

Nano-Technology in Herbal Medicines: Advancements in Herbal Treatment

RUSHIKESH V. MATHPATI¹, YOGESH R. HARANGULE², SHYAMLILA B. BAVAGE³,
NANDKISHOR B. BAVAGE⁴

¹ B. Pharmacy Final Year Student, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India

² Department of Organic Chemistry, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

³ Department of Pharmacognosy, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

⁴ Department of Pharmaceutical Chemistry, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

Abstract— Herbal remedies have been used from years around the world; especially in India, herbal remedies are in high demand. The use of herbal remedies has increased because of their ability to treat various ailments with minimal side effects. Delivery of medicinal plants of plants / herbs as drugs is problematic due to low digestion, poor availability, low availability, biological instability and early metabolism. These herbal remedies can be overcome by gluing or combining them with suitable nanomaterials. The growing interest in Nano chemicals has produced many advances in recent years with a focus on the use of an engineering novel. Over the past decade, great strides have been made in developing new drug delivery systems (NDDS) from plant operations and extracts. By creating new formulations such as Nano herbal medicines such as nanoparticles, dendrimers, Nano crystals, Quantum dots, Nanosperes, Nano capsules, the herbal market is getting a positive response. This review will provide details on the application of pharmaceutical nanotechnology, nanoparticles, nanoparticles manufacturing techniques and their formulation.

Index Terms— Nanotechnology, Herbal remedies, Formulation techniques of nanoparticles, Standardization of herbal drugs, NDDS- Novel Drug delivery System

I. INTRODUCTION

For many years, herbal remedies and natural products have been used to treat disease. Unlike the widely used allopathic system, herbs contain thousands of compounds that work simultaneously to fight disease. The function of herbal remedies depends on the completeness of the various active ingredients, as all the ingredients contribute to co-operation and thus improve the value of treatment. Each functional area plays an important role and they are all related.

The integration of herbal remedies into the delivery system also helps to increase solubility, improved stability, toxicity protection, improved pharmacological function, improved tissue distribution, continuous delivery and protection against physical and chemical damage.

Most herbal remedies do not melt well in water due to their hydrophobic nature. These side effects reduce the availability of bioavailability and increase the approval of the system and therefore require repeated administration or increased dosage, and thus reduce the clinical use of herbal medicines. Therefore, nanoparticles can be used to increase the solubility of herbal drugs and help to make the drug locally lead to better performance and to facilitate patient adherence.

Due to certain restricted vegetable / plant extracts such as high pH acidity, liver metabolism etc. to be important. Nanoparticle can be used to access herbal

medicine in each organ that improves selection, drug delivery, efficiency and safety and thus reduces dosage and increases patient adherence. The need for a proper Nano particulate system is that it must be able to circulate in the bloodstream and must be small enough to reach the target cells and tissues. Herbal remedies can be applied to various organs such as the brain, lungs, liver, kidneys, intestinal tract, etc.

The global market for a product using nanotechnology is estimated to reach US \$ 1trillion by 2015. In 2006 the Indian and Australian governments offered to launch the Australia-India Science Research Funding Program. The global market value of Nanomedicine was \$ 63.8 billion and \$ 72.8 billion in 2010-2011 respectively. The market is projected to grow to \$ 130.9 billion in the 2016 financial year.

Herbal remedies testing is a basic requirement of the industry and another organization dealing with ayurvedic and pharmaceutical products. Legislation is an important step in establishing a consistent biological work, a consistent chemical profile, or simply a quality assurance program for the manufacture and manufacture of pharmaceutical drugs.

II. NANOTECHNOLOGY FOR HERBAL DRUGS

Before reaching the bloodstream, many herbal supplements will be exposed to the acidic pH of the stomach and some nutrients are linked to the liver. It appears; a large amount of herbal medicines may not reach the bloodstream. If the drug does not reach the right value in the infected region at a "low active level," then there will be no means of indicating the effect of the drug treatment. Nano-based herbalists will carry the right amount of medicine into their workplace by overcoming all obstacles such as pH of the stomach, body weight and increased long-term distribution of the drug into the bloodstream due to its small size.

