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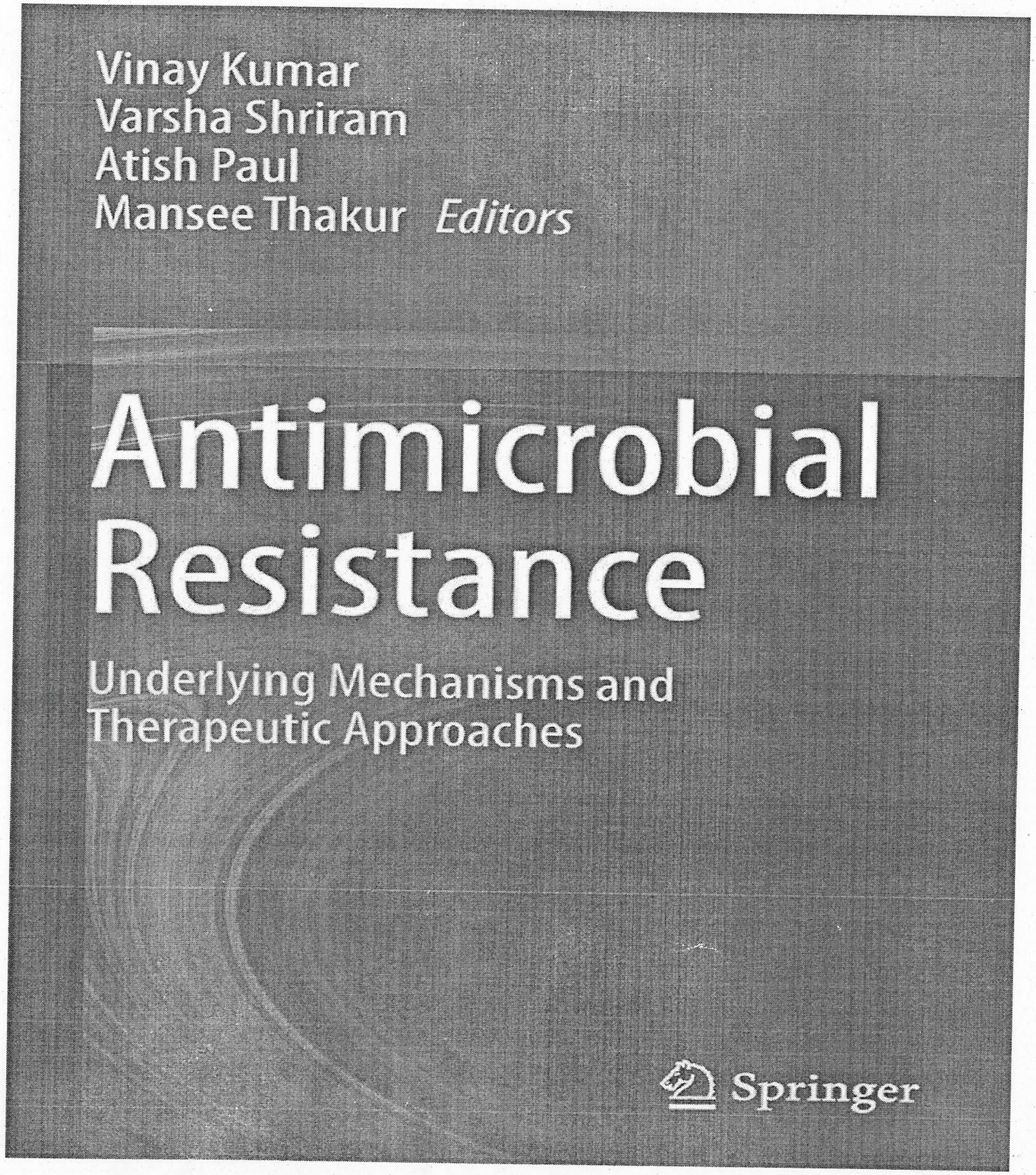

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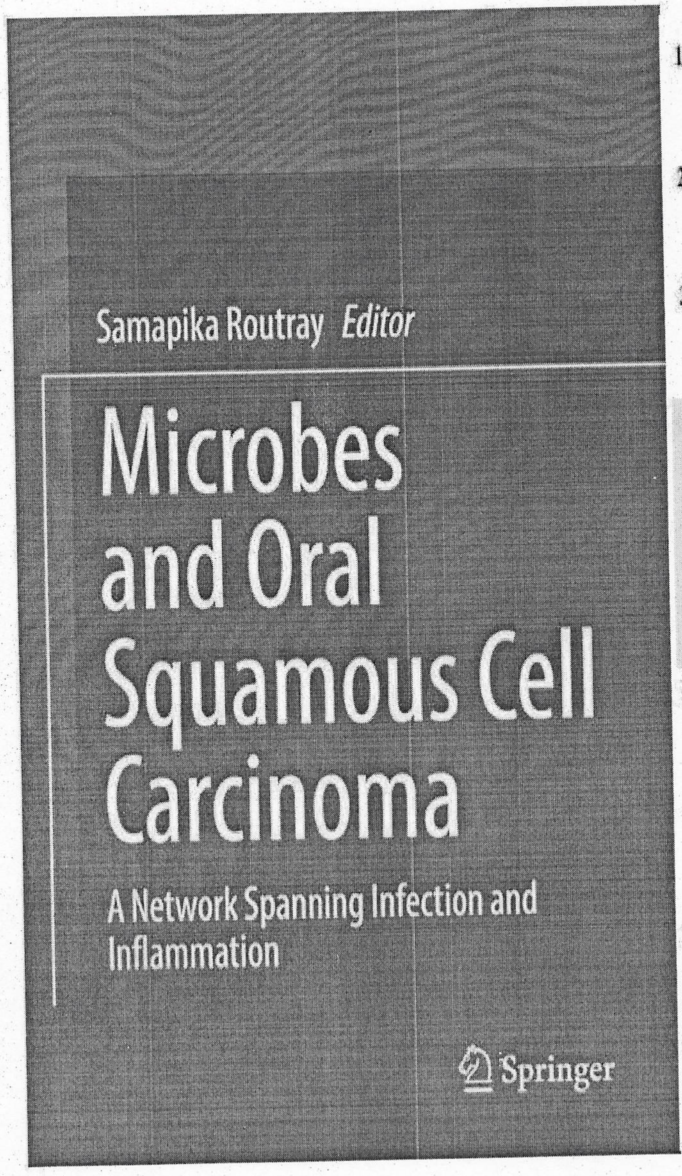

