

REVIEW ON GREEN NANOTECHNOLOGY

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Abstract

Green chemistry familiarly called as sustainable chemistry mainly focus on the designing of pharmaceutical products by processes that decreases the use of chemicals and hazardous substances generation, Now a days plant based medicines engineered with Novel drug deleivery like nanoparticles, microspheres etc plays a major role in the treatment oif several life threatening diseases by their quick drug deleivery to the target site. This review focus on the green chemistry principles for the formulation of pharmaceutical nanoparticles specially from plant based compounds and their formulation techniques. Green nanotechnology, in phyto formulations, maintains the environmental sustainability in the production of nanoparticles, providing harmless to human health and also to the environment. Enhancement of energy efficiency, reduction in waste production and emission of gases, and minimal consumption of non-renewable raw materials are the main advantages of green nanotechnology. Green chemistry offers a great opportunity to stop the adverse effects before their occurrence during the synthesis of nanoparticles.

Keywords: - Green Chemistry, Nano particles, Formulation.

INTRODUCTION

Plant derived natural products are used from ancient time for curing variety of disorders to humans as well as animals. The Modern way of medicines which are now in use mainly utilize herbs of traditional practices. The use of traditional plants was the oldest known type of medical care to humans. Since ancient times, people have employed herbal remedies as the major treatment option which is still practicing owing to its safety and cultural beliefs which have turned the society towards plant derived preparations. Herbal medicines are categorized by the WHO (World Health Organization) as finished labelled pharmaceuticals that include biologically active components of plants either their aerial or subterranean parts or other plant substantial or assortments. Now a days, plant based natural products and its derivatives occupys about 25% of the total pharmaceutical products which in turn serves as a theme for the emergence of novel drugs.¹ In the rural villages of India, nearly about 25,000 potent plant-based remedies are employed in folk medicine. More than 1.5 million people are using the traditional medicine system, which employs medicinal herbs for therapeutic, preventive and promotional purposes. In India, there are more than 7800 manufacturing facilities of pharmaceuticals are using 2,000 tonnes of herbs annually.² The emergence of green chemistry makes an improvement in the novel drug delivery system of plant or herbs based drug delivery systems like liposomes, nanoparticles etc which shows advantageous characteristics such as outrageous chemical and biological characteristics with macromolecular specificity and less toxicity which in turn making them favorable for introduction of novel plant based drugs.³ The designing of green extraction technique using green chemistry is now becoming a major area in the extraction of plant

products which produces less chemical used types of drug product minimizing the toxicity eventhough it is a naturally obtained herbal medicine. The chemical reagents and solvents used for extracting a particular compound in normal way makes them toxic as the therapeutic efficacy and possible interactions are not known. Thus the use of green chemistry principles in the field of synthesis, extraction, isolation, purification etc makes a product less vulnerable to hazards to human body.⁴

GREEN CHEMISTRY ⁵

Green Chemistry can be defined as the use of techniques that may lead to reduction or elimination for evolution of hazardous chemicals during any stages in the development of a pharmaceutical product. The use of twelve principle during the making process of any pharmaceutical product with more eco-friendly and efficient product with less wastage was proposed by Poul.T.Anastas in 1991.

Green Chemistry in Extraction Process ⁶“Green Extraction is the designing of extraction procedures which makes reduction in the consumption of energy using of alternative solvents and renewable natural products to ensure a safe and high quality of the extract. Green chemistry offers many advantages providing a way for avoidance or eliminating hazards and waste,as well as generating innovative and effective methodologies at minimal costs. To follow green extraction procedures on laboratory or industrial scale, three ideas has been covered up to approach an optimal use of substances required for extraction.

- (1) The existing process is optimized and improved
- (2) Use of equipment for wider range of products formulation rather than single product.
- (3) Innovative in process and procedures for alternative solvents

“Six principles of Green Extraction of Natural Products” should be taken in count by the industrial research scientists as a way to perform an innovative and green label, as an indication both in process and quality aspects of solid-liquid extraction.

Principle 1: Making Innovative selection procedures by using renewable natural resource

Principle 2: Selection of agro based or watery solvents for extraction procedures

Principle 3: Reduction in consumption of energy required during extraction by using recovery process through innovations.

