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Review Article

A REVIEW ON PROPERTIES, APPLICATIONS AND TOXICITIES OF METAL NANOPARTICLES

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ABSTRACT

Nanotechnology is a broad and novel technology related to all branches of science. However, in the Pharmaceutical industry, it plays an immense role in the drug delivery system. Nanotechnology applied on metal-based drug delivery systems varies; the size ranges from 100 nm or less. Metallic nanoparticles are existing the world from the 4th century. The noble metals, like gold and silver have attracted many researchers in the class of anticancer and anti-microbial. Metallic nanoparticles are not only used in the biomedical applications also have major functions in the domain of textiles, agriculture, photography, etc. Various metals are found in various applications in the biomedical industries. At the same time, the metallic nanoparticles have been evidences of remarkable toxicity in various studies. The rationale behind this topic was that the properties, applications and toxicity of individual metal nanoparticles. As this study have not been compiled and reported. So, in the current review, the gap was filled. The main sources for the preparation of the manuscript are Pubmed, Elsevier and google scholars. Keywords used includes metallic nanoparticles, reported toxicity of metals in drug delivery, applications of metals in drug delivery, history of novel metals in drug delivery, etc. Approximately 400 reviews and academic papers were reviewed to compose the manuscript and sorted by reference to the need for a manuscript.

Keywords: Nanoparticles, Metalnanoparticles, Toxicity, Gold, History of nanoparticles

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INTRODUCTION

Throughout research as well as in normal life, nanoscience and nanotechnology have become familiar terms. The development of nonmaterial's started shortly after the Creation of the universe when early meteorites used to develop nanoparticles and nanostructures [1]. Nanotechnology applies to the metals-specific branch of science and engineering, which has dimensions in the order of 100th of nm or less [2]. Nanoparticles commonly used in the biotechnology measure of particle size between 10 and 500 nm, rarely reaching 700 nm. Nano size of these particles allows for specific interactions with biomolecules on the cell surfaces and inside the cells in ways that can be described and assigned to the specific biochemical and physicochemical properties of such cells [3]. Nanomaterials is components with at least one dimension having the scale<100 nm. Now, Nanomaterials is an attractive field in medicine and agriculture, the discovery of nanomaterial has introduced a new field of science called nanotechnology, a concept that was first used by noriotaniguchi, a Japanese scientist from Tokyo University [4]. Nanoparticles are extremely attractive for several biomedical applications. Due to their capability to interact with the molecular or cellular process and the possibility to influence their functions [5]. Different types of nanoparticles used in pharmaceutical nanotechnologies are polymer nanoparticles, liposomes, dendrimers, polymer-drug conjugates and antibody-drug conjugates. Pharmaceutical nanotechnology typically classifies sustained and controlled delivery systems, stimulus-sensitive delivery system, and multifunctional system for combined therapeutic delivery, biosensing, diagnostics and site specific drug delivery [6].

The term metal nanoparticle is used to describe nano-sized metal with dimensions (length, width or thickness) within the size range 1-100 nm. Metal is substances with high malleability and the luster of electrical conductivity that willingly lose their electrons to form cations. Metal is naturally present in the Earth's crust and their distribution varies from one locality to another, resulting in spatial differences in the surrounding concentration [7]. Metallic nanoparticles have special properties, such as phonon surface resonance and optical properties. Metallic nanoparticles have shown various properties in the field of nanotechnology and have enabled certain new pathways in nanotechnology. Metallic nanoparticles have necessary functional groups. It can be produced and altered so that they can link to ligands, antibodies and drugs [8]. Noble metal, especially silver and gold, has attracted a great deal of attention from researchers in various fields of science and technology, such as catalysis, photography, the healthcare industry as anti-cancer and anti-microbial agents [9]. Priyadhashini KC, et al. studied an antimicrobial and anticancer activity of silver nanoparticles from edible mushroom and the authors intends to present green synthesis of silver nanoparticles and their application as antimicrobial and anticancer agents. [10]. DA Silva et al. studied recent advances in the use of metallic nanoparticles with anti-tumoral action and the authors are summarized the anti-tumor activities of 78 papers of various metallic nanoparticles, particularly the one's containing copper, gold, iron, silver and titanium in their composition [11].