Green Synthesis of Iron Oxide Nanoparticles and Its Biomedical Applications

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Chapter 5
Green Synthesis of Iron Oxide Nanoparticles and Its Biomedical Applications

Mansee Thakur, Smital Poojary, and Niharika Swain

Contents

5.1 Introduction

Iron deficiency anaemia (IDA) is one of the most prevalent malnutrition disorders with serious short-term and long-term complications. It mainly affects infants, adolescents and pregnant women because of their high iron demand (Stoltzfus 2001a, b). In children, iron deficiency is often associated with neurocognitive impairment leading to psychomotor and cognitive abnormalities (Black et al. 2008; Grantham-McGregor and Ani 2001; Lozoff et al. 2007; McCann and Ames 2007). During pregnancy, IDA has also been associated with increased risk of low birth weight, premature delivery, perinatal mortality of babies and young children as well as

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Abstract

Rapid development of nanotechnology had made availability of nanoparticles in various biomedical applications. Due to the hazardous effects of chemical and physical synthesized nanoparticles, the research has now focussed on "green nanotechnology". The plant-based nanoparticles have shown many advantages as compared to other chemical, physical and biological mode of nanoparticle synthesis. In this chapter, we made an effort to explore in depth about the various methodology and the biomedical utility of one of green synthesized nanoparticles, i.e. iron oxide nanoparticles (IONPs). In addition, the potential use of IONPs in diagnostic and therapeutic aspect of various human diseases is also highlighted with specific reference to its impeding application in the treatment of iron deficiency anaemia (IDA), one of the widely spread nutritional disorders affecting mainly women and children.

Keywords (separated by " - ") Hematite nanoparticles - Green synthesis - Iron oxide nanoparticles (IONPs) - Iron deficiency anaemia

maternal death (Rasmussen 2001; Lozoff et al. 2006; Brabin et al. 2001; Clark 2008). Furthermore, a causal relationship between iron deficiency anaemia and six health outcomes: infant mortality, maternal mortality, birth outcomes, morbidity, quality of work and child growth have also been observed and notified by WHO, INACG and the Edna McConnell Clark Foundation in May 2000 (Stoltzfus 2001a, b).

The clinical and diagnostic evaluation of an individual suffering from IDA includes a wide variety of factors. There may be presence of symptoms like fatigue, poor exercise tolerance, headache, diminished work capacity, impaired thermoregulation, poor memory, restless leg syndrome, immune dysfunction, gastrointestinal disturbances and pica, the desire to eat ice or dirt. In addition to this, physical signs like pallor, koilonychia (spooning of the nails) and shortness of breath, etc. also aid to clinical diagnosis of patients (Schümann et al. 2007; Haas and Brownlie IV 2001; Oppenheimer 2001; Beard 2001). In IDA, peripheral blood smear shows a significant feature—microcytic hypochromic RBCs. These findings are consistent with derangement in other haematocrit parameters like decrease and increase in the levels of mean corpuscular volume (MCV) and red blood cell distribution width (RDW), respectively. In addition, low serum iron level, high transferrin level or total iron-binding capacity (TIBC) and low serum ferritin also serve as important biochemical indicators of IDA (Miller 2013).

For the prevention and control of IDA, it is necessary to ingest appropriate amount of iron each day. The recommended daily dietary allowance for iron in non-pregnant adults is 8 mg, whereas for pregnant women is 27 mg (Khalafallah and Dennis 2012). Once IDA is diagnosed, the treatment options include oral iron supplementation, intravenous iron infusion or blood transfusion. Oral iron supplementation, most commonly with ferrous sulphate, is the least expensive approach but found to be associated with gastrointestinal side effects including nausea, diarrhoea and constipation. Moreover, abdominal pain, heart burn and vomiting were significantly observed in IDA patients treating with ferrous sulphate (Tolkien et al. 2015). It has also shown some detrimental effects such as change in colour of mucosa, ulcer formation, haemorrhages, epithelial changes, increased inflammatory cell count and fibrosis (Nadir 2015). Some studies indicate that lower doses of oral iron are still effective, but are associated with a lower incidence of side effects (Christensen et al. 2013; Bregman et al. 2013). Despite, there is sufficient information regarding iron metabolism, IDA and iron supplementation, the health consequences of IDA still continue to be a matter of research and debate.

