International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

A Review on Herbal Nanoparticles

Shelly Raghav, Yogendr Bahuguna, Deeksha Adhikari*
School of Pharmaceutical Sciences, SGRR University, Patelnagar, Dehradun, Uttarakhand, India

Date of Submission: 20-06-2021 Date of Acceptance: 03-07-2021

ABSTRACT
Now a days, the use of herbal medicines has increased because of their ability to treat different diseases with fewer side effects. Herbal medicines are used from historic time for remedy of diseases. Herbal drugs show their pharmacological action either due to specific constituent or due to blend of phytoconstituents. Pharmacological effect of the drug can be obtained only when its concentration ranges with in the therapeutic range. So, Novel Drug Delivery System (NDDS) play important role to enhance the efficacy of the herbal drug. Nano-sized drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines. Nanoparticle can be used to target the herbal medicine to individual organ which improves the selectivity, drug delivery, effectiveness and safety and thereby reduces dose and increases patient compliance. This review discussed about the advantages, types of nanoparticles, various methods of preparation and their characterization along with some marketed formulations of nanoparticles.

Keywords: Herbal medicines, Pharmacological effect, Novel drug delivery system, Nanoparticle.

I. INTRODUCTION

For beyond few decades, there has been significant development of Nanotechnology using nanoparticles. Nanotechnology plays important role in herbal medicines, especially in drug delivery system. Active phytoconstituents or standardized extracts are used for the preparation of Nanophytomedicines. Nanotechnology have a potential future for enhancing the activity and conquer the problems related to herbal plants.[1]

The herbal drugs can be utilized in a better form with enhanced potency by incorporating them into modern dosage forms. This may becarried outvia way of means of designing novel drug delivery systems which provide a therapeutic amount of drug to relevant site in the body to accomplish promptly and maintain the desirable drug concentration.[2]

Nanoparticles have been suggested to possess significant biological effects, indicating its potential as an alternative treatment for diseases. Their nanosized particles have high surface area to volume ratio which permit them to penetrate the cells more efficaciously, as compared to micro-sized particles.[3,4]

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Nanoparticles had been used as a physical approach to adjust and enhance the pharmacokinetic and pharmacodynamics effects of several types of drug molecules.The main aim in preparing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents as a way to obtain the site-specific action of the drug at the therapeutically optimal rate and dose regimen .[5,6]

Nanotechnology is approaching new paradigm for drug delivery system for their exclusive minute size and controlled release of the drug. This technology has been used to enhance the bioavailability by overcoming the drawbacks of the conventional dosage forms. This is feasible due the potential of the nanocarriers to protect the encapsulated drug molecule and transport it to various areas of the skin.[7,8,9]

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

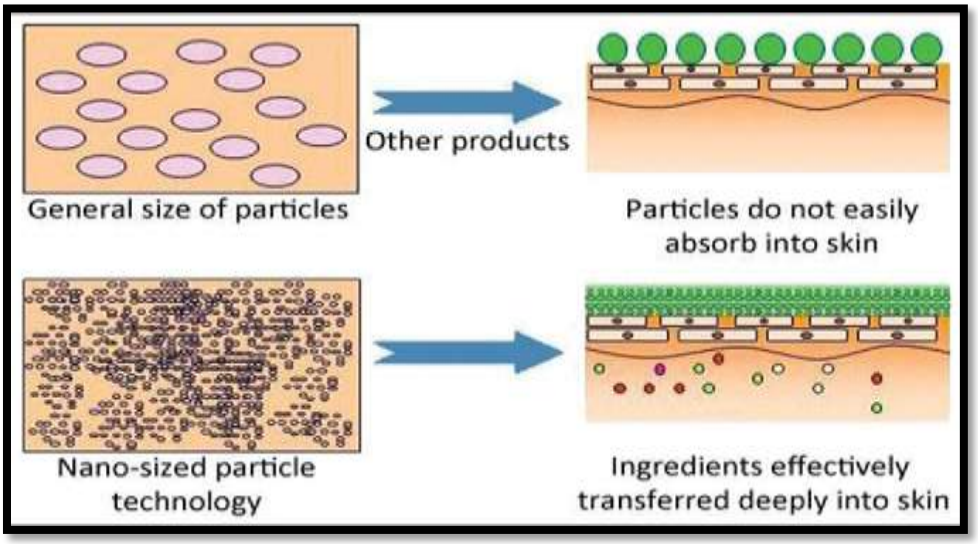

Figure 1. Transport of drug molecules through skin [10]

ADVANTAGES [11-15]

Advantages of using nanoparticles as a drug delivery system are as follows:

1. Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.
2. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
3. Enhanced shelf life of product.
4. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
5. They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
6. The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc.
7. Small sized nanoparticles can penetrate through smaller capillaries, which could allow efficient drug accumulation at the target sites.
8. Protection from physical and chemical degradation.
9. Hydrophilic as well as lipophilic both type of drugs can be incorporated.
10. Nanoparticles increases stability of drug/proteins against enzymatic degradation.

