A review of the biological synthesis of gold nanoparticles using fruit extracts: scientific potential and application

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Abstract. Gold nanoparticles (GNPs) are well-known nanomaterials that can be used for multiple biomedical applications. There are various methods for synthesis of GNPs using microorganisms and plants, particularly through the use of fruit extracts. Their use is due to the fact that fruit extracts are the natural concentrate of substances that possesses therapeutic properties. In this review, we aim to compare the recent studies concerning the methods for synthesis of GNPs from fruit extracts, the methods used to characterize the properties of GNPs and capping biomaterial and the potential applications of GNPs. The most frequently used methods to characterize GNPs and capping biomaterial are UV–visible spectroscopy, transmission or scanning electron microscopy, dynamic light scattering and Fourier transformation infrared spectroscopy techniques. Because of GNPs' optoelectronic properties, biocompatibility, stability and oxidation resistance, they can be used in areas such as electronics, chemical and biological sensing, tumour imaging, drug delivery and phototherapy.

Keyword. Biosynthesis; gold nanoparticles; fruit extracts; GNP properties; application.

1. Introduction

Nanoparticles (NPs) derived from noble metals play an important role in nanotechnology because of their wide range of applications [1–7]. The synthesis of NPs can be carried out using chemical (e.g., synthesis by sodium citrate) [8,9], physical (e.g., synthesis using laser ablation or microwave/ultraviolet radiation) [10–12] or biological methods (synthesis using bacteria, fungi or plants) [13–20]. Most of the chemical and physical methods are invasive and require the application of toxic compounds or harmful radiation. Moreover, chemical and physical methods of NP synthesis are expensive, labour-intensive, time-consuming and environmentally hazardous [21,22]. In physical and chemical NP synthesis, toxic substances are used to functionalize and stabilize NPs, complicating the ability of NPs to be used in medicine and pharmacy [23–25]. Currently, the goal of nanotechnology is to design NPs with well-defined size and shape and which are biocompatible and stable [26–30]. Moreover, biological methods of NP synthesis are cheap, sustainable, resource efficient, time-competent and eco-friendly [13,22].

In biological synthesis of NPs microorganisms, fungi, algae and plants are used [13,31–34]. There are multitude of reports on NP biosynthesis, including that of gold NPs (GNPs) using plant extracts [1–7,13,22,32–34]. The reason for choosing plants for NP biosynthesis is because they contain reducing agents such as proteins and second metabolites, which can possess therapeutic properties [1,13,22,32–34]. Plants present a high-reductive capacity to transform gold ions into metallic gold (table 1). Generally, the mechanism of biosynthesis

occurs by one of the two pathways, as biogenic synthesis or bioreduction [13]. In the case of biosynthesis using plant extracts, only bioreduction will result in GNPs [22]. There are many examples of using plant extracts (i.e., natural biomolecules such as peptides, terpenoids, polyphenols, sugars, alkaloids, phenolic acids and proteins) in the bioreduction of gold ions [13,22,32,33,35].

The mechanism of GNP formation can be divided into three stages: activation (reduction of gold ions and nucleation of reduced atoms), growth (spontaneous coalescence of small GNPs into large particles until they reach thermodynamic stability) and termination (where GNPs acquire the most favourable conformation) [33,35].

The usage of plant extracts to biosynthesize GNPs is not only convenient because they possess reducing biomolecules but also because of their stabilizing properties [13,22,32,33,35]. It has been suggested that the size and shape of GNPs are strongly dependent on the ability of plant extracts to stabilize GNPs [22,33]. Thus, optimization of the GNP synthesis process is very important, and the range of potential applications, especially in medicine and pharmacy, depends on the size and shape of GNPs [1–7,13,22,32–34].

The size and shape of GNPs are typically characterized using UV–visible spectroscopy, scanning or transmission electron microscopy (SEM/TEM), atomic force microscopy (AFM) and dynamic light scattering (DLS) techniques. There are other methods used to characterize properties of formed GNPs, primarily focusing on the optical (surface plasmon resonance — SPR), thermal, magnetic and electric properties [13,22,32,33,35].

Table 1. Biosynthesis of GNPs using plant extracts.

Latin or English name of plant	Part of plant	Solvent/physical factor	References
<i>Abelmoschus esculentus</i> L.	Seed extract	Water	[36]
<i>Acacia nilotica</i> L.	Leaf extract	Ethanol	[37]
<i>Achillea wilhelmisii</i>	Flower extract	Water	[38]
<i>Aerva lanata</i> L.	Plant extract	Water	[39]
<i>Allium cepa</i> L.	Leaf extract	Water	[40]
<i>Aloe vera</i> L.	Plant extract	Water	[41]
<i>Anacardium occidentale</i> L.	Leaf extract	Water	[42]
<i>Ananas comosus</i> L.	Fruit extract	Water	[43]
<i>Artocarpus heterophyllus</i> (Lam.)	Fruit extract	Water	[44]
<i>Avena sativa</i> L.	Stem extract	Water	[45]
<i>Averrhoa bilimbi</i> L.	Fruit extract	Water	[46]
<i>Bauhinia purpurea</i> L.	Flower extract	Water	[47]
Blackberry	Fruit extract	Water	[48]
Blueberry	Fruit extract	Water	[48]
<i>Callistemon viminalis</i> L.	Leaf extract	Water	[49]
<i>Camellia sinensis</i>	Leaf extract	Water	[50]
<i>Centella asiatica</i> L.	Leaf extract	Ethanol	[51]
<i>Chenopodium album</i> L.	Leaf extract	Water	[52]
<i>Chrysanthemum</i> L.	Flower extract	Water	[53]
<i>Cinnamomum zeylanicum</i>	Leaf extract	Water	[54]
<i>Citrullus lanatus</i>	Fruit extract	Water	[24]
<i>Citrus limon</i> L.	Fruit extract	Water	[55]
<i>Citrus reticulata</i>	Fruit extract	Water	[55]
<i>Citrus sinensis</i> L.	Fruit extract	Water	[55]
<i>Coffea arabica</i> L.	Fruit extract	Water	[56]
<i>Coleus amboinicus</i> L.	Leaf extract	Water	[57]
<i>Coriandrum sativum</i> L.	Leaf extract	Water	[58]
<i>Cornus mas</i> L.	Fruit extract	Water	[59]
<i>Couroupita guianensis</i> (Aubl.)	Fruit extract	Water	[60]
<i>Crocus sativus</i>	Plant extract	Water	[61]
<i>Cuminum cymium</i> L.	Seed extract	Water	[62,63]
<i>Cymbopogon schoenanthus</i> L.	Plant extract	Water	[64]
<i>Dioscorea bulbifera</i> L.	Tuber extract	Water	[65]
<i>Diospyros kaki</i>	Leaf extract	Water	[66]
<i>Euphorbia hirta</i> L.	Leaf extract	Water	[67]
<i>Garcinia cambogia</i> L.	Fruit extract	Water	[68]
<i>Garcinia mangostana</i> L.	Fruit extract	Water	[69]
<i>Genipa americana</i> L.	Fruit extract	Water	[70]
Grapes	Fruit extract	Water	[71]
<i>Hibiscus rosa-sinensis</i> L.	Leaf extract	Water/microwave radiation	[72]
<i>Hibiscus rosa-sinensis</i> L.	Leaf extract	Water	[73]
<i>Lawsonia inermis</i> L.	Leaf extract	Water	[74]
<i>Lycopersicon esculentum</i>	Fruit extract	Water/SDS	[75]
<i>Macrotyloma uniflorum</i> (Lam.)	Seed extract	Water	[76]
<i>Magnolia kobus</i>	Leaf extract	Water	[66]
<i>Malus domestica</i> (Borkh.)	Fruit extract	Water	[77]
<i>Mangifera indica</i> L.	Leaf extract	Water	[78,79]
<i>Medicago sativa</i> L.	Life plant	—	[80]
<i>Memecylon edule</i>	Leaf extract	Water	[81]
<i>Mentha × piperita</i> L.	Leaf extract	Water	[82]
<i>Mirabilis jalapa</i> L.	Flower extract	Water	[83]
<i>Murraya koenigii</i> L.	Leaf extract	Water	[84]
<i>Nitraria schoberi</i> L.	Fruit extract	Water	[85]
<i>Ocimum sanctum</i> L.	Leaf extract	Water	[86]
Olive	Leaf extract	Water	[87]
<i>Pelargonium graveolens</i>	Leaf extract	Water	[88]

