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Review

Nanoparticles, a Double-Edged Sword with Oxidant as Well as Antioxidant Properties—A Review

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Abstract: The usage of nanoparticles became inevitable in medicine and other fields when it was found that they could be administered to hosts to act as oxidants or antioxidants. These oxidative nanoparticles act as pro-oxidants and induce oxidative stress-mediated toxicity through the generation of free radicals. Some nanoparticles can act as antioxidants to scavenge these free radicals and help in maintaining normal metabolism. The oxidant and antioxidant properties of nanoparticles rely on various factors including size, shape, chemical composition, etc. These properties also help them to be taken up by cells and lead to further interaction with cell organelles/biological macromolecules, leading to either the prevention of oxidative damage, the creation of mitochondrial dysfunction, damage to genetic material, or cytotoxic effects. It is important to know the properties that make these nanoparticles act as oxidants/antioxidants and the mechanisms behind them. In this review, the roles and mechanisms of nanoparticles as oxidants and antioxidants are explained.

Keywords: nanoparticles; oxidant; antioxidant; ROS; oxidative stress

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1. Introduction

Nanoparticles are defined as materials with an overall size between 1 and 100 nanometres [1–3]. Their size, chemical reactivity, energy absorption, biological mobility, strength, surface area, sensitivity, and stability make them distinctive from bulk materials. These nanoparticles have recently emerged as major players in contemporary medicine, serving as anything from gene carriers for targeted cell distribution to contrast agents in medical imaging [1,4]. Based on the materials they are made of, these nanomaterials can be broadly classified as a metallic and non-metallic nanoparticles. Metallic nanoparticles (MNPs) are the nanoparticles that comprise inorganic metal, metal oxide cores, or metal-associated particles. Some of the commonly known metallic nanoparticles are aluminium [5], gold [6], iron [7], copper [8], silver [9], cerium [10], manganese [11], zinc [12], titanium oxide [13], nickel [14], quantum dots [15], etc. [16]. Non-metallic nanoparticles include ceramic-based nanoparticles, carbon-based nanoparticles, silica-based nanoparticles, and biological macromolecule-derived nanoparticles [16,17]. These nanoparticles are used in various applications including in the treatment of wastewater, for example, in heavy metal removal, as antibacterial agents, antioxidant agents, anticancer agents, drug delivery self-oxidation, etc. [18–25]. In general, antioxidants are compounds that prevent molecules from oxidizing, which can result in the production of free radicals. Eventually, polymerization and other chain reactions will occur.

A number of antioxidants, including glutathione, mycothiol, uric acid, bilirubin, albumin, bacillithiol, and superoxide dismutase, serve as protective mechanisms against oxidative stress. Antioxidants work to counter oxidants in some way. Natural or synthetic substances known as antioxidants can prevent or delay the cellular damage caused by oxidants such as reactive oxygen species (ROS), reactive nitrogen species (RNS), unstable ions and molecules, etc. [26,27]. ROS are free radicals comprising reactive oxygen ions and peroxides and are produced in the metabolism of any living system. ROS have harmful effects on biomolecules such as DNA, RNA, protein, and lipids, and cause most pathological diseases in humans [28]. As a result, excessive ROS production damages cells and tissues. When this ROS level increases, the weakening of antioxidant protection leads to oxidative stress [29] and damage to macromolecules including DNA, causing mutations and promoting tumour growth. Nanoparticles act as oxidants and tend to have a negative impact on living systems via oxidative stress. Some nanoparticles act as antioxidants to nullify the action of oxidants. An antioxidant molecule donates electrons to free radicals and neutralize them to limit the damage to the body [30]. Antioxidants are obtained through foods, and most known antioxidants are plant-derived products [31]. When nanoparticles are incorporated with these antioxidant metabolites, this enhances the antioxidant properties, and these nanoparticles are referred to as nano-antioxidants. Antioxidant properties have been reported in metal and metal oxide nanoparticles, carbon nanotubes, cerium oxide nanoparticles, gold nanoparticles, copper nanoparticles, and several forms of polymer-loaded antioxidant nanoparticles [32]. Some oxide nanoparticles have inherent physicochemical properties that allow them to scavenge reactive nitrogen and oxygen species and mimic an antioxidant molecule that has been shown to be effective in treating a variety of ailments brought on by oxidative stress [33–36].