Herbal remedies were selected for delivery through a Nano delivery system because of the following properties:

1. Patient non-compliance due to large doses and less effectiveness with the available formulations.

2. Effective chloroform, petrol, acetone, and methanolic extracts are available which may not be suitable for delivery as such.
3. At present the commercial product does not have specific information on various chronic diseases.
4. Some of the negative effects are associated with the construction currently on sale.
5. These are the bulk drugs so dose reduction is intended.

- Advantages of herbal nanoparticle delivery system

1. Show Nano particulate system delivers the herbal formulation directly to the site of actions EPR (enhanced permeation and retention) effect i.e. Improved fullness through obstruction due to small size and retention due to malignant lymphatic drainage such as a tumor.
2. The Nano Particle System transmits the formation of solutions directly to the operating site.
3. Reduce the dose of drug formulation.
4. Improved pharmacokinetic effect.
5. Decrease in the side effects.
6. Increased stability via encapsulation.
7. Increased efficacy and therapeutic index.
8. Indicates undocumented identification at the site of the disease without the inclusion of any ligand moiety.

- Types of Nano pharmaceuticals

- Polymeric nanoparticles.
- Solid lipid nanoparticles.
- Magnetic nanoparticles.
- Metal and inorganic nanoparticles.
- Polymeric micelles.
- Phospholipids micelles.
- Colloidal Nano-liposomes.
- Dendrimers.
- Nano crystals.
- Quantum dots.
- Nanosphere.
- Nano capsule.

- Techniques which are used for the preparation of Nano pharmaceuticals:

1. Complex coacervation method:
This is the process of separating the spontaneous phase of two liquids into colloidal systems, which arises as a result of the interaction of two highly resistant

polyelectrolytes when mixed into a strong solution. Includes three steps-

1. The formation of three invisible chemical classes.
2. Applying a liquid polymer fluid to an important object.
3. Making firmness difficult.

2. Co-precipitation method:

This method is a modification of the sophisticated method of storage of Nano scale core-shell particles. This method has been reported to provide good resistance to dispersion of drugs that do not dissolve in water

3. Salting-out method:

This method is based on the dissolution of non-electrolyte in water decreases over the addition of electrolyte. Acetone is preferred as a miscible solvent because of its soluble properties which are known to separate from aqueous solution by adding salt in the form of electrolytes. The spread of acetone from drops is a step in the right direction. This diffusion, which occurs in water mixing, can produce intermediate confusion leading to the formation of polymers in the form of nanoparticles.

4. Nanoprecipitation method or solvent displacement method:

As decaying nanoparticles meet the growing interest in drug delivery applications, a series of investigations are underway to understand how synthetic nanoparticles are synthesized using a delivery method only. This method is based on the placement of an internal polymer after solvent miscible transfer by water from a lipophilic solution, resulting in a decrease in tension between the two layers, which increases surface area and the formation of small droplets of living liquid without mechanical movement.

5. Solvent emulsification–diffusion method:

This method involves the preparation of o / w emulsion using a polymer-based oil phase such as PLGA and an organic solvent oil produced by a liquid phase containing a stabilizer in a large shear mixture followed by the addition of water resulting in the dispersing of the organic solvent, which led to the formation of nanoparticles.

6. Supercritical fluid methods:

Supercritical fluid (SCFs) can be liquid or gas and is used in addition to its critical point of temperature and pressure. SCFs are the most widely used carbon dioxide. Particles with a smooth surface, small particle size and free distribution and flow can be obtained with certain SCF techniques. Rapid Expansion of Supercritical Solutions (RESS), Supercritical Anti Solvent (SAS) and Particles from Gas Saturated Solutions (PGSS) are three groups of processes leading to fine flour production and monodisperse.

