Biomedical Applications of Green Synthesized-Metallic Nanoparticles: A Review

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Advances in the field of nanoscience and nanotechnology to modulate materials at nanoscale level has continued to have great impact on different disciplines of science and engineering as well as agriculture and medical fields. The surge in the utilization of benign and non-toxic biomolecules to engineer enhanced biocompatible nanomaterials has contributed to a large extent to the applications of nanomaterials in healthcare; an emerging sub-discipline termed nanomedicine. Among the several nanomaterials that have been produced, metallic nanoparticles occupy prime position owing to their optical, catalytic and biological characteristics. These nanoparticles, which are of different types existing singly as monometallic nanoparticles or in two or more metals as alloys have found extremely useful applications as antimicrobial, antioxidant, anticancer, antidiabetic, anticoagulant and thrombolytic agents amongst others. In this review, an attempt is made to project the different applications of green synthesized metallic nanoparticles in diverse areas of biomedicine, including the discussion of issues of toxicity and prospects of nanotechnology in biomedical field.

Keywords: Biomedicine, green synthesis, nanoparticles, nanomedicine, nanoscience, nanotechnology
1.0 INTRODUCTION

Nanotechnology is a current field of science that deals with handling of materials at the nanoscale. This branch of science has been evolving intensely and plays a central role in daily life as a result of the influence of their vast applications in all circles of human life. It is a field that deals with several structures of matter that have sizes in the order of a billionth (10⁻⁹) of a meter [1]. Nanotechnology comprises the creation, characterization including manipulation of components that have in any case one of its dimensions in the region of 1-100 nm in length. When the sizes of particle decrease lower than this dimension, the resultant material has its physical and chemical attributes transformed to make it different greatly from macroscale components [2].

Nanomaterials represent the major tools of nanotechnological applications, and such include nanowires, nanotubes, nanoflowers, nanocomposites, and nanoparticles which have been extensively studied, and fabricated through various processes involving manipulations to various sizes and shapes to fit into specific applications of desire. Nanomaterials include natural, incidental/byproducts or manufactured substances comprising particles, in a loose condition or as an agglomerate or as an aggregate and where, at least 50% accounted for the particles, and if any of the external dimensions are in the size range 1-100 nm [3]. Nanomaterials have properties that have made them extremely useful in biosensing, biological labeling, catalysis, antibacterial activity, antiviral activity, drug delivery, antioxidant applications, DNA sequencing and gene therapy in the recent years [4-8]. Owing to these valuable properties, nanomaterials have been employed for applications in electronics, catalysis, photonics, information technology, environmental remediation, cosmetics, drug delivery, biomedical, optics, chemical industries, mechanics, space industries, light emitters, energy science, non-linear optical tools and single electron transistors. Functionalization of nanomaterials enables directed delivery, transportation and distribution of nanoparticles to specific cell types, and this makes them particularly useful in gene delivery, bioimaging, and other diagnostic and therapeutic applications [9].

There exist a variety of nanoparticles but majorly metallic and non-metallic nanoparticles are widely recognized. Examples of such non-metallic nanoparticles are carbon, silicon, nitric oxide, chitosan, fullerences, and graphene oxide nanoparticles among others while some of the widely investigated metallic and metal oxide nanoparticles include cobalt, titanium, aluminium oxide, copper, silver, palladium, magnesium, manganese oxide, platinum, zinc oxide, magnetite and cerium dioxide [3, 7, 10]. Among these, metal nanoparticles are almost certainly the most studied and scientifically explored due to their exceptional properties that are attributable to elevated surface-to-volume ratio and metal specificities in activities at the nanoscale [11, 12].

The metallic nanoparticles, in relation to their exceptional surface, optical, chemical, biological, resonance, catalytic, and electronic properties have formed a central point of research these contemporary times, with foremost attention on biosynthesis and novel applications [13-20]. There are many techniques of synthesizing nanoparticles, and they can be largely described as ‘wet or dry processes’. Wet methods of synthesis are frequently referred to as “bottom-up” synthetic method since nanoparticles are assembled atom-by-atom through a process of nucleation while dry methods of synthesis are usually recognised as “top-down” methods since they embroil breaking down bulk compound into nanoparticles [21]. Numerous methods have been exploited for the synthesis of nanoparticles which include sono-chemical, laser irradiation, laser ablation, solvothermal, sputter deposition, and biological methods. However, biological synthesis remains the widely acceptable alternative that has received unrivalled focus [22]. The biological mode of creation of nanomaterials has led to the emergence of the sub-discipline of ‘green nanotechnology’. Green nanotechnology is described as the use of green chemistry, green engineering, and sustainability codes to eradicate or decrease the application and generation of lethal substances in the field of nanotechnology [23]. The emergence of green nanotechnology leading to biofabrication of biocompatible and less toxic nanomaterials has led to the upsurge in their applications in biomedicine. The present review chronicles some of the important biomedical applications of nanoparticles to guarantee improved healthcare delivery.

2.0 GREEN SYNTHESIS OF METALLIC NANOPARTICLES

Progresses in nanotechnology have advanced immensely from physical and chemical-based synthetic methods amongst which are pyrolysis, ablation, lithography, sol-gel technique, chemical vapor deposition, and electrodeposition. These methods are very costly and generate hazardous substances. However, green synthesis using biological molecules as means of bioreduction in the synthesis of metallic nanoparticles however has received wide approval and patronage, and would keep defining milestones in green nanotechnology.
due to the wide availability of probable biological agents [24]. Since the conventional chemical and physical methods of synthesis includes procedures involving toxic solvents, high energy and pressure which may be detrimental to the environment, biological methods offers a way out of these encounters in that it involves routes that are environmentally non-threatening. It is beneficial over chemical and physical methods because it is safe, modest, economical, quite reproducible, and often results in more stable materials [7].

Although chemical syntheses have some plusses, the application of toxic chemicals on the surface of nanoparticles and non-polar solvents in the procedure limits their applications especially in clinical fields. Therefore, several researchers endeavoured to develop unpolluted, biocompatible, non-toxic and eco-friendly techniques for nanoparticles synthesis [25]. The biological synthesis of nanoparticles has being carried out using different biomaterials such as bacteria [19, 20, 22, 26, 27], fungi and yeast [28, 29], microalgalae [30], arthropods and their exudates [8, 13, 14], enzymes [18, 31 -34] and plant biomass/extract [15-17, 35-42]. These biosynthesized nanomaterials have prospective applications in diverse areas such as diagnosis and treatment, development of surgical nanodevices and manufacturing of commercial products [43].

Cheviron et al [44] have identified three general aspects for consideration in green synthesis, these are; availability of solvent medium, use of non-toxic reductants, and environmentally safe nanoparticle stabilizers. These conditions have been sufficiently met using biological route of synthesis; thus the fabrication of nanoparticles via green route has attracted special attention of scientists worldwide for different applications. In addition, large-scale production of nanoparticles could be effortlessly achieved through this means. The wealth of biomolecules that can serve as bioreductants in the biofabrication of nanoparticles in various living things also contributes immensely to the growing development in green nanotechnology [7, 8, 15]. Extracts from different parts of plants (root, stem bark, leaf, fruit, flower and seed) encompass ample natural biomolecules such as flavonoids, alkaloids, saponins, vitamins, organic acids, pigments, tannins, steroids, and other nutritional compounds that serve the dual purpose of bioreduction and capping/stabilization in one-pot synthesis of metallic nanoparticles, making the technique to be facile. Plants have been used effectively in the biosynthesis of various nanoparticles such as cobalt, silver, gold, palladium, platinum, copper, zinc oxide, and magnetite [7, 45].

Nanoparticles have also been fruitfully biosynthesized by a range of agrowastes such as Cocos nucifera coir, corn cob, fruit seeds and peels, pod husks, bran, and palm oil mill effluent [7, 16, 36, 46, 47]. Also, enzyme-mediated biosynthesis of nanoparticles is a recent development in the biosynthetic field of nanotechnology. In most cases, active enzymes catalyse the creation of nanoparticles; however in some situations, enzymes can be denatured to discharge amino acids which in turn act as reducing and stabilizing agents in the creation of nanoparticles. Pure α-amylase, nitrate reductase, laccase, cellulase, ligninase, sulfite reductase, and crude keratinase [7, 18, 31]. Also, recently, the first references to xylanase for enzymatic synthesis of silver, gold and silver-gold alloy nanoparticles have been reported from our laboratory [32-34]. Pigments acquired from plants and microorganisms have been used for the biosynthesis of nanoparticles which have been testified to have some biological properties which make them appropriate for biomedical uses. Some previously reported include, cochineal [48], flexirubin [49], Streptomyces coelicolor klm pigment[33] [50], mel-anin, phycocyanin, actinorhodin, fucoxanthin, and C-phycocerythrin [7]. Moreover, biopolymers such as nucleic acids, proteins, and polysaccharide are decomposable or recyclable polymers which are obtained from organic materials and can be employed to bioproduce metallic nanoparticles. Some of the biopolymers that have been recounted for biosynthesis of nanoparticles are, chitosan for AgNPs and CuNPs [51], pectin for AgNPs [52], gelatin/pectin for PdNPs [53], crab shell for AgNPs [54], and gelatin for ZnO-NPs, and starch for CeO$_2$-NPs and CuO-NPs [55].