Table 1. (continued)

Latin or English name of plant	Part of plant	Solvent/physical factor	References
<i>Phyllanthus emblica</i> L.	Fruit extract	Water	[89]
<i>Polygonum fagopyrum</i> L.	Leaf extract	Water	[90]
<i>Prunus domestica</i> L.	Fruit extract	Water	[91]
<i>Psidium guajava</i> L.	Leaf extract	Water/microwave radiation	[92]
<i>Punica granatum</i> L.	Fruit extract	Water	[48,88,93]
<i>Pyrus</i> L.	Fruit extract	Water	[94]
<i>Rosa damascena</i>	Flower extract	Water	[95]
<i>Rosa hybrida</i>	Flower extract	Water	[96]
<i>Rosa rugosa</i>	Leaf extract	Water	[97]
<i>Solanum indicum</i> L.	Fruit extract	Water/microwave radiation	[98]
<i>Sorbus aucuparia</i> L.	Leaf extract	Water	[99]
<i>Tanacetum vulgare</i> L.	Fruit extract	Water	[100]
<i>Terminalia arjuna</i>	Fruit extract	Water	[101]
<i>Terminalia chebula</i>	Seed extract	Water	[102]
<i>Trianthema decandra</i> L.	Root extract	Water	[103]
<i>Trigonella foenum-graecum</i> L.	Seed extract	Water	[104]
<i>Ziziphus jujuba</i>	Fruit extract	Water	[105]

The unique physical properties of GNPs and their biocompatibility make them a useful tool in biomedical applications [2–7]. It has been demonstrated that GNPs synthesized from plant extracts would be effective as antibiotics and other drugs [5–7,33,35,106], practical for drug delivery [2,6,7,35] and useful as a vehicle of nucleic acids in gene therapy [4,5,7,32,35]. Studies has also examined the use of GNPs in breast cancers and other cancers [3,4,7,35] as well as their antimicrobial activity [1,7,33,35,106]. GNPs are also advantageous as biochips and contrast agents in diagnostic and therapy [2,3,5–7,35].

This review is devoted to the perspective of GNPs synthesized from fruit extracts. This method of gold ion bioreduction has been shown to be economical, efficient, time-saving and eco-friendly to obtain GNPs with specified properties [22,35]. The potential applications of GNPs synthesized from fruit extracts have been extensively studied [45,46,61,70,74,89,94,96,99,103]. This review describes, in detail, the methods of GNP synthesis using fruit extracts, the reducing potential of fruit extracts, mechanisms of reduction, parameters affecting biosynthesis and characteristics of the formed GNPs and their potential applications.

2. Synthesis of GNPs using fruit extracts

The synthesis of GNPs using fruit extracts has been reported for their ability to reduce gold ions to metallic gold (table 2, figure 1).

2.1 Preparation of fruit extracts

First, a defined amount of ripe fruit is washed in distilled or deionized water. Generally, there are two kinds of procedures

for preparing fruit extracts: at room or higher temperatures (temperatures below the boiling point). In both cases, the fruit was either crumbled by hand or mechanically disrupted (grinding, juicing and blending). The pulp was only removed from the hard fruit, e.g., in the case of *Citrullus lanatus* [24]. A defined amount of distilled water was added to the fruit before mechanical grinding. Additionally, intense stirring at room temperature was performed [59]. Next, the obtained mixture was either filtered immediately [46,71,94,98,101] or heated to temperatures below the boiling point [39,48,60,69,75,91]. The filtering was carried out once using paper filters, and then the filtrate was centrifuged [43,44,94]. Because of the properties of fruit extracts, they were stored in a refrigerator until the synthesis was performed.

2.2 Procedure of GNP synthesis

An aqueous solution of chloroauric acid (HAuCl_4) at concentrations from 0.5 to 30 mM was used in GNP synthesis from fruit extracts. The synthesis of the GNPs was carried out at room temperature [39,46,48,69,71,77,85,93,94,101], or the fruit extracts and/or HAuCl_4 solution were heated before mixing [43,56,59,75,91]. Synthesis was performed in the dark. The mixtures were stirred intensively to obtain a homogeneous solution. Two teams of researchers centrifuged the gold colloid solution at the end of the procedure to eliminate the organic compounds from the sample [43,44,94].

The process of the GNP synthesis using fruit extracts is quick and effective [7,14,33,45]. The visual effect of reducing the gold ions to metallic gold is the change of the mixture colour from light yellow or pink to dark red, purple or dark violet. The GNP synthesis proceeds usually after 2–30 min.

Table 2. Biosynthesis of GNPs using fruit extracts.