7. High-pressure homogenization method:

In this method, the lipid is compressed at high pressure (bar 100 to 2000) at very high shear pressures, resulting in low particle interference to micrometer or nanometer diameters. The high-pressure homogenization method is the most reliable and powerful method for the production of large scale Nano formulations for lipid carriers, lipid drug conjugate, SLNs, and emulsion emulsions.

8. Self-assembly methods:

Blending is a visual process in which pre-existing components, atoms, or molecules organize themselves into nanoscale controlled structures by physical or chemical reactions without any contribution from any external source.

9. Emulsion-Solvent Evaporation Method:

Emulsification-solvent explosion involves two steps. The first step requires the removal of the polymer solution from the wet phase. During the second step the polymer solvent evaporates, reducing polymer precipitation like Nano spheres. Nano particles are collected by ultracentrifugation and washed with refined water to remove the residues of any free and lyophilized drug reserves. Modification of this method is known as high pressure emulsification and solvent evaporation method. This method involves emulsion preparation and then under homogenization under high pressure followed by complete stirring to remove organic solvent. Size can be controlled by adjusting the dynamic scale, type and amount of dispersing agent, viscosity of organic components and water and temperature. However this approach can be applied to liposoluble-containing drugs and the limitations imposed by the problem of escalation. Polymers used

in this method are PLA, PLGA, Poly (caprolactone) \ (PCL), Poly (β - hydroxybutyrate) (PHB).

10. Double Emulsion and Evaporation Method:

The emulsion process and evaporation are limited to the negative concentration of hydrophilic drugs .Therefore the hydrophilic solution is applied using a double emulsion process, which involves adding strong chemical solutions to the organic polymer solution under strong stimulation to form emulsions. This w / o emulsion is placed in a second aqueous phase with continuous stirring to form a w / o / w emulsion. The emulsion was then removed from solvent application by evaporation and Nano particles could be separated by centrifugation at high speed. Synthetic nanoparticles must be thoroughly cleaned before lyophilization (Vandervoort et al., 2002). In this way the amount of hydrophilic component to be applied, the concentration of the solvent used, the density of the polymer, the volume of the liquid phase are variables that affect the formation of Nano particles (Ubrich et al., 2004).

- Advanced techniques for identification and characterization of Nano herbal medicine:

1. High performance Liquid chromatography (HPLC):

HPLC Preparation and Analysis is widely used in the pharmaceutical and computer cleaning industry. Vasicine, the major bioactive alkaloid of *Adhatoda vasica*, is measured by HPLC in two polyherbal drug formulas - *Shereeshadi Kashaya* and *Jastyadivati*, and its content is found to be 18.1 mg / 100 g in *Shereeshadi Kashaya* and 0.7 mg / 100g in *Yastyadivati*. *Triphala* suspension (antioxidant-rich herbal formulation) a mixture of *Emblica officinalis*, *Terminalia chebula* and *Terminalia bellerica* in equal proportions has been reported in the HPLC method using the RP18 column with a mobile acidic phase. Currently a very powerful process for the quality control of herbal remedies such as licorice.

2. High performance thin layer chromatography (HPTLC):

HPTLC is used for quality analysis and phytochemical measurements of pharmaceutical drugs and formulations. And with the help of HPTLC several samples can be analyzed simultaneously using a small number of cellular components. Gallic acid, rutin and

quercetin are important components of the *Terminalia chebula* measured in the form of HPTLC. The HPTLC process was used for simultaneous determination of two existing *Ashwagandha* biomarkers such as *Withaferin A* and β sitosterol d-glucoside. Glycoside (*Jamboline*), Tannin, Ellagic Acid and Gallic Acid present in the tincture of *Syzygium Jambolanum* tincture have been extensively tested for stability, durability, accuracy and measurement by HPTLC. The HPTLC method provides accurate, fast and cheap measurement control for diosgenin analysis.

