The establishment of Novel or Newer Drug Delivery Systems could be used to obtain all of the herbal constituents (NDDSs). The novel or newer drug delivery system not only aids in reducing the number of times the drug must be administered to overcome non-compliance, but also significantly boosts therapeutic value by boosting bioavailability and limiting toxicity. Herbal nanoscale drug delivery systems or plant derived medication has a promising future in overcoming problems and enhancing activities associated with plant derived medicines. As a result, nano-formulations are frequently being used for more precise and controlled drug delivery to target tissues. Nanostructured systems can enhance the effects of plant extracts, lowering dosage requirements, minimising side effects, and increasing their activity.

Keywords: Herbal Nanoparticles, Herbal Drugs, Nano Formulations, Nanofertilizers.

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INTRODUCTION

Our ancestors use of traditional medicines was based on their understanding of nearby medicinal plants that they had excavated and discovered. These days, dietary supplements are commonly used in conjunction with herbal or plant-based medicines. Plant parts that are fresh or dried can be used to make herbal medicines. Powder, tablets, teas, and capsules are the most common forms in which they are sold commercially.[1] Herbal medicines are known for their ability to eliminate and prevent diseases with fewer side effects than synthetic medications. Even though patients are aware that instant relief has a number of drawbacks and a lengthy recovery period, they are more likely to use synthetic alternatives than their natural medications. In order to improve the bioavailability and subsequently the pharmacological action of medicines derived from herbal sources, new and efficient methods and formulations must be developed. One of the advancements is the establishment of herbal nanoparticles.

The term "nanoparticle" refers to very small particles that range in size between 1 and 1000 nanometers and are invisible to the human eye. Herbal nanoparticles are simply colloidal systems containing plant-derived particles. These particles may be made of synthetic or organic polymers. Nanoparticles significantly differ from larger materials in terms of its chemical and physical characteristics additionally, they are made from liquid or solid materials such as dielectrics, semiconductors, and metals. Due to the effectiveness of nanoparticles in drug delivery, they can locate diseased cells and assist in delivering medications to them.[2]

India is a key contributor to the development of herbal or ayurvedic formulations that are standardised and therapeutically effective. When compared to synthetic drugs, herbal or plant products have fewer side effects or adverse effects that can be easily cured without affecting any other cells or organs inside the human body.[3-5] Thus, taking these benefits (Figure 1) into consideration for disease prevention and treatment, the current review is based on various herbal nanoparticles that are small

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in size but can exhibit various physical and chemical properties effectively without harming other organs of our body and also easily deliver the medication to the site of action.

Nanoformulations are used to deliver herbal or natural drugs to their sites of action or individual organs, which strengthens drug delivery, drug selectivity, safety, and effectiveness, promoting patient compliance and lowering dose. Drugs that are small enough to reach target tissues and cells and capable of circulating in the bloodstream can meet the needs of an ideal nanoparticulate system. Different organs can be targeted by herbal medications, including the gastrointestinal tract, liver, brain, kidney, and lungs.[6] In comparison to the allopathic system, which treats multiple diseases at once, herbal remedies contain thousands of constituents.[7] By incorporating herbal drugs into the delivery system, it is possible to improve the pharmacological activity, stability, and solubility, as well as the distribution of macrophages in the tissue, while also protecting the drug from toxicity, ensuring sustained delivery, and preventing chemical and physical degradation.[8] Most herbal medicines have poor water solubility due to their hydrophobic nature. These properties cause an increase in systemic clearance, necessitating an increased dose or repeated administration, limiting the clinical application of herbal remedies. Thus, nanoparticles are used to enhance the solubility of herbal drugs as well as to help localise the medication at a particular location, leading to improved patient compliance and efficacy.[9] The drug level is lowered below the therapeutic or desired concentration in the blood due to some limitations of the herbal extract actives, such as liver metabolism and high acidic pH instability, which results in a reduced therapeutic or desired effect.[10] The nanoparticles were regarded as the most important drug delivery system among various novel or more recent ones.[11] The establishment of a consistent chemical profile, consistent biological activity, or a quality assurance programme in the manufacturing and production of herbal drugs depends on standardisation.[12]

Herbal drugs are committed to health promotion, chronic disease therapy, and life-threatening conditions. When conventional drugs are ineffective in treating the disease, the use of herbals increases the effect.[13] When used for purely cosmetic reasons, such as fullerenes, nanotubes and nanodiamonds for skincare and hair care, nanoparticles are used as a treatment for a number of diseases and have been found to be more effective than conventional treatments. They are also used to protect plants, improve agricultural crops by increasing yields, fruit quality, and nutrient status, and treat wastewater and water for anti-microbial purposes.[14]

Nanoparticles have been utilised to treat a number of chronic diseases, for instance, inflammatory illnesses, cancer, Alzheimer's disease,[15] diabetes,[16] colitis,[17] antimicrobial,[18] anti-arthritis,[19] anti-analgesic,[20] antioxidant,[21] and antifungal.[22,23] These diseases are found to be more effectively treated with fewer side effects when treated with nanoparticles.

