Advanced Research Journal of Medical Sciences (ARJMS) ISSN 1740-3499, Vol. 10(1), pp. 254-258, September, 2024. Available online at www.advancedscholarsjournals.org © Advanced Scholars Journals

Review Research Paper

Revolution of Green Nanotechnology as Therapeutic agents: A Review

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Accepted 8th August, 2024.

Nature has an excellent hub to open more therapeutic ways by providing diversity in phytoconstituents. To increase the patient compliance by delivering active elements in a supportive way, a specific scientific path is needed. It is quite challenging to discover a phytochemical constituent for any lead therapeutic purpose. In past, drug discovery took several years to find out any leading compound to treat some particular disease. It was considered as a complex process to understand human system. As science progress, some target specific virtual processes have been introduced, which are cost effective and time saving methods. Nano-sized drug delivery system from herbal origin where drugs have been developed to enhance drug activity and to avoid repeated drug administration. Nano based herbal medicines will also minimizing synthetic medication associated problems. For the delivery of herbal medicine, nano based drug delivery system is of high demand which may bring some better therapeutic interventions in coming years.

Key Words: Herbs in nanotechnology, Medicinal Plants, Green Nanoparticles, Herb Therapeutics, Herbonanoceuticals

INTRODUCTION

The most developing field of research is biomedical science, which is increasing day by day. Biomedical research and development used ancient world history, cited in past history of natural products. In the ancient decades, new technologies and tools are being introduced for the welfare of the society. Perhaps, since thousands of years herbs have been fundamental sources of therapeutic considerations, but to become a part of biomedical research laboratories that are still under investigation. Several biomolecules had been studied and tested to check the validity and effectiveness against diseases. The new technology that is lesser than micro sizes has found its applications in medicine, science and engineering, and is termed as "Nanotechnology".[1-3]

However, it is new intervention in biomedical field, to yield metal-herb formulation by applying modern and old technologies. To synthesize nanomaterial, herb choice consideration depends upon its acceptability and

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bioactive potential nature. It should be cost effective with good physiological compatibility, and easily available to its natural origin with minimal side effects. Various ancient scripts also show evidence, about the existence of nano sized materials.[4, 5]This review demonstrated the new concept of "Herbonanoceuticals" in revolution of green nanotechnology thus highlighting the nanomaterial synthesis by using herbs for different biomedical applications.

Medicinal Plant Research

Medicinal herbs are gift of nature to mankind, that constitutes different bioactive molecules used in many drugs to fight against various diseases. Almost 60,000 years ago, fossil fuels recorded plant used as medicine. Literature showed the importance of medicinal plants in ancient civilizations tradition.[6, 7] For about thousands of years, herbs were considered as an integral part of medicinal system and their civilization. Studies revealed that herbal extracts were used as crude drug powder, tincture or in other formulation products.[8, 9]From ancient Indian culture, the "tulasiteerth" which used to give to devotees may be containing silver or copper nanomaterials. The active constituents of plants were extracted and modified to evaluate their biological prospective which finally led to the discovery of drug. However, some of active compounds are still in use as drug.[10-12] Almost 119 chemical compounds are being used as medicine worldwide, derived from some higher plants.

[13] As reported by World Health Organization (WHO) traditional medicine is in therapeutic practices for more than about hundred years, even before the development of modern medicine.[14] Medicinal plants are still considered as therapeutic choice in about 80% population of developing countries because of its cost effectiveness, acceptability, its availability and biocompatibility.[15]

Studies are documented on herbal medicines, the safety issues, treatment principles, therapeutics, validation and dosage forms of herbal medicines from ancient times. In perspective of physiological aliments including systems such as hepatic system, nervous system, digestive system, respiratory system, cardiac system, skin diseases, and reproductive system, the role of herbal medicine is emphasized in any patho-physiological illness. [16]For researchers, plant exploration is still very attractive research area because of its diversity and usefulness.

In future decades, medicinal plants in comparison to synthetic drugs become more popular with minimal side effects and showing eco-friendship nature.[17]In future research and development, more emphasis is required in this field by using new technologies, as the societies can apply the future medicine hold the hand of medicinal plants via bionanotechnology.