Principle 4: Designing to give co-products instead of getting wastes

Principle 5: Reduction in unit operations, favouring safest, robust process under control

Principle 6: Aiming to produce a not denatured natural extract free from contaminant

Importance of Green chemistry with pharmaceutical Nanotechnology^{11,12}

Green nanotechnology makes use of the concepts of green chemistry with green engineering. As per the report by ACS Green Chemistry Institute, the key challenges in green chemistry production of nanoparticles are

- (i) Barriers due to technical issue
- (ii) Way of handling the toxicity associated with nanomaterials

- (iii) Regulatory policies following for the synthesis of nanomaterials
- (iv) Industrial deployment in scale up procedures for nanomaterial production

Green nanotechnology offers reduction in the usage of energy and fuels utilized for a process through less material and renewable inputs. Green nanotechnology, in phytoformulations, maintains the environmental sustainability in the production of nanoparticles, providing harmless to human health and also to the environment. Enhancement of energy efficiency, reduction in waste production and emission of gases, and minimal consumption of non-renewable raw materials are the main advantages of green nanotechnology. Green chemistry offers a great opportunity to stop the adverse effects before their occurrence during the synthesis of nanoparticles.

NANOTECHNOLOGY

Nanotechnology is the emerging technology in pharmaceutical industries globally producing variety of scopes and opportunities for diagnosis and therapeutics of disease. Nanotechnology offers a development of a drug delivery system with optimization of a drugs pharmaceutical action with reduced toxicity especially in in vivo. Making such a delivery system is a challenging task which can be controlled by use of pharmaceutical nano-systems. Pharmaceutical nanotechnology consisting of two basic types, which are nano-materials and nanodevices, which play a key role in pharmaceutical nanotechnology.⁷Pharmaceutical Nanotechnology can be defined as the forming and developing small structures like atoms, molecules or compounds of size 0.1 to 100 nm with desired characteristics and properties, playing a key role in over coming several drawbacks of conventional dosage forms like low bioavailability, poor patient compliance, damage to healthy cells etc.⁸Based on their dimensions, nanomaterials are placed into four different classes,

- A) Zero-dimensional nanomaterials (0-D): Three dimensions in the nanoscale range. This category includes quantum dots, fullerenes, and nanoparticles.
- B) One-dimensional nanomaterials (1-D): one dimension outside the nanoscale. This category includes nanotubes, nanofibers, nanorods, nanowires, and nanohorns.
- C) Two-dimensional nanomaterials (2-D): two dimensions outside the nanoscale. This category includes nanosheets, nanofilms and nanolayers.
- D) Three-dimensional nanomaterials (3-D) or bulk nanomaterials: nanoscale in any dimension. This class includes bulk powders, dispersions of nanoparticles, arrays of nanowires and nanotubes, etc.

NANOPARTICLES

The Nanoparticles forms the basic fundamental component of nanotechnology. Nanoparticles are particles between 1 and 100 nanometers in size and are made up of carbon, metal, metal oxides or organic matter, exhibiting an unique physical, chemical and biological properties at nanoscale compared to their respective particles at higher scales which is due to a relatively larger surface area to the volume, increased reactivity or stability in a chemical process, enhanced mechanical strength, etc. which makes them in wider application.⁹ Tiny size and use of biodegradable materials are the two key characteristics in employing nanoparticles as a drug delivery system. They exhibit increased solubility and superior bioavailability because of their small particle size and large surface area. Crossing the blood brain barrier, entering to the lung system, endothelium of tumors and absorption through tight junctions of skin endothelial cells, give them added value. The Various types of cells can be easily absorbed and also the drug accumulation at target location due to nano size range.¹⁰

CLASSIFICATION OF NANOPARTICLES ⁹

Depending on their morphology, size and chemical properties, Nanoparticles are classified into different categories.

1. Carbon based Nanoparticles

The nanoparticles which are made up of carbon. Fullerenes, graphenes, carbon nanofibers and carbon nanotubes are the major classes of carbon-based NPs.

Fullerenes - It is spherical in shape and the carbon atoms present in it are held together by sp² hybridization. Nearly 28 to 1500 carbon atoms joined together to form the spherical structure. Diameter of 8.2 nm for single layered as well as 4 to 36 nm for multi-layered fullerenes.