Nanoparticles have better bioavailability characteristics, which increase their aqueous solubility and, as a result, lengthen the time that the drug will remain in the body before becoming ineffective. They also help to target the drug to the desired location. Essentially, various types of nanoparticles have emerged, and further processing for new techniques has been a concern in this century (Figure 2).

Pharmacological actions of the Nanoparticles formulations

Some herbal products that are established as powerful nanoparticles and are mentioned in the text are FDA-approved, while others are not. For instance, curcumin is synthesised using the wet-milling technique[23-25] and has potent anticancer and anti-tumor activity. Antineoplastic Paclitaxel works to combat breast and ovarian cancers, various tumour types, and for synthesis m ethods for nanoprecipitation are employed.[25-27] The anticancer agent berberin, which is used to treat various forms of cancer and inflammation, is made using the ionic gelation and emulsion methods.[28-30] The hydrophobically modified glycol encapsulates camptothecin, which has anticancer properties. Alzheimer's disease or dementia, which are caused by a combination of wet and dry processes, are both combated by ginkgo biloba (Liquid-phase or gas-phase grinding).[31,32] Specifically for rheumatoid arthritis, *triptolide* is used in cases of autoimmune and inflammatory diseases and is made using the nano encapsulation method.[33-35] *Salvia miltiorrhiza*, a phospholipid complex loaded anti-hyperlipidemic drug, works by enhancing blood stasis and is also used in cerebrovascular diseases.[36-39] *Quercetin* is an antioxidant with potent anticancer activity that is synthesised using Chitosan and Gelatin.[40-42] The lipid encapsulation method is used to create the drug *breviscapine*, which is used to treat pulmonary fibrosis, cardiovascular disease, and cerebrovascular disease.[43-45] *Naringenin* is produced using the nano precipitation method and has anti-tumor and hepatoprotective properties.[46,47] *Dodder* is generated using the nano precipitation method, has hepatoprotective properties, and fights carcinogenesis and ageing.[48-50] *Annual mugwort*, which has anti-malarial activity and is used to treat asthma, is created using the hydrophilic encapsulation method.[51,52] The hepatoprotective compound *silymarin*, which is produced using the cold homogenization method, protects against breast cancer and other liver diseases.[53-55] *Genistein*, an antioxidant compound made from chitosan microspheres and nano emulsions, is used to treat uterine and breast cancer, osteoporosis, cardiovascular disease, and osteoporosis.[56,57] *Centella asiatica* is created using the ionic gelation method and is used to treat cancer, allergies, leprosy, syphilis, and cancer.[58-60]

Herbal Nanoparticle Formulations and their benefits

Different herbal NPs were used in various pharmaceutical industries for the drug delivery process, which includes factors for improving efficacy and drug uptake in nano-form for drug formulation, which includes degradation mechanism and drug delivery system,[61] formulated drug stability, and FDA quality of drugs regulations. Because herbal drugs are widely used, NDDS were developed to combat various side effects.[62] Herbal nanoparticles can be used to reduce the toxicity of various drugs while also maintaining their therapeutic effects; thus, they can be used to improve the allocation of dissolution inside the blood and increase the retention or permeation of nanoparticles that can cross the BBB.[62] Ionic gelations (IG) are used to create microparticles and nanoparticles through electrostatic interactions between two ionic polymers with oppositely charged ions.[63,64] Micro-emulsion techniques are used to control particle size, morphology, geometry, surface area, and homogeneity, as well as to provide monodispersed nanoparticles.[63] Self-assembly procedures, which are low-cost and high-throughput for nanofabrication,[63-65] are used to organise atoms into ordered patterns using nanometer features without human intervention. By utilising emulsion solvent evaporation, wet mill, and melt emulsification techniques,[66] nano-suspension methods are used to prepare oral, suspensions, pulmonary, and ocular route suspensions. Table 1 contains some examples of nanoparticles, and Figure 3 summarises the various applications of nanoparticles.

Table 2 illustrates some of the therapeutic applications of herbal nanoparticles as well as their reported mechanism of action.

The phytoconstituents and phospholipid present in plant were added up with metal in specified condition resulting in formation of an herbal loaded nanoparticle.

Nanoparticles as the "nanofertilizers"

Nanotechnology is used to improve agricultural production by lowering losses and increasing input efficiency. Silver nanomaterials act as anti-microbial agents in food packaging. The primary goal of nanoparticle in agriculture is to reduce nutrient loss, increase spreadability, and increase yield through nutrient or pest management.[129] Nanomaterials increase the surface area of pesticides and fertilisers. The use of nanotechnology in various agricultural fields includes the use of nanopesticides and nanofertilizers to increase the nutrient levels of trial products without contaminating the soil and to provide protection against various insect pests and microbial diseases.[129] Nanotechnology is helping to revolutionise the food and agricultural industries by improving farming methods and increasing plant absorbability. Table 3 summarizes some of the nanoparticles used in agriculture.