Latin or English name of plant	Size and shape of GNPs	Methods used to characterize GNPs and capping biomaterial	GNPs antibacterial activity, cytotoxicity	References
<i>Ananas comosus</i> L.	Mean size 10 nm, spherical	UV-visible spectroscopy, SEM, FTIR	++	[43]
<i>Artocarpus heterophyllus</i> (Lam.)	Mean size 5 μ m, cubic polyhedron; 20–25 nm, spherical	UV-visible spectroscopy, SEM, FTIR	++	[44]
<i>Averrhoa bilimbi</i> L.	75–150 nm hexagonal, rhomboidal	UV-visible spectroscopy, SEM, FTIR	×	[46]
Blackberry	Mean size 100 nm, oblong-shaped	UV-visible spectroscopy, TEM, TGA	×	[48]
Blueberry	Mean size 200, spherical	UV-visible spectroscopy, TEM, TGA	×	[48]
<i>Citrullus lanatus</i>	5–25 nm, spherical	UV-visible spectroscopy, FTIR, TEM	×	[24]
<i>Coffea arabica</i> L.	Average size 59 nm, spherical	UV-visible spectroscopy, FTIR, XRD, SEM, DLS	×	[56]
<i>Cornus mas</i> L.	13–52 nm, spherical	UV-visible spectroscopy, FTIR, XRD, TEM, DLS, DSC	×	[59]
<i>Ciurapitia guianensis</i> (Aubl.)	Mean size 26 $\pm$ 11 nm, spherical, triangular	UV-visible spectroscopy, FTIR, XRD, TEM, DLS	(–)	[60]
<i>Garcinia cambogia</i> L.	Average size 17 nm, spherical, hexagonal	UV-visible spectroscopy, FTIR, XRD, TEM, SAED	×	[68]
<i>Garcinia mangostana</i> L.	Average size 32.96	UV-visible spectroscopy, XRD, TEM, DLS	×	[69]
<i>Genipa americana</i> L.	14.9–30.4 nm, spherical	UV-visible spectroscopy, FTIR, XRD, TEM, ESI-MS	(–)	[70]
Grapes	Spherical	UV-visible spectroscopy, FTIR, TGA	+, (+)	[71]
<i>Lycopersicon esculentum</i>	5–20 nm, spherical	UV-visible spectroscopy, FTIR, XRD, TEM	×	[74]
<i>Malus domestica</i> (Borkh.)	About 5 nm, spherical, triangular	UV-visible spectroscopy, FTIR and FT-Raman spectroscopy, XRD, SEM, TGA, fluorescence spectroscopy	+, (+)	[77]
<i>Nitraria schoberi</i> L.	Average size 30 nm, circle (plate)	UV-visible spectroscopy, SEM	×	[85]
<i>Prunus domestica</i> L.	Mean size 20 $\pm$ 6 nm, spherical	UV-visible spectroscopy, FTIR, TEM, DLS	×	[91]
<i>Punica granatum</i> L.	Mean size 400 nm, spherical	UV-visible spectroscopy, TEM, TGA	×	[48,88,93]
<i>Pyrus</i> L.	10–500 nm spherical, plate-like morphology, triangular, hexagonal	UV-visible spectroscopy, XRD, TEM, AFM, XPS	×	[94]
<i>Solanum indicum</i> L.	5–50 nm, spherical	UV-visible spectroscopy, FTIR, TEM	(–)	[98]
<i>Terminalia arjuna</i>	5–50 nm, spherical	UV-visible spectroscopy, FTIR, XRD, AFM, TEM, DLS	–	[101]
<i>Ziziphus jujuba</i>	Mean size 34.8 nm, spherical	UV-visible spectroscopy, TEM, CV	+	[105]

AFM–atomic force microscopy; CV–cyclic voltammetry; DLS–dynamic light scattering; DSC–differential scanning calorimetry; ESI-MS–electrospray ionization mass spectroscopy; FTIR–Fourier transform infrared spectroscopy; SAED–selected area diffraction; SEM–scanning electron microscopy; TEM–transmission electron microscopy; TGA–thermogravimetric analysis; XPS–X-ray photoemission spectroscopy; XRD–X-ray diffraction spectroscopy; ‘–’–GNPs do not show any antibacterial activity; ‘+’–GNPs show antibacterial activity; ‘×’–antibacterial or cytotoxic tests have not been made; (–)–GNPs do not show cytotoxicity against tumour cells; (+)–GNPs show cytotoxicity against tumour cells; ‘++’–GNPs show antibacterial activity with antibiotics.

Figure 1. Procedure of GNP synthesis from fruit extracts.

Figure 2. Three-stage process of GNP formation.

3. Mechanism of GNP synthesis using fruit extracts

3.1 Reducing potential of fruit extracts

Fruit extracts can reduce gold ions to metallic gold (figure 2) [22]. The source of fruit extracts influences the characteristics of GNPs because of their different reducing potentials and stabilizing ability. The reducing potentials of fruit extracts depend on the concentration and combinations of organic reducing agents [1]. The well-known reducing agents are second metabolites of plants such as sugars, terpenoids, polyphenols, alkaloids and proteins [22]. It has also been demonstrated that isolated flavonoids, flavonoid glycosides and vitamins (e.g., ascorbic acid) are able to reduce gold ions [33,35].

Fruit extracts usually contain high concentrations of reducing agents. For instance, blackberries, blueberries, grape, *Citrullus lanatus*, *Cornus mas* L., *Punica granatum* L. and *Terminalia arjuna* fruits contain increased amounts of flavonoids, phenolic compounds, anthocyanins, saccharides, ascorbic acid and other vitamins [24,48,59,71,93,101]. For this reason, the synthesis of GNPs from fruit extracts is very efficient, time-saving and economical. In many cases, only one drop of fruit extract is needed for synthesis of GNPs.

3.2 Mechanisms of the synthesis processes

Fourier transform infrared (FTIR) spectroscopy analysis of GNPs synthesized from *Terminalia arjuna*, *Polygonum fagopyrum* L., *Couroupita guianensis* (Aubl.), *Solanum indicum* L., *Malus domestica* (Borkh.), *Citrullus lanatus*, *Cornus mas* L. and grape revealed that flavonoids and phenolic compounds are found to be a reductant [24, 59,60,69,71,98,101]. Flavonoids are a large group of polyphenolic compounds, which are divided into several classes such as anthocyanins, isoflavonoids, flavonols, chalcones, flavones and flavanones [22]. It has been suggested that tautomeric transformations of flavonoids (from *enol*-form to *keto*-form) release a reactive hydrogen atom that can reduce gold ions to metallic gold [22]. The flavonoids' internal mechanism of transformation of ketones to carboxylic acids may also affect gold ion reduction [33].

In another case of GNP synthesis using *Garcinia cambogia* L. and *Pyrus* L. fruit extracts, the saccharides acted as reducing agents [68,94]. Currently, it is believed that the oxidation of a sugar aldehyde group to a carboxyl group by nucleophilic addition of a hydroxyl group causes the reduction of gold ions [33].

Figure 3. Fruits second metabolites involved in synthesis and stabilization of GNPs.