3.0 CHARACTERIZATION OF METALLIC NANOPARTICLES

Nanoparticles are characteristically categorized by their size, surface area, shape and dispersity nature. The common procedures implemented in their characterization are UV-visible spectrophotometry, Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), X-ray diffraction (XRD), dynamic light scattering and energy dispersive X-ray spectroscopy (EDX). The development of various metallic nanoparticles from their precursor metal salts gives representative peaks at different absorptions that can be examined using UV-visible spectrophotometry. For instance, noble metallic nanoparticles like Ag and Au absorb strongly within the visible region producing Amax of 400-450 nm and 500-560 nm, respectively, as a function of surface plasmon resonance (SPR) phenomenon occurring in metallic nanoparticles [56].
SPR originates from the resonant combined oscillations of the conduction electrons along the transversal pathway of the electromagnetic field. SPR band intensity and band width are predisposed by the dielectric constant of the medium, particle shape, and temperature [9]. Hence, UV-vis spectrophotometry examination is typically the first practice in characterization of metallic nanoparticles to monitor the formation of nanoparticles [56]. On making contact with the metal salt, the colour of biomolecular extract suspension employed for the synthesis changes and this is due to excitation of surface plasmon vibrations in the metal nanoparticles. The arrays of colour that developed depend on number of factors that include nature of the bioreductant, the mixing ratio and the particle size. Investigating the suspension using UV-vis spectrophotometry typically reveals a band having a determinable adsorption peak and from which the formation of respective metal can be confirmed. A progressive rise in the characteristic peak with increased reaction time and ratio of concentration of biomolecular extract with respect to the metallic salt solution clearly indicates the formation of nanoparticles [9]. A typical UV-vis spectrum in the bioformation of AgNPs is shown in Figure 1.

Fourier transform infrared (FTIR) spectroscopy is a surface chemical analytical method, which evaluates the infrared intensity against wave-number or wavelength of light. The nature of the functional groups and their participation through the bioreduction process can be roughly estimated using the FTIR spectroscopy [57]. The identification of the biomolecules involved in bioreduction is vital to develop new pathways in synthesis of nanoparticles. Generally, FTIR spectrum of crude extract and that of synthesized nanoparticles will be compared to collect facts about functional groups accountable for bioreduction. Figure 2 showed a typical spectrum of biosynthesized AgNPs. The X-ray diffraction (XRD) system is used to understand the structural information about crystalline nature of metallic nanoparticle. The X-rays can penetrate deep into the materials and give relevant information about the structure of the bulk. If the nanoparticles are fashioned in an amorphous structure, there will be no diffraction peak detected [56]. The widening of the peaks in XRD endorses the formation of particles in nanosize. The sizes of nanoparticles can thus be estimated using the Debye-Scherrer equation. This equation is generally used to estimate the particle size from the XRD data by determining the width of Bragg reflection in line with the following equation [58]:

$$d = \frac{K\lambda}{\beta \cos \theta}$$

where $d$ is the particle size in nm, $K$ is the Scherrer constant, $\beta$ is the full width half maximum, $\theta$ is half of Bragg’s angle and $\lambda$ is the wavelength of X-ray. A typical XRD spectrum of AgNPs is illustrated in Figure 3.

Scanning electron microscopy (SEM) affords information about the structure and morphology of the nanoparticles. Additionally, electron microscopic technique is used for the determination of mean size of nanoparticles using statistical software. Some researchers also employed atomic force microscopy (AFM) to unravel the structure of nanoparticles [59, 60]. TEM technique has superior resolution and magnification than SEM and the images give more precise information concerning shape, size and crystallography of the nanoparticles. Another benefit of TEM investigation over SEM images relates to the ability of TEM to differentiate between crystalline and amor-
phous structures with the aid of selected area electron diffraction technique (SAED) [56]. Elemental arrangement of metal nanoparticles can be recognized using energy dispersive X-ray spectroscopy (EDX) [61]. Each element has a distinctive atomic structure that produces a unique set of peaks on its spectrum which also leads to the characterization of the elements [9]. Figure 4 showed distinct features of biosynthesized AgNPs using TEM for investigation.

Figure 4: TEM micrographs (A), patterns of SAED (B) and EDX (C) of AgNPs biosynthesized using spider cobweb extract [13]

Silver nanoparticles have been proven to be strong antiviral agents against several viruses, which include the following families: retroviridae, paramyxoviridae, hepadnaviridae, poxviridae, herpesviridae, arenaviridae and orthomyxoviridae [63]. In addition, there are lesser chances of viruses becoming resistant to AgNPs as compared to conventional antiviral agents. The nanoparticles have multivalent connections with components of viral surface and cell membrane receptors which block viral access into the cells. As antiviral agents act directly and quickly on viral particles, they bind with virus coat proteins and disrupt either their function or structure. Though any sort of metal may exert certain antiviral potential, most exploration has been carried out to study the antiviral activity of AgNPs, showing that AgNPs are certainly the most active metal-based antiviral agents. The interaction of AgNPs interaction with viral biomolecules proposes that AgNPs have massive possibilities not only to face the challenges presented by viral infections, but also to augment the quality of existing antiviral therapies [64].

In some recent reports, Sharma et al [65] synthesized AgNPs by employing the extracts of Phyllanthus niruri, Andrographis paniculata, and Tinospora cordifolia. The particles were subsequently evaluated for antiviral activities against chikungunya virus. The in vitro cytopathic assay ranked antiviral activities of AgNPs as A. paniculata-AgNPs > T. cordifolia-AgNPs > P. niruri-AgNPs. Similarly, in cell viability test using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) dye, A. paniculata-AgNPs inhibited the virus to a maximum degree. The cell viability of CHIKV-infected

Figure 3: XRD pattern of AgNPs biosynthesized using keratinase of Bacillus safensis LAU 13 [31]
cells rose significantly from 25.69 to 80.76 and 66.8%, when treated with *A. paniculata*-AgNPs at MNTD and ½MNTD, respectively, indicating that the use of AgNPs as antiviral agents is achievable and could provide substitute treatment options against viral diseases which have no specific antiviral or vaccines available yet. Orlowski et al [66] reported the use of tannic acid (plant-derived polyphenol) to phytosynthesize AgNPs. The TA-AgNPs was reportedly 33 nm, served as an effective antiviral microbicide when applied upon the mucosal tissues with further adjuvant properties that enhanced anti-herpes simple virus-2 immune response. In a mouse model, herpes simplex virus 2 (HSV-2) infection was initiated through the vagina to determine immunity after treatment of the initial infection with TA-AgNPs, and later, after a re-challenge with the virus. The mice treated intravaginally with TA-AgNPs showed improved clinical scores and lower viral titres in the vaginal tissues soon after treatment.

Also, Rafiei et al [67] described the effectiveness of AgNPs against Foot-and-Mouth disease virus (FMDV), which is a contagious, and acute infectious disease of domestic and wild ruminants. The mode and interaction action of AgNPs were examined, cytotoxicity of AgNPs on the baby hamster kidney 21 (BHK-21) cell line was also determined by MMT assay, while the anti-FMDV action of the particles was assessed by plaque assays at different times of infection. It was revealed that the AgNPs at non-toxic concentrations could inactivate the virus prior to entry into the cell or during infiltration, but not after adsorption. In another related research, spherical AgNPs of 7-32 nm biosynthesized using leaf extract of *Carica papaya* were revealed to possess antiviral activities through molecular docking study with good binding affinity against non-structural protein 1 of dengue type 2 virus [68]. Rai et al [64] concluded that depending on the interaction and virucidal effects of AgNPs against viruses such as, hepatitis B virus, HIV-1, herpes simplex virus type 1, respiratory syncytial virus, tacearibe virus, monkey pox virus, and influenza virus which have been reported in various studies, it can be predicted that AgNPs can act as protective antiviral shields. Thus, they can offer the prospect of developing broad-spectrum antiviral drugs.

### 4.2 Antimicrobial Activities of Nanoparticles

This Drug/antibiotic resistance is an increasing phenomenon [69-77] and there is necessity for the development of new and more effectual drugs [78] against microbes. Resistance in bacteria can be attributed to horizontal gene transfer of the antibiotic resistance genes, adjustment in the antibiotic target, mutational changes in the biofilm formation and efflux pumps [79]. Antibiotic resistance patterns of microorganisms have led to the dread about the emergence and re-emergence of multidrug-resistant (MDR) parasites and pathogens. Therefore, modification in antimicrobial compounds to augment their latent bactericidal prospective is a main area of research in modern era and nanotechnology provides an excellent platform to transform and develop the important properties of metal in the form of nanoparticles having potential applications as cell labellers, biomarkers, contrast agents for bioimaging, antimicrobial agents, and drug delivery schemes [80]. The unique physicochemical characteristics of nanomaterials have positioned them to exercise multiple actions against multidrug resistant bacteria for broader applications. It was predicted that the particles rendered the drug-resistant isolates vulnerable by a series of attacks; comprising deformation of structural integrity of bacterial cell wall to stimulate entry of particles, in addition to the enhancement of the entry of antibiotic via the carrier action of the particles [35]. There are two core manner of nanoparticles action on microbial cells. First, it directly damages the cell membrane and components. Second, it induced the release of reactive oxygen species (ROS) that destroys the molecular machinery of the cell by oxidative damage. ROS production may lead to inactivation of proteins, RNA and DNA within the cell. Thus, nanoparticles can be utilized for nano-functionalisation of surface of biomedical instruments such as glass surfaces, catheters amongst others [79]. Metallic nanoparticles of copper, titanium, magnesium, gold, silver and zinc have been proven to be bactericidal at nano-levels. Among the particles, silver possesses significant physicochemical and biological activities as antimicrobial agent [64].

### 5.0 SILVER NANOPARTICLES (AgNPs)

Literature has reported the use of biosynthesized AgNPs as antimicrobial agents. Jassim et al [2] reported the biosynthesis of AgNPs using *Carica papaya* juice as bioreductant. The spherical AgNPs produced has average diameter of 75.68 nm and was effective as an antibacterial agent against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. In a closely related research, spherical AgNPs biosynthesized using leaf extract of *Carica papaya* with sizes ranging from 7 to 32 nm exhibited excellent antibacterial activities against *P. aeruginosa* and *K. pneumoniae* [68]. Moreover, enzyme catalysed synthesis of AgNPs as active antimicrobials have been reported. Greenly synthesized spherical AgNPs from fungal xylanases of *A. niger* and *T. longibrachiatum* with sizes ranging from 15.21–77.49 nm by Elegbede et al [32] had excellent antimicrobial activity against and...
activities of 63.20–88.10 and 82.20–86.10% against tested bacteria and fungi respectively.