The role of nanopesticides in protection of plants

Nanomaterials have properties such as improved crop yield with lower environmental toxicity, and plants can play an important role in bioaccumulation into the food chain. The effects of nanoparticles on phytotoxicity and plant growth include zinc, alumina, zinc oxide in seed germination and root growth in corn, lettuce, and cucumber, and sulphur nanoparticles in tomato. Zinc is essential for protecting plant cells from oxidative stress and managing reactive oxygen species.[129] Nanopesticides protect plants from leaching, degradation, photolysis, volatilization, controlled release, uniform spreading, improving leaf adhesion and bio-interactions, reducing genotoxicity and cytotoxicity, reducing pesticide loss, and reducing treatment frequency.[146] Table 4 contains some examples.

Solid Nanoparticles for Skincare treatment

Nanomaterials used in skincare treatments, such as nanopigment, nanosomes, and nanoemulsions, can differ in shape, molecular structure, and specific interactions with the environment and living world. Nanoparticles have the ability to alter cosmetic product properties such as transparency, chemical reactivity, colour, and solubility.[156] However, some nanoparticles have a delivering agent property that aids other present ingredients in penetrating the skin as well as in homogenising coloured pigment

Figure 1: Advantages of nanoparticles.

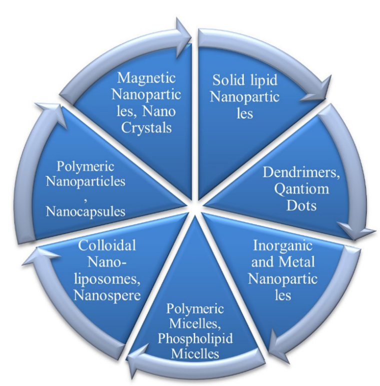

Figure 2: Types of Nano Pharmaceuticals.

Table 1: Benefits of Herbal Nanoparticles.

Sl. No.	Formulation	Active ingredient present	Biological activities	Preparation Method	Benefits	References	FDA Approved
1	Nanoparticles loaded with *Berberine* (Figure 4).	Berberine	Antineoplastic activity.	Ionic gelation methods are used.	It prevents *H. pylori* growth.	63, 64	NA
2	Solid liquid nanoparticles of Curcuminoids	Curcuminoids	Antioxidant, anti-inflammatory, anti-tumor, anti-platelet aggregation, anti-amylodin and anti-malarial.	Micro-emulsion techniques are used.	It aids in increasing activity as well as improving the stability of the Curcuminoids.	63	Yes
3	Artemisinin nanocapsules	Artemisinin	Anti-cancer	Self assembly procedure was used.	It helps in the prolonged drug release of polyelectrolytes via self-assembly on natural drug crystals as well as controlled release.	63-65	Yes
4	Nanoparticles of the *Cuscuta chinensis*	Lignan and Flavonoids	Antioxidants and hepatoprotective properties. It regulates the immune system and delays ageing. Some studies found immune-stimulatory, anti-aging, and anti-cancer effects.	Nanosuspension methods are used.	It improves solubility.	66	Yes
5	*Quercetin* nanoparticles	Quercetin	Anti-bacterial, anti-oxidant, anti-tumor and anti-proliferative effects.	Nano participation techniques are used.	It contributes to increased bioavailability.	67	NA

distribution in cosmetics. Nowadays, everyone wants to look fit and fine as well as young and attractive, so nanoparticles are used in cosmetics for better results such as deeper penetration into the skin, better UV protection, long-lasting effect, and can enhance the colour with finishing quality and the nano scale ingredients.[157] Physical sunscreens contain active ingredients such as zinc oxide, which aids in the blocking of UV A and B radiations. Nanotechnology is used in colour cosmetic products to help with deeper skin penetration and improving skin texture with good hydration properties. Table 5 lists some solid nanoparticles that are used in skincare.

Nanoparticles in Wastewater and Water Treatment Purposes

Water bodies may contain harmful chemicals and heavy metals derived from fertilisers, oils, pesticides, and industrial wastes, which can cause serious health problems in both animals and humans. Pathogens from human and animal excretion can contaminate water sources and become major sources of an epidemic. As a result, there is still a strong link between clean water and a healthy life. Nanotechnology is critical in wastewater purification. The use of nanomembranes aids in the separation of various pollutants, dyes, and heavy metals found in wastewater. Nanocomposites, zero-valent metallic nanoparticles, carbon nanotubes, and metallic oxide nanoparticles are examples of

Table 2: Herbal nanoparticles and mechanism of action.

