REVIEW ARTICLE

Green Biosynthesis of Nanoparticles for Targeted Drug Delivery

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Abstract

The matter at its molecular or atomic level is engineered and manufactured through a technique called Nanotechnology. It has contributed in various fields of science, including material science, biology, chemistry, and engineering. Various research studies have suggested that crude extract of plant can enhance the activity of green synthesized nanoparticles (NPs), like gold (Au) and silver (Ag). However, one drawback of NPs is its toxicity. The altered size, shape or surface chemistry of NPs help in passive or active drug targeting. If the size, shape or surface chemistry of NPs is altered, drug targeting can be helped passively or actively. Changing the size, shape or surface chemistry of NPs can help drug targeting actively or passively. On the other hand, green synthesis is said to be environment friendly in which extract of plant is used as capping as well as a reducing agent. So, green synthesis of NPs is important when studying different pathogens. In recent years, nanotechnology has been applied in treating health-related problems, which showed promising results, mainly in the treatment of cancer. The present review discusses the historical and the latest development, drawbacks, , and the challenges faced in the field of green biosynthesis of NPs, along with its wide application.

Keywords: Gold nanoparticles, Green biosynthesis, Nanoparticles, Silver nanoparticles.

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Introduction

Use of advance technology for synthesizing nanoparticles plays a major role in the biomedical and human health care fields for producing a wide range of products (Pal *et al.,* 2011). Nanotechnology means material at the atomic level can be manipulated through biological, chemical and physical approaches (Cauerhff and Castro, 2013). During the 19th century, nanoparticles of gold and silver were used by artist of Mesopotamia to create a gleaming effect on pots and utensils (Faraday, 1987). This is said to be the concept of the modern property of nanoparticle, scientifically provided through Michael Faraday in his paper "Experimental relation of Gold and other metal to Light" (Faraday, 1987; Singh *et al*., 2011). Richard Feynman in 1959 gave the term Nanotechnology, which was the marked initiation in the Nanotechnological world (Singh *et al*., 2011). By using green nanotechnology and the biotechnological tool, an environment friendly technique is evolved to produce non-toxic products all over the world (Joerger *et al.,* 2000; Chauhan *et al.,* 2012). As the biological method or green method used for synthesizing nanoparticle have varied nature, are stable and have accurate dimension therefore their synthesis is a one-step process. Synthesis can be processed at physiological condition like temperature, pressure, pH, at a negligible cost (Ingale and Chaudhari, 2013). So the nanoparticles for their potential applications are characterized through various characterization techniques, for that it can be used in drug delivery as well as in the biomedical field. For the synthesis of nanoparticles, clean biological root is needed (Lekshi *et al.,* 2012). This includes various approaches like reduction in solution, photochemical and chemical reaction in aggregated molecules for thermal decomposition of nanoparticle compound (Awwad and Salem, 2012) microwave assisted process, radiation assisted, electrochemical and lately green chemistry root (Ravindra *et al.,* 2012). For the synthesis of environment friendly as well as Pharmaceuticals and biomedical field materials such as plant extract (root, stem, bark, leaf, flower), fungi, bacteria and enzymes are being used because they do not produce toxic chemicals during synthesis (Gokulakrishnan *et al.,* 2012). Nanoparticles have huge applications in the field of genomics, immune response enhancement, biosensor, clinical chemistry, and also perform targeted drug delivery (Diva *et al.,* 2012).

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Green Nanotechnology

The methods of synthesis of a nanoparticle are physical, chemical, biological and hybrid technology (Fig. 1) (Mohanpuria *et al.,* 2008; Tiwari *et al.,* 2008; Luechinger*et al.,* 2010). Toxic end products are produced by conventional physical and chemical approaches which are hazardous to the environment. The nanoparticles used by these approaches are not used for medical purposes as it may create health issues, exclusively in the clinical field (Parashar U.K. *et al.,* 2009; Parashar V. *et al.,* 2009). The use of conventional method for nanoparticle synthesis at a large scale with its mentioned size and shape in less time is done but they are complicated, of high cost, ineffective and the most important they are outdated. In the recent years,huge interest has been developed in environment friendly synthesis of nanoparticle which do not produce toxic product during its manufacturing

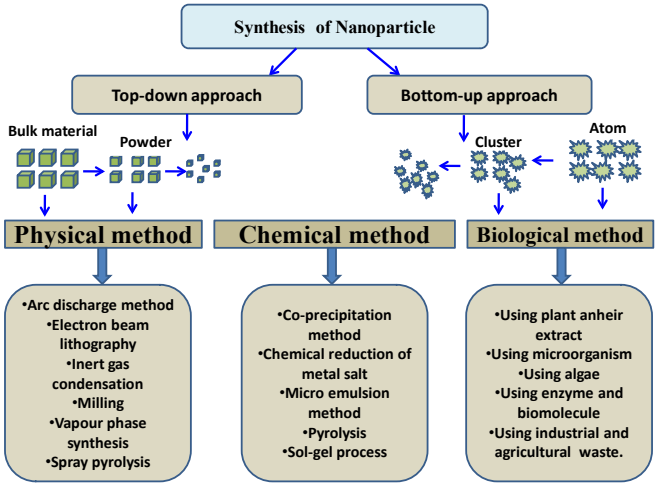

Fig. 1: Different approach and method for synthesizing nanoparticle

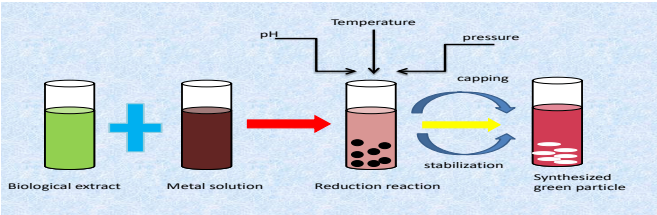

Fig. 2: Biological synthesis of nanoparticle

(Daniel and Astruc, 2004; Li *et al*., 2011; Chauhan *et al.,* 2012). This can be gained by a gentle synthesis which takes place through biological nature like using a biotechnological tool which is said to be safe and environmentally sound for fabrication of nanomaterial that is the best substitute for conventional physical and chemical method (Joerger *et al.,* 2000). This gave rise to the concept of green nanobiotechnology or green technology.