From the previous paragraph, it is clear that nanoparticles can act as oxidants and antioxidants. In this review, the mechanisms of metal and non-metal nanoparticles as oxidants and their potential negative effects, as well as the mechanisms of antioxidant activity of nanoparticles and their advantages, have been discussed in detail.

2. Mechanism of Nanoparticles as Oxidants

The imbalance caused due to increased pro-oxidants and lessened antioxidants within the cell is referred to as cellular oxidative stress [37–39]. One of the most prevalent types of oxidative stress is the generation of reactive oxygen species, such as the superoxide radical ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), hydroxyl radical (OH), nitric oxide (HNO), and peroxynitrite (NO_3) [38]. The characteristics that contribute to the generation of nanoparticle-induced ROS are as follows: the active surface of the nanoparticle, the size of the nanoparticle, photoactivation, toxins, metal ion dissolution, and nanoparticle interactions with biomolecules (Figure 1). Nanotoxicity is heavily influenced by oxidative stress, as depicted in Figure 2 [37]. ROS production within cells after the cellular entry of nanoparticles (NP) and the intracellular release of nanoparticles leads to increased ROS levels in the mitochondria, decreased ATP levels causing a flux in the tricarboxylic acid (TCA) cycle, and lowered cardiolipin, one of the important phospholipids required for the functioning of mitochondria [40,41], thus leading to mitochondrial dysfunction. Important contributors to NP-induced ROS include the reactive surface of NP with pro-oxidant functional groups, surface redox activation on transition metal-based NPs, and interactions between particles and cells [42,43].

Where positively charged nanoparticles interact electrostatically with negatively charged groups on the membrane surface, the plasma membrane is prone to rupture. By interacting with anionic and cations, gold nanoparticles with either a negative or positive charge modify the membrane's surface charge, producing a net surface charge [44,45]. In the rupture of the endothelial cell membrane, the form of the nanoparticles is also crucial since needle-shaped nanoparticles are more likely to cause harm than sphere- or flat-shaped nanoparticles [46,47]. Nanoparticles are able to diffuse more easily at elevated temperatures since their surface-area-to-volume ratio is high. It is because of this property that nanoparticles can sinter at lower temperatures than larger particles [48]. The formation

of reactive groups on the particle surface is caused by the structural/chemical imperfections of particles. When these reactive groups react with oxygen molecules, it leads to the production O^{2-}, followed by the Fenton reaction, where more ROS is produced [49]. The Fenton reaction, or a Fenton-like reaction, is influenced by NPs, and involves the dissociation of metals ions from NPs. Dissociated metal ions can inhibit cellular enzymes, disrupt membrane structure, interfere with electron-shuttling processes, lower redox potential, lower mitochondrial membrane potential, and again increase intracellular ROS. Furthermore, NPs have been shown to generate intracellular ROS by disrupting electron transfer, raising the ratio of NADP+/NADPH, and interfering with mitochondrial function. The above processes yield superoxide anions, which can then combine with nitric oxide radical (NO) to form reactive nitrogen species (RNSs), such as peroxynitrite anion, nitrogen oxide radical, nitrate anion, carbonate anion, etc. These free radicals can kill cells by damaging proteins, lipids, and nucleic acids, and lead NP-induced genotoxicity, oncogenesis, multidrug resistance, aging, etc. [50–55]. Many studies have been conducted to prove that NPs could cause ROS-mediated toxicity in vitro and in vivo [56].

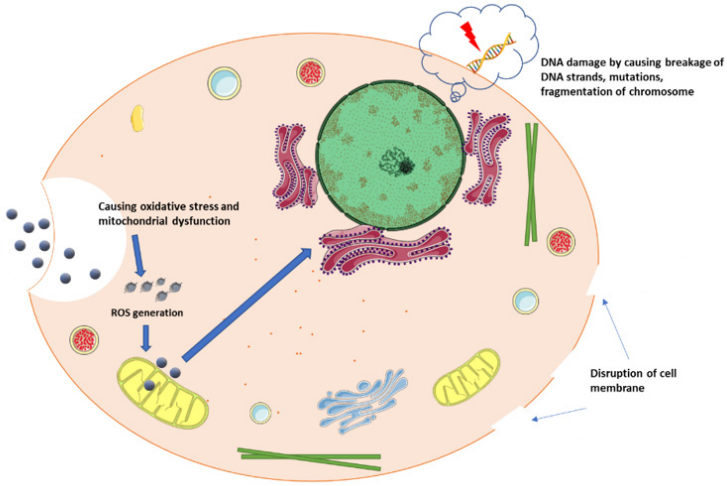

Figure 1. Mechanism of nanoparticles as oxidants (inspired from Khanna et al. [37]).