Sl. No.	Disorders	Herbals Acting	Mechanism of Action	References
1	Anti-inflammatory	Embelin, curcumin, quercetin, sylimarin, *Allium sativum, Zingiber officinale, Elettaria cardamomum, Piper nigrum*, Ginseng, Green tea, Rosemary, Cinnamon, Thymoquinone, *Magnolia officinalis*, Caffeic Acid Phenethyl Ester, Piceatannol.	These herbal drugs help to reduce the activation of mediators of inflammation such as TNF-α, Cox-2, Nrf2, C-Reactive Protein (CRP), Malondialdehyde (MDA), Prostaglandin (PGE2), IgE, Interleukin 1 beta (IL-1ß), moreover NF-KB (Nuclear Factor κB), which reduces inflammation. Thymoquinone significantly decreased the expression of cytokines that promote inflammation (TNF-, IL-6, and IL-1), KEAP1, iNOS, inflammatory markers Cox-2, and Nrf2 at both the protein and mRNA levels.	68-88
2	Anti-cancer	*Curcumin,* Manikya Bhasma, Resveratrol, Topotecan, *Magnolia officinalis*, *Camptotheca acuminata* Decne.	Curcumin therapy for pancreatic and breast cancer cells, as well as melanoma. Manikya Bhasma observed a reduction in cellular viability of cancer cell lines in a dose-dependent manner, as well as the ability to overcome cancer relapses. Resveratrol inhibits the growth of various types of cancer, particularly colon and prostate cancers. Topotecan aids in the formation of an interpolate with the cleavage complex topoisomerase-I/DNA, which disrupts the cell cycle, damages the DNA strand, and forces cancer cells to undergo apoptotic death. CPT (Camptothecin) - HGC (Hydrophobically altered Glycol Chitosans) has potent anti-tumoral activity that has been linked to high accumulation in tumours and prolonged blood circulation, as confirmed by near infrared studies.	89-99
3	Colitis	*Green Tea,* Thymoquinone, *Ginger, quercetin, silymarin,* Exosomes of grapes, *Embelin,* Caffeic Acid Phenethyl Ester.	Thymoquinone treats sodium dextran sulfate-induced mice with colitis by reducing Myeloperoxidase (MPO) activity and Malondialdehyde (MDA) levels with an glutathione levels rising, a sign of progress in the damaging of tissues associated with colitis. GDNPs have activities, such as reducing CAC and acute colitis within the AOM-DSS and mouse models for DSS, and improving intestinal repair in the DSS mouse model. Administration of the drug orally, Ginger-Derived Lipid Vesicle with siRNA-CD98 (GDLVs) drug aids in particularly targeting to the tissue of the colon, leading to a reduction in CD98 expression for colitis. GELNs, or ginger ELNs treat IL-22-dependent mouse colitis mechanism.	70, 100-107
4	Anti-oxidant	Curcumin, *Elettaria cardamomum*, Garlic, Clove, *Magnolia officinalis*, silymarin.	*Elettaria cardamomum* has anti-oxidant properties. Antioxidant enzyme activities such as superoxide dismutase, glutathione peroxidase, and catalase are influenced by silymarin.	108-110

Sl. No.	Disorders	Herbals Acting	Mechanism of Action	References
5	Anti-fungal	Curcumin, Clove, *Azadirachta indica* (neem), *Zingiber officinale, Allium sativum, Ocimum gratissimu, Aloe vera.*	These herbal drugs aid in increasing the zone of inhibition, indicating anti-fungal activity. Ginger acts by inhibiting the growth of *C. albicans*, and curcumin is also effective in inhibiting fungal growth. These herbs work by inhibiting C-14-demethylase (a cytochrome P450 [CYP450] enzyme that prevents the demethylation of the fungal membrane's primary sterol.	110-113
6	Anti-arthritis	*Piper nigrum*, Green Tea, Rosemary, Garlic, *Zingiber officinale, Piper nigrum, Swarnabhasma, Triphala, Withania sominifera*.	These drugs work by both targeting and suppressing Prostaglandins (PGs) by inhibiting the Cyclooxygenase (COX) enzyme. Upregulation of *Withania sominifera* extract is used in Th1/Th2 immunomodulation conditions in *in vitro* studies, which reported its mononuclear cells of synovial fluid in RA patients. Ginger extract reduced the formation of leukotrienes and prostanoid, which has an anti-inflammatory effect in cases of muscle pain and arthritis.	114-117
9	Alzheimer's Disease	Green Tea, Brahmi, *Ginkgo biloba*, green tea, peppermint tea, *Salvia officinalis*.	Brahmi protects cells in the striatum, hippocampus, and prefrontal cortex from DNA damage and cytotoxicity, which are linked to Alzheimer's disease, as well as promoting free radical scavenger mechanisms. It works by protecting cholinergic neurons, lowering anti-cholinesterase activity when compared to galantamine, rivastigmine, and donepezil. Herbal green teas contain compounds that can stimulate neurotransmitters and improve memory recall. These herbs increase acetylcholine levels in the brain, which improves memory recall and treatment of dementia.	118-120
12	IBD	Thymoquinon, Silymarin, Quercetin.	Oral drug implementation of an *N. sativa* Extract encapsulating an alginate microcapsule (NSE) was shown to be an efficient and effective strategy for delivering TQ into the colon for the treatment of IBD (Inflammatory Bowel Disease). Varshosaz *et al*. demonstrated that UC animal model induced by acetic acid, oral administration of silybinin-loaded Eudragit NPs reduced TNF and IL-6 activities while enhancing IBD indications. Glycoside-rutin regulates oxidative stress and body weight by lowering serum Nitrous Oxide (NO), Malondialdehyde, and GSH (Glutathione) concentrations.	121-125
14	Analgesic	Buchu plant, *Coriandrum sativum*	Buchu plant extracts were more effective in pain management when combined with Ag-NPs than when used alone or with the drug aspirin, and the combination of *C. sativum* extract of leaves and AuNPs was more effective than the *C. sativum* extract alone.	126-128