Due to hazardous effects of iron supplementations, it has become essential to search for other modes of iron supplementation which could be more efficient in IDA treatment with no or minimal side effects or toxicity. Hence, this chapter focusses on the potential use of one of the emerging technologies, i.e. "nanotechnology" as drug delivery system in the treatment of IDA.

Nanotechnology makes a major contribution to develop and even revolutionize several sectors of technology and industry, i.e. information technology, environmental science, medicine, homeland security, food safety, energy and transportation (Thangadurai et al. 2020a, b). In diagnostic medical science, nanotechnology offers early detection molecular imaging where sensitive biosensors are made of nano-scale components (e.g., nano-cantilevers, nanowires and nano-channels), which has the potential to identify genetic and molecular events, providing the ability for the detection of unusual molecular signals associated with malignancy. Meanwhile, it has shown tremendous potential to revolutionize a wide variety of drugs by making them more personalized, compact, simpler, safer and easier to administer (Boisseau and Loubaton 2011; George 2015; Yashveer et al. 2014).

Nanoparticles (NPs) are the objects ranging in size from 1 to 100 nm. Currently, different metallic NPs are produced, which include silver, gold, iron oxide, zinc oxide, copper nanoparticles, etc. NPs are used for a variety of purposes, ranging from medical treatments to the use of solar and oxide fuel batteries for energy storage in various branches of industry, even extending to the wide incorporation into various materials of daily use such as cosmetics or clothing (Dubchak et al. 2010; Hasan 2015). The two basic approaches that include various synthesis methods of nanoparticles are "top down and bottom up" (Fig. 5.1). The first approach "top-down" method includes break down of solid materials into smaller pieces by applying external force. Several physical, chemical and thermal techniques that serve as the necessary energy resources for NP formation come under this approach. The second approach "bottom-up" involves assembling of nanomaterials from atoms and molecules. In this approach, no waste materials need to be removed or are formed, and nanoparticles having smaller size can be obtained easily (Iravani 2011; Makarov et al. 2014; Möschwitzer 2010).

During the synthesis of nanoparticles, it is very important to control the size and surface area of the nanoparticles, which can be synthesized by three methods: chemical, physical and biological. Several adverse effects were observed in association with chemical and physical effects due to the use of toxic chemicals and high energy, respectively. Hence, these methods were somehow not acceptable in the treatment of various diseases or in medical applications. Alternative to these methods, biological approaches such as plant extracts (Shankar et al. 2004; Ahmad et al. 2011; Prasad et al. 2012; Swamy and Prasad 2012; Prasad and Swamy 2013; Prasad 2014; Bhattacharyya et al. 2016; Buhroo et al. 2017; Joshi et al. 2018; Rahman et al. 2020), microorganisms (Klaus et al. 1999; Konishi et al. 2007; Prasad et al. 2016), fungi (Vigneshwaran et al. 2007; Prasad 2016, 2017; Prasad et al. 2018a) and enzymes (Willner et al. 2006) provide eco-friendly mode of synthesis of

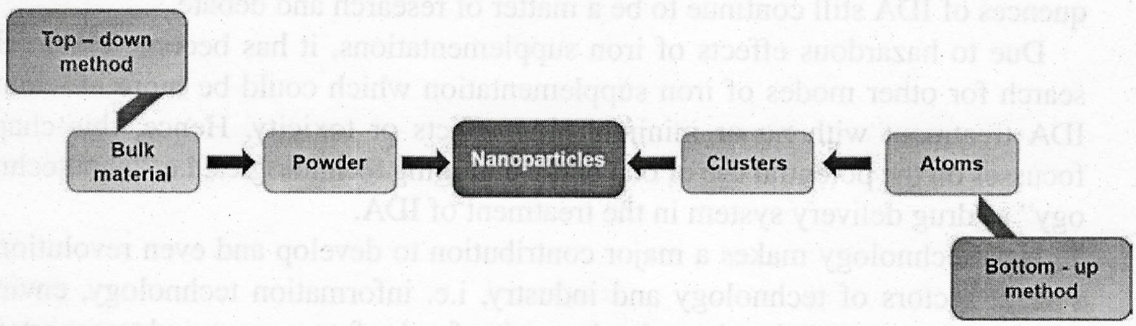

Fig. 5.1 Schematic diagram of top-down and bottom-up method

nanoparticles. The development of these eco-friendly methods of nanoparticles synthesis is evolving as a major nanotechnology branch by providing its contribution in various fields, for example applications of silver NPs in dental treatment and surgery and application of gold NPs in sunscreen lotions (Kim et al. 2010; Kyriacou et al. 2004; Hasan 2015).