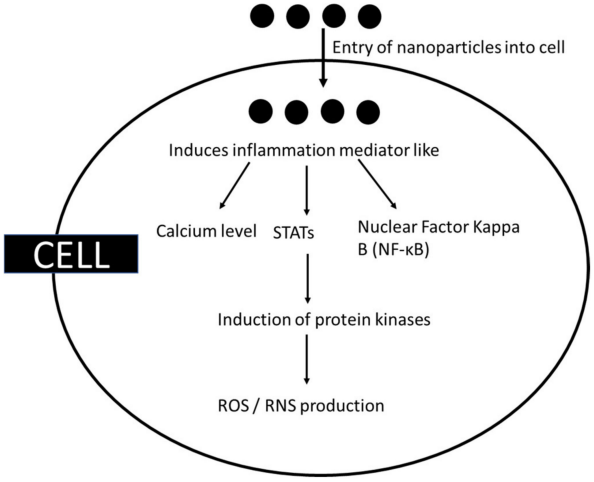

Figure 2. ROS generation by metal nanoparticles.

Ingestion, inhalation, and injection are the three basic routes through which nanoparticles may enter the body. Through inhalation, nanoparticles settle down on the mucous, causing inflammatory responses and oxidative stress in the lungs and damaging the epithelial cells, thus releasing interleukins responsible for inflammation. This causes diseases such as asthma, metal fume fever, fibrosis, carcinogenesis, etc. [57]. The use of nanoparticles

in consumer products and biomedical applications has led to the ingestion of nanoparticles that then reach the gastrointestinal tract. Then, nanoparticles enter the blood and other organs, interacting with gastrointestinal tract mucosa and affecting the luminal components, mucosa, and microbiome of the gastrointestinal tract [58]. The injection of nanoparticles mostly happens while using NPs for drug delivery or as contrast agents. This leads to hemolysis, platelet activation, and platelet aggregation [59]. Once they enter the bloodstream, they may produce unfavourable biological outcomes in a wide range of organs considered secondary sites of contact. They have been shown to spread to a variety of organs, including the kidneys, brain, spleen, liver, and heart. As the kidneys play an important role in xenobiotic elimination, renal clearance can eliminate NPs absorbed in systemic circulation. The physicochemical properties of NPs play a vital role in translocation, and their migration to remote areas is a major concern for toxicity [60]. As they enter the organs, they induce ROS production, oxidise proteins, and damage DNA, which can be detected by carbonyls and estimating 8-hydroxy-2′-deoxyguanosine. In most instances, oxidative stress blocks antioxidant enzymes, including catalase, superoxide dismutase, and glutathione peroxidase, and depletes non-enzymatic antioxidants such as glutathione, vitamin E, and vitamin C [61,62].

2.1. Metal-Based Nanoparticles as Oxidants

Metal nanoparticles can drive redox processes, resulting in the continuous endogenous generation of ROS in a positive feedback loop, causing major genotoxicity. The chronic oxidative stress that occurs following exposure to metal NPs is mediated by the upregulation of inflammatory mediators such as nuclear factor kappa B (NF-κB), signal transducer and activator of transcription (STATs), mitochondrial dysfunction, and higher intracellular calcium levels [63] (Figure 3). They can either directly or indirectly activate the mitogen-activated protein kinase pathways leading to the production of reactive free radicals [64,65]. As mentioned earlier, the physiochemical properties of metal NPs such as size, configuration, composition, shape, surface area, functionalization, charge, magnetic property, etc., have a direct/indirect and significant impact on the induction of oxidative stress [66] and lead to genotoxicity or cellular toxicity. NPs are directly responsible for causing ROS to form when they are in the acidic environment of lysosomes. NPs have been proven to cause damage to the DNA strands and change gene expression [64,65]. It was reported that ROS generation caused by hydrophilic NPs such as titanium oxide can lead to cancerous growth. In one study, titanium NPs was found to cause benign mouse fibrosarcoma that later became malignant [65].