It has been demonstrated that many plant extracts can reduce gold ions to metallic gold due to reductive properties of proteins, but their reducing ability differs because of various amino acid sequences [22,33]. In most cases of GNP synthesis from fruit extracts (e.g., *Ananas comosus* L., *Artocarpus heterophyllus* (Lam.), *Averrhoa bilimbi* L. and *Prunus domestica* L.), the proteins were found to be a reducing agent [43,44,46,91,94].

FTIR analysis of GNPs synthesized from the *Genipa americana* L. fruit extract revealed that genipin, genipaol, geniposide and ranolazine can act as reducers of gold ions.

It was also suggested that citric and ascorbic acids can reduce gold ions to metallic gold during the synthesis process using the extract from *Lycopersicon esculentum* [75].

3.3 Stabilizing ability of fruit extracts

Flavonoids, saccharides, proteins, citric and ascorbic acids can act as potential reducing agents in GNP synthesis from fruit extracts (figure 3) [107,108]. However, knowledge concerning the molecular mechanism of the process regulating

size and shape and stabilization of GNPs is lacking. As mentioned above, the final size and shape of GNPs are acquired in the termination stage of synthesis. In this stage, GNPs reach the most energetically favourable conformation [33]. The ability of fruit extracts to stabilize GNPs plays an important role in this process [7,22,33]. Previously, it has been shown that the same biomolecules which are responsible for reduction of gold ions also support subsequent stability of GNPs [7,22,32,33,35]. For instance, the flavonoids from the *Trigonella foenum-graecum* extract were responsible for reducing gold ions, and the authors assumed that the carboxylate group can stabilize GNPs [104].

The stability of GNPs can be studied using the DLS method. In the case of colloidal solutions, the potential zeta value $PZ \leq |-30|$ mV corresponds to stable GNPs [13,55,109]. Otherwise, fruit extracts may contain agglomerates of biomolecules, which also have a surface charge, and, for this reason, the interpretation of DLS results should be carefully examined. The electrostatic interactions occurring among the individual agglomerates can be attracted (positive and negative charges) or combined with another and

not repelled, as in the case of the stable sample [109]. The GNPs synthesized using *Garcinia mangostana* L., *Citrullus lanatus*, *Couroupita guianensis* (Aubl.), *Genipa americana* L. and *Prunus domestica* fruit extracts were stable for three weeks after completion of synthesis [24,60,69,70,91].

4. Characterization of GNPs

The characterization of GNPs in size, shape and other properties is very important, as these parameters determine their range of application (table 2).

4.1 Shape and size of GNPs

The optical properties of the synthesized GNPs were characterized using UV–visible spectroscopy. The position of the maximum absorption (SPR) band corresponds to the definite shape (spheres, nanorods and triangles) and size of GNPs [110,111]. When more than one dimension can be distinguished in the NP shape, the same number of SPR bands will be visible in the absorption spectrum [13,104]. According to the Mie theory, the isotropic GNPs will exhibit one SPR band, while the anisotropic GNPs will show more than one SPR band [111]. In most cases of GNPs synthesized from fruit extracts, the position of the SPR band was in the range of wavelengths that corresponds to small and large spheres [13,54]. Such GNPs were synthesized using the fruit extracts from *Terminalia arjuna*, *Solanum indicum* L., *Ananas comosus* L., *Coffea arabica* L., *Citrullus lanatus*, *Cornus mas* L., *Couroupita guianensis* (Aubl.), *Garcinia cambogia* L., *Ziziphus jujuba*, *Genipa americana* L., *Garcinia mangostana* L., *Punica granatum* L., *Lycopersian esculentum*, *Prunus domestica*, *Pyrus* L., blueberries and grape [24,43,48,56,59,60,68–71, 75,91,93,94,98,101,105]. The oblong-, cubic polyhedron-, hexagonal-, triangular-, rhomboidal-, shell- and plate-shaped GNPs were observed in synthesis from blackberries, *Artocarpus heterophyllus* (Lam.), *Averrhoa bilimbi*, *Punica granatum* L., *Couroupita guianensis* (Aubl.), *Garcinia cambogia* L., *Malus domestica* (Borkh.) and *Nitraria schoberi* L. fruit extracts [44,46,48,60,68,77,85]. The UV–visible spectroscopy results were confirmed by various microscopic methods (table 2).

The size of GNPs has also been studied by the DLS method [56,60,69,91,93]. The DLS method shows the hydrodynamic diameter of the GNPs, i.e., the diameter of NP with thickness of a capping bimolecular layer and the hydration shell [112,113]. The results from the hydrodynamic diameter of GNPs synthesized from fruit extracts revealed that the particles were not homogeneous in size and, for this reason, the values of their average size (Z-Ave) are not authoritative because of their large polydispersity [109,112].

4.2 Additional methods for GNP characterization

The X-ray diffraction (XRD) spectroscopy results have shown that GNPs are crystalline in nature [48,56,59,60,64,69,77, 101], whereas the results obtained using cyclic voltammetry (CV) concluded that shifting of the cathodic peak to the negative potential is caused via biomolecules from fruit extracts, thereby stabilizing GNPs [96].

The differential scanning calorimetry (DSC) method has been utilized to study the impact of temperature on the *Cornus mas* L. fruit extract following GNP synthesis [59]. The DSC results showed temperature-dependent processes related to the decomposition of the organic molecules from fruit extracts, crystalline rearrangements in the GNPs and characteristic transformations in fruit extracts. This could exert a specific influence of the GNPs on the stabilizing biomolecules [59]. Unfortunately, the lack of recent studies makes it difficult to fully interpret the preliminary results.

The thermogravimetric analysis (TGA) studies have been performed to test the thermal stability of GNPs [48,71,77]. The TGA and DSC results exhibit differences in the interpretation of temperature ranges of approximately 300°C, which should be considered.

4.3 Parameters of synthesis that affected size and shape of GNPs

The well-known factors that can affect GNP formation are reagent concentration, temperature, reaction time and pH [33].

The influence of reagent concentration on GNP synthesis using *Solanum indicum* L. has been observed [98]. The process was more effective when the concentration of the fruit extract and/or HAuCl₄ solution was increased. The temperature is the second factor that has a strong influence on synthesis process results. Increased temperature speeds up the process and makes it more effective [91,98]. Additionally, the rapid synthesis process could affect the size and shape of GNPs [46]. It has been observed that when the synthesis process is faster the size and anisotropic nature of the GNPs increase [46,68].