Table 3: Applications of nanoparticles as the "nanofertilizers" in enhancing agricultural crops.

Sl. No.	Crops	Nanofertilizers	Beneficial effects	References
1	Sesame (*Sesamum indicum*)	Mg and Chitosan nanoparticles.	It provided drought resistance.	130
2	Black cumin (*Nigella sativa*)	Zn, Mg, and Fe nanoparticles.	It aids in increasing yield and essential oil production.	131
3	Wheat (*Triticum aestivum*)	Chitosan nanoparticles.	It increased yield, growth, and biochemical properties.	132,133
4	Pea (*Pisum sativum*)	FeO nanoparticles.	Root development has improved.	134
5	Common bean (*Phaseolus vulgaris*)	Zn, Ti and Fe nanoparticles.	It improved biochemical traits and growth, and it increased N uptake.	135
6	Basil (*Ocimum basilicum*)	Si nanoparticles.	Under salinity stress, it improved growth, photosynthetic pigments, and biomass.	136
7	Cotton (*Gossypium* sp.)	Zn nanoparticles.	It enhanced growth under salinity stress.	137
8	Coffee (*Coffea arabica*)	Chitosan, B and Zn nanoparticles.	It aids in the improvement and enhancement of growth.	138,139
9	Moringa (*Moringa peregrina*)	Fe and Zn nanoparticles.	It boosted biomass and growth.	140
10	Barley (*Hordeum vulgare*)	Bioorganic nanofertilizers.	It raises the yield.	141
11	Pomegranate (*Punica granatum*)	B and Zn nanoparticles.	It improved crop yields, fruit quality, and nutrient status.	142
12	Lettuce (*Lactuca sativa*)	Mn and Fe nanoparticles.	It promotes growth.	143
13	Alfalfa (*Medicago sativa* L.)	Fe oxides and Fe chelate nanoparticles.	It improved the biochemical and growth parameters.	144
14	French bean (*Phaseolus vulgaris*)	Chitosan and carbon monotubes nanoparticles.	It enhanced nutrient uptake, growth, and water uptake.	145

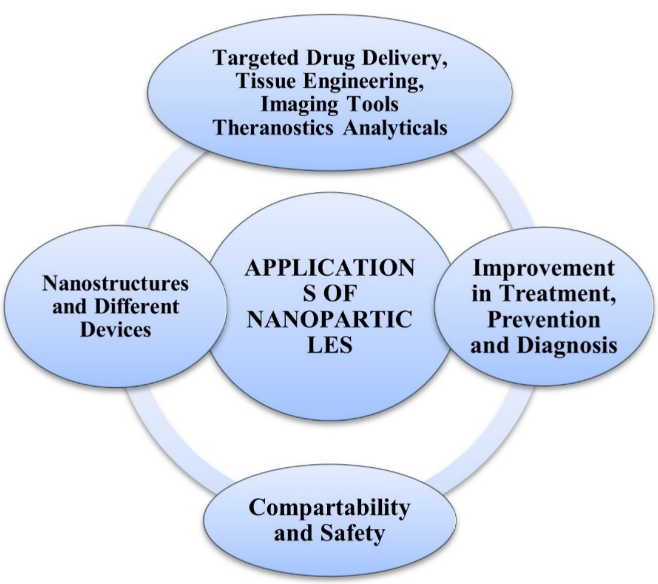

Figure 3: Applications of nanoparticles.

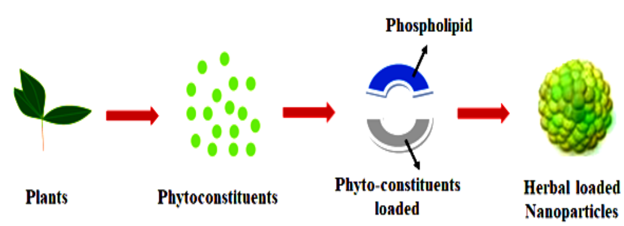

Figure 4: Herbal Drug Loaded Nanoparticles.

nanomaterials that are rarely used in waste water treatment. Silver nanoparticles are commonly used most effective antibacterial agents that aid in the death of *E. coli* in the water The fundamental principle of wastewater treatment is to accelerate natural processes so that water can be easily purified.[164] Silver solutions can be applied to the ceramic water filter by dipping or brushing. Water purification with nano-membranes aids in the elimination of chemical and biological contaminants.[165] Different chemical

Table 4: Nanopesticides in protection of plants.