Specifically, functionalized nanoparticles, such as metallic nanoparticles can overcome such weaknesses of conventional therapies, such as low water solubility or lack of target specificity [12]. Optical properties of metal nanoparticles had been studied in great detail. Investigations on optical properties, reason bridge gap between an atom property and a bulk material. Metal nanoparticles have unique properties, which are significantly dependent on their scale, shape, composition and dielectric constant [13-15]. This study is mainly focused on the various metals used in the pharmaceuticals and their properties, toxicity and applications of the metallic nanoparticles.

History and development

The strengthening of ceramic matrixes through the incorporation of natural asbestos nanofibers more than 4500 y ago [16]. There are natural sources such as rocks, plants, and animals also create all kinds of natural nanomaterials [17]. Nanoparticles have a long history. The gold metal, first mined near Varna in 5th millennium B. C. Artisans used nanoparticles, the popular Lycurgus cup made from dichloric glass as far back as Rome in the 4th century, as well as in the 9th century in Mesopotamia to generate a glittering effect on the surface of objects [18]. Michael Faraday, who first turned to metallic nanoparticles for beautiful stained glass in color. And, in his groundbreaking paper in 1857, he introduced the scientific jargon for the optical properties of nanometer-scale metals [19]. It is well established that a remarkable shift in properties takes place when thin leaves of gold or silver are placed on the glass and heated to a temperature well below a red heat (~500 °C) [20]. Metallic film consistencies are broken. The implication is perhaps that white light is now transferred freely, reflections are depleted correspondingly, the electrical resistivity is increased tremendously [21]. Nearly 100 y later Turkevich *et al.* used microscopic electronic investigations to demonstrate that the ruby-colored colloids developed by Faraday's

preparatory routes contain gold particles with average sizes of 6±2 nm [22]. Colloidal silver was first synthesized in 1880s by Mathew Carey Lea of Philadelphia. In the 20th century, colloidal silver was commonly used in the photographic film industry, found by X-ray diffraction to be metallic silver [23]. Carey Lea colloidal silver normally scales 7-10 nm [24]. In 1902, Alfred C. Barnes invented Argyrol, a new silver antiseptic drug, derived from the Greek word, silver Argyros. It plays a significant role in wiping out infection in the upper respiratory tract. No ciliary toxicity, no systemic toxicity and no pulmonary risks were reported [25]. Silver has a lot of medicinal benefits and treats a variety of diseases. This has both antiseptic and antibacterial properties. In 1890, the bacteriologist Robert Koch discovered that K [Au (CN) 2] potassium gold cyanide had anti-microbial activity against the Tubercle bacillus at small concentrations and from there gold is used in modern medicine [26]. Michel Peyrone synthesized cisplatin (platinum, which contains anti-cancer drugs) in 1845 [27]. Alfred Werner elucidated the structure of cisplatin in 1893 thus, Roserberg studied the function of cisplatin for antitumor. Gold nanoparticles were used in the 17th and 19th centuries to treat fever and syphilis [28], respectively. In the late 1960s, Moyer and Monafo developed 0.5 percent silver nitrate solution to treat burn wounds [29]. The copper and zinc complexes have been used to treat numerous diseases, including inflammatory and degenerative diseases [30]. For the first time Paracelsus used zinc sulfate in his prescription, which pioneered the biomedical field for the application of zinc-based drugs in therapeutic applications. Ancient Romans and Greeks have used copper and copper compounds to deal with burns, cough and ear infection. In 1832, copper was considered to be able to improve immunity against cholera. These have also been commonly used to treat anemia, eczema, syphilis, tuberculosis, etc., [31, 32]. Further, the newest material, titanium and its alloys are employed in biomedical applications, including dentistry [33].