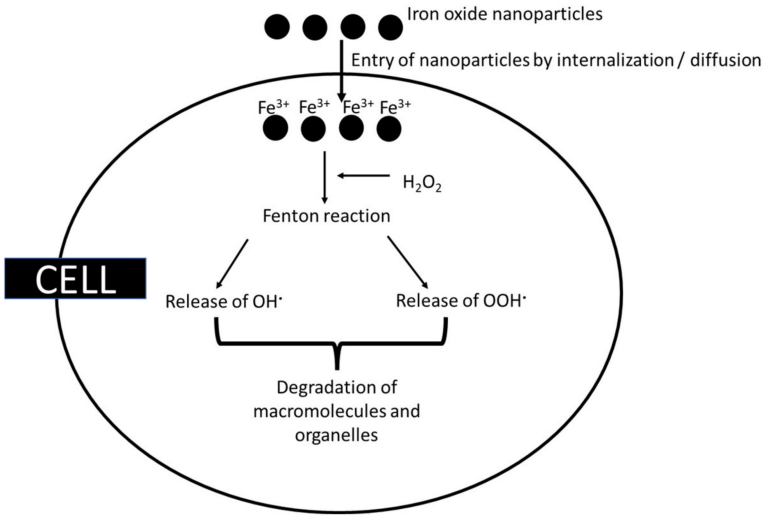

Figure 3. Oxidative damage caused by iron oxide nanoparticles.

2.1.1. Iron Nanoparticles as Oxidants

Through the Fenton reaction, iron nanoparticles produce redox-active iron and hydroxyl ions in the presence of hydrogen peroxide (refer to Equation (1)) [67,68], leading to the release of hydroxyl radicals. A particular illustration of the Fenton reaction is the Haber–Weiss reaction. In order to create a reactive species that can oxidise a wide range of organic substrates, hydrogen peroxide and ferrous salts must react. If Fe^{2+} can be produced from Fe^{3+} again, iron may have catalytic properties [69]. Superoxide radicals also liberate Fe^{2+} from ferritin, an intracellular iron-storage protein, or other proteins with $[4Fe\text{-}4S]^{2+}$ clusters that favour the Fenton reaction. Furthermore, NADH triggers the Fenton reaction by reloading Fe^{2+} from Fe^{3+} [67].

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{\cdot} + OH^{-} \quad (1)$$

Furthermore, ferrous iron can be converted to ferric iron, which can then react with superoxide radicals to restart the reaction. Additionally, ferric iron can form superoxide radicals when it reacts with peroxide radicals [67,70]. A variety of diseases, including neurodegenerative diseases, cardiovascular disorders, and cancers, have been linked to these compounds in the body. During ferrite-based ROS-mediated cancer therapy, these iron oxide nanoparticles are converted by hydrogen peroxide to produce highly toxic hydroxyl free radicals, which leads to tumour cell death in the acidic microenvironment of the tumour [70,71]. These free radicals can also damage biological macromolecules and the organelles of cells [72] (Figure 4). A positive feedback loop formed by iron accumulation, oxidative stress, and protein aggregation was found to produce toxicity in the cells [73,74]. It was found that citrate-coated iron oxide nanoparticles have protein oxidation [75].Various proteins, including α-synuclein are found to aggregate as a result of iron accumulation and oxidative stress, which might lead to Alzheimer's and Parkinson's diseases [76]. Ahamed et al. [77] reported that iron nanoparticles induced cytotoxicity by identifying higher levels of LDH, and defence in the antioxidant system was observed due to the generation of ROS caused by iron accumulation. As a result of ROS, permeabilization of the outer mitochondrial membrane releases soluble proteins into the cytosol where caspase activation occurs, resulting in apoptosis. Van den Bos et al. [78] found that dextran-coated SPIONs show lipid peroxidation, which is dose-dependent, but in lower amounts these iron oxides are not particularly toxic [79].