The GNPs size and shape are strongly dependent on the pH of the synthesis process [94]. The GNPs synthesized from the *Pyrus* L. extract at acidic, normal and alkaline pH showed triangular, spherical and hexagonal; plate-like and spherical and hexagonal and triangular shapes, respectively. The differences in the size of the synthesized GNPs were from 10 to 500 nm, depending on the pH range [94]. In contrast, Ganeshkumar *et al* [93] did not find a correlation between the pH, temperature, time of sample storage and the size and shape of the GNPs synthesized from the *Punica granatum* L. fruit extract. Interestingly, it is opposite to the results obtained previously for biosynthesized GNPs [45,86,93,114–117]. It has been shown that stability of GNPs synthesized from fruit extracts was independent of pH [91,93,94].

5. Potential applications of GNPs synthesized using fruit extracts

5.1 Application of GNPs as antibiotics or in anticancer therapy

The synthesized GNPs are useful for multiple biomedical applications, particularly in testing pharmaceutical level antibacterial activity. Commercially available antibiotics become less and less effective because of bacteria immunization, hence, searching for new generation antibiotics becomes critical [31,106].

GNPs synthesized from the *Terminalia arjuna* fruit extract did not exhibit antibacterial activity against four strains of bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, *Proteus vulgaris* and *Klebsiella pneumonia* [101]. However, GNPs synthesized from the *Ziziphus jujuba* and grape fruit extracts have exhibited antibacterial activities against the following bacteria *Staphylococcus aureus*, *Citrobacter koseri*, *Bacillus cereus*, *Pseudomonas aeruginosa* and *Escherichia coli* [71,105]. The concentration of GNPs synthesized using the *Ziziphus jujuba* fruit extract significantly influenced their antibacterial activities. With the increased GNP concentration, the diameter of the zone of inhibition increased as well. The GNPs synthesized from the grape fruit extract have the best antibacterial activity against *Citrobacter koseri*. Interestingly, in both antibacterial tests, Ciprofloxacin was used as a positive control. Compared with the diameter of the zone of inhibition, it was shown that antibacterial activity against *Staphylococcus aureus* of GNPs synthesized from the *Ziziphus jujuba* fruit extract was greater than that of Ciprofloxacin.

The antibacterial activity of GNPs is dependent not only on the bacterial strains but also on the shape, size and concentration of the GNPs [13,103,118,119]. The observed effect is dependent on the specificity of the interaction between the GNPs, the capping biomolecules and the outer cell wall of the bacteria [13]. Some testing have shown that GNPs have weak antibacterial activity, probably due to low concentration, but when GNPs are in contact with other substances, their antibacterial activity increases [120]. The antibacterial tests for GNPs synthesized from the *Ananas comosus* L. and *Artocarpus heterophyllus* (Lam.) fruit extracts are examples of this phenomenon [43,44]. The antibacterial activity of GNPs was examined for three kinds of antibiotics: ampicillin, penicillin and bavistin. The tests were carried out against bacteria: *Aspergillus flavus*, *Aspergillus niger*, *Escherichia coli* and *Streptobacillus*. The results revealed increased antibacterial activity for the combination of the antibiotics and GNPs compared with the antibiotics alone. The exception is the bacterium *Aspergillus flavus* where no activity was observed. Bavistin alone and bavistin with GNPs exhibited activity only against *Aspergillus niger*. Ampicillin and penicillin, and their combination with GNPs showed activity against *Escherichia coli* and *Streptobacillus*. The differences in antibacterial activities of the pure antibiotics and those combined with the GNPs

are slight, but there is a trend towards increased effects in each of the discussed cases.

New nanomaterials are often tested for cytotoxicity. If the acquired nanomaterial is to be used as a next generation medicine, e.g., in anticancer therapy, a strong cytotoxic effect will be expected. The cytotoxicities of the GNPs synthesized using the *Solanum indicum* L. and *Genipa americana* L. fruit extracts have been tested [70,87]. The (3-(4,5-Dimethylthiazolyl-2)-2,5-Diphenyltetrazolium bromide) cell proliferation assay (MTT) was used to assess cytotoxicity of GNPs on HeLa and MCF-7 cell lines (human cervical cancer and human breast cancer). After treatment of HeLa and MCF-7 cells with GNPs, it was found that cellular morphology did not change. The tests were carried out for different GNP concentrations. Both cell lines sustained viability when the concentration of GNPs was greater than 100 M, thereby concluding that the synthesized GNPs were not cytotoxic. Whereas, for the GNPs synthesized from the grape fruit extract, cytotoxicity was observed for HeLa cells using the MTT test [71]. Approximately, 60 mg ml⁻¹ of GNP concentration was sufficient to obtain 50% inhibition of viability (IC₅₀).

It is a noteworthy observation regarding the relationship between GNP concentration and their effect. Furthermore, it appears that GNP cytotoxicity tests are similar to antibacterial tests, i.e., concentration, size and shape of GNP dependency. It has been previously noted that GNP size influences cytotoxicity [121].

5.2 Application of GNPs in drug delivery

It has been proposed to apply the GNPs synthesized from the *Punica granatum* L. fruit extract in drug delivery [93]. The GNPs were functionalized via the 5-fluorouracil and folic acid. The percentage of haemolytic activity strongly depends on the GNP concentration. It was concluded that haemolytic activity less than 5% would be suitable for *in vitro* applications [93]. *In vitro* studies have been revealed fast release of 5-fluorouracil from the folic acid-GNPs over the first hour, then a slow and constant release over 47 h. The toxicity of GNPs has also tasted. The survival rate and morphology changes of zebrafish larvae affected by free 5-fluorouracil, folic acid-GNPs and folic acid-GNPs with the absorbed 5-fluorouracil have been taken into consideration. The embryo survival percentage decreased with the increased concentration of the 5-fluorouracil and the folic acid-GNPs with the absorbed 5-fluorouracil. Additionally, cytotoxicity tests (MTT) for the MCF-7 cells showed that folic acid-GNPs with the absorbed 5-fluorouracil had a lower IC₅₀ than free 5-fluorouracil.

The presented results show a very promising alternative in drug delivery application. Moreover, since folic acid is the specific ligand of the folic acid receptor, which is present on the cell membrane, the obtained results may provide new potential for anticancer therapy [122,123].

5.3 Application of GNPs as drugs

The GNPs synthesized from the *Cornus mas* L. fruit extract have been tested as a component of psoriatic skin lesion cream [59]. Cortisone cream is currently available as an effective treatment, but it cannot be used for extended periods of time, and some patients are unable to tolerate it. In these instances, an emollient cream is used. The effect of the emollient cream, cortisone cream and cream with the GNPs has been examined on patients with psoriatic lesions. The effects of the creams were tested on two parts of the patients' skin: the epidermis and derma. As expected, the best effect was acquired using the cortisone cream. The application of the emollient cream at the epidermis and derma levels did not have an effect. A positive anti-inflammatory effect was observed mainly at the dermis level for cream with the GNPs. As the emollient cream did not show increased therapeutic effects, the cream with GNPs may be a viable alternative for patients with psoriatic lesions.