Nobel metals in nanoparticles

Nanoparticles of metal or metal oxides are considered as metallic nanoparticles. These approaches are used widely for therapeutic applications, diagnostic applications and other fields like optics, photophysics, catalysis, electronic and magnetic materials. Owing to their relatively high chemical activity and association specificity, they have gained substantial interest in the last few years. Nanoparticles have distinctly different physicochemical properties with metal nanoparticles compared to their voluminous counterparts due to their large surface-to-volume ratio, including most of the highly active undisciplined metal sites [34]. Metal nanoparticles are predominantly used for medical purposes as carriers of biomolecules (drugs, peptides, antibodies, nucleic acid, aptamers, etc.,). Metal nanoparticles are submicron-scale entities made of pure metals such as gold, platinum, silver, titanium, zinc, cerium, iron and thallium or their derivatives of oxides, hydroxides, sulfides, phosphates, fluorides, and chlorides [35] Metal nanoparticles themselves have been commonly used as targeted therapy for many diseases such as cancer, cardiovascular disease, diabetes, retinal disorders, a neurodegenerative disorder, microbial infections, etc. also used for the delivery of biomolecules [36]. In this article focuses on the noble metals and their properties, applications, and toxicity.

Gold nanoparticles

Metallic nanoparticles have been highly utilized for biomedical applications. Of various nanoparticle, gold nanoparticles (AuNPs) have provoked considerable attention due to their unique optical properties. Much research has examined the optical characteristics of AuNPs with various sizes and shapes over the last two decades. Au NPs' special optical properties emerge from the effect of size confinement [37] and the intense, vibrant color of a colloidal gold solution caused by the absorption of surface plasmon resonance (SPR) [38]. AuNPs band surface plasmon resonance (SPR) and their significant physical properties depend on their morphology, such as shape, solvent, surface ligand, core power, temperature, and physiology [39]. Au NPs can be used as tools for the detection of single-molecule surface-enhanced Raman scattering (SERS) [40]. Due to their specific characteristics, AuNPs have received significant engross from distinct areas of science: high X-ray absorption coefficient, ease of structural manipulation, specific control of the physical and chemical properties of the particles [41], extreme binding affinity to thiols, disulfides and amines [42], remarkable optical adjustable and unique electronic properties [43].

Applications of AuNPs

Significant features of AuNPs used in photodynamic therapy (PDT) include selective fluorescence quenching and SPR absorption. The PDT used for oncological diseases and other skin or infectious diseases employs photosensitizers as light-sensitizing agents and a laser [44]. AuNPs have gained primary importance as an x-ray contrast agent because it represents a high coefficient of X-ray absorption, ease of synthetic processing, non-toxicity, colloidal stability and targeted delivery surface functionalization [45]. Further, AuNPs are active Nanocarriers for theranostic drugs such as peptides, proteins [46, 47], plasmid DNAs (pDNAs), small interfering RNAs (siRNAs), and chemotherapy agents. Besides, Nanorods and nanocages of colloidal gold are good candidates for drug delivery. AuNPs have been applied to detect various analytes such as metal ions, anions and molecules such as saccharides, nucleotides, proteins and toxins as effective sensors [48].