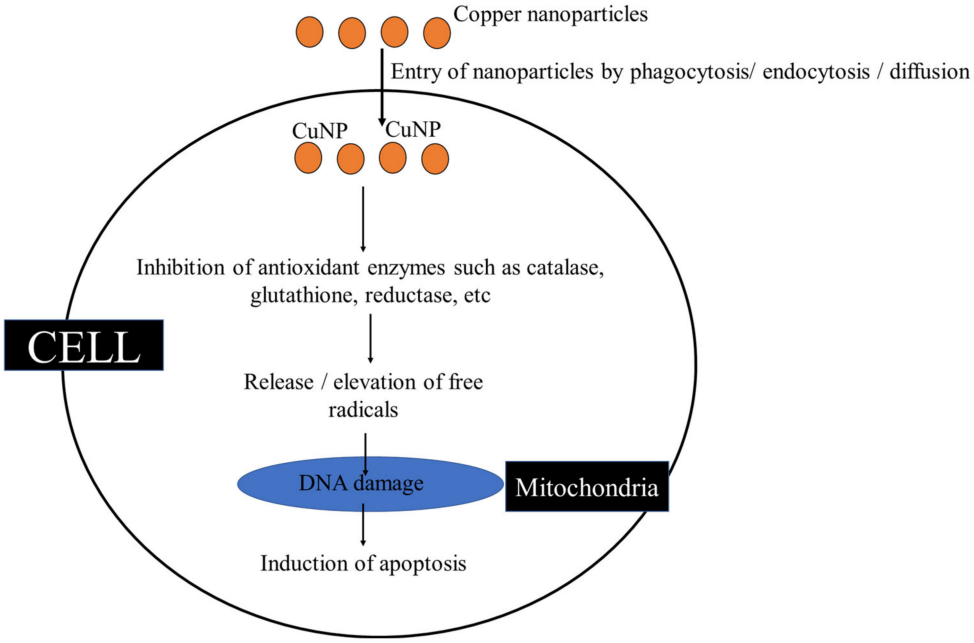

Figure 4. Oxidative damage caused by copper nanoparticles.

2.1.2. Copper Nanoparticles as Oxidants

Copper nanoparticles (CuNP) are widely used as they possess various bioactivity, including antimicrobial activity [80]. They do induce ROS generation where the biological responses are dependent on the amount of ROS released, the type of cellular pathways, etc. Copper nanoparticles act as pro-oxidants, meaning that they induce ROS production or inhibit antioxidants, thereby increasing oxidative stress [81]. The intake of CuNP by immune cells is through phagocytosis, endocytosis, passive diffusion, etc. Passive uptake does take place by direct interaction by modulating the NLRP3 inflammasome. Copper nanoparticles interact with cell surface receptors and activate intracellular pathways including the MAPK pathway, TLR4 pathway, and lectin pathway for the entry and induction of inflammation [81,82]. Fahmy et al. [83] recorded the inhibitory action of copper nanoparticles against cellular antioxidant enzymes such as catalase and glutathione reductase and increase the glutathione peroxidase activity. This suggests that copper nanoparticles are not only able to generate reactive oxygen species, but also inhibit the antioxidant defences of cells (Figure 5). Fahmy et al. [83] also found that co-treating CuNP with antioxidant resveratrol increased the life of cells. The cytotoxicity of Cu^{2+} was found to be caused by DNA damage and apoptosis-mediated cell death [83,84]. Similarly, a study by Zhou et al. [85] observed that, on exposure to copper nanoparticles, there was a higher apoptotic rate. It was also recorded that copper nanoparticles administered by intranasal instillation are tend to accumulate in the liver by entering into the mucosa, encountering severe damage. This results in the release of ROS from liver cells, triggering an oxidative stress response that leads to ER stress and cell apoptosis [86]. There was an increased ROS production leading to genotoxicity and cancer formation in CuNPs treated with *Mytilus galloprovincialis* [87].