II. LIMITATIONS

In spite of these advantages, nanoparticles also have following limitations:

1. Their small size and large surface area can lead to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms.
2. Small particles size and large surface area readily result in limited drug loading and burst release.
3. Smaller the particle size greater the surface area, this property makes nanoparticles very reactive in the cellular environment. [11-16]

CLASSIFICATION OF NANOPARTICLES

Nanoparticles are classified based on many forms, such as based on materials, based on size, based on surface, and based on shapes.[17] Example primarily based totally on coating material and based on the use for the study purpose the classification of nanoparticles given in the below figure 2.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

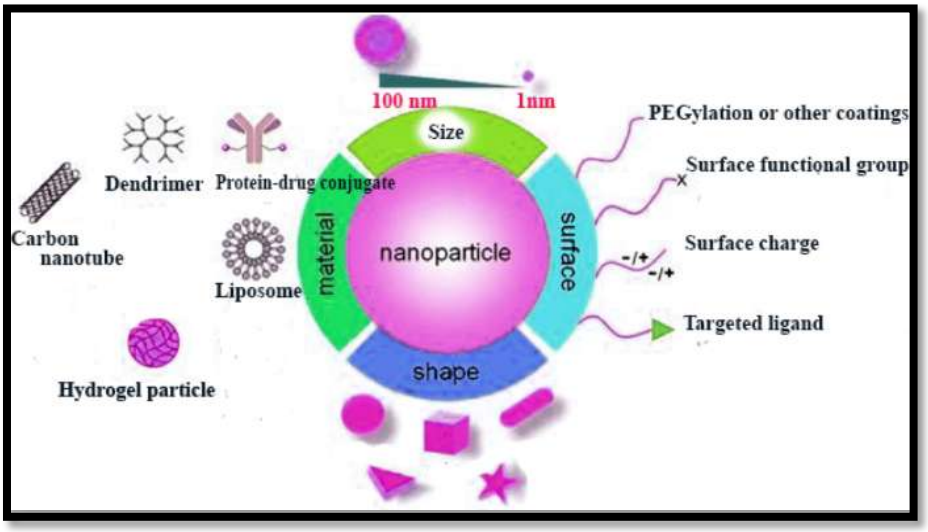

Figure 2. Schematic representation of nanoparticles [18]

There are two types of nanoparticles which are given below:-

a) Inorganic nanoparticles
b) Organic nanoparticles
c) Carbon based nanoparticles

1. **Inorganic nanoparticles-** These are particles that are not made up of carbon. Metal and metal oxide based nanoparticles are generally categorised as inorganic nanoparticles.

a) Metal based: Nanoparticles that are synthesised from metals to nanometric sizes either by destructive or constructive methods are metal based nanoparticles.[19] The commonly used metals for nanoparticle synthesis are aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). The nanoparticles have distinctive properties such sizes as low as 10 to 100nm, surface characteristics like high surface area to volume ratio, pore size, surface charge and surface charge density, crystalline and amorphous structures, shapes like spherical and cylindrical and colour, reactivity and sensitivity to environmental factors such as air, moisture, heat and sunlight etc.

b) Metal oxides based: The metal oxide based nanoparticles are synthesised to modify the properties of their respective metal based nanoparticles. Metal oxide nanoparticles are synthesised mainly due to their increased reactivity and efficiency. The commonly synthesised are Aluminium oxide (Al2O3),Cerium oxide (CeO2), Iron oxide (Fe2O3), Magnetite (Fe3O4), Silicon dioxide (SiO2), Titanium oxide (TiO2), Zinc oxide (ZnO).[20]

2. **Organic nanoparticles-** Dendrimers, micelles, liposomes and ferritin, etc. are commonly knows the organic nanoparticles or polymers. These nanoparticles are biodegradable, non-toxic, and some particles such as micelles and liposomes has a hollow core, also known as nanocapsules and are sensitive to thermal and electromagnetic radiation such as heat and light. These unique characteristics makes them an ideal choice for drug delivery.

The drug carrying capacity, its stability and delivery systems, either entrapped drug or adsorbed drug system determines their field of applications and their efficiency apart from their normal characteristics such as the size, composition, surface morphology, etc. they are efficient and also can be injected on specific parts of the body that is also known as targeted drug delivery.[21]