Prasannaraj and Venkatchalam [81] also reported phyto-synthesis of AgNPs using the leaf, root bark, and bark of ten medicinal plants having sizes of 34-98nm with potent antibacterial activities. In investigation against two bio-fouling strains of *P. aeruginosa* and *S. epidermidis*, antibiofilm activity as high as 79.6% was recorded. Aqueous extract of *Enteromorpha compressa* was employed by Ramkumar et al [82] to synthesize spherical-shaped AgNPs of 4-24 nm in size that displayed potent antibacterial and antifungal potentials. The AgNPs inhibited *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus* and *S. paratyphi* by 10.5-12.0mm, while inhibition of *A. niger*, *A. flavus*, *A. ochraceus*, *F. moniliforme* and *A. terreus* occurred between 9.2 and 10.2 mm. Singh et al [83] utilized root extract of *Panax ginseng* to produce AgNPs which were spherical and sized 10-30nm. The monodispersed AgNPs absorbed at 412 nm and exhibited potent antibacterial action against *B. anthracis*, *V. parahaemolyticus*, *S. aureus*, *E. coli*, and *B. cereus*. Fresh leaf extract of *P. ginseng* also produced spherical and monodispersed AgNPs having sizes which ranged from 5-15 nm [87]. At 3µg/ml the AgNPs acted creditably well against *S. enterica*, *E. coli*, *V. parahaemolyticus*, *B. anthracis*, *S. aureus*, and *B. cereus*. Also, the AgNPs completely inhibited biofilm development by *S. aureus* and *P. aeruginosa* at 4 µg/ml. Qayyum and Khan [79] in an extensive phytosynthesis of AgNPs employed extracts of ten plants (*Caryota urens*, *Pongamia glabra*, *Hamelia patens*, *Calendula officinalis*, *Tectona grandis*, *Thevetia peruviana*, *Ficus petiolaris*, *Ficus busking*, *Juniper communis*, and *Bauhinia purpurea*). The monodispersed AgNPs were spherical, triangular, quasi-spherical and pentagonal shapes and had sizes of 1-70 nm. The AgNPs were active against *E. coli*, *K. pneumoniae*, *E. cloacae*, *S. mutans*, *S. aureus* and *C. albicans* with minimum inhibitory concentration (MIC) of 16-26 µg/ml.

Bhakya et al [84] demonstrated the use of *Helicteres isora* root extract for the synthesis of spherical AgNPs that maximally absorbed at 450 nm and have size range of 16-95 nm. Moreover, the AgNPs displayed good antibacterial activity against both Gram-negative and Gram-positive bacteria; *E. coli*, *V. cholerae*, *S. typhi*, *P. aeruginosa*, *B. subtilis* and *M. luteus*. Basu et al [85] also reportedly synthesized AgNPs using seed extract of *Dolichos biflorus* as the bio-reducing agent. The AgNPs demonstrated good antibacterial potential against *S. aureus*, *B. subtilis*, *E. coli* and *P. aeruginosa*. Lateef et al [13] have reported the use of cobweb extract to synthesize spherical-shaped AgNPs of 3-50 nm in size. The cobweb-AgNPs inhibited growth of bacterial isolates including *S. aureus*, *E. coli*, *K. granulomatis* and *P. aeruginosa* in the range of 10-17 mm. It was also validated that AgNPs improved the activities of ofloxacin, cefixime and augmentin, in the AgNPs-antibiotics synergy investigations. Inclusion of the AgNPs at 5 µg/ml as an additive in white emulsion paint led to total inhibition of *E. coli*, *P. aeruginosa*, *Aspergillus niger* and *A. fumigatus*.

Similarly, Azeez et al [35] synthesized AgNPs with cocoa bean extract (CBE). The synthesized CBE-AgNPs were spherical and fairly polydispersed (8.96–54.22 nm). The CBE-AgNPs presented substantial activities against three multi-drug resistant bacteria producing inhibition of 10-14 mm in plate assay. Also the AgNPs boosted activities of cefuroxime, ampicillin, erythromycin and cefixime by 42.9–100 %. It enhanced antimicrobial activities against *K. pneumoniae*, *E. coli*, *S. pyogenes*, *P. aeruginosa*, *S. aureus*, *A. flavus*, *A. fumigatus* and *A. niger* as antimicrobial additive in emulsion paint. In another related study, cocoa pod husk extract (CPHE) facilitated the synthesis of spherical AgNPs [36] of 4-32 nm in size. The CPHE-AgNPs inhibited growth of *E. coli* and *K. pneumoniae* by 10-14 mm at 40-100 µg/ml. CPHE-AgNPs also contributed to 42.9–100% improvement in the antibacterial activities of cefuroxime and ampicillin and excellently acted as antimicrobial additive in paint. Singh et al [86] also described the extracellular synthesis of AgNPs by culture supernatant of *Sporosarcina koreensis* DC4. The spherical AgNPs had sizes between 30-50 nm, and exhibited outstanding antimicrobial activities against *E. coli*, *V. parahaemolyticus*, *S. enterica*, *B. cereus*, *B. anthracis*, and *S. aureus*. Also, pod extract of *Cola nitida* mediated the synthesis of AgNPs as described by Lateef et al [16], with production of spherical-shape and polydispersed AgNPs of 12 to 80 nm. The AgNPs efficiently repressed the growth of *E. coli*, *P. aeruginosa* and *K. granulomatis* by 12-30 mm on agar plate. It also acted excellently against bacteria and fungi capable of deteriorating paint when used as an antimicrobial additive. Additionally, spherical shaped SEEr-AgNPs was reported by Dhayalan et al [88] through the activities of seed extract of *Embelia ribes* (SEEr) that exhibited excellent antibacterial activities against *E. coli* (20-28 mm) and *S. aureus* (22-27 mm). Lateef et al [15] explored seed and leaf extracts of *Synsepalum dulcificum* (miracle fruit plant) for the synthesis of AgNPs with the biofabrication of spherical and crystalline particles of 4-26 nm in size.

The AgNPs successfully inhibited growth of *P. aeruginosa* and *K. granulomatis* by 11-24 mm at MIC of 60 µg/ml. Also, the AgNPs displayed exceptional potencies against the *A. flavus* and *A. niger* by about 100% suppression of growth. Moreover, Lateef et al [14] synthesized anisotropic AgNPs using nest extract of paper wasp (*Polistes...
sp) with size range of 1250.9555 nm. The AgNPs displayed strong antibacterial activities with zones of inhibition from 12-33 mm and antifungal activities which ranged from 75.61 to 100%. Also, cell-free extract of *Bacillus safensis* LAU 13 (GenBank accession number KJ461434) has been documented to synthesize AgNPs [26], with growth inhibition of *C. albicans* at 11-15 mm and MIC of 40 µg/ml.

### 6.0 GOLD NANO PARTICLES (AuNPs)

Unlike silver, bulk gold is not acknowledged to have inherent antimicrobial properties. However, the properties of gold at nanoscale allow for robust particle functionalization, and researchers have explored the prospect of using AuNPs as antimicrobial agent. Also, the simultaneous reduction of Ag and Au ions in the mixed solution has led to the development of bimetallic Ag-Au nanoparticles with higher activities as antimicrobials compared to either of the monometallic AgNPs and AuNPs. Elegbede et al [33] described the biosynthesis of spherical and flower-shaped AuNPs with fungal xylanases obtained from *A. niger* and *T. longibrachiatus* with SPR at 545 and 560 nm, respectively. The particles which were 4.88 to 123.99 nm in size had maximum antibacterial activity of 44.3% at 100 µg/ml against *E. coli*, *K. granulomatis*, *P. aeruginosa*, and *S. aureus*. However, the AuNPs had maximum antifungal activity of 87% at 150 µg/ml against *A. niger*, *A. fumigatus*, and *A. flavus*. Ojo et al [22] synthesized AuNPs using cell-free extract of *B. safensis* LAU 13 producing polydispersed particles of 10-45 nm in size. The AuNPs presented growth inhibitions of 66.67-75.32% against *A. fumigatus* and *A. niger* at 200 µg/ml. Also, SEER-AuNPs synthesized using seed extract of *Emblica ribes* according to Dhayalan et al [88] displayed outstanding antibacterial activities against *S. aureus* (22-27 mm) and *E. coli* (28-34 mm). Basu et al [85] synthesized spherical and some irregular-shaped AuNPs using the seed extract of *Dolichos biflorus*. The AuNPs demonstrated poor antibacterial potential against *S. aureus*, *B. subtilis*, *E. coli* and *P. aeruginosa*.