Meaning of the green nanotechnology is to synthesise nanoparticle or nanomaterial through biological routes like microorganisms, plants, and their byproducts such as protein and lipid by using different biotechnological techniques. Use of a green technique is much better than the synthesis done through physical and chemical methods. For example, green technology eliminates various expensive chemical, and less energy is utilized and produces environment friendly by-products. To produce less harmful chemical by-products and products, the researchers, scientists, chemical technologists and chemists all over the world use the twelve principles of green chemistry as a research guide (Anastas and Warner, 1998; Kharissova *et al.,* 2013). Nanobiotechnology is used as an alternative path for synthesizing biocompatible stable nanoparticle (Narayanan and Sakthivel, 2011). As we know two different processes are used for the reduction and stabilization of NPs. The first process is the bottom-up approach and the second is the top-down approach. The bottom-up approach is applied in the synthesis through bio base, in which the synthesis takes place by the help of reducing and stabilizing agent (Fig. 2). There are three steps to be followed for synthesizing nanoparticles by the use of bio product. They are 1) Solvent used for synthesis should be chosen. According to many researchers, water is considered the best suited solvent for the synthesizing process. Sheldon stated that water is the best solvent among all other solvents used (Shanker *et al.,* 2016), 2) The reducing agent chosen for NPs synthesis should be environment friendly and 3) Nontoxic material should be chosen as capping agent so that the synthesized particle can become stable (Mohanpuria *et al*., 2008; Singh *et al*., 2011).

Factors Affecting the Synthesis of Nanoparticles

Synthesis, characterization and application of nanoparticles are affected by many factors. There is a change in nature of synthesized nanoparticle when they come in contact with different adsorbates as well as catalysts used. This report was given by different researchers working on this field (Ajayan, 2004; Somorjai and Park, 2008). Few of the researchers have reported effectual nature of nanoparticle synthesized which shows varied symptoms and inferences by changing environment and time as well (Pennycook *et al.,* 2012). A large number of factors affect the nanoparticle synthesis like pH of solution, temperature, extract concentration to be used, raw material concentration, size (Baker *et al.,* 2013).

Some dominant factors that affect nanoparticle biosynthesis are described below:

a. *Particular method or technique:* Various protocols are implemented for the synthesis of nanoparticle which ranges from physical technique that includes mechanical procedure up to the chemical and biological approaches by the help of organic, inorganic chemical and living organisms too. These techniques used have both benefits as well as drawbacks. Among all, the biological method use of nontoxic and environmental friendly material are conjugated in green technology for synthesizing nanoparticle , so they are said to be favourable for the environment and widely accepted more than traditional methods (Kharissova *et al.,* 2013; Vadlapudi and Kaladhar, 2014).

b. *pH:* In the synthesis of nanoparticles in green technology, pH plays an important role. It has significant effects on morphology, surface area and size of NPs. This was reported by a number of researchers (Gardea-Torresdey *et al*., 1999; Armendariz *et al.,* 2004). Control over the size of nanoparticle can be done by adjustment of pH in solution medium.

c. *Temperature:* The other important parameter which influences the synthesis of nanoparticle is temperature among all three methods. The requirement of the temperature in physical method should be higher than 350°C and in chemical method the requirement is below 350°C. In many of the cases nanoparticle synthesized through green technique needs the temperature below 100°C or the nature of nanoparticle built (Rai *et al.,* 2006).

d. *Pressure:* For the nanoparticle synthesis pressure to play an important role. When on the reaction medium pressure is applied shows effects on size and shape of nanoparticle synthesized (Abhilash, 2012). The biological material rate of reducing metal ion is much faster when ambient pressure is provided (Tran *et al.,* 2013).

e. *Time:* The duration of time also influences the nanoparticle synthesis by using green technique. When the reaction medium is incubated according to the length of time, the quality and the type of synthesized nanoparticle are greatly influenced (Darroud *et al.,* 2011). Likely the character of

nanoparticles change according to the time and is affected by the process of synthesis, light exposure and storage condition (Kuchibhatla *et al.,* 2012; Mudunkotuwa *et al.,* 2012). if synthesized NPs are stored for longer period they may shrink or grow. They have their shelf life and therefore their potentiality is affected.

f. *Preparation cost:* Cost plays an important role in synthesis of nanoparticle which should be controlled and regulated to assist the potential application of nanoparticle in modern days. Therefore, effectiveness of cost in the process of producing nanoparticle is an important factor. Thus, the synthesis of nanoparticle with physical and chemical approaches is more cost effective, so the biological method used for synthesis of nanoparticle is less cost effective and is done on a large scale.

g. *Particle shape and size:* The properties of nanoparticle are determined by particle size. For example, when the size of a nanoparticle reaches the nanometre scale, their melting point decreases. There are many reports on this (Akbari *et al.,* 2011). The energy of differently configured nanoparticle is similar, that helps in transforming their shape easily (Yacaman *et al.,* 2001). The energy type used to analyze nanoparticle enhances the change in shape of a particular nanoparticle. Therefore, the effective nature and shape of particle synthesized influence their chemical property (Baer *et al.,* 2013).

h. *Pore size:* The size of the pore affects the quality and application of nanoparticles. Pore size and surface modification of biomolecule has provided efficient drug delivery of various molecule (Ruckenstein and Kong, 1999).

i. *Environment:* The nature of nanoparticles is determined by the environment of the surrounding. Through oxidation and reduction process in much of the environment, a single nanoparticle turns out to be core -shell nanoparticle. Soon after absorbing material or showing reaction with other material (Sarathy *et al.,* 2008). Nanoparticle synthesized by the biological approach forms a coating which is thick and large-sized (Lynch *et al.,* 2007). On the other hand, the environment also affects the physical and chemical nature of the nanoparticle synthesized. Some examples show the effects of the environment on synthesized nanoparticle nature. When crystalline zinc sulphide nanoparticle was placed from wet to dry condition their nature changed due to the change in environment. Due to changes in environmental condition, chemical nature of Cerium nitrate NPs may vary (Kuchibhatla *et al.,* 2012).