Biological synthesis of NPs also known as "green nanotechnology" is in alliance with the improvements of the environmental sustainability of negative-facetted processes. This approach also includes cost-effectiveness and is free from dangerous and toxic chemicals. This biological approach is gaining attention of most of researchers as metallic NPs of various shapes, sizes, contents and physicochemical properties can be synthesized with less or no toxicity. It involves the development of green nano-products, and then the use of these nano-products in support of sustainability (Shah et al. 2015). These syntheses can be done in a single step by using bacteria, actinobacteria, yeasts, moulds, algae and plants or their products (Prasad et al. 2016, 2018b; Nadaroglu et al. 2016, 2017). As plants have great potential to detoxify, minimize and remove metals, they provide a promising, quick and cost-effective approach in removing metal-borne contaminants (Nadaroglu et al. 2017). Synthesis process is initiated in the aqueous solution of metal ions by adding extracts obtained from plant parts such as leaves, roots, bark, stem and fruit. With the phytoconstituents present in the plant extract, such as sugar, flavonoid, protein, enzyme, polymer, organic acid, phenolic compounds, amines, alkaloids and pigments, which act as a reducing agent, the bioreduction of metal ions into nanoparticles takes over (Cicek et al. 2015; Narayanan and Sakthivel 2010; Mukhopadhyay and Yadav 2011; Park et al. 2016; Siddiqi and Husen 2016).

Due to their incredible properties, nanomedicine has tremendous prospects for the improvement of the diagnosis and treatment of human diseases. In addition, the green synthesis of nanoparticles provides a convenient, simple and environment-friendly way which minimizes the side effects of chemical and physical methods by preventing the use of toxic chemicals and formation of harmful/dangerous by-products (Nadaroglu et al. 2017; Parveen et al. 2016) The primary goal of green nanotechnology is to curtail forthcoming environmental and human health risks associated with the use of nanotechnology products and to inspire the substitution of existing products with a more environmentally friendly nano-product.

5.2 Plant-Based Synthesis of Iron Oxide Nanoparticles (IONPs)

In the current scenario, metallic nanoparticles (NPs) are currently a hotspot of interdisciplinary research due to their inherent potential for diverse nanotechnological applications. Therefore, scientists are actively trying to explore new and groundbreaking approaches to establish cost-effective strategies for coping with both environmental and human health-related problems (Blakemore 1975; Prabhu 2018).

Box 5.1: Synthesis of Iron Oxide Nanoparticles from Plants

Green Synthesis and Characterization of Iron Oxide Nanoparticles (IONPs) Using *Spinacia oleracea* Leaf Extract (Smital and Mansee 2018)

For biological synthesis of IONPs, *Spinacia oleracea* leaf extracts are prepared from hydroponically as well as soil grown plant (for comparison). About 20–25 g of fresh and healthy leaves of *S. oleracea* are weighed, washed thoroughly with double distilled water, cut into small pieces and allowed to boil in 100 mL of double-distilled water using water bath at 70 °C for 15–20 min. After boiling, the colour of the aqueous solution changes from watery to brown color. The extract is allowed to cool at room temperature. Then, the solution is filtered using Whatman filter paper no. 42 and stored at 4 °C for further experiments. Further, the extract is mixed with 0.1 M $FeCl_2$ and 0.1 M $FeCl_3$ in the ratio 1:2 under constant stirring at 80 °C for 15 min. In the next step, 0.1 M NaOH is added to the mixture under constant stirring at 20 °C, and it is allowed to stir for more 45 min. The mixture is cooled and washed with ethanol several times to remove the impurities if any. Finally, ethanol is added to the pellet followed by sonication and kept in oven for drying. The black solid particles obtained are characterized using sophisticated instruments such as UV spectroscopy, scanning electron microscopy-energy dispersive spectroscopy (SEM-EDS), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and atomic absorption spectroscopy (AAS) to confirm the presence, size, morphology, state and Fe content of biosynthesized nanoparticles.

Biosynthesis of Iron Oxide Nanoparticles Using *Sida cordifolia* Plant Extract (Pallela et al. 2019):

S. cordifolia plant is washed thrice with tap water and allowed to shade dry. Dried plants are cut into fine pieces and powered using pulverizer. The powder is extracted in the Soxhlet apparatus using methanol. The concentrated crude extract is refrigerated for further use. For synthesis, 0.01 M iron nitrate solution (precursor) is prepared with double-distilled water, stirred for 30 min and further boiled at 60 °C for 5 min. To 10 mL of boiled precursor solution, 5 mL of *S. cordifolia* extract is added under constant stirring. Deep brown colour is observed after addition of plant extract. The mixture is centrifuged at 10,000 rpm for 10 min with acetone, ethanol and DI water repeatedly. The dried precipitate powder is annealed at 300 °C for 8 h to obtain deep red–colored α-Fe_2O_3 nanoparticles. The physico-chemical characteristics are analysed using UV-Vis spectrophotometer, SEM-EDX, XRD, TG-DTA and FTIR.

Biosynthesis of Iron Oxide Nanoparticles Using *Glycosmis mauritiana* Leaf Extract (Amutha and Sridhar 2018):

Weigh 100 g of fresh healthy leaves of *G. mauritiana* and keep aside for shade dry. The dried leaves are finely powdered using blender. Soak the powdered leaves in 200 mL double-distilled water for overnight at 4 °C and boil the rinsed mixtures for 10 min. The extracts are allowed to cool at room