Also, AuNPs was synthesized via an environmentally benign process using seed extract of *Elettaria cardamomum* according to Rajan et al [89]. The AuNPs which were crystalline spherical particles exhibited activity against the pathogenic bacterial strains of *E. coli*, *S. aureus* and *P. aeruginosa*. Swain et al [90] biofabricated AuNPs by employing both leaf and root extracts of *Vetiveria zizanioides* (VZ) and *Cannabis sativa* (CS). Both VZ-AuNPs and CS-AuNPs were detected to be spherical-shaped with average size estimated as 40 nm by SEM analysis. The *in vitro* antifungal activities of the AuNPs against *Penicillium* sp, *A. flavus*, *Aspergillus* sp, *A. fumigatus*, *Fusarium* sp and *Mucor* sp showed inhibition of 3.8-4.8 mm. Leaf extracts of *Carica papaya* (CP) and *Catharanthus roseus* (CR) and the mixture of these two extracts (CPCRM) were used to synthesize AuNPs according to Muthukumar et al [91]. The morphology for CP-AuNPs, CR-AuNPs and CPCRM-AuNPs as revealed by SEM were spherical, triangular and hexagonal structures, while HR-TEM revealed that the CP-AuNPs, CR-AuNPs and CPCRM-AuNPs had sizes of 2-20, 3.5-9 and 6.18 nm respectively. The synthesized AuNPs presented exceptional activities towards *S. aureus*, *B. subtilis*, *E. coli*, and *P. vulgaris*, exhibiting maximum zone of inhibition of 20 mm against *E. coli*. Generally CPCRM-AuNPs presented greater antibacterial activities against the bacterial strains than CP-AuNPs and CR-AuNPs. The MIC against the pathogens ranged from 62.5 to 250 µg/ml for CP and CR-AuNPs, and 15.625 to 125 µg/ml for CPCRM-AuNPs.

### 7.0 SILVER-GOLD ALLOY NANO PARTICLES (Ag-AuNPs)

Bimetallic nanoparticles have gained attentions in their synthesis and applications, owning to the fact that they combine attributes of the monometallic components and by altering the molar ratios of the two metals. Unique bimetallic nanoparticles can be created with very good properties for diverse applications. Amongst such bimetallic nanoparticles of importance is Ag-AuNPs, which have been synthesized using the biological route. Ag-AuNPs with a single surface plasmon resonance (SPR) band located at an intermediate position between the SPR band of monometallic Au and Ag nanoparticles, may have lower toxicity compared to AgNPs, thereby enhancing the biocompatibility for biomedical applications. Unlike Ag and AuNPs, the reports on biomedical applications of green Ag-AuNPs are scanty, thereby necessitating intensive investigations on the potentials of the bimetallic material.

The antibiofilm efficiency of Ag-AuNPs biosynthesized from γ-proteobacterium *Shewanella oneidensis* MR-1 was explored by Ramasamy et al [92]. The Ag-AuNPs was tested against *E. coli*, *P. aeruginosa*, *Enterococcus faecalis*, and *S. aureus* and evaluated for biofilm inhibition using crystal violet. It was recorded that the Ag-AuNPs inhibited all strains efficiently at 250 µM. *E. coli* biofilm formation was totally inhibited at particle concentrations as low as 10 µM.

Also, Ojo et al [22] synthesized Ag-AuNPs with cell-free extract of *B. safensis* LAU 13 yielding mainly spherical Ag-AuNPs of 13-80 nm in size. Furthermore, Ag-AuNPs presented more outstanding antifungal property than AuNPs biosynthesized from the same extract reported in...
the same work with growth inhibitions of about 83.33% (A. niger) and 90.78% (A. fumigatus) at 200 µg/ml. Also, Lateef et al [24] demonstrated the green synthesis of Ag-AuNPs using the seed, seed shell, leaf, and pod extracts of Cola nitida. According to TEM analysis, the seed, seed shell and leaf extract-mediated Ag–AuNPs had almost spherical morphology in the size range of 17-90 nm, while anisotropic structures of sphere, triangle, rod, and hexagon of 12-91 nm in size were obtained in the pod extract-mediated Ag-AuNPs. All Ag-AuNPs were studied for possible antifungal activities. At 150 µg/ml, 100% inhibition of A. flavus was realized with all the Ag-AuNPs. However, growth inhibitions of 69.51-75.61 and 76.83-100% were realized for A. niger and A. fumigatus respectively.

8.0 OTHER METALLIC NANOPARTICLES

Several other metallic nanoparticles have been fabricated by researchers through the green approach, and some of them are hereby reviewed. Jayandran et al [93] synthesized copper nanoparticles (CuNPs) using the fruit extract of lemon. The nanoparticles which were reportedly spherical have sizes of 60-100 nm, and they also displayed antibacterial activities against some clinical bacterial isolates. Caroling et al [94] also reported the antibacterial activities of spherical CuNPs fabricated using Phyllanthus emblica extract which had sizes of 65-184 nm. The green synthesis of spherical CuO nanoparticles of 5-10 nm using the extract of Gloriosa superba was also reported to display antibacterial potentials [95].

Bala et al [96] reported that spherically shaped greenly synthesized zinc oxide nanoparticles (ZnONPs) displayed significant antibacterial activities. The crystalline nanoparticles was synthesized using Hibiscus sabdariffa leaf extract and had sizes between 16-300 nm. Bhuyan et al [97] explored Azadirachta indica leaf extract to synthesize spherical ZnONPs of 9.6-25.5 nm in size with potent antibacterial activities. Also, Lingaraju et al [98] synthesized ZnONPs using stem extract of Ruta graveolens which displayed antibacterial activities. The ZnONPs were approximately 28 nm is sizes and had hexagonal wurtzite shape.

Titanium dioxide nanoparticles (TiO2NPs) were biofabricated using Psidium guajava leaf extract [99] with potent activities against clinical bacterial strains. The spherical nanoparticles were averagely 32nm and showed agglomerations. Moreover, Leucas aspera mediated cerium dioxide (CeO2) nanoparticles was described by Malleshappa et al [100] which was reportedly multifunctional in activities including its antibacterial potency. The CeO2 NPs synthesized were relatively uniform microspheres with sizes of 4-13 nm. Arumugam et al [101] also synthesized of CeO2 NPs using the leaf extract of Gloriosa superba. The spherical particles averaged 5 nm showed potent antibacterial activity. Also, iron based nanoparticles biosynthesized using Aloe vera gel were indicated to possess antibacterial activities [102]. The nanoflower and conical-shaped particles had sizes of 18-21 nm. Naseem and Furrukh [103] also reported the antibacterial activities of iron nanoparticles greenly synthesized using leaf extracts of Laurus inermis and Gardenia jasminoides. The particles had sizes that ranged from 21-32 nm and were hexagonal in shapes.

9.0 ANTIOXIDANT ACTIVITIES OF NANOPARTICLES

Studies on the capacities of biosynthesized metallic nanoparticles to scavenge free radicals gave an initiative about the relationship and activity of the nanoparticles with the biomolecules that exist in living systems. Antioxidants mostly play a dynamic role in the performance of biological systems by scavenging toxic free radicals. Antioxidants check oxidative injuries that are generated by oxidative stress to cellular components such as DNA, proteins and lipids, and minimize the menace of age-related chronic diseases. Measurements of antioxidant potentials are still to a large extent restricted to biological moieties [104]. Studies on antioxidant activities of metallic nanoparticles have been earlier reported [105-107].

Reactive oxygen species (ROS) are said to excite or stimulate auto-oxidation and thermal oxidations of lipids which are connected with damage of membrane and aging in living organisms [105]. Hydrogen peroxide is a weak oxidizing agent that can deactivate some enzymes directly by the oxidation of important thiol groups. It crosses cell membrane swiftly, and inside the cell, it can possibly react with Fe2+ and Cu2+ to form hydroxyl radicals. Hydroxyl (OH) radicals have very short half-life and are among the most lethal and reactive free radicals with huge oxidative power, which combines rapidly with virtually all molecules in its immediate vicinity. It hastens several biological disorders such as cataracts, carcinogenesis, inflammation, atherosclerosis, mutation, ageing and cell death [89]. It can freely react with superoxide radicals, resulting to vascular system impairment which then leads to conditions such as multiple sclerosis and juvenile diabetes [106]. Nitric oxide (NO) is involved in many biological processes or functions, such as: smooth muscle relaxation, neurotransmission, antitumor, blood pressure regulation, and antimicrobial activities. However, it also adds to oxidative damage, because it has the ability to react with superoxide to form the peroxynitrite anion, which can produce DNA fragmentation and initiate lipid peroxidation [108]. Thus, production of nitric oxide must be tightly controlled to restrain the harmful effects.
There are several techniques of assessing the antioxidant potentials of materials. Of the in-vivo and in-vitro assessment of antioxidant activities, in-vitro assays are simple, cost-effective, reproducible and convenient. The 2, 2-diphenyl-1-picrylhydrazyl (DPPH) is basically used for testing initial radical scavenging potentials of a compound or extract, and it offers a speedy and uncomplicated way to assess antioxidant activity [109]. The DPPH is a stable nitrogen free radical which accepts hydrogen electrons or atoms from antioxidant materials. A change of colour in the ethanolic solution of DPPH is detected once it reacts with an antioxidant, which is as a consequence of the scavenging action of antioxidant on DPPH by liberating or donating hydrogen to form the stable DPPH which is yellow-coloured.

Moreover, ABTS radicals are produced from the oxidation of ABTS by potassium persulfate and it is an excellent tool for appraising the antioxidant potential of the hydrogen-donating and chain-breaking antioxidants [110]. Also, ferric ion reducing antioxidant power (FRAP) is an antioxidant assay employed to estimate the degree of the antioxidant competence of foods, beverages and nutritional supplements comprising polyphenols. The use of FRAP assay gives rapid and easy way to calculate antioxidant activities [109]. Nanotechnology has expanded the range of materials that can scavenge free radicals in the environment and in living entities.