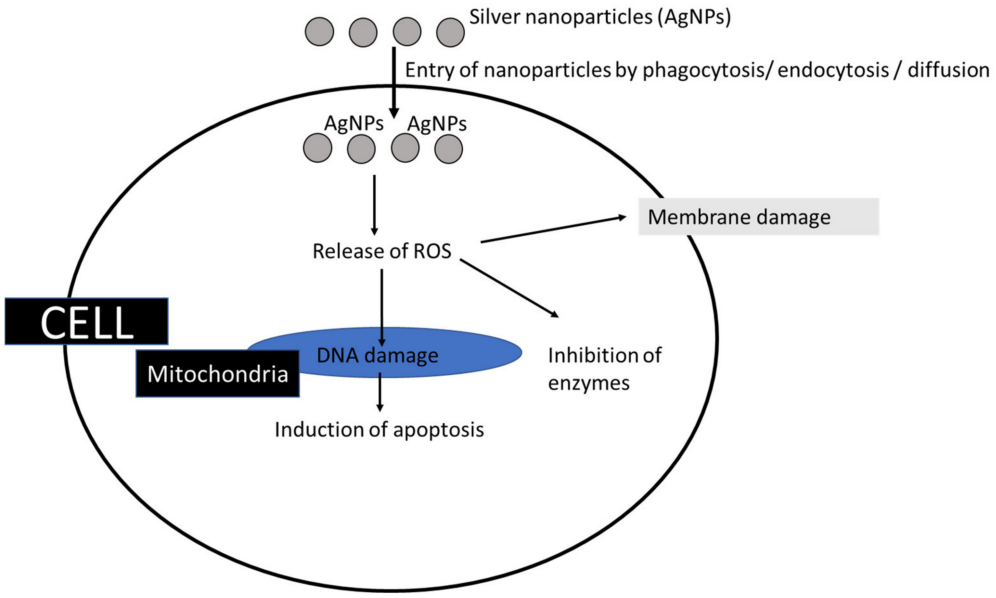

Figure 5. Role of silver nanoparticles as oxidants.

2.1.3. Silver Nanoparticles as Oxidants

Silver nanoparticles (AgNPs) possess unique properties and can be used in various biomedical and environmental fields, as well as healthcare-related products, etc., for their antimicrobial properties [88,89],

These characteristics are attributed to their higher ability to induce ROS. In addition to interacting with the cell membrane, AgNPs internalize and enter the cell through diffusion or membrane damage [90]; mostly, Ag^{+} dissociates from the nanoparticle core and stimulates ROS production [86,91,92]. The ROS produced are cytotoxic (even the AgNPs are directly cytotoxic) and the genotoxic effects mostly lead to apoptosis/membrane damage/enzyme inhibition etc. (Figure 6). When the silver nanoparticles react with membrane

proteins containing sulfur, enzymes and proteins bound to the membrane become inactive. By attacking the membrane, silver nanoparticles can disrupt the respiratory chain and reduce energy production. They also attack unsaturated fatty acids on cell membranes and alter membrane fluidity, thereby impairing cell function by destroying membrane permeability and integrity [93,94]. It is reported that silver nanoparticles could cause apoptosis by the activation of caspase in-vivo [95].

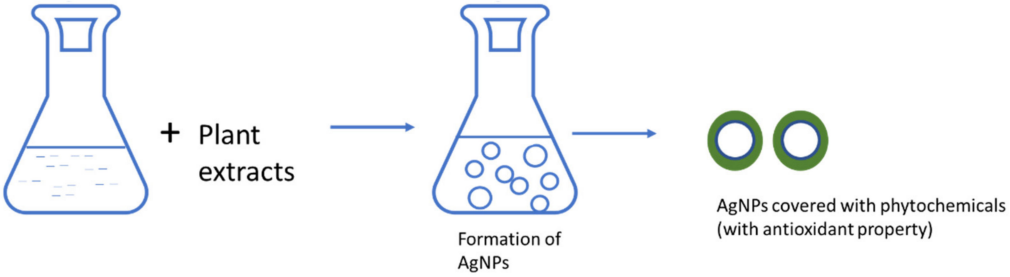

Figure 6. Silver nanoparticles with antioxidant property.

2.1.4. Other Metal/Non-Metal Nanoparticles as Oxidants

The particle surface of a nanoparticle has a major role in ROS generation [96]. SiO• and SiO_2• are the radicals seen on quartz nanoparticles which are believed be involving in formations of hydroxyl and oxygen radicals [97,98]. Sometimes the reactants are present in the environment [99]. The reactive sites of nanoparticles such as Si either donate or accept electrons from molecular oxygen, leading to the formation of oxygen radicals which participate in the generation of other ROS [100]. The size of the particles plays a major role in the generation of ROS [97,98], and chromium and other metals such as vanadium NPs form ROS through Fenton reactions [101]. Metal-based NPs have been found to promote NF-κB pathways for ROS generation [102]. Carbon nanotubes induce ROS after being internalized; single-walled carbon nanotube-induced NADPH-mediated ROS leads to mitochondrial failure and pulmonary damage [103]. Carbon nanotubes can also cause genotoxic effects by interacting with DNA, causing aberrant cell development and, ultimately, leading to carcinogenesis and fibrogenesis [104]. The addition of carbon nanoparticles to lung surfactant enhanced the number of nicotinic coenzymes of NAD+, NADH, NADP+, and NADPH in the cell [105]. These are responsible for causing ROS generation and oxidative stress.