Toxicity of AuNPs

AuNPs are typically considered non-toxic, inert and biocompatible as bulk gold. Indeed, Various studies have been reported that AuNPs cause adverse effects when cells pick them up and preserve them because these nanoparticles can transform into potent catalysts. According to the research of Yan-Peng Jia *et al.*, The study concluded that gold nanoparticles are toxic when it's used in biological systems at certain concentration levels. Also, they have summarized from *in vitro* work that gold nanoparticles also induce endogenous reactive oxygen species (ROS) development after entering the cells, leading to additional oxidative stress-related cytotoxicities, such as DNA damage, cell death (apoptosis and necrosis) and consequent cell cycle arrest. ROS is thus among the basic function, which causes the harmful effects [49]. Another research found that AuNPs cause damage to DNA, confirming their genotoxicity [50]. Oxidation of protein and polyunsaturated fatty acid, eventually leading to a deliberate alteration in mitochondrial function, which is the primary cause of cell death. With the aid of DiOC6(3) dye, mitochondrial damage caused by spherical PEG-AuNPs on K562 cells after 24-72 h treatments were assessed by monitoring changes in the capacity for mitochondrial transmembrane [51]. In addition, AuNPs induces toxic material leakage due to pH variations, cell damage due to being contacted with membrane lipids and proteins, endocrine disturbance, gene expression modification, cellular morphology changes [52].

Silver nanoparticles

Silver nanoparticles (AgNPs) are nanoparticles of silver, in the range of 1 to 100 nm. Silver nanoparticles have remarkable properties that aid in molecular diagnostics, medications, and instruments used in various medical procedures. It has been well known that silver ions and silver related compounds are highly toxic to micro-organisms including 16 major bacterial species [53]. Silver nanoparticles are extremely efficient to absorb and scatter light, depending on the particle surface size, the shape of the particle and the refractive index. The strong interaction of silver nanoparticles with light occurs because, when excited by light at specific wavelengths, the conduction electrons on the metal surface undergo a collective oscillation called a surface plasmon resonance (SPR), this oscillation results in extremely strong dispersion and absorption properties. As particles of aggregate, the optical properties of silver nanoparticles changes and the conduction electrons near each particle surface are delocalized and shared by neighboring particles. As this happens, the frequency of the surface plasmon changes to lower energy, allowing the peaks of absorption and dispersion to shift to longer wavelengths. UV-Visible spectroscopy can be used to track the stability of nanoparticle solutions as an easy and reliable tool [54, 55]. It is a known fact that the shape of silver nanostructures can influence its physical and chemical properties drastically. Silver nanostructures commonly used for biomedical applications include

silver spherical nanoparticles, nanowires, nanorods, nanoplates and nanotubes [56].

Applications of AgNPs

AgNPs function as an antibacterial is wide-ranging, affecting gram-positive as well as gram-negative bacteria [57]. Silver nanoparticles work on and penetrate the bacterial cell wall, causing structural changes in the cell membrane such as cell membrane permeability and cell death or by releasing silver ions via nanoparticles, these ions can interact with and inactivate the thiol groups of many essential enzymes [58]. Then, there is the production of reactive oxygen species, likely created by silver ions inhibiting a respiratory enzyme and attacking the cell itself. AgNPs have also been shown to suppress HIV-1, Tacaribe virus (TCRV), hepatitis B virus (HBV), recombinant respiratory syncytial virus (RSV), the monkeypox virus, murine rotavirus (MNV)-1, and influenza A/H1N1 virus. This is usually observed as strong radiosensitizers and/or photo-sensitizers. It has been stated that grapheneoxide@Ag-doxorubicin-DSPE-PEG2000-NGR (GO@Ag-DOX-NGR) exhibits excellent chemophotothermal therapeutic efficacy, tumor-targeting properties, laser-controlled drug release functions of NIR and *in vivo* murine tumor model X-ray imaging capability [59]. The AgNPs have shown promising effects on antitumors. Low concentrations of AgNPs have been documented to cause DNA damage and chromosomal aberrations (genotoxicity), although no significant cytotoxicity has been recorded [60].

Toxicity of AgNPs

The deleterious effects of free silver ions on humans and all life forms entail severe bluish-gray discoloration of the skin (argyria) or eyes (argyrosis) and exposure to soluble silver compounds can result in toxicity such as damage to the liver and kidneys; Inflammation of the eyes, skin, respiratory and intestinal tract; and unfavorable changes in blood cells [61]. Al Gurabi *et al.*, studied Ag nanoparticles were studied with *in vivo* in various organs such as the liver, kidney, lungs, spleen and brain in different subjects, after exposures by inhalation or subcutaneous injection. Silver nanoparticles has demonstrated more toxicity in terms of cell viability, lactate dehydrogenase leakage and production of reactive oxygen species (ROS) compared with other nanoparticles [62].