5.4 Application of GNPs in agriculture

Possible applications of GNPs in the field of agriculture crops and seed germination of endangered plant species have been proposed [101]. The impact of GNPs synthesized using the *Terminalia arjuna* fruit extract on seed germination and vegetative growth of *Gloriosa superba* has been examined. It was found that the GNPs had a positive influence on seed germination, node elongation and vegetative growth. This was based on the comparative observations of seeds not treated with GNPs. There was a strong dependence between the GNP concentration and seed germination and vegetative growth of *Gloriosa superba*.

5.5 Application of GNPs in catalysis

It has been proposed to apply GNPs synthesized from *Garcinia cambogia*, *Lycopersicon esculentum* and *Prunus domestica* L. as catalytic agents and colorimetric sensors [68,75,91]. The catalytic activity of GNPs is well-known [124–126]. The catalytic activity of the GNPs synthesized from the *Garcinia cambogia* L. and *Prunus domestica* fruit extracts against toxic 4-nitrophenol was studied [68,91]. It was demonstrated that the catalytic activity of GNPs synthesized from *Garcinia cambogia* L. depends on their shape and size [68]. Sodium dodecyl sulphate (SDS)-stabilized GNPs synthesized from *Lycopersicon esculentum* were proposed as colorimetric sensors for pesticide detection (methyl parathion) [75]. The pesticide, after catalytic hydrolysis in alkaline medium, produced the 4-nitrophenolate ions. The new signal in the UV–visible spectrum at approximately 400 nm was potentially due to the 4-nitrophenolate ions.

6. Conclusion

Biosynthesis of GNPs using plant extracts is a well-known eco-friendly, time-saving, non-laborious and cheap process,

while GNPs synthesized using fruit extracts are relatively a new field in nanotechnology.

Fruit extracts have a strong ability to reduce gold ions to metallic gold. This is due to large concentration of substances such as flavonoids, flavonoid glycosides, saccharides, proteins and vitamins, which possess reductant properties. Fruit extracts are useful not only because of their reduced environmental impact, but also because they can produce high amounts of GNPs. Compared with the use of fruit extracts and whole plant extracts, the use of fruit extracts is cheaper, simpler and more effective. For these reasons, fruit extract-mediated synthesis of GNPs has attracted attention during recent years. Rapid and non-complicated processes of synthesis from fruit extract yield GNPs of various sizes and shapes. Unfortunately, currently used GNP synthesis methods from fruit extracts give a wide range of GNP size distribution. In the future, improved procedures are needed to better define the size of GNPs, as well-defined size is crucial in biomedical applications, specifically on the antibacterial and cytotoxic impact of GNPs.

Fruit extracts, like whole plant extracts may stabilize GNPs. Stabilized GNPs produced using fruit extracts are free from contamination. Despite this, procedures that prolong the GNP stabilization are needed.

Properties of GNPs synthesized from fruit extracts make them an interesting nanomaterial, providing advanced applications as new generation antibiotics, drug delivery, environmental protection, catalysts of the reduction reaction and agriculture.

References

- [1] Mittal A K, Chisti Y and Banerjee U Ch 2013 *Biotechnol. Adv.* **31** 346
- [2] Youns M, Hoheisel J D and Efferth T 2011 *Curr. Drug Targets.* **12** 357
- [3] Pauwels E K and Erba P 2007 *Drug News Perspect.* **20** 213
- [4] Gindy M E and Prud'homme R K 2009 *Expert Opin. Drug Deliv.* **6** 865
- [5] Sperling R A, Rivera Gil P, Zhang F, Zanella M and Parak W J 2008 *Chem. Soc. Rev.* **37** 1896
- [6] Boisselier E and Astruc D 2009 *Chem. Soc. Rev.* **38** 1759
- [7] Arvizo R R, Bhattacharyya S, Kudgus R, Giri K, Bhattacharya R and Mukherjee P 2012 *Chem. Soc. Rev.* **41** 2943
- [8] Turkevich J, Stevenson P C and Hillier J 1951 *Discuss Faraday Soc.* **11** 55
- [9] Kimling J, Maier M, Ovenke B, Kotaidis H, Ballot H and Plech A 2006 *J. Phys. Chem. B* **110** 15700
- [10] Nikov R G, Nikolov A S, Nedyalkov N N, Dimitrov I G, Atanasov P A and Alexandrov M T 2012 *Appl. Surf. Sci.* **258** 035016
- [11] Ngo V K T, Nguyen D G, Huynh T P and Lam Q V 2016 *Adv. Nat. Sci.: Nanosci. Nanotechnol.* **7** 17
- [12] Yang S, Wang Y, Wang Q, Zhang R and Ding B 2007 *Colloids Surf. A* **301** 174
- [13] Timoszyk A, Niedbach J, Śliżewska P, Mironczyk A and Koziol J J 2017 *J. Nano Res.* **48** 114