3. Mechanism of Nanoparticles as Antioxidants

Metallic nanoparticles, in particular, have been found to have enzyme-like antioxidant properties which can scavenge free radicals and lower ROS concentrations. Metallic NPs, such as magnetic, silver, and gold NPs, appear to offer promising potential for treating and preventing illnesses caused by excessive ROS production [106–108]. Nanotechnology, in conjunction with materials science, has significantly reduced free-radical generation during nanoparticle creation, and these nanoparticles are called nano-antioxidants [109]. Nano-antioxidants are nonorganic NPs functionalized with antioxidants or antioxidant enzymes for use as delivery systems for antioxidants, as well as NPs with intrinsic antioxidant properties. Significant antioxidant properties include superoxide dismutase, catalase, oxidase, and peroxidase-mimicking activity. Metallic NMs may have a significant antioxidative effects due to their ability to bounce between different multiple oxidation states [108]. The mechanism of nanoparticle antioxidant activity is unclear and yet to be discovered.

The nano-antioxidant properties of nanoparticles are mostly depending on the method by which they are synthesized, as there are numerous preparation techniques such as the solvent displacement method, supercritical fluid technology, emulsion or solvent evaporation, the templating technique, and the nanoprecipitation technique. The antioxidant activity of novel metal nanoparticles such as silver, gold, and the transition metal oxides of copper oxide and nickel oxide, is extensively employed and studied. Coupling/incorporating

various phytochemicals into single or bimetallic combinational NPs enhances antioxidant activity. Antioxidant characteristics rely on chemical composition, nature, stability, surface-to-volume ratio, size, surface coating, and surface charge [51]. Certain oxide nanoparticles, because of their intrinsic physicochemical characteristics, can scavenge reactive nitrogen and oxygen species and mimic antioxidant molecules or antioxidant enzymes [52,53]. Another mechanism of nanoparticles for quenching free radicals depends on the ability of a nanomaterial to quench alkyl peroxyl radicals by converting them to hydroperoxides [54].

3.1. Silver Nanoparticles as Antioxidants

In an earlier section, the oxidant properties of silver nanoparticles that can inhibit cell growth by interfering with membrane proteins or signaling pathways were discussed. Furthermore, the ability of silver nanoparticles to interact with sulfur groups of proteins, especially on antioxidant enzymes, and interfere in antioxidant activity, was considered. A huge number of articles on the antioxidant activity of silver nanoparticles have been published in recent years [109]. Using nanoparticles as radical scavengers, for their redox potential, or as carriers for antioxidant compounds are developing fields of research in the science of oxidative stress [94]. The antioxidant properties of AgNPs might be depended on methods of preparation (Figure 6), but in most cases AgNPs are prepared using plant extracts [110,111]. These phytochemicals do help inform us on nanoforms and the antioxidant activity of AgNPs. Ansar et al. [112] synthesized Ag NPs from *Brassica oleracea* leaves with a good scavenging percent ranging from 60 to 80%. The abundance of surface-generated flavonoids and phenolics as capping agents could be the reason for antioxidant activity of these nanoparticles [110]. AgNPs mediated by aerial parts of *Lavandula stoechas* was reported to scavenge DPPH radicals of 75% at 25 mg/mL through their phytochemical constituents' such as phenols, terpenoids and flavonoids [111].