Platinum nanoparticles

Platinum nanoparticles (PtNPs) are usually within the sort of suspension or colloid of nanoparticles of platinum during a fluid, usually water. Physical properties of pt Nps such as brownish red or black color, spherical, rod, cubes and tetrahedral in shape. Size is about 2 and 10 nm [63, 64].

Applications of PtNPs

Platinum-based nanomaterials have been shown as excellent therapeutic agents [65]. Platinum compounds such as cis-platin, carboplatin and oxaliplatin are frequently used in chemotherapy, especially in the treatment of ovarian and testicular tumors [66]. Since platinum group compounds are cytotoxic, tea capped platinum nanoparticles were investigated for his or her toxic behaviour towards human cancer cells. It was also important to examine if these are toxic to both the healthy and cancer cells, similar to the platinum complexes such as cis-platin and carboplatin used in the treatment of cancer. They have many side effects like nausea, vomiting, nephrotoxicity, neurotoxicity, ototoxicity, hematuria and alopecia. Cervical cancer cells (SiHa) were, therefore, treated with different concentrations of tea capped platinum nanoparticles. The influence on cell viability, nuclear morphology and cell cycle distribution showed that the proliferation of SiHa cells was inhibited by platinum nanoparticles. The tea polyphenol capped platinum nanoparticles exhibited excellent viability at a concentration between 12.5 and 200 μgml−1 for twenty-four and 48 h. A significant dose-dependent decrease in cell viability was noticed with increasing concentration of nanoparticles. When the concentration is enhanced, the area is additionally enhanced alongside the massive size of the tea polyphenol. The particle size and their agglomeration are equally responsible for the cytotoxicity of platinum nanoparticles [67]. Although platinum alloys have been used in the coronary artery disease, neuromodulation devices and catheters, [68] they're not selective for cancer because they influence both the traditional cells and cancer cells, resulting in many complications. Functioned platinum nanoparticles have shown size_ and shape_dependent specific and selective therapeutic properties [69, 71]. In many cases, platinum nanoparticles containing other organic substances have also been used as pro_drug [65, 72]. Manikandan *et al.* [73] have shown that tiny platinum nanoparticles (5–6 nm) are biocompatible and exhibit apoptosis-inducing properties [74, 75]. This ability is enhanced manifold when they are coated with polymers or fortified with phytochemicals. For instance, the herbal extracts, generally used for green synthesis of nanoparticles, contain phenol, sugar and acids, which act as reducing as well as stabilizing agents. Such phytochemicals in combination with cis_platin synergism apoptosis in breast cancer and cervical cancer [63, 67, 76]. A combination of platinum nanoparticles with ion irradiation has been found to enhance the efficiency of cancer therapy [77].

Toxicity of PtNPs

Toxicity stemming from platinum nanoparticles can take multiple forms. One possible interaction is cytotoxicity or the power of the nanoparticle to cause necrosis. A nanoparticle can also interact with the cell's DNA or genome to cause genotoxicity [78]. These effects are seen in altered levels of gene expression measured through protein levels. Last is the developmental toxicity that can happen in an organism's growth. Developmental toxicity looks at the impact the nanoparticle has on the expansion of an organism from an embryonic stage to a later point. Most nanotoxicology research is done on cyto_ and geno_toxicity as both can easily be done in a cell culture lab.