3. UPLC:

Ultra-performance liquid chromatography (UPLC) has been used to test for chemical reactions and chemical instability between traditional and granule decoctions.

4. Liquid chromatography-Mass spectroscopy (LC-MS):

LC-MS has become an option in many stages of drug development.

LC-MS analysis of amino glycosides showed that these drugs are highly soluble in water, show low binding to plasma proteins, and are more than 90% excreted in the kidneys. In addition this method assists in the analysis of amino glycosides in plasma samples with ion chromatography. Pharmacokinetic studies of Chinese herbal remedies using LC-MS.

5. Gas chromatography - mass spectroscopy (GC-MS):

It is a system used to identify large amounts of matter in the ecological and biological systems. The identification and processing of chemical compounds present in the manufacture of polyherbal oil (*Megni*) containing nine ingredients, mainly *Myristica perfrumens*, *Eucalyptus globulus*, *Gaultheria procumbens* and *Mentha piperita* analyzed the GC-MS method. 35 flexible chemicals are isolated and identified.

6. Capillary Electrophoresis:

The CE method was developed to test a single herbal drug in terms of definition, sensitivity and accuracy. Several CE studies on herbal remedies have been reported and two types of therapeutic compounds namely alkaloids and flavonoids have been widely studied. Moreover, the analysis time of the CE method

was twice as short as that of the HPLC and the solvent consumption was more than 100 times higher. CE instruments have been used, such as CE-diode array detection, CE-MS and CE-NMR. Some Herbal Drug

Nanoparticles with their method of preparation and application presented in Table1.

Table 1: herbal drug nanoparticles

Sr. No.	Formulations	Active ingredients	Biological activity	Method of preparation	Benefit of formulation	References
1.	Berberine-loaded nanoparticles	Berberine	Anti-neoplastic activity	Ionic gelation method.	H.pylori growth inhibition	2,40
2.	Curcuminoids solid lipid nanoparticles	Curcuminoids	Antitumor, antioxidant, antiplatelet aggregation and anti-inflammatory, antimalarial.	Micro-emulsion technique.	-increase in activity -Enhanced stability of curcuminoids	40,
3.	Artemisinin Nano capsules	Artemisinin	Anticancer	Self-assembly procedure.	- achieving prolonged drug release through self-assembly of polyelectrolytes on natural drug crystals. - controlled release	9,40,
4.	Nanoparticles of cuscuta chinensis	Flavonoids and lignans	-Hepatoprotective and antioxidant effects -Used to improve sexual function, prevent senescence and regulate the immune system. Some studies showed anticancer, antiaging and immunostimulatory effects.	Nano suspension method.	Enhanced solubility	41
5.	Quercetin Nanoparticles-	Quercetin	antioxidant, anti-proliferative, antitumor, antibacterial	Nano participation technique	- improve the bioavailability	42

CONCLUSION

India can emerge as a major country and play a leading role in producing a balanced, effective ayurvedic treatment. Conventional ayurvedic remedies can only be obtained if herbal products are tested and analyzed using modern stabilization methods such as TLC, HPLC, HPTLC, LC-MS, GC-MS, Capillary

Electrophoresis and others. The development of analytical techniques will serve as a quick and clear tool for herbal research; assists manufacturers to set standards and definitions of quality and results in increasing the effectiveness of medical, safety and shelf- herbal medicine. In addition, all pharmaceutical manufacturers must adhere to the WHO guidelines for quality control.