10.0 SILVER NANO-PARTICLES (AgNPs)

Greenly synthesized spherical AgNPs from fungal xylanases of A. niger and T. longibrachiatum as reported by Elebgele et al [32] were described to present excellent antioxidant activities. They displayed high free radical scavenging potentials against DPPH (37.48-79.42 %) at concentration of 10-100µg/ml, and hydrogen peroxide (20.50-96.50%) at 1-40µg/ml. Azeeq et al [39] reported the use of AgNPs synthesized using pod extract of Cola nitida to grow Amaranthus caudatus. The AgNPs increased the DPPH antioxidant activities of A. caudatus grown with 25 -100 ppm of the AgNPs by 6.48-43.30% with the 50ppm of AgNPs inducing the plant extract with smallest IC_{50} of 0.67 mg/ml. Prasannaraj and Venkatachalam [81] evaluated antioxidant activity of biosynthesized AgNPs using XTT (sodium 2,3,-bis(2-methoxy-4-nitro-5-sulphophenyl)-5-[(phenylamino)-carbonyl]-2H-tetrazolium inner salt. The release of ROS, such as OH radicals, could be a general mechanism of cell death prompted by use of antibiotics [111]. The treatment with the biosynthesized AgNPs led to 3 to 4-fold increase in ROS generation in S. epidermidis, E. coli, P. aeruginosa, K. pneumoniae, P. vulgaris and S. aureus to promote bactericidal action. Also, AgNPs biosynthesized using the cell-free extract of B. safensis LAU 13 by Lateef et al [27] scavenged DPPH by 40.56-89.40% at 20-100 µg/m which were clearly better than those of quercetin and β-carotene standards. Also, the ferric ion reducing powers of the AgNPs were in the range of 1.84-2.42 at 20-100 µg/ml.

In another study, Lateef et al [16] reported that AgNPs biosynthesized using the pod extract of C. nitida scavenged DPPH and ferric ion. The AgNPs exhibited a strong antioxidant activity with IC_{50} of 43.98 µg/ml against DPPH and a ferric ion reduction power of 13.62-49.96% at 20-100 µg/ml. Similarly, Bhakya et al [84] in a related report elucidated the production of AgNPs using the seed extract of Embelia ribes (SEEr). The synthesized SEEr-AgNPs (5-35 nm) displayed good antioxidant activities in the DPPH free radical scavenging and the phosphomolybdenum assays. The IC_{50} of 100 and 60 µg/ml was recorded DPPH scavenging as well as phosphomolybdenum assay (involving reduction of Mo (VI) to Mo (V)) respectively.

The CPHE-AgNPs synthesized using cocoa pod husk extract (CPHE) described by Lateef et al [36] also presented excellent antioxidant activities of 32.62-84.50% at concentrations of 20-100 µg/ml in DPPH radical assay. The IC_{50} of quercetin and β-carotene which were standards used were 430 and 710 µg/ml respectively, while that of CPHE-AgNPs was 49.70 µg/ml. Also, the ferric ion reducing potentials of CPHE-AgNPs ranged from 14.44-83.94% at concentrations of 20-100 µg/ml compared to β-carotene (11.53-65.38%), and quercetin (12.05-100%) at 0.2-1.0 mg/ml. The AgNPs synthesized with leaf extract of Aristolochia indica described by Shammugam et al [104] displayed excellent antioxidant activities with maximum activity of 81.19% obtained at 100 µg/ml in the DPPH scavenging test, while the highest activity of 64.01% at 100 µg/ml of AgNPs was obtained in ABTS scavenging assay.

Also, AgNPs biosynthesized with the leaf extract of Sola-num nigrum by Jinu et al [111] was assessed for antioxidant activities against reactive oxygen species (ROS) generation. The accumulation of ROS was increased by 3-fold in AgNPs treated K. pneumoniae, S. epidermidis and
P. aeruginosa than S. aureus strains. Ravichandran et al. [112] elucidated synthesis of BAgNPs with leaf extract of Artocarpus altilis. The BAgNPs were polydispersed, spherical and has particle sizes of 34-38nm. BAgNPs displayed good antioxidant activity on DPPH with performance of 79.79% at 100 µg/ml. The IC50 of 51.17 µg/ml was obtained.

Moreover, the spherical TT-AgNPs synthesized employing the leaf extract of Talinum triangulare (TT) by Elemike et al. [114] scavenged DPPH by 30-88% using concentration of 25-100 µg/ml. Silver nanoparticles biosynthesized with lipid extract from Acutodesmus dimorphus as reported by Chokshi et al. [115]. The micrograph established the production of spherical-shaped, polydispersed AgNPs having 2.20nm size. The AgNPs in investigations for antioxidant potentials produced IC50 values of 14.41 and 6.91 µg/ml to scavenge ABTS and DPPH respectively. Also, Moteriya and Chanda [115] synthesized AgNPs mediated by flower extract of Caesalpinia pulcherrima with excellent antioxidant activities via the various tests conducted. The IC50 was estimated to be 70, 55 and 38.5 µg/ml for the scavenging of DPPH, ABTS and superoxide ion, respectively while the FRAP activity of 8.8 Mg⁻¹ was obtained. Lateef et al. [117] reported that AgNPs synthesized using extracts from spider cobweb (CB), pod (KP), seed (KS) and seed shell (KSS) of Cola nitida displayed excellent antioxidant activities with respect to hydrogen peroxide scavenging activity assay which resulted in activities obtained in the range of 77-99.8%, with almost instantaneous clearance of the turbid solution of H2O2 prepared in phosphate buffer.

11.0 GOLD NANOPARTICLES (AuNPs)

Rajan et al. [89] reported that AuNPs synthesized using the aqueous extract of Elettaria cardamomum seeds displayed good antioxidant activities when studied through the DPPH, nitric oxide and OH radicals scavenging assays. The particles scavenged DPPH by 19.87 to 62.18% at concentrations of 1.25-20 µl, while it exhibited about 64.44% activity at concentration of 200 µl against nitric oxide. Also, 67.5% inhibition of the hydroxyl radical was obtained. Recently, Elegbede et al. [33] used fungal xylanases obtained from A. niger and T. longibrachiatum to fabricate AuNPs. The spherical and flower-shaped AuNPs had sizes which ranged from 4.88 to 123.99 nm, and displayed elevated antioxidant potentials by scavenging DPPH by 42.91-53.79% at 10-100 µg/ml and H2O2 by 74-96 % at 1-40 µg/ml.

In another study, Dhayalan et al. [88] elucidated the excellent antioxidant activities of AuNPs synthesized using the seed extract of Embelia ribes (SEEr) in the DPPH free radical scavenging and the phosphomolybdenum assays.

The IC50 of 20 µg/ml was recorded for DPPH, while 40 µg/ml was recorded for phosphomolybdenum assay. Sathishkumar et al. [118] described the synthesis of CGAuNPs using the fruit extract of Couroupita guianensis. TEM micrographs showed uniformly sized anisotropic CGAuNPs which were spherical, hexagonal and triangular having mean size of ~25 nm. CGAuNPs exhibited excellent antioxidant potentials having IC50 of 36 µg/ml for the hydroxyl radical scavenging effect and 37 µg/ml for DPPH. Also, the superoxide scavenging activity of CGAuNPs was reported to rise with increasing concentrations and had maximum inhibition of 89.8%. Abbai et al. [119] described the synthesis of spherical-shaped Siberian ginseng gold nanoparticles (Sg-AuNPs) using the stem extract of Eleutherococcus senticosus with a Z-average hydrodynamic diameter of 189 nm shown by DLS. The Sg-AuNPs was assessed for antioxidant potentials using DPPH and the IC50 value of 250 µg/ml obtained was significantly higher than its corresponding salt. Abel et al. [120] biofabricated AuNPs using Cassia tora leaf powder. The TEM images confirmed the formation of nearly spherical AuNPs of about 57 nm. The antioxidant potential of the AuNPs was evaluated via catalase activity and nitric oxide scavenging assays. Catalase is said to be an ever-present antioxidant enzyme with capability to degrade hydrogen peroxide into water and oxygen. Thus, the rise in catalase activity corresponds to rise in antioxidant activity. About 60% rise in catalase activity was achieved with treatment of 100 µg/ml of AuNPs. Also, nitric oxide inhibition was recorded to be about 70% with the AuNPs in the range of 25-75 µg/ml.

12.0 OTHER METALLIC NANOPARTICLES

Subbaya and Selvam [121] reported the antioxidant activities of spherically shaped greenly synthesized copper nanoparticles using Hibiscus rosasinensis leaf extract as the bioreductant and stabilizer. Also, ZnONPs synthesized using stem extract of Ruta graveolens reported by Lingaraju et al. [98] were reported to display potent antioxidant activities. Spherical FeO nanoparticles biosynthesized using Amaranthus spinosus leaf extract with sizes ranging from 58-530 nm were also reported to possess antioxidant properties [122].

13.0 METALLIC NANOPARTICLES AS ANTICOAGULANTS

Blood clots formation greatly depends on the coagulation factors which have resulted into several diseases relating to thrombosis. This includes stroke, pulmonary embolism, deep venous thrombosis (DVT), acute coronary syndrome (ACS) and acute myocardial infarction (AMI). Blood clot formed from contagion may also damage tissues leading to organ failure [123], often linked with car-
diovascular disorders, autoimmune reactions, allergic responses, injuries, and emergence of cancer [124, 125]. Anticoagulants are the basis of therapy for the prevention and treatment of thrombosis related diseases [126]. They are also referred to as blood thinners and are capable of manipulating the various pathways of blood coagulation. The commonly used chemical anticoagulants such as warfarin and heparin products, rivaroxaban are closely-linked with adverse drug events as well as increased readmission rates with severe thrombotic events, while administration of dabigatran may be accompanied by grave haemorrhage [126].