Graphenes - It is an allotropic hexagonal framework consists of honey comb lattice from the carbon atoms as a two dimensional planar surface. It is formed of thickness around 1 nm.

Carbon Nano Tubes (CNT) - Carbon Nano Tubes (CNT) are a type of graphene nanofoil with a honeycomb lattice of carbon atoms expressed as hollow cylinders to form nanotubes. The diameter of CNT are lesser than 0.7 nm for single layered and 100 nm for multi-layered CNT. The length may vary from a few micrometers to several millimetres.

Carbon Nanofiber - It is similar to that of CNT but the graphene nanofoil is made to a cone or cup shape rather than the regular cylindrical tubes.

2. Organic nanoparticles

Most commonly made organic nanoparticles are Dendrimers, micelles, liposomes and ferritin, etc. They are biodegradable and non-toxic in nature and some organic NP like micelles and liposomes form a hollow core, also called as nanocapsules and are very sensitive to thermal and electromagnetic radiations, making them an ideal choice for novel drug delivery. Apart from the normal physical characteristics like size, composition and surface morphology, the drug carrying capacity, stability either as entrapped drug or adsorbed drug make them an efficient application in the field of drug delivery. They can also be injected to specific parts of our body providing targeted drug delivery.

3. Inorganic nanoparticles

The nanoparticles that are not made up of carbon. Mainly metal based NP and Metal oxides based NP are the two main categories.

METAL BASED NP

Metal based Nanoparticles are directly synthesised from metals in nanometric sizes by the use of destructive or constructive methods. Almost all the metals can be synthesised into their nanoparticles. The commonly used metals for nanoparticle synthesis are aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag), Platinum (Pt) and zinc (Zn). These nanoparticles have distinctive properties of surface characteristics like higher surface area to volume ratio, size of pores, charge on the surface and its 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.

METAL OXIDES BASED NP

The metal oxide based nanoparticles, mainly modify the properties of their respective metal based nanoparticles. Due to the increased reactivity and efficiency than their respective metals, metal oxide nanoparticles are normally used. The commonly synthesised are Aluminium oxide (Al_2O_3), Cerium oxide (CeO_2), Iron oxide (Fe_2O_3), Magnetite (Fe_3O_4), Silicon dioxide (SiO_2), Titanium oxide (TiO_2), Zinc oxide (ZnO). These metal oxides based nanoparticles have an extra properties when compared to their metal counterparts. For example nanoparticles of the metal iron (Fe) instantly oxidises to iron oxide (Fe_2O_3) in the presence of oxygen at room temperature that increases its reactivity compared to iron nanoparticles.

SYNTHESIS OF NANOPARTICLES^{13,14,15,16}

Two main approaches are used for the synthesis of nanomaterials

1. Top-down approaches
2. Bottom-up approaches.

TOP DOWN APPROACHES

In the Top-down approaches, the nanostructured materials are made by division of the bulk materials. Top-down methods include mechanical milling, electro spinning, electrolaser ablation, lithography, etching, sputtering, and electro-explosion.

BOTTOM DOWN APPROACH

The alternative approach of creating less waste and hence the more economical, is the 'bottom-up'. Bottom-up approach is the buildup of a material from the bottom from the level of atom-by-atom, molecule-by-molecule, or cluster-by cluster. Many of these techniques are still under development or are just beginning to be used for commercial production of nano powders. Some of them are chemical vapor deposition, spinning, sol gel, pyrolysis, chemical reduction

MECHANICAL MILLING

Mechanical milling is a cost effective method for producing nanomaterial by blending of different phases. It is mainly used for silver nanoparticles. It is aimed in the reduction of particle size, emerging them into different phases using milling equipment such as ball mill or by mechanical activation. Mechanical milling is used to produce aluminum/nickel/magnesium/copper-based nanoalloys, and many other nanocomposite materials. Ball-milled carbon nanomaterial are considered in providing an opportunity to satisfy environmental remediation, energy storage, and energy conversion demands.

ELECTROSPINNING

Electro spinning is a simplest top-down methods to produce nanofibers typically from polymers. coaxial electro spinning is mainly used, comprises of two coaxial capillaries. In these capillaries, two viscous liquids, or a viscous liquid as the shell and a non-viscous liquid as the core, can be used to form core-shell nanoarchitectures in an electric field. It is useful for production of core-shell ultrathin fibers of several cm on a larger scale.