Sl. No.	Nanopesticides	Host plant	Pathogen/Disease	Effects	References	FDA Approved
1	AgNPs	Tomato (*S. lycopersicum*)	Various fungal diseases *Alternaria solani*/ Early blight	It aids in the reduction of disease symptoms and also inhibits fungal growth.	147,148	Yes
2	CeO2	Tomato (*S. lycopersicum*)	*Fusarium oxysporum*/ Wilt	It facilitates in disease suppression by 35-57%.	149	Yes
3	Chitosan nanoparticles	Pearl millet (*Pennisetum glaucum*)	*Sclerospora graminicola*/Downy mildew	It assist in disease resistance development.	150	Yes
4	Ti and Si nanoparticles	Wheat (*Triticum aestivum*)	*Blumeria graminis*/Powdery mildew	It reduces the severity of the disease by 84-93%.	151	Yes
5	CuO	Tobacco (*Nicotiana tabacum*)	*Ralstonia solanacearum*/Bacterial wilt	It has antibacterial properties.	152	Yes
6	Zn nanoparticles	Sugar beet (*Beta vulgaris*)	*Cercospora beticola*/Cercospora leaf spot	It supports in the reduction of disease severity and incidence.	153	Yes
7	Silver nanoparticles (AgNPs)	Tomato (*Solanum lycopersicum*)	*Fusarium oxysporum*/Wilt	It has antifungal properties.	154	Yes
8	Chitosan nanoparticles	Tomato (*S. lycopersicum*)	*Rhizoctonia solani*/Early blight	It facilitates in the reduction of pathogenic infection.	155	Yes

processes such as chlorination, ultraviolet light, flocculation, different physical methods such as distillation, sedimentation, filtration, and various biological methods such as active carbon and sand filters[164] are used to purify water. Table 6 lists some nanoparticles that are used in waste water and water treatment.

Plants, in addition to nanoparticles, have been reported to be used in waste water treatment. Shittu and Ihebunna[184] successfully removed heavy metals from water using silver nanoparticles biosynthesized from Piliostigma thonningii aqueous leaves extract. Thus, more such herbal technologies for waste water treatment can be developed and used in households to clean water and live a healthy life.

Herbal products effective against COVID-19

Since coronavirus is a virus with a high rate of human-to-human transmission that first appeared in Wuhan, Hubei, China and was brought on by the coronavirus 2 that causes severe acute respiratory syndrome and has zoonotic origins. Some herbal products can help prevent COVID-19 and boost immunity.[185] It is a viral infection that causes respiratory infections and pneumonia. Table 7 lists some herbal products that are effective against COVID-19.

Future prospect for the Nano-sized Herbal medicines

Herbal and natural remedies have demonstrated outstanding performance even in the field of critical health issues, but they occasionally fail at the point of appropriate delivery system. And some targeted drug delivery systems and nanoparticles are now overcoming this factor. Where patients were suffering as a result of a lack of a suitable delivery system, these herbal products embedded with appropriate moieties to provide a perfect formulation as healers.[200] Transdermal nanoparticles are

Table 5: The Solid Nanoparticles Used for Skincare Purposes

Sl. No.	Name of the nanoparticles	Applications	References
1	Silver Nanoparticle (Ag NPs)	They are utilized as coloured pigments, antifungal agents, and antimicrobial agents in a variety of cosmetics.	158
2	Copper Nanoparticles	They are used for both biocidal and anti-aging purposes.	159
3	Gold Nanoparticles (Au NPs)	They serve as an anti-aging agent, a carrier, a colourant, and a preservative.	160
4	Aluminum oxide	It is applied to cosmetics such as mineral foundations, concealers, and foundations rather than skincare products.	156
5	Nanoparticles of Titanium Dioxide and Zinc Oxide (TiO_2 and ZnO NPs)	Because of their ability to scatter as well as reflect UV-B and UV-A radiations, they are used as an inorganic UV filter.	161
6	Carbon based nanoparticles	Fullerenes, nanodiamonds for skincare, and nanotubes for haircare are examples of these materials.	162, 163
7	Silica nanoparticles	These nanoparticles are used in products that are rinsed off as well as products that are left on to improve the texture of the product and provide a matte finish (i.e., opaque) where applied.	156

Table 6: List of Nanoparticles in Waste water and Water Treatment Purposes.