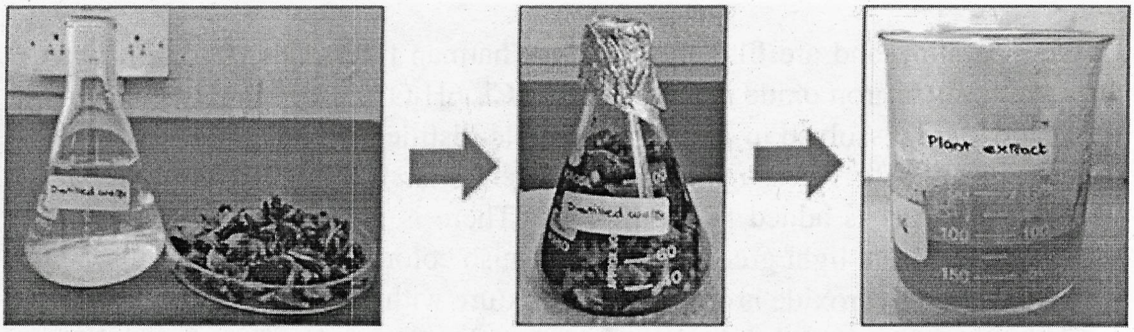

Fig. 5.2 Initial step of preparing *Spinacia oleracea* plant extract for nanoparticle synthesis

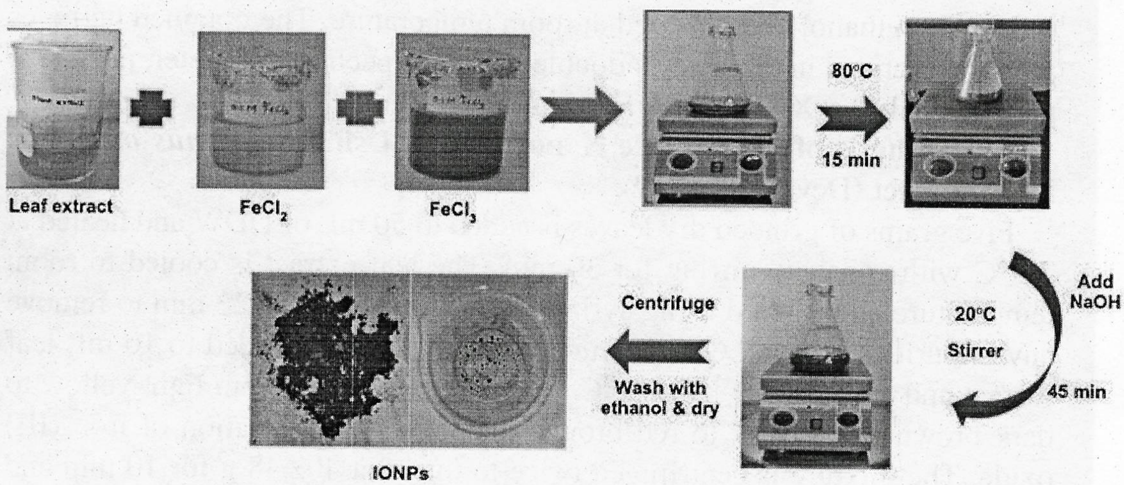

Fig. 5.3 Green synthesis of IONPs using *Spinacia oleracea* leaf extract, $FeCl_2$, $FeCl_3$ and NaOH

et al. 2011). This method involves the plant extracts, fungi microorganisms like bacteria, etc. In this process, phytochemicals and aqueous matrixes replace the chemical compounds and organic solvents, respectively. As with any chemical and biochemical reaction, variables such as reaction temperature, iron precursor concentration, leaf extract concentration and reaction time have crucial effects on the yield of the reaction (Jassal et al. 2016; Harshiny et al. 2015; Ehrampoush et al. 2015; Latha and Gowri 2014).

Unfortunately, nanomaterial production from microorganisms is less monodispersed, and the synthesis rate is slow compared to plant synthesis (Dhillon et al. 2012). The process of nanoparticle synthesis using microorganisms involves complex steps like microbial sampling, isolation and culturing. As there are use of microorganisms, there is more maintenance requirement. The process is slow along with low productivity of microorganisms as compared to plant-based synthesis. It requires downstream processing for recovery which is not required in plant-based nanoparticle synthesis (Parveen et al. 2016; Singh et al. 2016). In the synthesis process, the bioactive components found in the plant extract serve as reduction and capping agents and reduce the metal ions to NPs. No additional surfactants or capping agents are therefore necessary for the synthesis. The metal ions in the aqueous salt solution are reduced to form small nucleation centres. Such nucleation centres increase in size temperature and are filtered through Whatman filter paper (No.42). For the synthesis of iron oxide nanoparticle, $FeCl_3 \cdot 6H_2O$ and $FeCl_2 \cdot 4H_2O$ (1:2 molar ratios) are dissolved in 100 mL of double-distilled water and heated at 80 °C under mild stirring using magnetic stirrer. After 10 min, 20 mL of *G. mauritiana* extract is added to the mixture. There is an immediate color change observed from light green to dark brownish color. Again after 10 min, 20 mL of sodium hydroxide is added to the mixture with the rate of 3 mL per minute to allow uniform precipitation of iron oxides. The mixture is cooled down to room temperature, and by decantation, magnetite iron oxide nanoparticles are obtained. The magnetites are washed thrice with double-distilled water and thrice with ethanol and air dried at room temperature. The obtained particles are characterized using UV-vis double bean biospectrophotometer, nano size particle analyzer, XRD, FTIR, SEM and HR-TEM.