j. *Proximity:* The properties of most of the nanoparticle alter when a single or isolated nanoparticle are contacted with other nanoparticles (Baer *et al.,* 2008). This behavioural change in such nanoparticle can give rise to turns of nanoparticles. The proximity effect of nanoparticles like particle charging, substrate interaction and magnetic property shows a great implication.

k. *Other factors:* Plants are rich source of secondary metabolite which plays a role in reduction and stabilization of synthesized nanoparticle. Though their composition differs in different part of plants, the type of plant and the most important is the process used for extract preparation (Park *et al.,* 2011). Synthesized nanoparticles are also affected by the various intracellular and extracellular enzymes produced by different microorganism (Haverkamp *et al.,* 2007). For the purification of synthesized nanoparticle, the chosen method influences quality as well as quantity of nanoparticle. On the basis of gravitational force, a centrifugation process is used to separate the nanoparticle The chromatography technique is also applied for separation of nanoparticles on the basis of mobile and stationary phase coefficient (Jimenez *et al.,* 2003). The nanoparticle separation is important in the field of pharmaceutical and biomedical industry (Kowalczyk *et al.,* 2011).

Why Nanoparticles are Metal

Nanoparticles show an antimicrobial activity and it also helps in developing various diagnostic tool (Ravindra *et al.,* 2012). Some of the nanoparticle are said to be attractive probe of biological marker due to its small size that is 1 to 100nm. Their strong affinity to the targeted protein enhancer delay their aggregation. It depends on the type of surface modification, photoemission, electrical and heat conductivity, surface catalytic activity in improved manner (Sahayaraj and Sathiyamoorthy, 2011). There are various type of nanoparticle formed by different metals, like gold, silver, copper etc, which are described below.

Green Biosynthesis of Gold NPs

From the last few decades nanoparticles synthesized by using various metals have shown increasing importance because of their exclusive physical and chemical property and therefore are said to be the most researched topic from past few decades (Sahoo and Parveen, 2007; Safari and Zarnegar, 2014). Because of the great interest in nanoparticle synthesis researchers had a considerable focus on physical and chemical methods which include chemical reduction, hydrothermal, sol-gel, reverse micelle, ion sputtering, etc. (Kumar *et al.,* 2013; Ahmed *et al.,* 2015a) but these two methods are expensive and not environment friendly as they produce toxic components. Therefore, the different approaches other than physical and chemical methods applied were called the biological approach in which naturally occurring reagent like plant extract, bacteria, fungi etc can be used as reducing as well as stabilizing agent for synthesis (Krishnaswami *et al.,* 2014; Ahmed *et al.,* 2015a,b). Synthesis of nanoparticle through gold has attracted more because of their application in different fields such as antimicrobial, catalytic, electronic, in the biomedical field etc.

Green Biosynthesis of Silver NPs

The demand for Silver nanoparticles has increased in various fields such as medical, food, consumer, healthcare, for industrial purposes because of their peculiar physical and chemical properties (Mukherjee *et al.,* 2001; Li *et al.,* 2010; Gurunathan *et al.,* 2015). As they have a unique property so they have various applications which include antibacterial agent, healthcare related products, medical device coating, in pharmaceutical and food industry, in drug delivery, applied as an anticancer agent and the most effective anticancer drugs to kill the tumors (Chernousova and Epple, 2013). Nano size of a silver particle can change their physical, chemical and biological properties

because of their surface to the volume ratio, so they are used for various purposes (Li *et al.,* 2001; Sharma *et al.,* 2009). Considering all physical, chemical and biological methods for synthesizing silver nanoparticle, the best is the biological approach as it does not produce any toxicity.

Green Biosynthesis of Copper NPs

Nanoparticles synthesized through Copper are used in different fields like industrial engineering, technological field, agriculture etc. For the synthesis of Copper nanoparticles, biotechnology has used different biological, physical and chemical approach to produce nano size particles with exclusive function. Copper nanoparticles have antibacterial properties which have increased their demand in the field of agriculture research. This leads to the establishment of clean, cost-effective as well as systematic biosynthetic technology (Shobha *et al.,* 2014). Nanoparticles synthesized by using copper have attracted the researcher more in comparison to silver and gold, as they are available at low cost (Han *et al*., 2006). Because of the catalytic, electrical, antifungal, antibacterial applications, copper nanoparticles have achieved significant importance in the field of nanotechnology as well as nanomedicine (Ponce and Klabunde, 2005; Huang *et al.,* 2008). Various processes for synthesizing copper nanoparticles are used. One of the processes is thermal reproduction (Joerger *et al.,* 2000), polyol method (Park *et al.,* 2007) etc. But in recent few years, syntheses mediated by plant have acquired much more interest because of their simple and ecofriendly approach.

Green Biosynthesis of ZnO NPs

Nanoparticles produced through metal oxide have wide range as they are applicable in various fields like electronic, photonic devices (Engelbert *et al*., 2011; Zbigniew *et al*., 2017) and the biomedical field (Ramos *et al.,* 2017). Advancement in the field of green synthesis brought zinc oxide nanoparticles application in the nanomedicine field. Much research has concluded that Zinc nanoparticles have the antimicrobial property (Justin and Thomas, 2012).

Green Biosynthesis of Iron NPs

Recently much research has reported the potentiality of iron nanoparticles in terms of environment remediation. Materials at nano scale such as nano adsorbants, nano catalyst, nano filteration, nano biocides are used for remediation as well as tackling water pollution. Among other metals, iron nanoparticles are more advantageous to overcome environmental pollution. Because of the large surface area to the volume ratio, iron nanoparticles in the field of environmental remediation showed a great interest (Lin *et al*., 2008; Gui *et al*., 2012).

Green Biosynthesis of Titanium Dioxide NPs

In the world of nanotechnology research, synthesis of nanoparticles is done. Recently, Titanium dioxide is being used to synthesize nanoparticles which is applied in various fields due to their optical property, high chemical stability, and most importantly, they do not produce any toxicity (Hoffmann *et al.,* 1995; Fujishima *et al.,* 2000). Recently much interest is shown by the researchers as it resists microbe against various metal ions, antibiotic and also developed resistant strain (Gong *et al.,* 2007). It also shows antibacterial property (Allahverdiyev *et al.,* 2011).