Sl. No.	Name of the nanoparticles	Applications	References
1	Zinc Nanoparticles	Because it has negative reduction properties, it is widely used in wastewater treatment for pollutant reduction. It is also used in Sequencing Batch Reactors (SBR) to inhibit nitrifying bacterial growth, resulting in a decrease in NH_4^+-N removal.	166-168
2	TiO_2 Nanoparticles	They are photocatalyst nanoparticles that are widely used in pathogen removal from wastewater treatment and have the ability to kill viruses such as MS2 bacteriophages, Herpes simplex virus, poliovirus 1, and hepatitis B virus. In some countries, Nano-TiO_2 is used to provide safe and pure drinking water.	169-173
3	Zinc Oxide Nanoparticles	It is used to reduce biological nitrogen treatment from wastewater and has substantial anti-bacterial activity against a variety of pathogenic bacterias.	174-176
4	Iron Nanoparticles	It has been tested for its ability to detoxify vinyl chloride, hexachlorocyclohexane (lindane), Chlorinated Organic Compounds (COCs), trichloroethane, and carbon tetrachloride. Organic dyes, nitroaromatic compounds, phenols, inorganic anions, nitrates, radio elements, halogenated and chlorinated organic compounds, and phosphates are also removed.	177, 178
5	Silver Nanoparticles	It possesses good anti-microbial properties and can be used as an antimicrobial agent and are used for water disinfection against various viruses, bacteria, pathogens and fungi.	179

Sl. No.	Name of the nanoparticles	Applications	References
6	Zerovalent Metal Nanoparticles	Zerovalent metal nanoparticles are employed for the clean-up of wastewater, contaminated soils, and sediments. due to their distinct properties of optical, mechanical, magnetic, electronic, and catalytic (Zinc, silver, and Fe were common zerovalent metal nanoparticles).	180, 181, 129, 64
7	Metal Oxide Nanoparticle	It can be used against a variety of environmentally friendly industrial wastewater treatment methods. heavy metals, including nickel, lead, copper, chromium, cadmium, mercury and arsenic are also removed.	182, 183

Table 7: List of some Nanoparticles effective against COVID-19.

Sl. No.	Herbal Nanoparticles	Mechanism of action	Inhibit virus	References
1	Silvestrol	It aids in inhibiting eIF4A, with an EC_{50} of 1.3 nM.	Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV).	186
2	Gallic acid	According to molecular docking tests, it has a high affinity for RdRp (RNA-dependent RNA polymerase).	SARS-CoV-2, also referred to as the Severe Acute Respiratory Syndrome Coronavirus-2.	193
3	Withanone	It aids in the interaction and binding at the TMPRSS2 catalytic site (transmembrane protease).	SARS-CoV-2, also known as the "severe acute respiratory syndrome Coronavirus 2.	187
4	*Alpinia officinarum*	A molecular docking test revealed that it has a high affinity for the PLpro.	SARS-CoV-2, (Severe Acute Respiratory Syndrome Coronavirus 2).	188
5	Ouabain	It works by preventing MERS-CoV entry into Vero cells using the HCS assay, IC_{50}: 0.08 μM	Middle East Respiratory Syndrome-Related Coronavirus, or MERS-CoV.	189
6	Tannic acid	It inhibits 3CL Protease, with an IC_{50} of 3 M.	SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus).	190
7	Griffithsin	It works by inhibiting the function of the spike protein during entry.	MERS-CoV	191
8	Escins	It works by lowering IL6 and TNF-α levels in NHC and HCLE cells, with EC_{50} values of 1.5 and 2.4 mg/mL, respectively.	SARS-CoV	192
9	Dihydrotanshinone	It works by preventing MERS-CoV entry through pre and post attachment assays.	MERS-CoV	196
10	Daidzin	The virtual docking test shows that it has a higher binding affinity for Heat Shock Protein A5 (HSPA5) Substrate Binding Domain ß (SBDß).	SARS-CoV-2	194
11	Theaflavin-3-gallate	It aids in the inhibition of 3CLPro function, with an IC_{50} of 7 M.	SARS-CoV	197

less persistent than oral and intravenous nanoparticles.[201] Every year, new herbal nanoformulations are introduced into clinical trials, primarily for anticancer and antimicrobial trials. The current publication summarises various patents and novel nano formulations, such as resveratrols, carotene, epigallocattchin-3-gallate, curcumin, quercetin, gallic acid, and fish oil.[202]

In the case of laboratory models, the novel formulations with antioxidant and anti-inflammatory activities were characterised by toxicity or efficacy.[195] However, further investigation using novel nano formulations or patents is warranted.[198] The newer and novel developing nanotechnology-based drug delivery systems faces difficulties related to the viability of the scalability process, which provides a therapeutic innovative technique quickly to the recent market, as well as the potential for obtaining a versatile system for the fulfilment of multiple therapeutic and biological requirements.[205] Nanoparticles have toxicological effects; a new subfield of toxicology called nanotoxicology has emerged to study the unfavourable effects of nanoparticles.[203]