REFERENCES

- [1] Patel JS et al., Nanotechnology: A new approach in Herbal Medicine. American Journal of Pharmtech Research. 3(4); 2013: 275-288.
- [2] Sharma M et al., Applications of Nanotechnology Based Dosage Forms for Delivery of Herbal Drugs. Research and reviews: journal of pharmaceutics and nanotechnology. 2(1); 2014: 23-30.
- [3] Thapa RK et al., Herbal Medicine Incorporated Nanoparticles: Advancements in Herbal Treatment. Asian journal of biomedical and pharmaceutical sciences. 3(24); 2013: 7-14.
- [4] Dhiman A et al., Novel Herbal Drug Delivery System (NHDDS): the need of Hour.2012 International Conference on Environment, Chemistry and Biology. 49(34); 2012: 171-175.
- [5] Abirami A et al., Herbal nanoparticle for anticancer potential- a review. World journal of pharmacy and pharmaceutical sciences. 3(8); 1014: 2123-2132.
- [6] Shahu AN et al., Nanotechnology in herbal medicines and cosmetics. International. Journal Research. Ayurveda Pharm. 4(3); 2013: 472-474.
- [7] Choudhary N and Sekhon B et al., An overview of advances in the standardization of herbal drugs. Journal Pharm Educ Res. 2(2); 2011: 55-70.
- [8] [Ansari](#) SH et al., Influence of nanotechnology on herbal drugs: A Review. J Adv. Pharm Technol Research. 3(3); 2012: 142–146.
- [9] Yadav D, et al. Novel approach: Herbal remedies and natural products in pharmaceutical science as Nano drug delivery systems. International Journal of Pharmacy and Technology. (3)3; 2011: 3092–3116.
- [10] Kharat A and Pawar P et al., Novel drug delivery system in herbals. International journal of pharmaceutical, chemical and biological sciences. 4(4); 2014: 910-930.
- [11] Abhilash M et al., Potential applications of Nanoparticles. International Journal of Pharma and Bio Sciences 1(1); 2010: 1-12.
- [12] Sahni JK et al., Promising Role of Nano pharmaceuticals in Drug Delivery. Pharma Times. 43; 2011; 16–8.
- [13] Lachman L and Lieberman HA., the Theory and Practice of Industrial Pharmacy. New York; 3 rd Ed: pp. 420.
- [14] Sheehan D, Blackwell W. Physical biochemistry. 2009; 285.
- [15] Fessi H, et al., Nano capsule formation by interfacial polymer deposition following solvent displacement. Int J Pharm. 1989; 55:R1- 4.
- [16] Back BM.et al., Department of pharmaceutics and biopharmacy, Eur. J Pharm Science. 2010; Oct.9.
- [17] Jung J, Perrut M.et al., Particle design using supercritical fluids: Literature and patent survey. Journal of Supercrit Fluids. 20; 2001: 179–219.
- [18] Pal SL et al., Nanoparticle: An overview of preparation and characterization. Journal of Applied Pharmaceutical Science. 1(6); 2011: 228-234.
- [19] Chimezie A et al., HPLC analysis of nicotinamide, pyridoxine, riboflavin and thiamin in some selected food products in Nigeria. Afr J Pharm Pharmacol. 2(2); 2008: 29-36.
- [20] Saravanan J et al., A simple and validated RP-HPLC method for the estimation of methylcobalamin in bulk and capsule dosage form. Int J Chem Pharm Sci. 1(2); 2010: 323-324.
- [21] Choudhary N, Sekhon B et al., An overview of advances in the standardization of herbal drugs. J Pharm Educ Res.2 (2); 2011:55-77 (Anupam S, Krishan L, Handa SS. Standardization: HPLC determination of vasicine in polyherbal formulations. Pharm Biol; 30(3); 1992: 205-208.)
- [22] Bose A et al., A review on latest developments in the standardization of ayurvedic drugs. International journal of pharmaceutical research and bio-science. 3; 2012: 96-119. (Singh DP, Govindarajan R, Rawat AKS. High-performance liquid chromatography as a tool for the chemical standardization of *Triphala* an ayurvedic formulation. Phytochem Anal. 19(2); 2007: 164-168.)