Nanoparticles Green Synthesis

The word 'Green' is not related to color here, rather it gives the perception of nanoparticle synthesis from metal salts like iron, copper, gold etc., by using biological active compounds that shows reducing property. The dead and live micro-organisms, animal and plant extracts are used to derive several biological active components. The biological compatibility of biological active compounds depends upon the reducing capability, solubility and affectivity nature. For potential therapeutic effects biological active compounds are used for the production of metal nanoparticles. The best therapeutic potential can be achieved in combination, where the herbs as active components can reduce nanoparticles and stabilize them. By using herbal extracts, synthesis of silver and gold nanoparticles was reported by Gardea-Torresdey et al.[18, 19]To synthesize green nanoparticles, several plant extracts, vitamins, sugar, biodegradable polymers, and microorganisms are being used. However, in plant extracts active key component is polyphenol that is considered as best reducing agent, as their side chain (OH) groups are accountable for stabilization of nanoparticles. In nanotechnology field gold shows an excellent biocompatibility and inertness, therefore its use is very extensive. Dried powder of *Anacardium occidentale* leaf and water-soluble molecules like polyols are being used to synthesize gold, silver, gold core silver shell and gold silver alloy type nanoparticles.[20] Geetha et al. was reported that flowers of *Couroupitaguianensis* produced gold nanop articles and presented its synthesis as one step process and is very cost effective.[21] By extracting aqueous root of Morindacitrifolia, Suman et al. synthesized gold nanoparticles.[22]

Studies proposed by using extract of *Pelargonium zonale* leaf gold nanoparticles were synthesized rapidly *in situ*, that acts as high stabilized and non-toxic reducing agentson high power ultrasound.[23] To reduce gold salt, about 3.5 minutes time used to take for reaction in an aqueous solution under ambient conditions. In the absence of light at about 4 ºC, it has an average life span of 8 weeks. An average size of 80% synthesized particles is about 9-15nm with a diameter range from 8-20nm. In tea infusions gold nanostructures were synthesized by Lin et al., used surface assisted laser desorption mass spectrometry to prove phyto chemical presence on nanosur face structure. Arunachalam and Annamalai (2013)is reported the reduction property of aqueous leaf extract of *Chrysopogonzizanioides*, biosynthesized goldnanop articles which could have cytotoxic, antibacterial and antioxidant property.[24]

Seeds of *Mimosa pudica* were used by Iram et al., reported for the production of about 6nm diameter silver nanoparticles from an isolated glucoxylans. [25] By using bran extracts of an aqueous sorghum, bio-reduction of silver salt was been reported by Njagi et al. [26] Magneto-sensitive nanoparticle is a new emerging trend in green methods to produce targeted delivery carriers. By using bio-reduction methods, several plant extracts, fungus and bacteria are being used for the production of iron-based nanoparticles. Machado studied by using different tree leaf extracts like green tea, pomegranate and oak, which in aqueous solution is capable of reducing iron to zero valent iron. Hence the extracts are therefore used for green production of zero valent iron nanoparticle.[27]The antioxidant property of dry leaf extracts is higher than non-dried leaf extracts. Spherical ions with nanostructures were produced by Wang et al. from extracted Eucalyptus leaf which shows reducing capability of polyphenols. [28] *Brassica juncea* L. plant extract is mixed copper and zinc oxide for the synthesis of nanoparticles.[29]In hospitals, the products containing copper surfaces are being used for the process of sterilization because copper has an active biocidal activity. The copper nonmaterial'scontains toxic behavior to some biological systems like bacteria, fungi, helminthes, etc. In nature zero valent, copper nanoparticle is common that shows good biological affectivity. Different herbal extracts are being used to synthesize copper oxide nanoparticles. Rod shaped copper oxide nanoparticles were synthesized by using *Carica papaya* leaf extract, that was proposed by Sankar et al.[30]

Applications of Green Nanoparticles

Properties of nanoscale dimension is totally different from properties of metals in bulk form. In human body both of them plays a significant role as therapeutic agents. [31] When biologically active compounds conjugated with these nanoparticles, active potential of compound has been exhibited. Sometimes, concrete effects of conjugated compound with nanoparticles have been found. For green synthesis, the extracted compounds from medicinal plants have some medicinal uses. Herbal extract in combination with nanoparticle is more potent towards dreadful diseases like cancer, diabetics, heart strokes, kidney stones, etc. Nanoproducts has been reported that antioxidant, anti-diabetic, anti-cancer, anti-microbial, drug delivery, anti-arthritic effects of these green nanoparticles have been established.[32][33]