Green Biosynthesis of Gold-Silver Alloy NPs

Metallic alloys like Au-Ag alloy have the peculiar property in them. They have various applications in photonics, pharmaceutical industry, biological tagging, etc. (Wang *et al.,* 2006; Som and Karmakar, 2009; Doria *et al.,* 2010). Their activities depend on their size, composition and shape (Link *et al.,* 1999) for different purposes. Au-Ag alloy is used like as cell biomarker and also used in measurement of drug taken by cancer cell (Balogh *et al.,* 2006). Various methods like physical and chemical are used for the synthesis of Au-Ag nanoparticles. Recently, it has been reported that synthesis of metal alloy can be done by using biomass of fungus and mushroom (Senapati *et al.,* 2005; Sawle *et al.,* 2008; Philip, 2009).

Green Biosynthesis of Cadmium Sulfide NPs

Various sources are used for preparing cadmium sulphide nanoparticle like cadmium nitrate, cadmium acetate, cadmium chloride, cadmium oxalate as well as cadmium sulphate. Among the different semiconducting materials, cadmium sulphide used for the synthesis of nanoparticlesis given more importance because of their use in drug delivery system or as a carrier in drug delivery to the desire site (Goud *et al.,* 2016). Various challenges are faced by different researchers working in the field of nanotechnology for developing clean, environment field, nontoxic protocol (Prasad, 2017). Therefore, the green synthesis approach like using plant extracts, microbes, metabolites like a capping agent gives ecofriendly and nontoxic effect other than different approaches (Kang, 2008; Reddy, 2016).

Why is green synthesis

Synthesis through green approaches shows advancement over physical and chemical methods due to cost-effective, ecofriendly, simply scaling up for large scale synthesis of nanoparticle. In green synthesis, high pressure, energy, temperature and toxic chemicals are not needed.

The Green Route for Biosynthesis of Nanoparticle

For synthesizing nano and micro length scaled inorganic material that has contributed for developing new and unexplored field of research on basis of biosynthesis of nanoparticle, nontoxic and safe reagent is used (Salam *et al.,* 2012). Among all the green processes for synthesizing nanoparticle plants are supposed to be easy and simple process for producing nanoparticle at large scale. They are collectively called as biogenic nanoparticles (Fig. 3).

Biological Method

Preparation of extract through bio-organism behaves as reducing and capping agent in synthesis of nanoparticle. The bio organism extracts for synthesizing nanoparticle have different bio-molecules like protein/ enzyme, polysaccharide, amino acid and vitamin which help in reducing metal ion by combining with them. They are said to be environment friendly though they are chemically complex. Much research has reported on the synthesis of nanoparticle through various compounds present in bio organism (Sahayaraj and Rajesh, 2011) because of its ecofriendly nature and simplicity. The biological synthesis of nanoparticles created a marked importance.

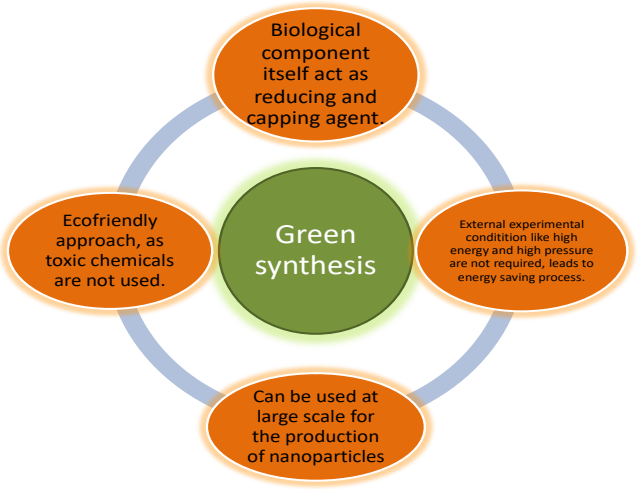

Fig. 3: Merits of green synthesis

Nanoparticle Drug Delivery System

As we know that the nanoparticles have potential ability to reduce toxic compound of therapeutic agents in their surrounding cells and also increase the number of drug in targeted cell so they have become centre for attraction in drug delivery (Tolaymat *et al.,* 2010). The nanoparticles that are characterized are further coated with drugs and established into the body. After reaching the specific site, they function accordingly. The significance of targeted drug delivery is that they move the drug specifically to the sites of infection which are treated without any harm to the body (CD Creative Diagnostics, 2018). The small volume of nano carrier depicts the physical, chemical and biological characteristics which make them advantageous to be used as medicine. Nanoparticle with its physical, chemical and biological characteristic are used up by the cell in the easy manner than the larger molecule; therefore, they are stoutly applied as equipment for delivery in recently used biological active cells. The drug is combined by cell specific object to mostly composed particle. In the drug delivery system, many of the small particles are involved like dendrimers, liposomes, silicon, carbon material and magnetic nano carrier. As we know that peculiar properties of nanoparticles are related to their small size that is 1-100 nm and their large surface to its volume ratio, the drug delivery system supplies required dose with less side effects and toxic production. Overall, nanoparticles solve the problem which is related to drug solubility and bioavailability. The nano carrier helps in protecting the drug from harmful environment. Their origin may be organic or inorganic that can be prepared from various polymer ceramic, metals etc.

Among all metals, silver is more profitable preferable than others. It has antibacterial, antifungal, antioxidant and physiochemical properties in comparison to the bulk materials like optical, electrical, thermal and catalytic property (Tolaymat *et al.,* 2010; Le Ouay and Stellacci, 2015; Phull *et al.,* 2016). In spite of various therapeutic agents, silver nanoparticles are alternative strategy for drug delivery system to cure cancer as they directly or indirectly targeting tissue of tumour. It was seen that if drug is accumulated at its required side, it enhances the effectiveness of anticancer therapy. Different silver nanoparticles synthesized through the green approach have anticancer activity that offers the opportunity for new treatment.

Challenges in Green Chemistry

In the recent years, we have seen immense advancement and growth in the field of nanotechnology. The new development and discoveries are considered centre for attraction in medical treatments as they are powerful, less toxic curative that they can enter into the area of disease and behave as magic bullets. Different researchers in pharmaceutical industries have developed some nanomedicine that are being successfully developed as well as accepted for clinical use. But still nanomedicine fields are at their early stage with little success stories; therefore, the review has explored huge challenges that experienced while developing nano based therapeutic.