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

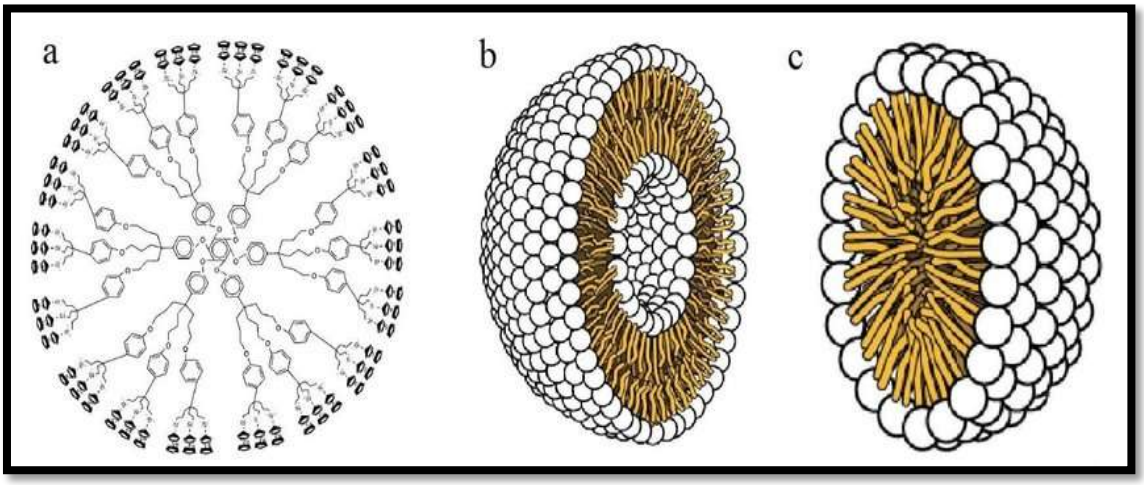

Figure 3. Organic nanoparticles: a – Dendrimers, b – Liposomes and c – micelles [22]

3. **Carbon based-** The nanoparticles made completely of carbon are knows as carbon based. They can be classified into fullerenes, graphene, carbon nano tubes (CNT), carbon nanofibers and carbon black and sometimes activated carbon in nano size.[23]

a) **Carbon Nano Tubes (CNT):** Carbon Nano Tubes (CNT), a graphenenanofoil with a honeycomb lattice of carbon atoms is wound into hollow cylinders to form nanotubes of diameters as low as 0.7 nm for a single layered and 100 nm for multi-layered CNT and length varying from a few micrometres to several millimetres. The ends can either be hollow or closed by a half fullerene molecule.

b) **Carbon Nanofiber:** The same graphenenanofoils are used to produce carbon nanofiber as CNT but wound into a cone or cup shape instead of a regular cylindrical tubes.

c) **Fullerenes:** Fullerenes (C60) is a carbon molecule that is spherical in shape and made up of carbon atoms held together by sp2 hybridization. About 28 to 1500 carbon atoms forms the spherical structure with diameters up to 8.2 nm for a single layer and 4 to 36 nm for multi-layered fullerenes.[24]

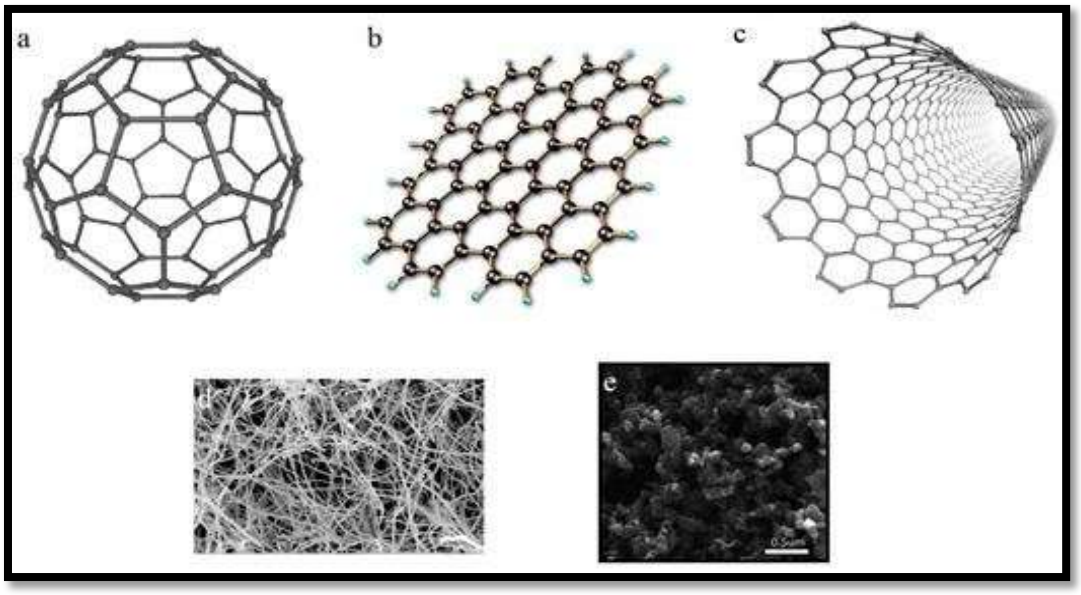

Figure 4. Carbon based nanoparticles: a- fullerenes, b- graphene, c- carbon nanotubes, d- carbonnanofibers and e- carbon black [22]

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

PREPARATION OF NANOPARTICLES

1) **High Pressure Homogenizations-** A liquid with a high pressure (100-2000 bar) push through a narrow gap (in the range of few microns) by a homogenizers. The fluid moves at very short distance with high velocity (over 1000 km/h), very high shear stress, cavitations forces disrupt the particles down to the submicron range. High pressure homogenization can be done by two methods:[25]

a) **Hot homogenization technique:**This process will take place in the presence of a higher temperature than the melting point of the lipid. The pre-emulsion will form when the drug is loaded with melted lipids in the presence of a hot aqueous solution of surfactants. Finally, the nanoparticles will be formed.