Platinum nanoparticles have the potential to be toxic to living cells. In one case, 2 nm platinum nanoparticles were exposed to 2 differing types of algae so as to know how these nanoparticles interact with a living system [79]. In both species of algae tested, the platinum nanoparticles inhibited growth, induced small amounts of membrane damage, and created a large amount of oxidative stress. In another study, the researcher tested the consequences of differently sized platinum nanoparticles on primary human keratinocytes. The authors tested 5.8 and 57.0 nm PtNPs. The 57 nm nanoparticles had some hazardous effects, including decreased cell metabolism but the effect of the smaller nanoparticles was much more damaging. The 5.8 nm nanoparticles exhibited a more deleterious effect on the DNA stability of the first keratincoytes than the larger nanoparticles. The damage to DNA was measured in individual cells using single_gel electrophoresis via the comet assay [80].

Nickel nanoparticles

Nickel nanoparticles (NiNPs) are typically 10_14 nm with specific surface area (SSA) within the 30-50m^2/g range and also available with a mean particle size of 50-100 nm range with a selected surface area of approximately 5_10m^2/g. NiNPs find potential applications in various fields, including electronics, magnetism, technology and biomedicine. Optical properties of NPs are highly dependent on the size of particles. Magnetic properties of the $NiFe_2O_4$ with an inverse spinel structure can be explained in terms of the cations distribution and magnetization originates from Fe^{3+} ions at both tetrahedral and octahedral sites and Ni^{2+}ions in octahedral sites [63].

Applications of NiNPs

It is employed within the treatment of prostate enlargement so as to spice up the function of T_cells and goes to work and perform more efficiently. β_sitosterol inhibits neoplastic cell proliferation by decreasing the expression of PCNA or signalling. It inhibits the secretion of proinflammatory cytokines and tumor. β-sitosterol have antinflammatory efficacy inhibiting cholesterol absorption in the lower intestine, thereby reducing excess of cholesterol in the blood, preventing atherosclerosis [81]. Ahmed AS *et al.*, investigated the NiNPs usage on plants. It controls fusarium wilt on lettuce and tomato. NiNPs inhibits the mycelial proliferation and aporulation of fungal pathogens [82].

Toxicity of NiNPs

A study has shown effects on interleukin on NiNPs, may cause the amount of peroxidase and catalase was decreased and

malondialdehyde was increased. Interleukin-4 and interferon-ɣ Were cytokines that were significantly increased within the experimental group, compared with the controls. Thus, increase of interleukin with a rise in nickel oxide nanoparticles could create a disturbance within the production of interleukins by impacting the system within the body. An identical state of the condition could also occur within the case of increased humoral immune reaction [81]. Another was reported on the toxicity of NiNPs on continuous inhalation. It causes death due to adult respiratory distress syndrome (ARDS). Also, it causes acute tubular necrosis [83].

Palladium nanoparticles

The mean diameter of monodispersed palladium nanoparticles (PdNPs) might be controlled from 17 to 30Å in a one-step reaction by changing the quantity of protective polymer Poly (N-vinyl-2-pyrrolidone) (PVP). Palladium may be a rare and valuable that belongs to the platinum group elements. It's largely employed as a lively catalyst material in automotive catalytic converters but finds also apply within the electronic engineering, biomedical and jewelry sectors [64].