Firstly, it is important to know the reason for the development of nanomedicine. Nanoparticle shows there peculiar property at the atomic, cellular and molecular levels but not visible in bulk material (Emerich and Thanos, 2006) due to their high surface to volume ratio. Nanoparticles are able to produce three dimensional structures which is pliable to design drug delivery system that is further used as they may fulfil many required properties like potentiality to overcome biological barrier, ability to deliver hydrophobic water soluble molecule and also have potentiality to select the target site in the body.

Biological Barrier in Drug Delivery

There are numerous biological barriers for drug which create hindrance for them in reaching to their deliberated site. The delivery of the drug blood-brain barrier (BBB) creates hurdles in the delivery of drugs (Xiaowei, 2018). In circulation, drugs need to overcome a few barrier for reaching the target. The blood brain barrier (BBB) limits the spreading of hydrophobic molecule in Cerebro-spinal fluid and is a great hurdle for treating many of the CNS as well as brain disorder Many nanoparticles are planned for delivering drug over blood brain barrier (BBB) which include liposome, nanosphere and cation albumin nanoparticle. Delivery of hydrophobic compound shows consequential obstacles in pharma industry as formulating hydrophobic drugs needs toxic solvent and surfactants like Cremophore and Tween, which impair distribution of drug and shows several harmful effects. Therefore, newly synthesized nanoparticles-based medicines require to successfully overcome various hindrance before it is approved to go in market. So, nanostructure development is to be done with suitable component and their properties. Nanotechnology is being widely used for commercial production all over the world. But still there is little information in concern of increasing human, animal and environment expose to nanoparticles specially silver nanoparticles, as well as the risk related to short and long term toxicity

Conclusion

With this we come to the conclusion that nanotechnology is said to be the science that deals with production, approaches and the most important manipulation of particles. Because of their advanced characteristics, they are applicable in many fields like farming, nanofertilizers, petroleum, clothing etc. Green synthesis

of nanoparticle is said to be ecofriendly in nature therefore it is important when different pathogens are studied. It is applied for the treatment of various health related problems. Various methods are applied for nanoparticle synthesis that is physical, chemical and biological with the help of plant, microorganism and many other sources. Characterization of the nanoparticles is done by the manipulation of their size and shape. It was observed by many of the researchers that certain changes in shape and size of medicine and their properties is done through activated nanoparticle. A small drug with large activity targets the specific site. In recent days nanoparticles have become popular transport system of medicine. So, synthesis of nanoparticles may serve in the field of biomedical industries in developing various drugs for the ailment related to living beings. Though nanoparticles based drug is seeking great attention because of its therapeutic behaviour, certain challenges have been encountered during the development of nanoparticles, which have to be tackled in near future.

References

Abhilash, B.D.P. 2012. Synthesis of zinc-based nanomaterials: A biological perspective. *IET Nanobiotechnology* **6**(4):144-148.

Ahmed, S., Ahmad, M., Swami, B.L. and Ikram, S. 2015a. A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: A green expertise. *Journal of Advanced Research* **7**(1):17-28.

Ahmed, S., Ullah, S., Ahmad, M. and Swami, B.L. 2015b. Green synthesis of silver nanoparticles using Azadirachtaindica aqueous leaf extract. *Journal of Radiation Research and Applied Sciences* **9**(1):1-7.

Ajayan, P.M. 2004. Nanotechnology: how does a nanofibre grow? *Nature* **427**(6973):402-403.

Akbari, B., Tavandashti, M.P. and Zandrahimi, M. 2011. Particle size characterization of nanoparticles: A practical approach. *Iranian Journal of Materials Science and Engineering* **8**(2):48-56.

Allahverdiyev, A.M., Abamor, E.S., Bagirova, M. and Rafailovich, M. 2011. Antimicrobial effects of $TiO_{(2)}$ and $Ag_{(2)}O$ nanoparticles against drug-resistant bacteria and leishmania parasites. *Future Microbiology* **6**(8):933-940.

Anastas P.T. and Warner J.C. 1998. *Green Chemistry: Theory and Practice*, Oxford University Press, New York, NY, USA.

Armendariz, V., Herrera, I. and Peralta-Videa, J.R. 2004. Size controlled gold nanoparticle formation by *Avena sativa* biomass: use of plants in nanobiotechnology. *Journal of Nanoparticle Research* **6**(4):377-382.

Awwad, A. and Salem, N.M. 2012. Green synthesis of silver nanoparticles by mulberry leaves extract. *Journal of Nanoscience and Nanotechnology* **2**(4):125-128.

Baer, D.R., Amonette, J.E., Engelhard, M.H., Gaspar, D.J., Karakoti, A.S., Kuchibhatla, S., Nachimuthu, P., Nurmi, J.T., Qiang, Y., Sarathy, V., Seal, S., Sharma, A., Tratnyek, P.G. and Wang, C.-M. 2008. Characterization challenges for nanomaterials. *Surface and Interface Analysis* **40**(3-4):529-537.

Baer, D.R., Engelhard, M.H. and Johnson, G.E. 2013. Surface characterization of nanomaterials and nanoparticles: important needs and challenging opportunities. *Journal of Vacuum Science and Technology A* **31**(5):050820.

Baker, S., Rakshith, D. and Kavitha, K.S. 2013. Plants: emerging as nanofactories towards facile route in synthesis of nanoparticles. *BioImpacts* **3**(3):111-117.

Balogh, L.P., Lesniak, W., Sinani, V.A., Bielinska, A.U., Sun, K., Nair, B.M., Waite, E., Kariapper, M.S.T. and Khan, M.K. 2006. Labeling of cells with silver and gold host-guest nanocomposites, NSTI Nanotechnology Conference and Trade Show, Boston, Rosewell Park Cancer Institute, 7-11 May, CRC Press, Taylor and Francis Group, Vol. 2, p. 462.

Cauerhff, A. and Castro, G.R. 2013. Bionanoparticles, a green nanochemistry approach. *Electronic Journal of Biotechnology* **16**(3):1-10.