b) **Cold homogenization technique:**The drug is melted in the lipid melt, and quickly cooled using cryogenic systems like liquid nitrogen or ice nitrogen. Then make it into dispersing powder form using powder mill. Then homogenize at room temperature or below to get a nanoparticle.[26]

2) **Dispersion of preformed polymers-** For the preparation of biodegradable nanoparticles from polymers such as poly (lactic acid) (PLA); poly (D, L-glycolide), PLG; poly (D, L-lactide-co-glycolide) (PLGA) and Poly (cyanoacrylate) (PCA), dispersion of preformed polymer method is used.[27] This technique can be used in various ways as follow:

a) **Solvent evaporation method:** In this method, there is formation of o/w emulsion prepared by emulsification of drug and polymer mixture in aqueous solution which contain emulsifying agent, which result in formation of stable emulsion. After that by using pressure reduction method or continuous stirring, organic solvent is evaporated. The homogenizer speed, nature and stabilizer concentration along with the property of polymer effect size of nanoparticle.[28]

b) **Spontaneous emulsification or solvent diffusion method:** In this method, two phase solvent is used, one is water miscible and other is water immiscible. In this method interfacial turbulence is created, by immediate diffusion between two solvents (which are differing in phase) which lead to the formation of small particles. A reduction in particle size can be gained by increasing the concentration of water miscible solvent both the above described method can be used for preparation of hydrophilic and hydrophobic drugs.

c) **Salting out:** This method involves the mixing of saturated aqueous solution of polyvinyl alcohol (PVA) into an acetone solution of the polymer under magnetic stirring resulting in the formation of o/w emulsion. The precipitation of the polymer occurs when sufficient amount of water is added to external phase to allow complete diffusion of the acetone from internal phase into aqueous phase.

3) **Polymerization method-** Polymerization of monomers in an aqueous solution form the basis of this method. Two different techniques are used for the preparation in aqueous solution.

a) **Emulsion polymerization:** This method involves emulsification of monomer in non-solvent phase.

b) **Dispersion polymerization:** This method involves dispersion of monomer in non-solvent phase. [29]

4) **Coacervation or ionic gelation method-** This method involves a preparation of two aqueous phases, of which one is the polymer chitosan, adi-block co-polymer ethylene oxide or propylene oxide (PEO-PPO) and the other is a polyanion sodium tripolyphosphate which are mixed, due to mixing positively charged amino group of chitosan interacts with negative charged tripolyphosphate to form coacervates with a size in the range of nanometer. when electrostatic interaction take place between two aqueous phases coacervates are formed, and when two molecules interact due to ionic force, resulting in transition from liquid phase to gel phase at room temperature this is known as ionic gelation method.

5) **Supercritical fluid technology (SCF)-** Supercritical fluid technology has been a alternative to prepare biodegradable micro and Nanoparticles. Solvent which remain fluid in a single phase regardless of pressure above critical temperature are known as supercritical fluid. Super critical CO2 is the most widely used supercritical fluid.[30] Two principles have been developed for the production of nanoparticles using supercritical fluids:

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

a) **Rapid expansion of supercritical solution (RESS):** In traditional RESS, the solute is dissolved in a supercritical fluid to form a solution, followed by the rapid expansion of the solution across an orifice or a capillary nozzle into ambient air. The high degree of super saturation, accompanied by the rapid pressure reduction in the expansion, results in homogenous nucleation and thereby, the formation of well-dispersed particles.[31]

b) **Rapid expansion of supercritical solution into liquid solvent (RESOLV):** A simple, but significant modification to RESS involves expansion of the supercritical solution into a liquid solvent instead of ambient air, termed as RESOLV.In RESOLV the liquid solvent apparently suppresses the particle growth in the expansion jet, thus making it possible to obtain primarily nanosized particles.[32-34]

CHARACTERIZATION OF NANOPARTICLES

Nanoparticles are generally characterized by their size, morphology and surface charge, using such advanced microscopic techniques as scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). The average particle diameter, their size distribution, and charge affect the physical stability and the in vivo distribution of the nanoparticles.[35]

1) **Size:** The particle size and distribution is most commonly measured using electron microscopy. The images of Scanning Electron Microscope (SEM) and Transmission Electron Microscope (TEM) are used for the measurement of particles.[36]

2) **Surface area:** The surface area to volume ratio of a nanoparticle has a huge influence on its properties. The surface area is most commonly measured using BET analysis.