Biosynthesis of Iron Oxide Nanoparticles Using *Plantanus orientalis* Leaf Extract (Devi et al. 2019):

Five grams of grinded dry leaves is added to 50 mL of DDW and heated at 70 °C with constant stirring for 30 min. The leaf extract is cooled to room temperature and filtered using syringe filter of pour size 0.22 mm to remove any impurities present. One gram of $Fe(NO_3)_3 \cdot 9H_2O$ is added to 10 mL leaf extract and stirred for 1 h at 25 °C. The colour changed from light yellow to dark brown and slowly to red brown, indicating the formation of iron (III) oxide. The mixture is centrifuged twice to thrice at 402.48 g for 10 min and washed with alcohol twice. The red-brown colour sample obtained is dried at room temperature. The sample is analysed for various characteristics using UV-vis spectrophotometer, SEM-EDX, XRD, DLS, TEM and FTIR.

During earlier times, conventional chemical and physical methods were in high demand for nanoparticle synthesis. Owing to their drawbacks, now the focus has been shifted to more eco-friendly, less expensive and safer biological method for NP production (Ebrahiminezhad et al. 2018). In chemical synthesis, toxic reducing agents such as sodium borohydride and hydrazine hydrate are used, which cause undesired detrimental impacts on the environment, plant and animal life. It also involves the formation of dangerous by-products and chemical precursors. Similarly, high amount of energy is required for synthesis of NPs by physical methods (Saif et al. 2016; Mandal et al. 2006; Jebali et al. 2011; Thakkar et al. 2010). The NPs synthesized by chemical and physical methods lose their reactivity due to aggregation of air exposure (Kim et al. 2008), magnetism and dispersibility (Wu et al. 2008). In addition to their low production rate, both these methods are also expensive and time-consuming processes.

In order to overcome the limitations posed by conventional methods, there has been a growing demand for rapid and eco-friendly synthesis of nanoparticles, i.e. *"green synthesis"* (Figs. 5.2 and 5.3). Green synthesis will help to minimize the use of toxic materials and increase process efficiency (Sharma et al. 2009; Schröfel by sequestrating more metal ions and surrounding nucleation sites to form the NPs. These NPs are closely associated with the organic moieties present in the extract of plants which aid in the NP capping process. For instance, biosynthesized IONPs have large surface area to volume ratio and, therefore, high surface energies (Mittal et al. 2013; Kumar and Yadav 2009). In the plant extract, phytochemicals directly transform iron ions to IONPs. Such biomolecules contain a number of water-soluble metabolites (e.g. polyphenols, carbohydrates, alkaloids, phenolic acids and proteins) and coenzymes that can act as biosynthesis reaction reducers and stabilizers (Jassal et al. 2016; Njagi et al. 2011). Reaction conditions (i.e. temperature, concentration of iron precursor, quantity of plant extract and duration of reaction) and plant extract chemical specifications (i.e. preparation temperature, concentration, pH and phytochemical molecules) have important impacts on the physicochemical properties of the resulting nanoparticles (Harshiny et al. 2015; Ehrampoush et al. 2015; Latha and Gowri 2014). Table 5.1 represents different plant extracts used in the synthesis of iron oxide nanoparticles and differences in their physicochemical characteristics. The whole process takes place in a single-step reaction at room temperature and occurs rapidly and easily. The synthesis eradicates the need to use dangerous chemicals and poisonous solvents. Furthermore, waste products in the atmosphere can be easily disposed of because they are mainly made up of plant biomaterial. The overall synthesis process is simple, cost-effective, reproducible and sustainable. Additionally, this approach can be used to achieve stable NPs of desired size and morphology (Shahwan et al. 2011; Raveendran et al. 2003). Biologically generated NPs thus possess superior properties compared to chemically synthesized NPs.

According to the study of Kalaiarasi et al., green synthesis of metallic nanoparticles by different plant parts such as the leaf, stem, seed and root has been proved to be the simplest, most cost-effective, reproducible and best candidates for fast and large-scale synthesis as compared to microorganisms (Kalaiarasi et al. 2010).

Table 5.1 List of few plant extracts used in the synthesis of iron oxide nanoparticles and its physicochemical characteristics

Plant	Part used	Iron precursor	Resulted IONPs	Size (nm)	Shape	References
Green tea	Leaves	$FeCl_2{\cdot}4H_2O$	Magnetite FeOOH	40–60	Irregular cluster	Shahwan et al. (2011)
Eucalyptus	Leaves	$FeSO_4{\cdot}7H_2O$	IONPs ZVI NPs	20–80	Spherical	Wang et al. (2014a, b)
Soyabean	Sprouts	$FeCl_3{\cdot}6H_2O$	Magnetite	8	Spherical	Cai et al. (2010)
Caricaya papaya	Leaves	$FeCl_3{\cdot}6H_2O$	Magnetite	Irregular	Irregular	Latha and Gowri (2014)
Salvia officinalis	Leaves	$FeCl_3$	Fe_2O_3	5–25	Spherical	Wang et al. (2015)
Black tea	Leaves	Ferrous sulphate	FeOOH, Fe_2O_3	40–50	Round	Ali et al. (2016)
Oolong tea	Leaves	$FeSO_4{\cdot}7H_2O$	ZVI, Fe_3O_4, FeOOH, Fe_2O_3	40–50	Spherical	Huang et al. (2014)

Several researchers reported green synthesis of IONPs using plant extracts. Green synthesis of iron nanoparticles was performed using green tea (*Camellia sinensis*) extract which is a cheap and local source in a study by Hoag et al. The nanoparticles were obtained without the addition of any surfactant or polymer since polyphenols present in plant act as a reducing agent as well as a capping agent (Hoag et al. 2009). For the production of IONPs, plant extract derived from agro waste (*Sorghum* sp.) such as Sorghum bran extract was used, and degradation of bromothymol blue dye was observed using these NPs (Njagi et al. 2011). Synthesis of magnetite nanoparticles was also performed using extract from the plantain peel. The authors have proposed that these NPs have the ability for toxic metals and dyes to be bioremediated (Venkateswarlu et al. 2013).