CD Creative diagnostics®.(2018) CD Bioparticles products. Properties and Application of Silver Nanoparticles. Available from: https://www.cd-bioparticles.com/t/Propertiesand-Applications-of-Silver-Nanoparticles_60.html

Chauhan, R.P.S., Gupta, C. and Prakash, D. 2012. Methodological advancements in green nanotechnology and their applications in biological synthesis of herbal nanoparticles. *International Journal of Bioassays* **1**(7):6-10.

Chernousova, S. and Epple, M. 2013. Silver as antibacterial agent: Ion, nanoparticle, and metal. *Angewandte Chemie International Edition: Early View* **52**:1636-1653.

Daniel, M.-C. and Astruc, D. 2004. Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. *Chemical Reviews* **104**(1):293-346.

Darroud, M., Ahmad, M.B., Zamiri, R., Zak, A.K., Abdullah, A.H. and Ibrahim, N.A. 2011. Time-dependent effect in green synthesis of silver nanoparticles. *International Journal of Nanomedicine* **6**(1):677-681.

Diva, B., Lingappa, K. and Dayanand, A. 2012. Antibacterial activity of nanogolparticles synthesezed by *Bacillus* sps. *Journal of Ecobiotechnology* **4**(1):43-45.

Doria, G., Larguhinho, M., Dias, J.T., Pereira, E., Franco, R. and Baptista, P.V. 2010. Gold-silver-alloy nanoprobes for one pot multiplex DNA detection. *Nanotechnology* **21**:255101.

Emerich, D.F. and Thanos, C.G. 2006. The pinpoint promise of nanoparticle based drug delivery and molecular diagnosis. *Biomolecular Engineering* **23**(4):17184.

Engelbert, R., Peter, M., Chen, H., Srebri, P. and Geoffrey, A.O. 2011. Nanoparticle films and photonic crystal multilayers from colloidally stable size-controllable zinc and iron oxide nanoparticles. *ACS Nano* **5**(4):2861-2869.

Faraday, M. 1987. Experimental relations of gold (and other metals) to light. *Philosophical Transactions of the Royal Society B* **147**:145-181.

Fujishima, A., Rao, T.N. and Truk, D.A. 2000. Titanium dioxide photocatalysis. *Journal of Photochemistry and Photobiology C: Photochemistry Reviews* **1**:1-21.

Gardea-Torresdey, J.L., Tiemann, K.J., Gamez, G., Dokken, K. and Pingitore, N.E. 1999. Recovery of gold (III) by alfalfa biomass and binding characterization using X-ray microfluorescence. *Advances in Environmental Research* **3**(1):83-93.

Gokulakrishnan, R., Ravikumar, S. and Raj, J.A. 2012. *In vitro* antibacterial potential of metal oxide nanoparticles against antibiotic resistant bacteria pathogens. *Asian Pacific Journal of Tropical Disease* **2**(5):411-413.

Gong, P., Li, H., He, X., Wang, K., Hu, J. and Zhang, S. 2007. Preparation and antibacterial activity of Fe_3O_4@ Ag nanoparticles. *Nanotechnology* **18**:604-611.

Goud, B.S., Suresh, Y., Annapurna, S., Singh, A.K. and Bhikshamaiah, G. 2016. Green synthesis and characterization of cadmium sulphide nanoparticles. *Materials Today: Proceedings* **3**(10):4003-4008.

Gui, M., Smuleac, V., Ormsbee, L.E., Sedlak, D.L. and Bhattacharyya, D. 2012. Iron oxide nanoparticle synthesis in aqueous and membrane systems for oxidative degradation of trichloroethylene from water. *Journal of Nanoparticle Research* **14**:1-16.

Gurunathan, S., Park, J.H., Han, J.W. and Kim, J.H. 2015. Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by *Bacillus tequilens* is and *Calocybe indica* in MDA-MB-231 human breast cancer cells: Targeting p53 for anticancer therapy. *International Journal of Nanomedicine* **10**:4203-4222.

Han, W.K., Choi, J.W., Hwang, G.H., Hong, S.J., Lee, J.S. and Kang, S.G. 2006. Fabrication of Cu nanoparticles by direct electrochemical reduction from CuO nano particles. *Applied Surface Science* **252**:2832-2838.

Haverkamp, R.G., Marshall, A.T. and Van Agterveld, D. 2007. Pick your carats: nanoparticles of gold-silver-copper alloy produced in vivo. *Journal of Nanoparticle Research* **9**(4):697- 700.

Hoffmann, M.R., Martin, S.T., Choi, W.Y. and Bahnemann, D.W. 1995. Environmental applications of semiconductor photocatalysis. *Chemical Reviews* **95**:69-96.

Huang, Z., Cui, F., Kang, H., Chen, J., Zhang, X. and Xia, C. 2008. Highly dispersed silica-supported copper nanoparticles prepared by

precipitation-gel method: A simple but efficient and stable catalyst for glycerol hydrogenolysis. *Chemistry of Materials* **20**:5090-5099.

Ingale, A.G. and Chaudhari, A.N. 2013. Biogenic synthesis of nanoparticles and potential applications: An eco-friendly approach. *Journal of Nanomedicine and Nanotechnology* **4**(2):1-7.

Jimenez, V.L., Leopold, M.C., Mazzitelli, C., Jorgenson, J.W. and Murray, R.W. 2003. HPLC of monolayer-protected gold nanoclusters. *Analytical Chemistry* **75**(2):199-206.

Joerger, R., Klaus, T. and Granqvist, C.G. 2000. Biologically produced silver carbon composite materials for optically functional thin film coatings. *Advanced Materials* **12**(6):407-409.

Justin, T.S. and Thomas, J.W. 2012. Antimicrobial applications of nanotechnology: Methods and literature. *International Journal of Nanomedicine* **7**:2767-2781.

Kang, S.H. 2008. Microbial synthesis of CdS nanocrystals in genetically engineered *E. coli*. *Angewandte Chemie International Edition* **47**(28):5186-5189.

Kharissova, O.V., Dias, H.V.R., Kharisov, B.I., Perez, B.O. and. Perez, V.M.J. 2013. The greener synthesis of nanoparticles. *Trends in Biotechnology* **31**(4):240-248.