3) **Composition:** The chemical or elemental composition determines the purity and performance of the nanoparticles. The composition measurement is usually carried out by X-ray photoelectron spectroscopy (XPS). Some techniques involve chemical digestion of the particles followed by wet chemical analysis such as mass spectrometry, atomic emission spectroscopy and ion chromatography.[37]

4) **Surface morphology:** The nanoparticles have various shapes and surface structures that plays important role in exploiting its properties. Some of the shapes include spherical, flat, cylindrical, tubular, conical and irregular shapes with surface like crystalline or amorphous with uniform or irregularities on the surface. The surface is generally determined by electron microscopy imaging techniques like SEM and TEM.[38]

5) **Surface charge:**The surface charge of a nanoparticle determines its interactions with the target. Zeta potentiometer is used for the measurement of surface charges and its dispersion stability in a solution.[36]

6) **Crystallography:** Crystallography is the study of atoms and molecules arrangement in crystal solids. The crystallography of nanoparticles are carried out by a powder X-ray, electron or neutron diffraction to determine the structural arrangement.[39

MARKETED FORMULATION OF HERBAL NANOPARTICLES

S.No.	Nanoparticle	Indication	Method of preparation	References
1.	Curcumin	Potent Anticancer and Antitumor	Wet-milling technique.	40, 41, 42
2.	Paclitaxel	Acts against several tumours, ovarian and breast cancers.	Nanoprecipitation	43, 44, 45

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

3.	Berberin	Inflammation and several cancers	Emulsion, Ionic gelation	46, 47, 48
4.	Camptothecin	Potent anticancer	Encapsulated with hydrophobically modified glycol	49
5.	Ginkgo biloba	Alzheimer's dementia	Combination of Dry and wet process.	50
6.	Triptolide	Anti- arthritis	Nano encapsulation	51, 52, 53
7.	Salvia miltiorrhiza	Anti-hyperlipidaemia	Phospholipid complex loaded	54, 55, 56, 57
8.	Quercetin	Potent anticancer	Gelatin and chitosan loaded.	58, 59, 60
9.	Breviscapine	Anti-cardiovascular	Lipid encapsulation	61, 62, 63
10.	Naringenin	Antioxidant, Antiinflammatory.	Nano precipitation	64, 65
11.	Dodder	Acts against carcinogenesis and Antioxidant	Nano precipitation	66, 67, 68
12.	Silymarins	Hepatoprotective	Cold homogenization	69, 70, 71
13.	Genistein	Used in cardiovascular diseases, breast and uterine cancer also in osteoporosis .	Nano emulsion and chitosan microsphere	72, 73
14.	Centellaasiatica	Acts as anti-anxiety, also used in leprosy, cancer, syphilis and allergy.	Ionic gelation.	74, 75, 76

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

15.	Annual mugwort	Antimalerial Also used for Asthma	Hydrophilic encapsulation	77, 78
16.	Artemisinin	Anticancer	Self assembly procedure	77
17.	Cuscutachinensis	Hepatoprotective and antioxidant effects	Nanosuspension method	68
18.	Glycyrrhizic acid loaded nanoparticles	Anti-inflammatory antihypertensive	Rotary-evaporated film ultrasonication method	79
19.	Taxel-loaded nanoparticles	Anticancer	Emulsion solvent evaporation method	80, 81
20.	Bacoside	Memory enhancing	Microemulsion probe sonicator method	82

III. CONCLUSION

Predominantly, this reviewshows that nanotechnology has great prospects for delivering herbal drugs and nutraceuticals, and in mild of the overall health problems, its usage for effective disease prevention and health merchandising is important and to be anticipated.The combination of nanotechnology with traditional herbal medicine may offer a beneficial tool in designing future herbal medicine with better bioavailability profile and less toxicity. The main aim of this review was to describe the advantages, types of nanoparticles and different techniques involved in preparation of nanoparticles.

REFERENCES

[1]. Goyal A, Kumar S, Nagpal M, Singh I, Arora S: Potential of novel drug delivery systems for herbal drugs. Indian journal of pharmaceutical education and research 2011; 45:225-35.

[2]. Bonifácio BV, Silva PB, Aparecido M, Ramos S and Maria K: Nanotechnology-based drug delivery systems and herbal medicines: a review. International journal of nanomedicine 2014; 9:1-15.

[3]. Ovais M, Khalil AT, Raza A, Khan MA, Ahmad I, Islam NU et al. Green synthesis of silver nanoparticles via plant extracts: beginning a new era in cancer theranostics. Nanomedicine, 2016; 11(23):3157-3177.

[4]. Bobo D, Robinson KJ, Islam J, Thurecht KJ, Corrie SR. Nanoparticle-based medicine: a review of FDA-approved materials and clinical trials to date. Pharmaceutical Research, 2016; 13(10):23732387.

[5]. Vila A, Sanchez A, Tobio M, Calvo P, Alonso MJ. Design of biodegradable particles for protein delivery. J Control Release 2002; 78: 15-24.

[6]. Mu L, Feng SS. A novel controlled release formulation for the anticancer drug paclitaxel (Taxol(R)): PLGA nanoparticles containing vitamin E TPGS. J Control Release 2003; 86: 33-48.

[7]. Gupta D, Nguyen P, Yu M. Nanoparticles for superior pharmacokinetics and enhanced efficacy. J Dev Drugs 2014;3:2.

[8]. Gao D. Drug design for cancer: Gold nanoparticleliposome hybrids for drug delivery and monitoring. Drug Des 2013;2:2.

[9]. Lopes CM. Therapeutics delivery: Innovations technology approaches. Drug Des 2014;3:3.