Green Nanoparticles as an Anti-cancer agent

Geetha et al. reported the flowers of *Couroupitaguianesis* produced gold nanoparticles, and checked its anti-cancer activity by DNA fragmentation, MTT assay and comet assay for DNA damage. [21] Gold nanoparticles were synthesized by an aqueous extract of rhizome of *Dysosmapleiantha,* which showed anti-metastatic activity against HT-1080 cells. The gold nanoparticles prepared in this experimentation shows interference with action polymerization pathway that can inhibit migration of HT-1080 cells. The gold nanoparticles were also shows non-toxic property to cell proliferation.[34]Particles prepared by using edible mushroom *Pleurotus florida* showed best anti-cancer activity for human lung carcinoma against A-549 and human chronic myelogenous leukemia bone marrow (K-562).[35]

Mukherjee et al. reported the preparation of an aqueous extract of Ecliptaalba leaves hybridized with doxorubicin has developed clean, efficient, fast, eco-friendly, low-cost biocompatible gold nanoparticles for inhibiting breast cancer cells.[36]Green gold nanoparticles were synthesized by Venkatpurwar et al. reported using reducing agent prophyrancan acts as a carrier for anticancer drug doxorubicin hydrochloride.[37] The conjugation of gold nanoparticles with doxorubicin hydrochloride shows hydrogen bonding has been confirmed by spectroscopic examination.

Drug Delivery by Green Nanoparticles

Metal particles are effective to carry drug to their targeted sites due to high surface area to volume ratio. Drug effectively can be mediated by particles with very small volume of drug. Drug can be attached to surface of particle or should be loaded in hollow sphere inside metal nanoparticles. The drug releases into the biological system is slow and has sustain process. Nanoparticles with size of about 40nm are considered as safe green particles for targeted drug delivery process because of non-cytotoxic nature.[25] Particles synthesized from fruit extract of *Punica granutum* are being used for targeted drug delivery to cancerous cells.[32]

Green nanoparticles as an anti-microbial agent

One of an important monosaccharide is Xylose that is used to synthesized gold nanoparticles and is found in cottonseed hulls, straw and pecan shells. Xylose shows effectiveness against gram positive bacteria and has strong anti-bacterial activity.[38] An effective anti-bacterial activity against gram positive *Staphylococcus aureus,* gram negative *E. coli*, and anti-fungal activity for *Fusarium oxysporum* and *Aspergillus niger* has been exhibited by gold nanoparticles, being synthesized from leaf of Cinnamomum zeylanicum.[39] Using standardized well diffusion methods from an aqueous extract of *Terminalia chebula*areused to synthesized gold nanoparticle that showed marvelous anti-microbial activity for gram positive bacteria like *S. aureus* rather than gram negative bacteria like *E. coli*.[40] Gold nanoparticles extracted from banana peel showed anti-microbial activity towards bacterial and fungal cultures.[41]

Ajitha et al. used extracted leaf of *Plectranthusamboinicus* for the synthesis of silver nanoparticles, which potentiates an anti-microbial activity.[42, 43] Extracts of ethyl acetate and methanol has been used for the synthesis of silver nanoparticles by using *Cocous nucifera* tree, which was being used against human bacterial pathogen such as *Salmonella paratyphi, Bacillus subtilis and Klebsiella pneumonia* as an efficient anti-microbial agent.[44]

CONCLUSION

One of challenging area of nanotechnology is green nanotechnology, with its widespread applications in research and pharmaceutical health care products. For the development of nanoparticles, green nanotechnology has huge potential and is a highly active field of research. By approaching different techniques, different types of nanoparticles can be synthesized. The research advancement indicates expansion of green medicine, as they are trending in different application areas with different types of green nanoparticles which are being synthesized from different types of green plants. However, it should be highly concerned to develop conventional standardized technique for the synthesis of green nanoparticles, which would be helpful for better understanding and also yielding of novel nanoparticles. Most of the studies and reports are highly concerned to the issues of toxicity. Hence, there is anecessity to combat such issues in order to improve drug efficacy. New vistas and possibilities expand green medicine and green nanotechnology research. In future, less explored green nanoparticles would expectedly require robust by exploration of novel and efficient nanoproducts.

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