The more intricately structured Nanotherapeutic products are highly expensive than the conventional product alternative, which are intended to reduce total cost of medical care.[199] Health care policies, pharmaceutical regulatory environments, demographics, and the broader economic environment all have an impact on the marketed nanomedicine-related drugs.[207] Companies specialising in nanomedicine have used specific strategies[209] to meet highly competitive market challenges. Taking increased investments and research efforts in nanotherapeutics into account, 200 EU healthcare system were introduced with an increase in the number of newly marketed nanomedicinal products. the use of nanotherapeutic products in the national drug reimbursement strategy had a significant effect on its availability across the health or human care system.[204] Because nanoparticles of matter particulate have already polluted bio environments, precautions must be taken to prevent environmental hazards caused by nanomaterials that are intentionally generated.[208] By meeting international standards for biocompatibility and toxicology, as well as probing the targeted efficiency of the Nanoparticles,[206] various new challenges were included.

In the future, nano pharmaceuticals may be effective in altering the human body in ways we are unable to imagine currently, but it is critical as a factor of risks and benefits of using Nano pharmaceuticals.

CONCLUSION

All plant product manufacturers should adhere to WHO quality control guidelines. Herbal nanoparticles applications in waste water treatment, agricultural applications for plant protection, skincare treatments, and various disease conditions such as antioxidant, cardiovascular diseases, anticancer, anti-malarial, anti-anxiety, liver and kidney tonic diseases were discussed in the current review. Plant metabolites such as triptolide, paclitaxol, savianolic acid B, and ginkolic acid are responsible for the medicinal properties of the plants. Different types of herbal drugs have low absorption, poor aqueous solubility, slow pharmacological actions, physical instability, and lower bioavailability, so different drug delivery systems with nanocarriers are being developed to overcome these disadvantages. Due to their larger surface area to volume ratios and small size, nanoparticles drug carriers aid in the bio-distribution and pharmacokinetics of therapeutically active agents. Rather than having specific site actions, nanoparticles can increase their stability, bypass blood barriers, and improve hydrophobic compound solubility. Not only have herbal nanoparticles helped with health issues, but they have also helped with the economy and making our lives easier, such as in the oil recovery process, agriculture, and so on. The hilarious pandemic, COVID-19, engulfed the world in 2019. Strategies are being developed to keep this deadly disease at bay. Many synthetic approaches have been developed for the same purpose, and parallel herbal techniques are being implemented to mitigate the effects of synthetic approaches. The time required by those which use herbal nanoparticles is the major challenge they face. The major challenge that herbal nanoparticles face is the time required for those that are currently in the early stages of development and waiting for recognition. With the acceleration of critical diseases, treatment measures should be multiplied as well, but with the restriction of fewer side effects, and literature predicts that it is most efficiently possible with herbal nanoparticles, which are an amalgamation of traditional base with modern approach.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NPs: Nanoparticles; **BBB:** Blood Brain Barrier; **NDDS:** New drug delivery system; **FDA:** Food and Drug Administration; **H. pylori**: Helicobacter pylori; **Ti:** Titanium; **TNF:** Tumor necrosis factor; **Cox:** Cyclooxygenase; **Nrf2:** Nuclear factor erythroid; **KEAP1:** Kelch like ECH-associated protein 1; **iNOS:** Inducible nitric oxide synthase; **NF-KB:** Nuclear factor kappa B; **mRNA:** Messenger ribonucleic acid; **DNA:** Deoxyribonucleic acid; **GDNPs:** Gross domestic product nanoparticles; **AuNPs:** Gold nanoparticles; **GSH:** Glutathione; **IBD:** Inflammatory bowel disease; **TQ:** Thymoquinone; **RA:** Rheumatoid arthritis; **Th1/Th2:** T helper cell type 1 and T helper cell type 2; **DSS:** Azoxymethane (AOM)/Dextran Sodium Sulfate; **CAC:** Colitis-associated cancer; **siRNAs:** Small interfering RNAs; **GDLVs:** Ginger-derived lipid vesicles; **Mg:** Magnesium; **Zn:** Zinc; **Fe:** Iron; **FeO:** Iron oxide; **Si:** Silicon; **Mn:** Manganese; **UV A/B:** Ultraviolet A and B; **SBR:** Sequencing batch reactors; **NH_4-N:** Ammonium; **MS2:** Emesvirus zinderi; ***E. coli*:** *Escherichia coli*; **COCs:** Chlorinated organic compounds; **eIF4A:** Eukaryotic initiation factor-4A; **EC_{50}:** Half maximal effective concentration; **nM:** Nanometer; **RdRp:** Viral protein RNA-dependent RNA polymerase; **TMPRSS2:** Transmembrane serine protease type II; **PLpro:** Papain-like protease; **MERS:** CoV-Middle East respiratory syndrome related coronavirus; **SARS:** CoV-severe acute respiratory syndrome coronavirus; **3CLPro:** 3-chymotrypsin-like cysteine protease; **HSPA5:** Heat Shock Protein A5; **SBDß:** Substrate binding domain ß; **EU:** European Union.

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