[10]. Mamillapalli V, Atmakuri M.A, Khantamneni P, Nanoparticles for Herbal Extracts, Asian Journal of Pharmaceutics, 2016.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

[11]. Kreuter J. Nanoparticles. In Colloidal drug delivery systems, J, K., Ed. Marcel Dekker: New York, 1994; pp 219-342.
[12]. Gaur A, Mindha A, Bhatiya Al, Nanotechnology in medical sciences, Asian Journal of Pharmaceutics, 2008; 80-85.
[13]. Sapra P, Tyagi P, Allen TM, Ligand-targeted liposomes for cancer treatment, Current drug delivery, 2005; 2:369-381. http://dx.doi.org/10.2174/156720105774370159PMid: 16305440.
[14]. Patel J, Patel N. An overview of phytosome as an advanced drug delivery system. Asian J PharmaSci 2009;4:363-71.
[15]. Chang CH, Huang WY, Lai CH, Hsu YM, Yao YH, Chen TY, et al. Development of novel Nanoparticles shelled with heparin for Berberine delivery to treat Helicobacter pylori. ActaBiomater 2011; 7: 593-603.
[16]. Mohanraj VJ, Chen Y, Nanoparticle a review, Tropical Journal of Pharmaceutical Research, 2006, 5:561-573.
[17]. Nalla A, Chinnala KM (2017) Novel herbal drug delivery system-an overview. WJPPS 6(8):369–395.
[18]. V Sandhiya and U. Ubaidulla, A review on herbal drug loaded into pharmaceutical carrier techniques and its evaluation process, Future Journal of Pharmaceutical Sciences, 2020;6:51.
[19]. Salavati-niasari M, Davar F and Mir N 2008 Synthesis and characterization of metallic copper nanoparticles via thermal decomposition Polyhedron 27 3514–8.
[20]. Tai C Y, Tai C, Chang M and Liu H 2007 Synthesis of Magnesium Hydroxide and Oxide Nanoparticles Using a Spinning Disk Reactor 5536–41.
[21]. Tiwari D K, Behari J and Sen P 2008 Application of Nanoparticles in Waste Water Treatment 3 417–33.
[22]. Ealias AM, P. Saravanakumar, A review on the classification, characterisation, synthesis of nanoparticles and their application, IOP Conf. Series: Materials Science and Engineering, 2017;032019.
[23]. Bhaviripudi S, Mile E, Iii S A S, Zare A T, Dresselhaus M S, Belcher A M and Kong J 2007 CVD Synthesis of Single-Walled Carbon Nanotubes from Gold Nanoparticle Catalysts 1516–7.
[24]. Ramesh S, Sol-Gel Synthesis and Characterization of 2013.
[25]. Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine: NMB2010; 6 Supply 1 :e9-e24.
[26]. Belletti D, Riva G, Luppi M, Tosi G, Forni F, VandelliMA RB (2017) Anticancer drug-loaded quantum dots engineered polymeric nanoparticles: diagnosis/ therapy combined approach. Eur J Pharm Sci 107:230–239.
[27]. M.N Ravi, U Bakowsky, C.M. Lehr, Biomaterials, 2004, 25, 1771-1777.
[28]. M Zambaux, X. F Zambaux, R. Gref, P. Maincent, E. Dellacherie, M. Alonso, P. Labrude, C. Vigneron, J. Control.Release, 1998, 50, 31-40.
[29]. G. Puglisi, M. Fresta, G. Giammona, C.A Ventura, Int. J. Pharm. 1995, 125, 283-287.
[30]. J. Jung, M. Perrut, J.Supercritical Fluids, 2001, 20, 179-219.
[31]. Weber M, Thies M C Understanding the RESS process. In: SunYP, editor. Supercritical fluid technology in materials science and engineering: synthesis, properties, and applications. NewYork:Marcel Dekker; 2002, 387–437.
[32]. Meziani MJ, Pathak P, Hurezeanu R, Thies MC, Enick RM, Sun YP. Supercritical fluid processing technique for nanoscale polymer particles. AngewChemInt Ed2004; 43:7047.
[33]. Meziani MJ, Pathak P, Wang W, Desai T, Patil A, Sun YP. Polymeric nanofibers from rapid expansion of supercritical solution. IndEngChem Res2005; 44:4594–8.
[34]. Hutchenson KW. Organic chemical reactions and catalysis in supercritical fluid media. In:SunYP, editor. Supercritical fluid technology in materials science and engineering: synthesis, properties, and applications. NewYork: Marcel Dekker; 2002, 87–188.
[35]. Mcbride A, Price DN, Lamourex LR, Elamaoued AA, Vargas JM, Adolphi NL, et al. Preparation and characterization of novel magnetic nano-in-microparticles for site-specific pulmonary drug delivery, Mol. Pharm, 2013; 10:3574-81.
[36]. Marsalek R 2014 Particle Size and Zeta Potential of ZnO APCBEE Procedia 9 13–7.
[37]. Sharma V and Rao L J M 2014 An overview on chemical composition, bioactivity and processing of leaves of Cinnamomumtamala. Crit. Rev. Food Sci. Nutr. 54 433–48.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