The successful synthesis of maghemite nanoparticles was reported by Martínez-Cabanas et al. (2016) using chestnut tree (*Castanea sativa*) extracts, eucalyptus (Eucalyptus globulus), gorse (*Ulex europaeus*) extracts, and pine (*Pinus pinaster*) extracts. The authors in their analysis selected *E. globulus* as the best alternative for green iron (III) oxide nanoparticles synthesis (Martínez-Cabanas et al. 2016). Ali et al. (2016) reported using black tea leaf extract for Fe_2O_3 nanoparticle synthesis, while iron (III) oxide nanoparticles were successfully synthesized using aqueous green, black and oolong tea extract (Ali et al. 2016).

Senthil et al. attempted the green synthesis of Fe_3O_4 nanoparticles using the *Tridax procumbens* leaf extract at room temperature in which carbohydrates found in the plant extract have been responsible for the synthesis of NPs (Senthil and Ramesh 2012). Leaves of three plants native to Australia, namely *Eucalyptus tereticornis* (A), *Melaleuca nesophila* (B) and *Rosmarinus officinalis* (C), have been explored by Wang et al. to study the efficacy of synthesized iron nanoparticles and used as heterogeneous Fenton-like catalyst for decolouration of azodye (Acidblack194) and total organic carbon (TOC) (Wang et al. 2014a, b). Biosynthesis of metal nanoparticles using plant extract provides major advantages over other biological systems such as reducing the cultivation and downstream processing costs, quick manufacturing processes and non-hazardous waste (Table 5.2). In addition, plant-mediated synthesis of INPs is one of the strategies for enhancing the physicochemical and biological

Table 5.2 Comparison between nanoparticle synthesis using plants and other biological materials (microorganisms, fungi, bacteria, etc.)

Plant-based nanoparticle synthesis	Other biological material nanoparticle synthesis
Single-step reaction	Complex steps are involved in reaction
Quick manufacturing process	Slow manufacturing process
Reduction in cultivation and downstream processing costs	Expensive cultivation and downstream processing
Very low maintenance is required	More maintenance is required
Non-hazardous wastes are formed	Hazardous wastes are formed
More productivity	Low productivity
Advantages of preserving properties, i.e. particle size and monodispersity	Particle size and monodispersity not well maintained

operations, which transform superoxide into H_2O_2. The therapeutic effects of nanozymes include applications for anti-ageing effects, anti-inflammatory effects, anti-oxidation effects, neuroprotection, promotion of stem cell growth, etc. (Wang et al. 2016).

5.3.3 *Role of IONPs in Hyperthermia and Photothermal Therapy (PTT)*

Hyperthermia is a thermal therapy in which energy sources such as microwaves, radio waves, ultrasonic energy and magnetism generate heat near a local or systemic tumour. Recently, it has been realized that conventional cancer treatment approaches suffer from many drawbacks such as side effects, drug resistance, poor on-the-spot drug availability and rapid renal clearance. Such problems have allowed the researchers to combine hyperthermia with chemotherapy and radiotherapy. The intratumorally injected IONPs produce heating effect in magnetic hyperthermia after exposure to an external magnetic field and induce cell death near the tumour site (Cheraghipour et al. 2012). Because of weak cellular architecture, cancer cells are very susceptible to being affected by the small rise in the temperature around them. Additionally, the temperature of the ambient atmosphere can be raised up to 55–60 °C using hyperthermia technique, which can be very well resisted by normal healthy cells but not by cancer cells. In addition, IONPs can be used to prepare synergistic, balanced nanohybrids for magnetic hyperthermia and photothermia. Photothermal therapy is also feasible using other nanoparticles such as gold, copper, silver, carbon nanotubes and graphene NPs, such as anisotropic nanostructures. Certain IONP morphologies are also developed for the treatment of photothermal diseases such as cancer, neuromusculoskeletal disorders and thyroid gland abnormalities (Boca et al. 2011; He et al. 2014).

In the perspective of use of IONPs in photothermal therapy (PTT), Niu et al. developed a nanosystem consisting of poly-encapsulated IONPs (Fe_3O_4), indocyanine green (ICG) and perfluoropentane (PFP) (lactidecoglycolide) (PLGA) nanoparticles for NIR-induced PTT. These multifunctional NPs have shown to enhance tumour ablation in MCF-7 tumour experiments in mice when irradiating as NIR laser and can act as a potent anti-tumour photothermal agent (Niu et al. 2017). Multifunctional IONPs are often planned and have performed better than their unifunctional equivalents. PEGylated Fe/Fe_3O_4 NPs were formed in this context to exhibit triple functions comprising PTT, targeting and MRI (Zhou et al. 2014). Shen et al. (2013) synthesized Fe_3O_4 NPs coated with carboxymethyl chitosan, which showed extremely low toxicity and high PTT performance with additional advantage of easy manufacture protocol for multiple applications.