Applications of PdNPs

Palladium adsorbs about 1000 times its own volume of hydrogen when brought to dull redness. Their catalytic activity is thanks to the dissociation of molecular hydrogen into the atomic state: $H2 \rightarrow 2H$. Palladium nanoparticles doped with Chitosan–graphene are employed as a biosensor for glucose estimation [84]. Palladium nanoparticles on graphene oxide have also been used as recyclable heterogeneous catalyst for the reduction of nitrogen using sodium borohydride. Since the recovered catalyst is often used for five cycles, it is often used in a large-scale reduction of nitrogenous. It's also been utilized in the reduction of methylthionine chloride, azo dye and nitrophenol. The nanoparticles exhibited excellent degradation of the above dyes and thus, both palladium and platinum are extensively utilized in oxidative addition and reductive elimination of hydrogen. Platinised asbestos is employed in many catalytic [75] reactions. As an example, (i) within the contact process for the manufacture of H_2SO_4, (ii) in Ostwald process for the oxidation of NH_3 to NO for the manufacture of HNO_3, (iii) oxidation of methanol to formaldehyde and (iv) decomposition of hydrazine to nitrogen and ammonia. Platinum-gold dendrimer-like nanoparticles supported on polydopamine graphene oxide reduce nitrophenol to aminophenol [85]. The power to catalyze the reduction depends on platinum to gold ratios. Palladium nanoparticles are fabricated from S. persica root extract, and their catalytic activity was examined within the Suzuki coupling reactions of aryl halides with benzeneboronic acid in water to biphenyl [86]. The efficiency of the conversion rate as a function of your time and yield follows the order iodobenzene>bromobenzene>chlorobenzene, although the highest conversion occurred within the first 2 min. The palladium nanoparticles as catalyst are often successfully reused for less than three cycles. In another study, the common myrtle leaf extract was used for the assembly of Pd/TiO_2 nanoparticles [87]. The authors have demonstrated that Pd/TiO_2 nanoparticles as a highly efficient, stable and recyclable catalyst for the ligand-free Suzuki–Miyaura coupling reaction.

Toxicity of PdNPs

Exposure to Pd-NPs was reported to induce different toxic effects on various cellular models. The assessment of cell viability in human colon adenocarcinoma Caco-2 cells and HaCaT keratinocytes, treated with Pd-NPs, revealed only minor effects, maybe associated with the cellular stress caused by the NP application [88]. On the opposite hand, Wilkinson *et al.* [89] showed that the exposure of primary bronchial epithelial cells (PBECs), and lung carcinoma epithelial cells (A549) to stimulate the upper and lower tract, respectively, to Pd-NPs resulted during a concentration-dependent cytotoxicity. Of note, PBECs were markedly more suffering from Pd-NPs than A549 cells. In line with these findings, apoptosis was induced during a dose-dependent manner by Pd-NPs in PBECs, but not in A549 cells [89]. Nanoparticle chemical composition appeared also applicable to work out cellular viability effects since individual PdNPs resulted in less cytotoxicity compared to bimetallic Pt-Pd-NPs on human epithelial cervical cancer HeLa cells [90]. Such enhanced effect might be ascribed to a synergistic action of both components. Also, the sort of NP surface coating was shown as a possible influencing factor for the Pd-NP toxicological profile. Recent research on the mechanism of palladium toxicity suggests high toxicity if measured on an extended timeframe and at the cellular level within the liver and kidney. Mitochondria seem to possess a key role in palladium toxicity via the mitochondrial membrane potential collapse and depletion of the cellular glutathione (GSH) level. Until that recent work, it had led to believe that palladium was poorly absorbed by the physical body when ingested [91].

CONCLUSION

In the present century, metallic nanoparticles are highly demanded in the area of drug delivery and drug targeting. In the study of natural products, green synthesis of nanoparticles is strongly implicated. This review pedestals the development of metallic nanoparticles in the area of antimicrobials, anti-cancer, anti-inflammatory, degenerative diseases, dentistry and immunity boosters have paid great attention. In addition, numerous studies, evidence cytotoxicity and the additional toxicity profiles is included. As metallic nanoparticles have good potential for drug targeting and drug delivery, similar toxicity was also raised. So, proper understanding and selection of metal could avoid the remarkable adverse effects. From the countless research on metallic nanoparticles, very few products are existing in the market. Gaps from research to market through proper pilot study, development, technology, characterization and testing have to be eliminated. As far as metal nanoparticles are a great choice for cancer drug delivery, with appropriate establishments, sophisticated technology in formulating and extensive clinical studies provides the great platform for several diseases.

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All the authors are contributed equally to this work.

CONFLICT OF INTERESTS

The authors hereby confirm that there is no conflict of interest.

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