- [14] Pantidos N and Horsfall L E 2014 *Nanomed. Nanotechnol.* **5** 233
- [15] Castro L, Blázquez L, Muñoz J A, González F G and Ballester A 2014 *Rev. Adv. Sci. Eng.* **3** 1
- [16] Sintubin L, De Windt W, Dick J, Mast J, van der Ha D, Verstraete W *et al* 2009 *Appl. Microbiol. Biotechnol.* **84** 741
- [17] Ahmad A, Mukherjee P, Senapati S, Mandal D, Khan M I, Kumar R *et al* 2003 *Colloids Surf. B* **28** 313
- [18] Rai M, Yadav A and Gade A 2009 *Biotechnol. Adv.* **27** 76
- [19] Bar H, Bhui D K, Sahoo G P, Sarkar P, De S P and Misra A 2009 *Colloids Surf. A* **339** 134
- [20] Irvani S and Zolfaghari B 2013 *Biomed. Res. Int.* **2013** 1
- [21] Malarkodi Ch, Rajeshkumar S, Vanaja M, Paulkumar K, Gnanajobitha G and Annadurai G 2013 *J. Nanostruct. Chem.* **3** 30
- [22] Makarov V V, Love A J, Sinitsyna O V, Makarova S S, Yaminsky I V, Taliansky M E *et al* 2014 *Acta Nat.* **1** 35
- [23] Srivastava S K, Yamada R, Ogino Ch and Kondo A 2013 *Nanoscale Res. Lett.* **8** 70
- [24] Gan P P, Ng S H, Huang Y and Li S F Y 2012 *Bioresour. Technol.* **113** 132
- [25] Maiti S, Barman G and Laha J K 2014 *Int. J. Sci. Eng. Res.* **5** 1226
- [26] Khan M R and Rizvi T F 2014 *Plant Pathol. J.* **13** 214
- [27] Rana S, Bajaj A, Mout R and Rotello V M 2012 *Adv. Drug Deliv. Rev.* **64** 200
- [28] Murphy C J, Gole A M, Stone J W, Cisco P N, Alkilany A M, Goldsmith E C *et al* 2008 *Acc. Chem. Res.* **41** 1721
- [29] Alkilany A M and Murphy C J 2010 *J. Nanopart. Res.* **12** 2313
- [30] Shah M, Fawcett D, Sharma S, Tripathy S K and Poinern G E J 2015 *Materials* **8** 7278
- [31] Vadlapudi V and Kaladhar D S V G K 2014 *Middle-East J. Sci. Res.* **19** 834
- [32] Shankar S S, Ahmad A, Pasricha R and Sastr M 2003 *J. Mater. Chem.* **13** 1822
- [33] Mittal J, Batra A, Singh A and Sharma M M 2014 *Adv. Nat. Sci.: Nanosci. Nanotechnol.* **5** 043002
- [34] Kumar V and Yadav S K 2008 *J. Chem. Technol. Biotechnol.* **84** 151
- [35] Santhoshkumar, Rajeshkumar S and Venkat Kumar S 2017 *Biochem. Biophys. Rep.* **11** 46
- [36] Jayaseelan C, Ramkumar R, Rahman A A and Perumal P 2013 *Ind. Crop. Prod.* **45** 423
- [37] Majumdar R, Bag B G and Maity N 2013 *Int. Nano Lett.* **3** 53
- [38] Andeani J K, Kazemi H, Mohsenzadeh S and Safavi A 2011 *Digest J. Nanomater. Biostructures* **6** 1011
- [39] Kirubha R and Alagumuthu G 2014 *Int. J. Pharm.* **4** 195
- [40] Parida U K, Bindhani B K and Nayak P L 2011 *WJNSE* **1** 93
- [41] Chandran S P, Chaudhary M, Pasricha R, Ahmed A and Sastry M 2006 *Biotechnol. Prog.* **22** 577
- [42] Shen D S, Mathew J and Philip D 2011 *Spectrochim. Acta A* **79** 254
- [43] Basavegowda N, Sobczak-Kupiec A, Malina D, Yathirajan H S, Keerthi V R, Chandrashekar N *et al* 2013 *Adv. Mater. Lett.* **4** 332
- [44] Basavegowda N, Kumar G D, Tyliczszak B, Wzorek Z and Sobczak-Kupiec A 2015 *Ann. Agric. Environ. Med.* **22** 84
- [45] Armendariz V, Herrera I, Peralta-Videa J R, Jose-Yacamán M, Troiani H, Santiago P *et al* 2004 *J. Nanopart. Res.* **6** 377
- [46] Rimal Isaac R S, Sakthivel G and Murthy Ch 2013 *J. Nanotechnol.* **906592** 1
- [47] Radha R, Murugalakshmi M and Kokila Rani S 2016 *Int. J. Interdiscip. Res.* **2** 306
- [48] Nadagouda M N, Iyanna N, Lalley J, Han Ch, Dionysiou D D and Varma R S 2014 *ACS Sustainable Chem. Eng.* **2** 1717
- [49] Kumar P, Singh P, Kumari K, Mozumdar S and Chandra R 2011 *Mater. Lett.* **65** 595
- [50] Vilchis-Nestor A R, Sánchez-Mendieta V, Gómez-Espinosa R M, Camacho-López M A and Arenas-Alatorre J A 2008 *Mater. Lett.* **62** 3103
- [51] Das R K, Borthakur B B and Bora U 2010 *Mater. Lett.* **64** 1445
- [52] Dwivedi A D and Gopal K 2010 *Colloids Surf. A* **369** 27
- [53] Liu Q, Liu H, Yuan Z, Wei D and Ye Y 2012 *Colloids Surf. B* **92** 348
- [54] Smitha S L, Philip D and Gopchandran K G 2009 *Spectrochim. Acta A* **74** 735
- [55] Sujitha M V and Kannan S 2013 *Spectrochim. Acta A* **102** 15
- [56] Reddy Bogireddy N K, Martinez Gomez L, Osorio-Roman I and Agarwal V 2017 *Adv. Nano Res.* **5** 253
- [57] Narayanan K B and Sakthivel N 2010 *Mater. Charact.* **61** 1232
- [58] Narayanan K B and Sakthivel N 2008 *Mater. Lett.* **62** 4588
- [59] Olenic L and Chiorean I 2015 *Int. J. Latest Res. Sci. Technol.* **4** 16
- [60] Sathishkumar G, Pradeep K J, Vignesh V, Rajkuberan C, Jeyaraj M, Selvakumar M *et al* 2016 *J. Molec. Liq.* **215** 229
- [61] Vijayakumar R, Devi V, Adavallan K and Saranya D 2011 *Phys. E* **44** 665
- [62] Shalaby T I, Shams El-Dine R S and Abd El-Gaber S A 2015 *Nanosci. Nanotechnol.* **5** 89
- [63] Sneha K, Sathish Kumar M, Lee S Y, Bae M A and Yun Y S 2011 *J. Nanosci. Nanotechnol.* **11** 1811
- [64] Shankar S S, Rai A, Ahmad A and Sastry M 2005 *Chem. Mater.* **17** 566
- [65] Ghosh S, Patil S, Ahire M, Kitture R, Jabgunde A, Kale S *et al* 2011 *J. Nanomater.* **354793** 1
- [66] Song Y, Jang H K and Kim B S 2009 *Process Biochem.* **44** 1133
- [67] Annamalai A, Christina V L, Sudha D, Kalpana M and Lakshmi P T 2013 *Colloids Surf. B* **108** 60
- [68] Rajan A, Meena Kumari M and Philip D 2014 *Spectrochim. Acta A* **118** 793
- [69] Lee K X, Shameli K, Miyake M, Kuwano N, Khairudin N B B T A, Mohamad S E B T *et al* 2016 *J. Nanomater.* **8489094** 1
- [70] Kumar B, Smita K, Cumbal L, Camacho J, Hernández-Gallegos E, De Guadalupe Chávez-López M, Grijalva M *et al* 2016 *Mater. Sci. Eng. C* **62** 725
- [71] Lokina S and Narayanan V 2013 *Chem. Sci. Trans.* **2** S105
- [72] Yasmin A, Ramesh K and Rajeshkumar S 2010 *Nano Convergence* **1** 1
- [73] Philip D 2010 *Phys. E* **42** 1417
- [74] Kasthuri J, Veerapandian S and Rajendiran N 2009 *Colloids Surf. B* **68** 55
- [75] Barman G, Maiti S and Konar Laha J 2013 *Nanoscale Res. Lett.* **8** 181
- [76] Aromal S A, Vidhu V K and Philip D 2012 *Spectrochim. Acta A* **85** 99