Several authors have employed green synthesis for various metallic nanoparticles as a result of their eco-friendly properties and reported anticoagulant actions of these nanoparticles. Abbasi et al [127] reported green synthesized spherical AgNPs of ~7 nm using aqueous extract of dried Juglans regia green husk which prevented blood clot within 72 h in a dose-dependent manner. The AgNPs of 10-45 nm in size synthesized using dried biomass of Diplazium esculentum (retz.) sw showed an anticoagulative activity with no noticeable blood clot following 24 h exposure [128]. Bridelia retusa fruit extract-functionalized AgNPs of average diameter of 68.49 nm also prevented the development of blood clots in human blood samples which proved the anticoagulant activity of the nanoparticles with potential application in nanomedicine [129]. Raja et al [130] also had similar result using pods of Peltophorum pterocarpum-synthesized AgNPs. Cocoa bean mediated-AgNPs of sizes between 8.96-54.22 nm demonstrated antiplatelet activity which prevented blood coagulation with no modification in the morphology of the red blood cells [35]. AgNPs mediated by extracts of Bacillus safensis [26], paper wasp nest [14], seed and leaf of Synsepalum dulcificum [15], cobweb, pods, seeds and shell of Cola nitida [117] (Figure 5), leaf of Petiveria alliacea [17] and fungal xylanases [32] inhibited aggregation of platelets thus preventing the clot formation over a long period of time as opposed to those lacking the nanoparticles. The result also compared well with EDTA-incorporated blood thereby suggesting the biosynthesized AgNPs as excellent substitutes to the conventional drugs which are short-termed in circulation, capital intensive and as well have harmful effects after a prolonged exposure of vital organs to such drugs.

Paul et al [131] used dried biomass of Momordica cochinchinensis (Lour) leaf to synthesize AuNPs and evaluated for the inhibition of coagulation of human blood plasma. The AuNPs was observed to have a lasting effect towards prevention of blood clotting after 24 h. Similarly, Kim et al [132] demonstrated the synthesis of AuNPs using aqueous earthworm extract without any additional reducing or capping agents to reinforce the anticoagulant activities of heparin by activated partial thromboplastin time (aPTT) assay for treatment. The heparin-AuNPs produced improvement of 134.8 % over the clotting time of heparin alone. Elegbede et al [33] described the inhibition of blood clot formation by the addition of the biosynthesized AuNPs using fungal xylanases. The presence of both antiplatelet aggregation as well as fibrinolytic activities in the nanoparticles was accountable for the anticoagulation activities. Similarly, we have demonstrated the use of AuNPs, and Ag-AuNPs as potent anticoagulants [20, 22, 24, 34], and also documented the prospects of metallic nanoparticles as both anticoagulant and thrombolytic agents to manage blood coagulation disorders in clinical nanomedicine [133].

Figure 5: Anticoagulant activities of biosynthesized AgNPs using extracts of cobweb (CB), kola pod (KP), kola seed (KS) and kola seed shell (KSS) [117].

14.0 METALLIC NANOPARTICLES AS THROMBOLYICS

Thrombosis is a symptom of vascular blockage because of thrombotic formation in a critical blood vessel. Thrombolytic therapy is a major treatment of thrombosis involving the dissolution of thrombi by the application of thrombolytics which include streptokinase (SK), urokinase (UK) and tissue type plasminogen activator (t-PA). Conversely, the use of these thrombolytics has resulted into bleeding complications (i.e hemorrhagic side effects) owing to their non-targeting administration and non-specific activation, which endangers the safety as well as limits the utilization of the drugs in therapeutics. Hence, several efforts have been applied to solve this problem via safely and selective delivery of thrombolytics to the sites of vascular occlusion and its controlled release [134].
Thrombolytic activity test of *Cassia auriculata*-AgNPs was demonstrated by Dhandapani and Iyer [135]. The particles dissolved blood clot within 45 min. In our laboratory likewise, the demonstration of appropriate blood clot dissolution has been carried out using biosynthesized AgNPs by extracts of bacteria, paper wasp nest, seed and leaf extracts of *S. dulcificum* (miracle fruit plant), cobweb, pod, seed and seed shell of kolanut, leaf of *P. alliacea* and crude enzyme [14, 15, 17, 26, 32, 117]. In our report, thrombolytic activities of 55.76-89.83 % were obtained for some of these biosynthesized AgNPs (Figure 6).

Biosynthesized AuNPs using bacterial extract of *B. safensis* was also able to stimulate the dissolution of clot in treatment with blood clot within 5 min of reaction [22], while comparable results were obtained when AuNPs biosynthesized using bacterial extract and crude xylanases were used as thrombolytic agents [20, 33]. The nanoparticles induced dissolution of blood clot within 5 min of reaction with the optical micrographs showing the dispersal of cells as a result of the reaction of blood clot with biosynthesized AuNPs. The mechanisms of thrombolytic activities of nanoparticles have been proposed where fibrin could be degraded by nanoparticles (mechanism 2) as indicated in the plate assay of Harish et al [136]. On the other hand, plasminogen can be triggered by AgNPs to releasing plasmin which in turn causes the lysis of the blood clot (mechanism 1). Inhibition of the activities of inhibitors by nanoparticles may also prevent of plasminogen and plasmin. The two mechanisms could occur together, thereby resulting to the pronounced thrombolytic activities as obtained in these studies.

15.0 APPLICATIONS OF METALLIC NANO PARTICLES IN WOUND HEALING

Metal nanomaterials as single conjugates have proved to possess potential wound healing properties. Coupling of nanoparticles with other wound dressing materials promotes the removal of microbes from the site of wound which would otherwise cause interruption and delays the normal phases of healing. Topical application of chitosan-capped AgNPs has been recently shown to accelerate the healing of a burn wound where it decreased the inflammatory reaction and consequently, reducing the length of repair phase [137]. In Katas et al [138], AgNPs was used as excellent healing wound dressings because of the acceleration of reepithelization and increased performance at clearing bacteria from infected wounds.

The particles also inhibited proinflammatory cytokines such as interferon gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) [138]. AgNPs have been extensively used in the preparation of ointment for burns, dressing for pressure ulcer wound and clinical devices for effective avoidance of microbial infections [139, 140]. In an *in vitro* model, treatment with AgNPs caused a significant reduction in the production of inflammatory cytokines and oxidative stress to promote healing in human keratinocytes and dermal fibroblasts [141]. Furthermore, topical application of AgNPs on burn wounds in mice led to reduction in number of neutrophils and production of interleukin (IL-6). However, the particles induced elevated levels of IL-10, TGF-β, vascular endothelial growth factor (VEGF) and interferon gamma (IFN-γ).

In another *in vivo* study, Nejad et al [142] reported the incorporation of AgNPs with poly (dopamine methacrylamide-co-methyl methacrylate) (MADO), which was applied to cutaneous wounds, with total healing achieved within two weeks in the treated samples in comparison with the partial healing of the untreated group. The application of AgNPs in normal wounds have been highlighted by Hamdan et al [143], with such influences as reduction of inflammation by modulating cytokines, reduced lymphocyte infiltration and enhanced reepithelization; all leading to promotion of wound healing. However, the long usage of AgNPs for wound healing may be hampered by toxicity, development of blue-gray colouration of healed areas and the emergence of silver-resistant microbes [144-146].
Conjugation of nanomaterials with pathogen-specific antibodies may be applied for photothermal therapy. Sherwani et al [147] demonstrated improved activity of AuNP-conjugated photosensitizer against Candida albicans that was used to infect wounds in mice. The topical application of AuNPs improved the healing of the infected wound. A similar study by Naraginti et al [148] showed that AuNPs when applied to cutaneous wounds in rats enhanced healing with improved re-epithelialization, granulation tissue formation and increased extracellular matrix (ECM) deposition and collagen fibre. AuNPs combined with cryopreserved human fibroblasts (CrHFC-AuNPs) have also been applied topically to burn wounds in rats. CrHFC-AuNP- treated wounds displayed an enhanced overall healing rate, reduced inflammatory phase and increased collagen deposition [149].

16.0 APPLICATIONS OF METALLIC NANO PARTICLES AS ANTICANCER AGENTS

Cancer is not a solitary disease; rather it is a group of diseases with every organ or system having the capability to develop a distinct set of diseases. It is developed through diverse signaling mechanisms including cell proliferation, angiogenesis and metastasis [150, 151]. The currently available anticancer therapies have adverse effect by affecting the functions of normal cells while administering excess drug and exposure to radiation [51]; thereby necessitating the need to develop new anticancer strategies. In order to address these therapeutic requirements, nano-sized molecular tools capable of distinguishing between malignant and non-malignant cells and also deliver lethal payload are being developed [150].

Current anticancer research has been devoted to the discovery of novel transition metal compounds rather than the platinum based pharmaceutical with various toxic side effects including gastrointestinal and haematological toxicity [151]. Metallic nanoparticles have been used in drug delivery especially in the treatment of cancer. Given to their large surface area and area to volume ratio, nanoparticles display a number of specific physicochemical attributes making them valuable by inducing cytoxicity in the treatment of cancer cells, and have therefore become formidable tool against cancers [152, 153]. In a study, Patra et al [154] showed that Au and AgNPs-based drug delivery systems significantly inhibited growth of B16F10 cells compared to free doxorubicin. In this case, the particles acted as drug delivery systems. It has been documented that biosynthesized nanoparticles are mostly biocompatible and highly suitable for biomedical applications [154-156]. Prabhu et al [157] demonstrated that AgNPs biosynthesized from leaf extract of Vitex negundo inhibited the proliferation of HCT 15 colon cell line and induced apoptosis in concentration-dependent manner. In another study, AgNPs were produced using phycocyanin obtained from Nostoc linckia, which displayed effective cytotoxicity against MCF-7 cells with IC50 of 27.79 ± 2.3 µg/ml [158]. Kuppusamy et al [159] utilized extract of Commelina nutiflora to synthesize AgNPs and AuNPs which caused reduction of cell viability and exercised improved cytotoxicity against HCT-116 colon cancer cells with IC50 of 100 and 200 µg/ml. Saratate et al [1] produced AgNPs using extract of Taraxacum officinale with elevated cytotoxic activity against human liver cancer cells (HepG2). In another report, AuNPs synthesized using carrageenan of marine red algae, displayed activities against HCT-116 and MDA-MB-231 cells [160].