- [23] Zhang Q, Ye M et al., Chemical analysis of the Chinese herbal medicine Gan-Cao (licorice). *J Chromatogr A*. 1216(11); 2009:1954-1969.
- [24] Kumar A et al., Estimation of gallic acid, Rutin, and Quercetin in *Terminalia chebula* by HPTLC. *Jordan Journal of Pharmaceutical Sciences*. 3(1); 2010: 63-68.
- [25] 25. Jirge SS et al., Development and validation of a novel HPTLC method for simultaneous estimation of beta-sitosterol- d-glucoside and Withaferin A. *Int J Pharm Pharmaceut Sci*; 3(Suppl 2); 2011: 227-230.
- [26] Shanbhag DA, Khandagale NA.et al., Application of HPTLC in the standardization of a homoeopathic mother tincture of *Syzygium jambolanum*. *J Chem Pharm Res*. 3(1); 2011: 395-401.
- [27] Kasthuri KT. et al., Development of GC-MS for a polyherbal formulation- MEGNI. *International Journal of Pharmaceutical sciences*, 2 (2), 2010, 81-83.
- [28] Li SL, et al. Decocting-induced chemical transformations and global quality of Du–Shen–Tang, the decoction of ginseng evaluated by UPLC–Q-TOF-MS/MS based chemical profiling approach. *J Pharm Biomed Anal* 53(4); 2010: 946–957.
- [29] Li SL, et al. UPLC– PDA–TOFMS based chemical profiling approach to rapidly evaluate chemical consistency between traditional and dispensing granule decoctions of traditional medicine formulae. *J Pharm Biomed Anal*.52 (4); 2010:468–478.
- [30] Mike Lee S, Edward Kerns H.et al., LC/MS applications in drug development. Milestone Development Services, Pennington, New Jersey. 1999:187-279.
- [31] 31. Shen AQ .et al. Tandem Method development of LC-MS analysis of aminoglycoside drugs: Challenges and solutions. *Answering Pharmaceutical Questions with Discipline and Ingenuity*; 5(2); 2010:567-569.
- [32] Binit Kumar Dwivedi, et al. Gas chromatography mass spectrometry (GC-MS) analysis of the hexane and benzene extracts of the Piper beetle from India. *J Med Plant Res*. 4(21); 2010: 2252-2255.
- [33] Gatkal S, et al. Safety of herbal medicine: a review. *International journal of pharmaceutical and chemical sciences*. 1(4); 2012: 1624-1639.
- [34] 34. Shaa YF.et al., Analysis of *Rhioxma Curcumae Aeruginosae* volatiles by solid-phase microextraction with gas chromatography-massspectrometry. *Z. Naturforsch*. 2004; 59(7-8): 533-537.
- [35] Ganzera M.et al., Quality control of herbal medicines by capillary electrophoresis: Potential, requirements and applications. *Electrophoresis* 29:2008; 3489–3503.
- [36] Wen HG, et al. Analysis of protoberberine alkaloids in several herbal drugs and related medicinal preparations by non-aqueous capillary electrophoresis. *J Sep Sci*. 28(1); 2005: 92-97.
- [37] 37. Pietta P. et al., Application of micellar electrokinetic capillary chromatography to the determination of flavonoid drugs. *J Chromatogr*; 549; 1991: 367-373.
- [38] Sombra LL.et al., Comparative study between capillary electrophoresis and high performance liquid chromatography in „guarana“ based phytopharmaceuticals. *J Pharm Biomed Anal* 36:2005; 989–994.
- [39] Tistaert C.et al., Chromatographic separation techniques and data handling methods for herbal fingerprints: A review. *Anal Chim Acta*. 690(2); 2011: 148–161.
- [40] Anupam Kumar Sachan* and Ankita Gupta.et al., A review on nanotized herbal drugs.*International journal of pharmaceutical sciences and research*.
- [41] Yen FL.et al., Nanoparticles formulation of *Cuscuta chinensis* prevents acetaminophen-induced hepatotoxicity in rats. *Food Chem Toxicol* 46:2008; 1771-1777.
- [42] Soheir N. et al.: Quercetin Nanoparticles: Preparation and Characterization. *Indian Journal of Drugs*. 2(3); 2014: 96-103.