- [77] Lokina S and Narayanan V 2017 *Int. J. Pharm. Bio. Sci.* **8** 203
- [78] Philip D 2010 *Spectrochim. Acta A* **77** 807
- [79] Muralikrishna T, Malothu R, Pattanayak M and Nayak P L 2014 *World J. Nano Sci. Technol.* **3** 66
- [80] Gardea-Torresdey L, Persons J G, Gomez E, Peralta-Videa J, Troiani H E, Santiago P *et al* 2002 *Nano Lett.* **2** 397
- [81] Elavazhagan T and Arunachalam K D 2011 *Int. J. Nanomed.* **6** 1265
- [82] Ali D M, Thajuddin N, Jeganathan K and Gunasekaran M 2011 *Colloids Surf. B* **85** 360
- [83] Vankar P S and Bajpai D 2010 *Ind. J. Biochem. Biophys.* **47** 157
- [84] Philip D, Unni C, Aromal S A and Vidhu V K 2011 *Spectrochim. Acta A* **78** 899
- [85] Rad M S, Sharifi J, Heshmati G A, Miri A and Jyoti Sen D 2013 *Am. J. Adv. Drug Deliv.* **1** 174
- [86] Philip D 2011 *Phys. E* **43** 1318
- [87] Khalil M M H, Ismail E H and El-Magdoub F 2012 *Arabian J. Chem.* **5** 431
- [88] Elia P, Zach R, Hazan S, Kolusheva S, Porat Z and Zeiri Y 2014 *Int. J. Nanomed.* **9** 4007
- [89] Ankamwar B, Damle C, Ahmad A and Sastry M 2005 *J. Nanosci. Nanotechnol.* **5** 1665
- [90] Babu P J, Sharma P, Kalita M C and Bora U 2011 *Front. Mater. Sci.* **5** 379
- [91] Dauthal P and Mukhopadhyay M 2012 *Ind. Eng. Chem. Res.* **51** 13014
- [92] Raghunandan D, Basavaraja S, Mahesh B, Balaji S, Manjunath S and Venkataraman A 2009 *Nanobiotechnology* **5** 34
- [93] Ganeshkumar M, Sathishkumar M, Ponrasu T, Dinesh M G and Suguna L 2013 *Colloids Surf. B* **106** 208
- [94] Ghodake G S, Deshpande N G, Lee Y P and Jin E S 2010 *Colloids Surf. B* **75** 584
- [95] Ghoreishi S M, Behpour M and Khayatkashani M 2011 *Phys. E* **44** 97
- [96] Naruzi M, Zare D, Khoshnevisan K and Davoodi D 2011 *Spectrochim. Acta A* **79** 1461
- [97] Dubey S P, Lahtinen M and Sillanpää M 2010 *Colloids Surf. A* **364** 34
- [98] Babu P J, Sharma P, Saranya S, Tamuli R and Bora U 2013 *Nanomater. Nanotechnol.* **3** 1
- [99] Dubey S P, Lahtinen M, Särkkä H and Sillanpää M 2010 *Colloids Surf. B* **80** 26
- [100] Dubey S P, Lahtinen M and Sillanpää M 2010 *Process Biochem.* **45** 1065
- [101] Gopinath K, Gowri S, Karthika V and Arumugam A 2014 *J. Nanostruct. Chem.* **4** 115
- [102] Kumar K M, Mandal B K, Sinha M and Krishnakumar V 2012 *Spectrochim. Acta A* **86** 490
- [103] Geethalakshmi R and Sarada D L V 2012 *Int. J. Nanomed.* **7** 5375
- [104] Aromal S A and Philip D 2012 *Spectrochim. Acta A* **97** 1
- [105] Kirubha R and Alagumuthu G 2014 *World J. Pharma. Sci.* **2** 146
- [106] Gupta A, Landis R F and Rotello V M 2016 *F1000 Res.* **5** 364
- [107] Shankar S S, Rai A, Ankamwar B, Singh A, Ahmad A and Sastry M 2004 *Nat. Mater.* **3** 482
- [108] Shankar S S, Ahmad A, Pasricha R and Sastry M 2003 *J. Mater. Chem.* **13** 1822
- [109] Muangnapoh T, Sanon N, Yusa S-I, Viriya-Empikul N and Charinpanitkul T 2010 *Curr. Appl. Phys.* **10** 708
- [110] Jain P K, Lee K S, El-Sayed I H and El-Sayed M A 2006 *J. Phys. Chem.* **110** 7238
- [111] Das A K and Raj C R 2011 *J. Colloid Interface Sci.* **353** 506
- [112] Philip D 2008 *Spectrochim. Acta A* **71** 80
- [113] Toy R, Hayden E, Shoup Ch, Baskaran H and Karathanasis E 2011 *Nanotechnology* **22** 115101
- [114] Zhang X, Yan S, Tyagi R D and Surampalli R Y 2011 *Chemosphere* **82** 489
- [115] He S, Guo Z, Zhang Y, Zhang S, Wang J and Gu N 2007 *Mater. Lett.* **61** 3984
- [116] Konishi Y, Tsukiyama T, Tachimi T, Saitoh N, Nomura T and Nagamine S 2007 *Electrochim. Acta* **53** 186
- [117] Gericke M and Pinches A 2006 *Hydrometallurgy* **83** 132
- [118] Shamailla S, Zafar N, Riaz S, Sharif R, Nazir J and Naseem S 2016 *Nanomaterials* **6** 71
- [119] Balakumaran M D, Ramachandran R, Balashanmugam P, Mukeshkumar D J and Kalaichelvan P T 2016 *Microbiol. Res.* **182** 8
- [120] Payne J R, Waghwan H K, Connor M G, Hamilton W, Tockstein S, Moolani H *et al* 2016 *Front. Microbiol.* **7** 607
- [121] Pan Y, Neuss S, Leifert A, Fischler M, Wen F, Simon U *et al* 2007 *Small* **3** 1941
- [122] Hilgenbrink A R 2005 *J. Pharm. Sci.* **94** 2135
- [123] Kim H, Jo A, Baek S, Lim D, Park S-Y, Cho K *et al* 2017 *Sci. Rep.* **7** 1
- [124] Hvolbæk B, Janssens T V, Clausen B S, Falsig H, Christensen C H and Nørkov J K 2007 *Nanotoday* **2** 14
- [125] Li G and Jin R 2013 *Nanotechnol. Rev.* **2** 529
- [126] Ma T, Yang W, Liu S, Zhang H and Liang F 2017 *Catalysts* **7** 1