Kowalczyk, B., Lagzi, I. and Grzybowski, B.A. 2011. Nanoseparations: Strategies for size and/or shape-selective purification of nanoparticles. *Current Opinion in Colloid and Interface Science* **16**(2):135-148.

Krishnaswamy, K., Vali, H. and Orsat, V. 2014. Value-adding to grape waste : Green synthesis of gold nanoparticles. *Journal of Food Engineering* **142**:210-220.

Kuchibhatla, S.V.N.T., Karakoti A.S. and Baer, D.R. 2012. Influence of aging and environment on nanoparticle chemistry: implication to confinement effects in nanoceria. *Journal of Physical Chemistry C* **116**(26):14108-14114.

Kumar, A., Chisti, Y. and Chand, U. 2013. Synthesis of metallic nanoparticles using plant extracts. *Biotechnology Advances* **31**:346-356.

Le Ouay, B. and Stellacci, F. 2015. Antibacterial activity of silver nanoparticles: A surface science in sight. *Nano Today* **10**(3):339-354.

Lekshmi, N.C.J.P., Sumi, S.B., Viveka, S., Jeeva, S. and Brindha, J.R. 2012. Antibacterial activity of nanoparticles from *Allium* sp. *Journal of Microbiology and Biotechnology Research* **2**(1):115-119.

Li, L., Hu, J., Yang, W. and Alivisatos, A.P. 2001. Band gap variation of size- and shape-controlled colloidal CdSe quantum rods. *Nano Letters* **1**:349-351.

Li, W.R., Xie, X.B., Shi, Q.S., Zeng, H.Y., Ou-Yang, Y.S. and Chen, Y.B. 2010. Antibacterial activity and mechanism of silver nanoparticles on *Escherichia coli*. *Applied Microbiology and Biotechnology* **8**:1115-1122.

Li, X., Xu, H., Chen, Z.-S. and Chen, G. 2011. Biosynthesis of nanoparticles by microorganisms and their applications. *Journal of Nanomaterials* **2011**:1687-4110.

Lin, K.-S., Chang, N.-B. and Chuang, T.-D. 2008. Fine structure characterization of zero-valent iron nanoparticles for decontamination of nitrites and nitrates in wastewater and groundwater. *Science and Technology of Advanced Materials* **9**:025015.

Link, S., Wang, Z.L. and El-Sayed, M.A. 1999. Alloy formation of gold-silver nanoparticles and the dependence of the plasmon absorption on their composition. *The Journal of Physical Chemistry B* **103**:3529-3533.

Luechinger, N.A., Grass, R.N., Athanassiou, E.K. and Stark, W.J. 2010. Bottom-up fabrication of metal/metal nanocomposites from nanoparticles of immiscible metals. *Chemistry of Materials* **22**(1):155-160.

Lynch, I., Cedervall, T., Lundqvist, M., Cabaleiro-Lago, C., Linse, S. and Dawson, K.A. 2007. The nanoparticle-protein complex as a biological entity: A complex fluids and surface science challenge for the 21st century. *Advances in Colloid and Interface Science* **134-135**: 167-174.

Mohanpuria, P., Rana, N.K. and Yadav, S.K. 2008. Biosynthesis of nanoparticles: Technological concepts and future applications. *Journal of Nanoparticle Research* **10**(3):507-517.

Mudunkotuwa, I.A., Pettibone, J.M. and Grassian, V.H. 2012. Environmental implications of nanoparticle aging in the processing and fate of copper-based nanomaterials. *Environmental Science and Technology* 46(13):7001-7010.

Mukherjee, P., Ahmad, A., Mandal, D., Senapati, S., Sainkar, S.R., Khan, M.I., Renu, P., Ajaykumar, P.V., Alam, M. and Kumar, R. 2001. Fungus-mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: A novel biological approach to nanoparticle synthesis. *Nano Letters* **1**: 515-519.

Narayanan, K.B. and Sakthivel, N. 2011. Green synthesis of biogenic metal nanoparticles by terrestrial and aquatic phototrophic and heterotrophic eukaryotes and biocompatible agents. *Advances in Colloid and Interface Science* **169**(2):59-79.

Pal, S.L., Jana, U., Manna, P.K., Mohanta, G.P. and Manavalan, R. 2011. Nanoparticle: An overview of preparation and characterization. *Journal of Applied Pharmaceutical Science* **1**(6):228-234.

Parashar, U.K., Saxena, P.S. and Srivastava, A. 2009. Bioinspired synthesis of silver nanoparticles. *Digest Journal of Nanomaterials and Biostructures* **4**(1):159-166.

Parashar, V., Parashar, R., Sharma, B. and Pandey, A.C. 2009. Parthenium leaf extract mediated synthesis of silver nanoparticles: a novel approach towards weed utilization. *Digest Journal of Nanomaterials and Biostructures* **4**(1):45-50.

Park, B.K., Jeong, S., Kim, D., Moon, J., Lim, S. and Kim, J.S. 2007. Synthesis and size control of monodisperse copper nanoparticles by polyol method. *Journal of Colloid and Interface Science* **311**:417-424.

Park, Y., Hong, Y.N., Weyers, A., Kim, Y.S. and Linhardt, R.J. 2011. Polysaccharides and phytochemicals: A natural reservoir for the green synthesis of gold and silver nanoparticles. *IET Nanobiotechnology* **5**(3):69-78.

Pennycook, T.J., McBride, J.R., Rosenthal, S.J., Pennycook, S.J. and Pantelides, S.T. 2012. Dynamic fluctuations in ultrasmall nanocrystals induce white light emission. *Nano Letters* **12**(6):3038-3042.

Philip, D. 2009. Biosynthesis of Au, Ag and Au-Ag nanoparticles using edible mushroom extract. *Spectrochimica Acta* **73**:374-381.

Phull, A.-R., Abbas, Q., Ali, A., Raza, H., Kim, S.J., Zia, M. and Haq, I. 2016. Antioxidant, cytotoxic and antimicrobial activities of green synthesized silver nanoparticles from crude extract of Bergeniaciliata. *Future Journal of Pharmaceutical Sciences* **2**(1):31-36.

Ponce, A.A. and Klabunde, K.J. 2005. Chemical and catalytic activity of copper nanoparticles prepared via metal vapor synthesis. *Journal of Molecular Catalysis* **225**:1-6.