ZnONPs have been reported to possess anticancer properties in a couple of studies. For instance Hassan et al. [161] found out that ZnONPs considerably declined elevated levels of oxidative stress markers and hepatocyte integrity, and also reduced high levels of serum of tumor alpha-fucosidase and markers alphafetoprotein when used against hepatocellular carcinoma HepG2, non-small cell lung cancer A549, and human prostate PC3. Also, DeLong et al [162] reported the efficacy of ZnONPs in inhibiting ERK enzyme and other cancer-associated kinases such as AKT, p70S6 K and CREB. ZnONPs has also been reported as an anticancer agent against human colon carcinoma LoVo, and HeLa among others [163, 164]. Zinc oxide was doped with rare earth metals such as lanthanum, Cerium and Neodymium facilitated by Gymnema sylvestre leaves extract, and they were reported to display anticancer activities in vitro against A498 (human kidney carcinoma) cell line and normal vero (African monkey kidney) cell lines [165]. Spherical copper oxide nanoparticles of 26–30 nm in dimension were synthesized by biological method using extract of Aculypha indica leaf and the cytotoxicity activity of the CuONPs was confirmed by MTT assay against MCF-7 breast cancer cell lines [166]. Nagajyothi et al [167] reported the synthesis of CuONPs (average size of 26.6 nm) using an aqueous black bean extract. The cytotoxic effect of the CuONPs was determined by sulforhodamine-B assay and results indicated that an increase of the mitochondria-derived reactive oxygen species (ROS) and initiation of the lipid peroxidation of the liposomal membrane, which influences the cytokinetic movements of cells and regulates the several signaling pathways. Also, clonogenic assay established that the NPs-incubated cancer cells were unable to proliferate well. Summarily, the CuONPs was shown to have ability to induce apoptosis and suppress proliferation of HeLa cells. CuONPs were synthesized using different plant extracts obtained from the leaves of Azadirachta indica, Murraya koenigii, Hibis-
Nanosilver was immobilized on TiO$_2$ nanometric fibers (Ag/TiO$_2$) which displayed cytotoxicity in both cancer cells (murine AT-84 oral squamous carcinoma cells) and macrophages (ATCC RAW 264.7). Concentration of 5 mg/ml was reported to prompt partial suppression of growth and migration of cancer cells, and 5.06 mg/l caused a comprehensive inhibition of proliferation and migration of murine AT-84 cells [170]. Environmentally safe synthesis of tellurium nanoparticles was reported by Brown et al [171] and explored. Cytotoxicity assays of the rod-shaped tellurium nanoparticles coated with polyvinylpyrrolidone (PVP) were performed using human dermal fibroblasts (HDF) and melanoma (skin cancer) cells for 24 and 48h. Treatment with nanoparticles at concentrations between 10 and 100 µg/ml presented no noteworthy cytotoxicity to HDF cells. But cytotoxic effect was observed in melanoma cells at the same concentrations. This proposes that the nanoparticles possess anticancer properties towards melanoma cells without being toxic to healthy cells.

**17.0 APPLICATIONS OF METALLIC NANO Particles IN DIAGNOSTICS**

Nanobiotechnology has been valuable as veritable tools to detect biomolecules and analytes showing their usefulness in diagnosis; the concept of nanodiagnoses [172]. Nanodiagnostics has enhanced the development of handheld devices that are simple to use and marketable [173], and provides novel ways of assessing patients with improved sensitivity and specificity. The deployment of nanodiagnostics is frequently found in applications to detect pathogens in communicable diseases and cancer biomarker in cancer therapy. These include nanoparticle-based, nanodevice-based and most importantly nanotechnology-based point-of-care tests (POCT) [174]. Several nanoparticles, particularly fluorescent, metallic and magnetic nanoparticles have been successfully utilized for the diagnosis of infectious diseases. Hepatitis B virus has been diagnosed in a simple and sensitive manner by using dot immunoassay through the quantum dots nanobeads (QDNB) [175]. Similarly magnetic nanoparticles possessing iron oxide core and silver shell have also been shown to be efficient in the early diagnosis of malaria [176].

Antibodies could also be used to functionalize nanomaterials for the detection of several diseases. Nanowire platform functionalized with ssDNA has been used for the detection of the BRAF mutation in breast cancer [177, 178]. Lin et al [179] reported the novel urinary nanomarker assay that was based on thrombin-sensitive iron oxide nanoparticles to detect thrombin activity and thus quantified thrombosis burden in vivo. In a mouse model of pulmonary embolism induced by thromboplastin, the circulating nanomarkers successfully accessed the local sites of thrombosis and release the reporter upon cleavage by thrombin [180]. Nanorobots dentrifices (dentifrobots), when used as mouth wash or toothpaste can cover all subgingival surfaces, thereby metabolizing any trapped organic matter into harmless and odourless vapours. Pathogenic bacteria in dental plaque are identified and destroyed, using properly configured dentifrobots [181]. Nanoparticles platforms have evolved and optimized to detect pathogens and cancer biomarkers making diagnostic procedures less cumbersome but more sensitive because most of the complex procedures are now integrated onto a simple device with capacity to be used for on the spot diagnosis [182]. Through these developments, integration of numerous assays into a single device becomes a possibility with advantages of reduction of sample volumes, consumption of less materials and timely analysis [183].

**18.0 MOSQUITOCIDAL, LARVICIDAL, ANTIPLASMODIAL AND TRYPANOCIDAL ACTIVITIES OF NANO Particles**

A new era of antimalarial method is evolving by the use of nanoparticles alone and/or in combination with generally used drugs and may characterise an innovative therapeutic approach for malaria treatment [184]. Leaf extract of *Anisomeles indica* was used for the synthesis of spherical AgNPs which displayed mosquitocidal activity against *Anopheles subpictus*, *Aedes albopictus*, and *Culex triaeniorhynchus* [185]. Cubic and spherical AgNPs was synthesized using the aqueous leaf extract of *Carissa spinarum* that displayed outstanding toxicity against larva of *A. subpictus*, *A. albopictus*, and *C. triaeniorhynchus* with LC$_{50}$ values of 8.37, 9.01 and 10.04 µg/ml, respectively. The AgNPs was found safer against non-target organisms *Diplonychus indicus*, *Anisops bouvieri* and *Gambusia affinis* [186]. Larvicidal activities of AgNPs against Anopheles mosquito larvae have been reported.
Lateef et al. [27] reported that AgNPs synthesized using the extract of *Bacillus safensis* displayed 100% mortality within 12h for all concentration applied and LC$_{50}$ was 42.19 µg/mL. Azeez et al. [35] reported that AgNPs synthesized using cocoa bean extract displayed LC$_{50}$ of 44.37 µg/ml against *Anopheles gambiae* mosquito larvae. Also, LC$_{50}$ of 43.52 µg/ml was reported for AgNPs synthesized using cocoa pod husk extract [36] which had larvicidal activity of 70-100% for all concentrations within 2 h of reaction.

Elumalai et al. [188] reported the use of the aqueous leaf extracts of *Leucas aspera* and *Hyptis suaveolens* to synthesize AgNPs with sizes ranging from 7-22 nm and 5-25 nm respectively. Both synthesize AgNPs displayed 100% larvicidal activity at 10 mg/l against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* with LC$_{50}$ of 4.02, 4.69, 5.06 mg/l and 4.63, 4.04, 3.52 mg/l for AgNPs mediated by aqueous leaf extracts of *Leucas aspera* and *Hyptis suaveolens* respectively. AgNPs synthesized using cheap seaweed extract of *Ulva lactuca* reported by Murugan et al. [189] was found to display mosquitocidal activities against *A. stephensi* with LC$_{50}$ values of 2.111-5261ppm for the instars and 6.860 ppm for the pupae. The antiplasmodial activity the AgNPs was evaluated against CQ-resistant (CQ-r) and CQ-sensitive (CQ-s) strains of *Plasmodium falciparum*, with IC$_{50}$ of 76.33 µg/ml (CQ-s) and 79.13 µg/ml (CQ-r). Jaganathan et al. [190] reported the synthesis of silver nanoparticles (EW-AgNPs) using *Eudrilus eugeniae* earthworms. The AgNPs was toxic to *Anopheles stephensi* larvae and pupae with the LC$_{50}$ being 4.8-8.5 ppm for the instars and 15.5 ppm for pupae. The biosynthesized AgNPs was evaluated for antiplasmodial activity against CQ-resistant (CQ-r) and CQ-sensitive (CQ-s) strains of *Plasmodium falciparum*. The IC$_{50}$ obtained were 49.3 µg/ml (CQ-s) and 55.5 µg/ml (CQ-r), while the IC$_{50}$ for chloroquine were 81.5 µg/ml (CQ-s) and 86.5 µg/ml (CQ-r) respectively. Leaf extract of *Cinnamomum zeylanicum* was used for the synthesis of AuNPs (spherical in shape with average size of 46.48 nm) which displayed mosquitocidal activity against *Anopheles stephensi* and *C. quinquefasciatus* [191]. Few reports have been recorded for the use of AuNPs as larvicidal agents. The biosynthesis of AuNPs using flower extract of *Couropita guianensis* was reported by Subramanian et al [192] and the AuNPs exhibited toxicity against the larvae, pupae and adults of *Anopheles stephensi* with LC$_{50}$ estimated at 17.36-24.57 ppm for the instars, 28.78 ppm for the pupa, and 11.23 ppm for the adult. Moreover, Ag-AuNPs have been investigated for larvicidal activities against larva of *Anopheles gambiae* and 100% mortality was obtained at 3, 24, 48 and 72 h for the seed, leaf, pod and seed shell-mediated Ag-AuNPs respectively [24].