3.2. Copper Nanoparticles as Antioxidants

As mentioned in the above section, CuNPs have oxidant activity; when they are green-synthesised, they possess antioxidant activity. In a study, greenly synthesized copper nanoparticles using avocado seeds have shown antioxidant activity of nearly 17% to 22% [113]. Similarly, Wu et al. [36] have recorded the maximum antioxidant activity of 21% for CuNPs produced using *Cissus vitiginea*, where the colour change from violet to yellow indicates that DPPH is decreased by donating hydrogen atoms with high scavenging activity [114]. In the above cases, the phytochemicals of the plant extract have a role in the enhancement of antioxidant activity. CuNPs were reported to increase plasma ferric-reducing ability and catalase activity, but interestingly decreased plasma Cu and ceruloplasmin levels [115]. The application of CuNPs on tomato leaves increased chlorophyll content, as well as enzymes such as ascorbate peroxidase, glutathione peroxidase, superoxide dismutase, and phenylalanine ammonia lyase, and non-enzymatic antioxidants such as vitamin C and glutathione. They also enhanced the quality of nutraceutical and commercial fruits by increasing non-enzymatic antioxidant components, including vitamin C, glutathione, flavonoids, firmness, total soluble solids, and titratable acidity [116]. At high concentrations, Cu-NPs also had a significant impact on the release of proinflammatory mediators from brain microvessel endothelial cells [117].

3.3. Iron Nanoparticles as Antioxidants

Iron oxide nanoparticles were reported to increase catalase activity, glutathione peroxidase, and ascorbate peroxidase by 225.08%, 223.04%, and 69.89%, respectively, in different tomato cultivars [118]. As like in the case of AgNPs and CuNPs, plant extract addition increased the antioxidant property of iron oxide nanoparticles. It was reported that iron nanoparticles synthesized using *Blumea eriantha* showed antioxidant activity with a percentage of 74.94% [119]. In a study, antioxidant capacity of iron nanoparticles synthesized using *E. robusta* leaves was found in a concentration-dependent manner [120].

3.4. Other Metallic/Non-Metallic Nanoparticles as Antioxidants

Fullerenes, as well as single-walled and multiwalled carbon nanotubes have been reported to have antioxidant properties and can be used preclinically to check for inflammatory arthritis and neurodegenerative diseases. Poly(ethylene glycol)-conjugated hydrophilic carbon clusters could act as immunomodulators that selectively target T cells to scavenge the intracellular oxygen radicals generated by antigen-stimulated T cells [121]. A study by Oliveira et al. [122] showed red propolis-embedded mesoporous silica nanoparticles to have good antioxidant activity, as the physicochemical integrity of the pharmacological characteristics is preserved as a carrier of isoflavonoids, flavonoids, and other chemicals present in red propolis extract.

Several forms of polymer-loaded antioxidant nanoparticles, metallic and metal oxide nanoparticles, and carbon nanotubes have also been shown to possess antioxidant properties [96]. Nano-antioxidants are capable of accessing, reacting, and responding as required to specific functions in targeted tissues. Nano-antioxidant therapy can be used in combination with conventional therapy to offer a viable treatment option for patients suffering from oxidative-stress-related conditions [123,124]. Due to their intrinsic physicochemical features, certain oxide nanoparticles can scavenge reactive nitrogen and oxygen species (RNS/ROS) and imitate the antioxidant molecule [125,126]. Nanomedicines can dramatically change the pharmacokinetic properties of antioxidant drugs while reducing their adverse effects. Furthermore, nanomaterials, including inorganic nanoparticles, possess inherent antioxidant capabilities which are demonstrated through direct reactions with ROS and/or emulating natural antioxidant enzymes, demonstrating significant ROS-scavenging potential. The development of ROS-scavenging or ROS-responsive antioxidative nanotherapies derived from organic materials, or inorganic/organic hybrid materials, has gained a lot of attention recently, with promising results in reducing oxidative damage in various animal models of various diseases [126]. Nanotechnology-based systems are now being used to prevent and treat aging-related pathological ailments such as Alzheimer's and Parkinson's diseases, as well as cardiovascular diseases, obesity, type 2 diabetes, and cancers [110].

4. Conclusions

The oxidation mechanisms of all nanoparticles are mostly ROS-mediated, and they can induce apoptosis in-vivo and in-vitro. The mechanism causing oxidative stress is slightly different amongst metal nanoparticles, and is dependent on size, surface chemistry, and shape of the nanoparticles. The antioxidant properties of the metal/non-metal nanoparticles are mostly rendered by the addition of plant extracts. Phytochemicals could nullify the oxidant nature of nanoparticles and give them antioxidant properties too.

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