Prasad, K.S. 2017. Synthesis of water soluble CdS nanoparticles and study of their DNA damage activity. *Arabian Journal of Chemistry* **10**:S3929-S3935.

Rai, A., Singh, A., Ahmad, A. and Sastry, M. 2006. Role of halide ions and temperature on themorphology of biologically synthesized gold nanotriangles. *Langmuir* **22**(2):736-741.

Ramos, A.P., Marcus, A.E.C., Camila, B.T. and Pietro, C. 2017. Biomedical application of nanotechnology. *Biophysical Reviews* **9**(2):79-89.

Ravindra, B.M., Seema, L.N., Neelambika, T.M., Gangadhar, S.M., Nataraja, K. and Vijaya, K.S. 2012. Silver nanoparticles synthesized by in-vitro derived plants and *Callus* culture of *Clitoria ternatea*; evaluation of antimicrobial activity. *Research in Biotechnology* **3**(5): 26-38.

Reddy, K.R. 2016. Green synthesis, morphological and spectral properties of CdS nanoparticles. *Indian Journal of Research in Pharmacy and Biotechnology* **4**:271.

Ruckenstein, E. and Kong, X.Z. 1999. Control of pore generation and pore size in nanoparticles of poly(styrene-methylmethacrylateacrylic acid. *Journal of Applied Polymer Science* **72**(3):419-426.

Safari, J. and Zarnegar, Z. 2014. Advanced drug delivery systems: Nanotechnology of health design: A review. *Journal of Saudi Chemical Society* **18**:85-99.

Sahayaraj, K. and Sathiyamoorthy, R. 2011. Bionanoparticles: Synthesis and antimicrobial applications. Science against microbial pathogens. *Science against Microbial Pathogens: Communicating Current Research and Technological Advances* **2011**:228-244.

Sahoo, S.K. and Parveen, S.P.J. 2007. The present and future of nanotechnology in human health care. *Nanomedicine* **3**:20-31.

Salam, H.A., Rajiv, P., Kamaraj, M., Jagadeeswaran, P., Gunalan, S. and Sivaraj, R. 2012. Plant: Green route for nanoparticles synthesis. *International Research Journal of Biological Sciences* **1**(5):85-90.

Sarathy, V., Tratnyek, P.G. and Nurmi, J.T. 2008. Aging of iron nanoparticles in aqueous solution: effects on structure and reactivity. *The Journal of Physical Chemistry C* **112**(7): 2286-2293.

Sawle, B.D., Salimath, B., Deshpande, R., Bedre, M.D., Prabhakar, B.K. and Venkataraman, A. 2008. Biosynthesis and stabilization of Au and Au-Ag alloy nanoparticles by fungus, *Fusarium semitectum*. *Science and Technology of Advanced Materials* **9**:035012-035018.

Senapati, S., Ahmad, A., Khan, M.I., Sastry, M. and Kumar, R. 2005. Extracellular biosynthesis of bimetallic Au-Ag alloy nanoparticles. *Small* **1**:517-520.

Shanker, U., Jassal, V., Rani, M. and Kaith, B.S. 2016. Towards green synthesis of nanoparticles: from bio-assisted sources to benign solvents: A review. *International Journal of Environmental Analytical Chemistry* **96**:801-835.

Sharma, V.K., Yngard, R.A. and Lin, Y. 2009. Silver nanoparticles: Green synthesis and their antimicrobial activities. *Advances in Colloid and Interface Science* **145**:83-96.

Shobha, G., Vinutha, M. and Ananda, S. 2014. Biological synthesis of copper nanoparticles and its impact: A review. *International Journal of Pharmaceutical Science Invention* **3**:28-38.

Singh, M., Manikandan, S. and Kumaraguru, A.K. 2011. Nanoparticles: A new technology with wide applications. *Research Journal of Nanoscience and Nanotechnology* **1**(1):1-11.

Som, T. and Karmakar, B. 2009. Core shell Au-Ag nanoparticles in dielectric nanocomposites with plasmon-enhanced fluorescence: A new paradigm in antimony glasses. *Nano Research* **2**:607-616.

Somorjai, G.A. and Park, J.Y. 2008. Colloid science of metal nanoparticle catalysts in 2D and 3D structures. Challenges of nucleation, growth, composition, particle shape, size control and their influence on activity and selectivity. *Topics in Catalysis* **49**(3-4):126-135.

Tiwari, D.K., Behari, J. and Sen, P. 2008. Time and dose-dependent antimicrobial potential of Ag nanoparticles synthesized by top down approach. *Current Science* **95**(5):647-655.

Tolaymat, T.M., El Badawy, A.M., Genaidy, A., Scheckel, K.G., Luxton, T.P. and Suidan, M. 2010. An evidence-based environmental perspective of manufactured silver nanoparticle in syntheses and applications: A systematic review and critical appraisal of peer-reviewed scientific papers. *Science of the Total Environment* **408**(5):999-1006.

Tran, Q.H., Nguyen V.Q. and Le, A.T. 2013. Silver nanoparticles: Synthesis, properties, toxicology, applications and perspectives. *Advances in Natural Sciences: Nanoscience and Nanotechnology* **4**(3): 033001.

Vadlapudi, V. and Kaladhar, D.S.V.G.K. 2014. Review: Green synthesis of silver and gold nanoparticles. *Middle-East Journal of Scientific Research* **19**(6):834-842.

Wang, A., Hsieh, Y., Chen, Y. and Mou, C. 2006. Au-Ag alloy nanoparticle as catalyst for CO oxidation: Effect of Si/Al ratio of mesoporous support. *Journal of Catalysis* **237**:197-206.

Xiaowei, D. 2018. Current strategies for brain drug delivery. *Theranostic* **8**(6):1481-1493.

Yacaman, M.J., Ascencio, J.A., Liu, H.B. and Gardea-Torresdey, J. 2001. Structure shape and stability of nanometric sized particles. *Journal of Vacuum Science and Technology B* **19**(4):1091-1103.

Zbigniew, S., Mieczyslaw, B., Katarzyna, D. and Grzegorz, C. 2017. Synthesis and characterization of iron oxide magnetic nanoparticles. *Nukleonika* **62**:73-77.