LITHOGRAPHY

It is a useful tool for developing nanospheres. It uses a focused beam of light or electrons. Lithography can be divided into two main types: masked lithography and maskless lithography. In masked nanolithography, nanopatterns are transferred into a large surface area by the use of a specific mask or template. Masked lithography can be given in terms of photolithography, nanoimprint lithography and soft lithography. Maskless lithography may be a scanning probe lithography, focused ion beam lithography, and electron beam lithography. In maskless lithography, nanopattern is carried without the use of mask.

SPUTTERING

The process which involves the bombardment of a solid with particles of high energy using gas to produce nanomaterial. Generally, sputtering is made to perform in an evacuated chamber, to that the gas is introduced. Gaseous ions are produced by the application of high volts in the cathode part, where the acceleration of positive ions takes place. When this ion hits continuously which results in atomic ejection from the target surface. WSe₂-layered nanofilms on SiO₂ and carbon paper substrates can be produced by sputtering using magnetron. This method is advantageous as it produces fewer impurities, and it is also effective in cost wise when compared with lithography.

LASER ABLATION

Laser ablation techniques use a laser beam to hit the target solid for producing nanoparticles. During this, because of the high energy of the laser radiation, the material gets vaporized. This technique is used for the production of metal based nanoparticles using green chemistry principles. The characteristics of nanoparticles like size and distribution is easily adjustable by changing the influence, wavelength, and laser pulse addition. Carbon nanomaterials, oxide composites and ceramics can also be prepared by using this process.

CHEMICAL VAPOR DEPOSITION (CVD)

CVD is used in the production of carbon-based nanomaterials. In CVD, formation of a thin film on the surface of the substrate is due to the chemical reaction of vapor-phase, if suitable only the sample has volatility. In the process of generation of carbon nanotubes by this technique, the substrate is evaporated under high temperature followed by the slower introduction of gaseous hydrocarbons. The application of high temperatures, leads to the decomposition of hydrocarbons which releases carbon atoms, then it is recombined for the formation of carbon nanotubes. The proper selection of catalyst plays a vital role in this process. It is a better technique producing 2D nanomaterials.

SPINNING

Spinning Disc Reactor (SDR) is used in this process where the temperature of the system can be controlled on the rotating disc present in the reactor which is filled up using nitrogen for removing oxygen inside. The disc is made to rotate at different speeds to pump the liquid precursor and water. As a result it leads to fusion of atoms and molecules together and gets precipitated. The liquid flow rate, disc rotation speed, liquid/precursor ratio, location of feed, disc surface, etc. are the controllable parameters in this process.

SOL-GEL TECHNIQUE

Sol-gel is the most preferred, simple and widely used method. Wet chemical technique where the Metal oxides and chlorides are used as precursors which are made to disperse in a co-liquid by using shaking, stirring or sonication as a result it forms both a liquid and a solid phase. Recovery is done by separating the phases using either sedimentation, filtration and centrifugation. The presence of moisture is removed by drying.

PYROLYSIS

Pyrolysis is the process where flame is used to burn the liquid which is made by using high pressure by a small hole. Nanoparticles are recovered by making them air classified to removes the gaseous molecules formed during the burning process. Sometimes laser is used instead of flame for burning providing high temperature than the flame. It is a simple, effective, continuous process. It is mainly used for the industrial production of nanoparticles on higher scale.

CHEMICAL REDUCTION

It is a wet-chemical method involving the reduction process of aqueous salts of metals. Reducing agents like citrate, borohydride etc are used to provide electrons for the metals in the reduction process producing zero valency nanoparticles. Three essential stages of this technique are namely, Reduction of metallic salts by the use of reducing agents, Ionic complex stabilization, and size controlling by the capping agent. The stabilizing agent, generally referred to as the capping agent, controls the achievable size of the nanoparticles. Both are added to the reaction mixture respondingly at some point. A single compound can act as both the reducing agent and also /capping agent. The reducing agent can be sodium borate, ascorbic acid, sodium triethyl borohydride, or some organic compounds such as hydrazine or toluene.

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