Panneerselvam et al. [193] exploited AgNPs synthesized using *Pteridium aquilinum* leaf extract to study the *in vitro* inhibition of *P. falciparum* and their mosquitocidal potentials against the malaria vector, *Anopheles stephensi*. The AgNPs produced IC$_{50}$ of 62.04 and 71.16 µg/ml against CQ-s and CQ-r strains. Larayetan et al. [194] reported the synthesis of AgNPs with crude extracts of *Calistemon citrinus* plant and the AgNPs displayed antiplasmodial activities with IC$_{50}$ ranging from 2.99-534 µg/ml. AgNPs and AuNPs were synthesized by both leaf and bark extract of *S. jambos* and the antiplasmodial potential against chloroquine sensitive (3D7) and resistant (Dd2) strain of Plasmodium falciparum was investigated by using 24h schizont maturation assay. IC$_{50}$ values of 24.22 -51.63 µg/ml were obtained for the particles [195]. Rajakumar et al. [196] reported the synthesis of PdNPs by using leaf aqueous extract of *Eclipta prostrata*, which was active against *Plasmodium berghei* in Swiss albino mice. The in vivo assay revealed reduction of parasitemia by 78.13 % in the biosynthesized PdNPs-treated mice group with an IC$_{50}$ value of 16.44 mg/kg/body weight. Also, the PdNPs showed IC$_{50}$ and IC$_{90}$ values of 8.70, and 18.49 mg/kg/body weight, respectively against NK65 strain of *Plasmodium berghei*.

Trypanosomes are accountable of the severe human diseases which can be illustrated in two main forms of trypanosomiasis which are the African and the American types. Human African trypanosomiasis or sleeping sickness as it is popularly known occurs in sub-Saharan African countries where the tsetse fly vector transmits the disease. The agent is the haemoflagellate parasite of the species *Trypanosoma brucei*, and particularly, the single *Trypanosoma brucei gambiense* accounts for more than 98% of cases that have been reported. Millions of people are affected by Sleeping sickness and is often deadly if untreated, and it is considered a serious public health problem. The American trypanosomiasis, normally recognized as ‘Chagas disease’, is caused by *Trypanosoma cruzi* and this signifies the most important parasitic disease in the Americas [197]. Although, there are very scanty reports on the use of nanoparticles in the treatment of trypanosomiasis, spherical AgNPs (4-9 nm) and AuNPs (7-22 nm) have been reported for the potential activity against *Trypanosoma brucei* [198]. AgNPs biosynthesized using the aqueous crude extracts of aerial parts of *Callistemon citrinus* plant was reported to display anttrypanosomal activities with IC$_{50}$ of 107.30 µg/ml [194]. Also, prodigiosin, a bioactive pigments extracted from cultures of *Serratia marcescens* and *Chromobacterium violaceum* was used for the synthesis of silver and gold nanoparticles, and this was reported to display *in vitro* growth inhibition of *Trypanosoma brucei gambiense* although, the activi-
ties obtained were lower than that of the pigment itself [199].

19.0 NANOTOXICOLOGY AND NANTOXICITY

Nanobiotechnology has been rapidly growing with a wide range application in nanomedicine throughout the world. The ultra-small sizes of nanoparticles make them immensely useful in various biomedical applications; however, the same property could enhance their adverse effects, representing toxicity to environment, human beings, animals and plants [183]. There is still dearth of information on the risks that may be associated with exposure to nanoparticles, especially on prolonged usage. Nanoparticles may get inhaled deep into the lungs by human beings and animals, thereby leading to various harsh effects and health disorder. The particles go into the bloodstream and accumulate in lungs and kidney causing pro-inflammatory effects such as inflammation, genotoxicity, protein fibrillation, oxidative stress, lipid peroxidation, lung diseases and pulmonary pathological changes. The effects of nanoparticles are also based on the type and property [183].

AgNPs is an essential class of nanomaterials for a range of medical applications that may have probable risks to human health, which have been documented through studies on the genotoxicity and cytotoxicity of AgNPs. AgNPs may prompt the expression level of genes involved in cell cycle apoptosis and progression, and some of the mechanisms involved in AgNPs toxicity include oxidative stress, the induction of ROS, apoptosis and DNA damage [200]. In Allium cepa assay, the genotoxic potentials of green synthesized AgNPs with the occurrences of chromosomal aberrations have been reported [201, 202], though with mild actions compared with the Ag+. Conversely, the cell-growth arresting property of the particles could be useful in treating cancerous cell. In vivo tests, the most noteworthy problem to be understood is the actual influence of AgNPs on health of humans and animals. Due to their ultra-small sizes, AgNPs have high mobility in diverse environments, and humans are simply exposed through means such as ingestion, contact, and inhalation, through which they can be translocated to other important organs and infiltrate into the cells.

Toxicity via inhalation of AgNPs has been explored on Sprague-Dawley rats over a period of 28 days. Results indicated that the male and female rats did not show any important changes in body weight compared to the concentration of AgNPs during the experiment. There were also no significant deviations in the blood biochemical and haematology values in either the male or female rats [203]. However, there have been reports that showed that lungs are primary target tissues affected by extended exposure to AgNPs via inhalation [204, 205]. Lee et al [206] also reported that AgNPs exposure modified the expression of numerous genes connected with neurodegenerative disease, motor neuron disorders and immune cell function, signifying potential immunotoxicity and neurotoxicity that may accompany contact with AgNPs. In contrast, some results suggested that AgNPs could not prompt genetic toxicity in bone marrow of the male and female rat [207], though exposure to more than 300 mg AgNPs could induce liver damage. Generally, very few reports on the in vivo toxicology of AgNPs exist, and in such cases, there are contrasting observations, so further investigation is required in this field to appraise precisely the exact impact of AgNPs, especially in commercial products to both humans and animals.

20.0 CHALLENGES IN THE DEVELOPMENT OF NANO-MEDICALS

Notwithstanding their benefits, the probable risks of nanomedicines to both the environment and humans cannot be disregarded. Therefore, appropriate screening of nanomaterials for efficacy, biosafety, long-time toxicity, immunological interactions and comprehensive pharmacokinetics in in vivo studies is very important before proceeding to carrying out clinical trials. The major challenges confronted by researchers before biosynthesized NPs can be taken into clinical phases are biocompatibility, route of administration and its dosage, effective uptake, retention and clearance, and combinatorial approach with FDA-approved anticancer drugs [208-210]. Similarly, for the active uptake of nanomedicine, appropriate diffusion and permeation through the cell and tissue barriers are crucial. Critical issues which are related with intravascular delivery of NPs include intestinal tissue infiltration, immune rejection, discharge of drug via dispersion into the cytoplasm, crossing of endothelium to reach the target sites, probable entry into nucleus, clearance in the spleen liver, and receptor-mediated entrance into the cells [210, 211]. All the aforementioned issues that border on regulations, efficacy and safety would have to be properly resolved before novel nanodrugs can take their rightful place in the clinical practice of nanomedicine. In this view, regulations of nanomedicines would continue to develop in combination with the innovations in applications in nano-based drugs.

21.0 PROSPECTS AND FUTURE TRENDS

The science of nanomedicine is presently among the most attractive areas of research. As result of the numerous researches in this field in the last two decades, about 1500 patents have already been filed and several dozens of clinical trials have been completed [212]. The treatment of cancer and the search for new antimicrobials
appeared to be the best example of diseases where both its diagnosis and therapy have very much benefited from nonmedical technologies. Precision in the use of nanoparticles for the discriminatory delivery of drugs to the tumour or cancerous cells, without distressing the physiology of the normal cells has undoubtedly contributed to the milestone achieved in the development of nanomedicals which is on the steady rise [213]. The numerous types of nanoparticles discussed in this review are not of uniform sizes. Therefore, more researches on nanomaterials are needed to create particles with consistency in properties that would impact positively on biocompatibility, drug loading and release of drugs.

Though, MeNPs have been significantly advanced for diagnostic purposes, the trend is likely to continue in view of the exploitation of several noble metals in diagnosis and therapy. It is expected that their applications would be extended vigorously in the diagnosis and treatment of most neglected parasitic infections such as trypanosomiasis, leishmaniasis among others. One major interest includes the fact that AuNPs appear to be well absorbed in soft tumour tissues thereby making tumours to be prone to radiation-based heat treatment for discriminatory and cautious eradication [213]. In spite of the overwhelming future prospect of nanomedicine and nano-drug delivery systems, its real impact in healthcare system, even in cancer therapy/diagnosis remains to be very limited. This attributes to the field being a new area of science with only two decades of real research on the subject and many key fundamental attributes still being unknown. The fundamental markers of diseased tissues including key biological markers that allow absolute targeting without altering the normal cellular process is one main future area of research. Ultimately, understanding of the molecular signatures of diseases would promote advances in nanomedicine. Other areas that need active researches include modelling of drug-cell interactions, development of animal models to study interactions, efficacies and toxicities of nano-based drugs. There is so much enthusiasm about the roles that nanomaterials may play in the development of personalized healthcare in the future, including the concept of nanodevices and nanorobots that can function in the diagnosis and repair mechanism of tissues. All these could be attained earlier than expected through concerted efforts by researchers using multidisciplinary approach.

22.0 CONCLUSION

This review examined the roles of metallic nanoparticles as novel nanomedicals in the development of the sub-discipline of nanomedicine. Several reports on the in vitro activities of MeNPs as antimicrobial, anticancer, antioxidental, anticoagulant, thrombolytic, larvicidal, antiparasite, wound healing, and diagnostic agents were reviewed. Similarly, the basic attributes of nanoparticles, their characterization and issues relating to their toxicity were discussed. The paper can serve as an interesting piece for researchers with bias for healthcare to understand the basics of nanotechnology, be abreast of issues or challenges in their translation to clinical practice and explore the prospects that nanomedicine offer in the development of personalized and improved healthcare for mankind.

Authors’ Contribution

AL conceived and designed the study and revised the manuscript. JAE collected data, contributed to data analysis tools and performed data analysis. POA, VOA collected data, and performed data analysis. All authors approved the final manuscript.

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