[38]. Hodoroaba V, Rades S and Unger W E S 2014 Inspection of morphology and elemental imaging of single nanoparticles by high- resolution SEM / EDX in transmission mode.
[39]. Yano F, Hiraoka A, Itoga T, Kojima H, Kanehori K and Mitsui Y 1996 Influence of ionimplantation on native oxidation of Si in a clean-room atmosphere Appl. Surf. Sci. 100-101 138–42.
[40]. Bisht S, Feldmann G, Son Si, Ravi R, Karikar C, Maitra A. Polymeric nanoparticles-encapsulated curcumin (nanocurcumin): a novel strategy for human cancer therapy. Journal of Nanobiotechnology. 2007; 5(3):2-18.
[41]. Sharma RA, Euden SA, Platton SL, Cooke DN, Shafayat A, Hewitt HR. Phase I clinical trial of oral curcumin: biomarkers of systemic activity and compliance. Clinical Cancer Research. 2004; 10:6847-6854.
[42]. Lim JK, Bisht S, Bar EE, Maitra A, Eberhart CG. A polymeric nanoparticle formulation of curcumin inhibits growth, colongenicity and stem like fraction in malignant brain tumors. Cancer Biology and Therapy 2011; 11:1-10.
[43]. Singla AK, Garg A, Aggarwal D. Paclitaxel and its formulation. International Journal of Pharmaceutics. 2002; 235:179-192.
[44]. Spencer CM, Faulds D. Paclitaxel-a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the treatment of cancer Drugs. Adis International Limited, Auckland, New Zealand 1994; 48(5):794-847.
[45]. Fessi H, Puisieux F, Devissaguet JP, Ammoury N, Benita S. Nano-capsule formation by interfacial polymer deposition following solvent displacement. International Journal of Pharmaceutics. 1989; 55:1-4.
[46]. Fukuda K, Hibiya Y, Mutoh M. Inhibition of activation protein 1 activity by Berberine in human hepatoma cells. Planta Med 1999; 65:381-383.
[47]. Lin JG, Chung JG, Wu LT. Effects of Berberine on arylamineNacetyl-transferase activity in human colon tumor cells. Am J Chin Med. 1999; 27:265-275.
[48]. Kim SA, Kwon Y, Kim JH, Muller MT, Chung IK. Induction of topoisomerase II-mediated DNA cleavage by a protoberberine alkaloid, Berberrubine, Biochemistry 1998; 37:16316-163124.
[49]. Chen KJ, Tang L, Garica MA, Wan H, Lu H, Lin WY. The therapeutic efficacy of camptothecin-encapsulated super molecular nanoparticle, Biomaterial 2012; 33:11621169.
[50]. Shinji S, Yasukazu T, Hatsue W, Kazuo K, Machiko I, Naoki M. Analysis of brain cell activation by nano sized particles of Ginkgo biloba extract. International Journal of Plant Physiology and Biochemistry. 2011; 3(3):28-33.
[51]. Ahmed S, Anuntiyo J, Malemud JC, Haqqi TM. Biological basis for the use of botanicals in osteoarthritis and rheumatoid arthritis: a review. Evid Based Complement Altern Med 2005; 2:301-308.
[52]. Wang B, Ma L, Tao X, Lipsky EP. Triptolide an active component of Chinese herbal remedy Tripterygiumwilfordii Hook F. inhibits production of nitric oxide by decreasing inducible nitric oxide synthase gene transcription. ArithritisRheumatis 2004; 50:2995-3003.
[53]. Mei Z, Chwn H, Wneg T, Yangand Y, Yang X. Solid lipid nanoparticles and microemulsion for tropical delivery of triploid. European Journal of Pharmaceutics and Biopharmaceutics. 2003; 56(2):189-196.
[54]. Zhou L, Chow M, Zuo Z. Improved quality control method for Danshen products – consideration of both hydrophilic and lipophilic active components. Journal of Pharmaceutical Biomedical Analysis 2006; 41:744-750.
[55]. Kang DG, Oh H, Sohn EJ, Hur TY, Lee KC, Kim KJ et al. Lithospermic acid B isolated from Salvia miltiorrhiza ameliorates ischemia/ reperfusion-induced renal injury in rats. Life Sciences 2004; 75:1801-1816.
[56]. Liu JR, Chen GF, Shih HN, Kuo PC. Enhanced antioxidant bioactivity of Salvia miltiorrhiza (Danshen) products prepared using nanotechnology. Phytomedicine 2008; 15:23-30.
[57]. Peng Q, Tao G, Jiao Z, Jie L, Dong Z, Zhirong Z. Enhanced the oral bioavailability of savianolic acid B by phospholipid complex loaded nanoparticles, Die PharmazieAn International Journal of Pharmaceutical Science. 2008; 63:661-666.
[58]. Kawai Y, Nishikawa T, Shiba Y, Satio S, Murota K, Shibata N et al. Macrophage as a

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 75-86 www.ijprajournal.com ISSN: 2249-7781

targeted quercetinglucurnoidsin human atherosclerotic arteries: implication in the anti-atherosclerotic mechanism of dietary flavonoids. Journal of Biological chemistry. 2008; 283(14):9424-9434.

[59]. Zheng Y, Hasworth IS, Zuo Z, Chow MS, Chow AH. Physicochemical and structural characterization of quercetin- beta-cyclodextrin complexes. Journal of Pharmaceutical Sciences. 2005; 94:1079-1089.