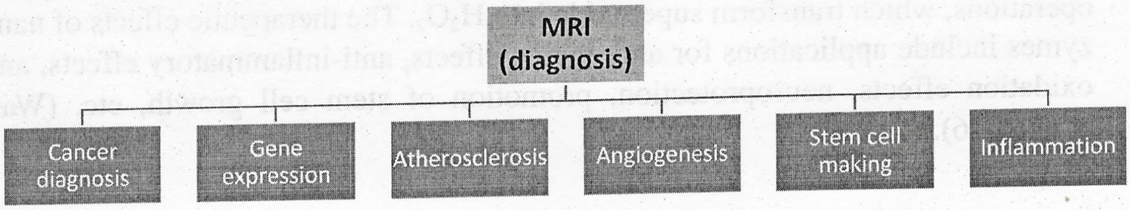

Fig. 5.5 Biomedical applications of IONPs in the diagnosis of disorders through magnetic resonance imaging

5.3.2 *Role of IONPs as Nanozymes*

Recent advances in nanotechnology have also been aimed at developing new enzyme mimetics (nanozymes) that exhibit biological oxidase, peroxidase, catalase and superoxide dismutase-like activities (Karim et al. 2018). Nanozymes are beneficial in many respects compared to natural enzymes, such as low cost, ease of mass production, robustness to harsh conditions, high stability, long-term storage and size/composition-dependent operation. Compared to other artificial enzymes, nanozymes also exhibit unique properties in terms of their size, shape, structure, composition-dependent catalytic action, integrated (multi) functions in addition to catalysis, broad surface area for further modification and bioconjugation, smart response to external stimuli, self-assembly capability, etc. Besides diverse applications in bionanotechnology, these nanozymes have been extensively studied in other several platforms ranging from biosensing and bioimaging to tissue engineering, therapeutics and beyond (Wei and Wang 2013).

Various nanomaterials based on metal and metal oxides, such as IONPs, gold, silver, copper and graphene nanosheets, MoS2 and WS2, exhibit horseradish peroxidase (HRP)-like properties. These enzyme-mimetic activities are demonstrated to be used in the construction of non-enzymatic biosensors to test the cancer diagnosis levels/concentrations of glucose, glutathione, cholesterol, H_2O_2, urea, creatinine and biomarkers. These biomolecules are well-known biomarkers for many diseases, so the biosensors that have been developed could be used as early diagnostic tools (Zheng et al. 2011).

Wei and Wang (2008) have developed a colorimetric method for H_2O_2 detection, where Fe_3O_4 magnetic nanoparticles (MNPs) were used as peroxidase mimic (Wei and Wang 2008). Fang et al. (2014) used nanocomposites of Fe_3O_4/reduced graphene oxide (rGO) as peroxidase mimics to prepare the modified glass carbon electrode for H_2O_2 electrochemical sensing (Fang et al. 2014). The corresponding oxidase substrate can be determined when an oxidase is combined with peroxidase mimic. Wei and Wang (2008) documented a sensitive and selective colorimetric approach to glucose detection by combining glucose oxidase with the Fe_3O_4 MNPs as the peroxidase mimic (Wei and Wang 2008). Moreover, nanozymes have been used for possible therapeutics by mainly replacing reactive oxygen species (ROS) and/or reactive nitrogen species (RNS). The ROS scavenging capabilities of nanozymes were mainly derived from their superoxide dismutase (SOD) mimicking

Residents in affected areas can use publicly available apps to find critical assistance and resources. Apps and maps can provide directions to hospitals with available beds, clinics that provide medical assistance with current wait times, open grocery stores and pharmacies, and places to buy personal protective equipment, among other things. This information could significantly improve outcomes and save lives in severely afflicted cities.[11]

CONCLUSION

Modern GIS technology relies on web-based applications, increased data sharing, and real-time data to assist users to make better decisions. These values are represented via dashboards, which have proven to be quite useful for sharing and studying SARS-CoV-2 coronavirus spread.[11]

COVID-19 outbreak awareness has surely been centered on dashboards. Another outbreak is not a question of if, but when and where it will occur. Viruses such as SARS-CoV-2 are unconcern ed with national or continental boundaries.[11]

GIS mapping is a useful tool and has scope for continued mapping of COVID. It can help in the prediction of disease spread. Using GIS mapping the extent of the spread of the disease can be tracked and specific measures for control of spread can be implemented in a targeted manner.

Therefore, for better preparedness, we need to keep tracking new outbreaks through GIS and promote further advances in Mapping technologies.

Limitations

Data show positive COVID-19 cases reported at only one tertiary care hospital. A broader picture can be painted if more COVID hospitals data are used.

Ethical consideration

Institutional Ethics Committee (IEC) of MGM Medical College, Navi Mumbai, Maharashtra, India reviewed and approved the research study entitled: "Community mapping of COVID-19 cases admitted during April to June 2020 at a Tertiary Health Care Hospital in Raigad District in Maharashtra, India" in the IEC meeting held on 10 July 2020 communicated vide their letter no. N-EC/2020/07/41 dated July 14, 2020.

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Conflicts of interest

There are no conflicts of interest.

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