[60]. Zhang Y, Yang Y, Tang K, Hu X, Zou G. Physiochemical characterization and anti-oxidant activity of quercetin loaded chitosan Nanoparticles. Journal of Applied Polymer Science. 2008; 107:891-907.

[61]. Zhu HB, Guan YY, He H, Lin MJ. Effects of scutellarein on diabetic rat aorta. ActaPharmcologicaSinica 2000; 21:353-366.

[62]. Gao R, Zhu BH, Tang SB, Wang JF, Ren J. Scutellarein inhibits hypoxia and moderately-high glucose-induced proliferation and VEGF expression in human retinal endothelial cells. ActaPharmacologicaSinica 2008; 29:707-712.

[63]. Chen P, Wang DH, Lei WY, Shen ZQ. Effects of scutellarin on thrombosis and platelet aggregation. J Kunming Med Univ. 2006; 27:1-5.

[64]. Yen LF, Wu TH, Lin LT, Chan MT, Lin CC. Naringenin loaded Nanoparticles improve the physiochemical properties and hepatoprotective effects of naringenin in orally administered rats with CCl4 induced acute liver failure. Pharm Res 2008; 26:893-902.

[65]. Bilati UE, DoelkerAllémann E. Nanoprecipitation versus emulsion-based techniques for the encapsulation of proteins into biodegradable nanoparticles and processrelated stability issues. AAPS Pharm Sci Tech 2005; 6:594-601.

[66]. Nisa M, Akbar S, Tariq M, Hussain Z. Effect of Cuscutachinensis water extract on 7, 12-dimethylbenz a anthracene- induced skin papillomas and carcinomas in mice. J Ethnaphamacol. 1986; 18:21-31.

[67]. Liu JH, Jiang B, Bao YM, An LJ. Effect of Cuscutachinensis glycoside on the neuronal differentiation of rat pheochromocytoma PC12 cells. Intern J DevelopmNeurosc. 2003; 21:277-281.

[68]. Yen FL, Wu TH, Lin L, Cham TM, Lin CC. Nanoparticles formulation of Cuscutachinensis prevents acetaminophen-induced hepatotoxicity in rats. Food ChemToxicol 2008; 46:1771-1777.

[69]. Samaligy MS, Afifi NN, Mahmoud EA. Evaluation of hybrid liposomes-encapsulated silymarin regarding physical stabilityand in vivo performance. Int J Pharm. 2006; 319:121-129.

[70]. Raffa V, Vittorio O, Riggio C, Cuschieri A. Progress in nanotechnology for health care,In: Minimally Invasive Therapy and Allied Technologies 2010; 19:127-135.

[71]. He J, Feng JF, Zhang LL, Lu WG, Hou SX. Freeze- drying of silymarin-loaded solid Nanoparticles. China J Chinese Mat Med. 2005; 30:110-112.

[72]. Usui T. Pharmaceutical prospects of phytoestrogens. Endocr J. 2006; 53:7-20.

[73]. Hua-Yan Li, Dong-Peng Wang, Tian-Ming Zhang, HaoLiRen, Fang-Yuan Xu, Zhu Guo Zhao et al. J NanosciNanotechnol. 2010; 10(4):2325-2331.

[74]. Bradwejn JT. A double blind, placebo-controlled study on the effects of Gotu Kola-(Centellaasiatica) on acoustic startle response in healthy subjects. J Clinic Pharmacol. 2000; 20:680-684.

[75]. Van Wyk BE. Medicinal Plants of South Africa. Briza Publications, Pretoria, 1997, 78-79.

[76]. Padamanaban G, Nagaraj AV, Rangarajan PN. Artimisinin-based combination with curcumin adds a new dimension to malaria therapy. CurrSci 2012; 102:704712.

[77]. Chen Y, Lin X, Park H, Greever R. Study of artemisininnanocapsules as anticancer drug delivery systems, Nanomedicine: Nanotechnol. Biol Med 2009; 3:316-322.

[78]. Sathyavathi GV, Gupta AK, Tandon N. Medicinal Plants of India, New Delhi (India), Indian Council of Medical Research 1987; 2:230-239.

[79]. Hou J, Zhou SW: Formulation and preparation of glycyrrhizic acid solid lipid nanoparticles. ACTA Academiaemedicinaemilitaristertiae 2008; 30:1043-5.

[80]. Yadav D, Suri S, Choudhary AA, Sikender M, Hemant, Beg NM, et al. Novel approach: Herbal remedies and natural products in pharmaceutical science as nano drug

delivery systems. Int J Pharm Tech 2011;3:3092-116.

[81]. Li D, Zhong X, Zeng Z, Jiang J, Li L, Zhao M, et al. Application of targeted drug delivery system in Chinese medicine. J Control Rel 2009;138:103-12.

[82]. Khot U.V., Pillai M.M.,Kininge P., Study of solid lipid nanoparticles as a carrier for bacoside, Int J Pharm Bio Sci, Volume 3| Issue 3 |JUL-SEPT|2013|414-426.