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REVIEW

Nanoparticles as Antioxidant Agents: A Comprehensive Review

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Abstract

This study seeks to provide a comprehensive overview of the latest progress in the antioxidant properties of nanoparticles. Nanoparticles (NPs) have emerged as a promising tool in several domains of science and industry, including their application as antioxidant agents. The main knowledge gaps seem to be in correctly identifying the make-up of the naturally occurring phytochemicals that give these nano-antioxidants their extraordinary pharmacology and drug-like properties. In many instances, that characterization is done using spectroscopy instrumentation such as fourier-transform Infrared (FT-IR), scanning electron microscope (SEM), and X-ray diffraction analysis (XRD). From literature appraisals, it was discovered that a lot of authors didn't properly characterize the phytochemicals—flavonoids, phenolics, or other phytochemicals in the plant extracts in the case of green synthesis, which bond with the metallic components. Due to the lack of proper isolation of phytochemicals in the plants, it is also uncertain if the increased activities registered for the nanoantioxidants are the result of one or numerous phytochemicals creating unique nano-moieties. Most often, plant extracts of the same species vary significantly in their chemical composition, and therefore making it challenging to replicate the research findings. In conclusion, there is an inadequate understanding of the long-term consequences of nanoparticles on human health, and some studies have raised concerns about their safety versus potential toxicity. Therefore, further studies on the toxicity of nanoantioxidants are necessary.

Keywords: Nanoantioxidants, Phyto chemicals, Toxicity profile, Nano particles, Nanomedicine

1. Introduction

The "nano era" has evolved recently in many different disciplines of research and industry. These are seen in the form of nanotechnology, nanoparticles, nanomaterials, nanofibers, nanoantioxidants, and nanoplates. Nanotechnology refers to the development and use of small, nanometer-sized materials based on their varied qualities. Generally, there are three basic groups of nanomaterials (NPs): nanoparticles, nanofibers, and nanoplates [1,2]. Nanoparticles have diverse use in the electronics sector, in medicine for drug delivery, as biosensors, in biotechnology, and in agriculture [3,4].

There are various types of nanoparticles that demonstrate antioxidant capabilities. For instance, reports indicates that organic nanoparticles such as melanin and lignin, metal oxide nanoparticles like cerium oxide, and metal nanoparticles like gold and platinum possess antioxidant capabilities. It has been established that these nanoparticles contain

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redox activity that is associated with radical trapping and/or activities similar to superoxide dismutase and catalase [5,6].

When nanoparticles are integrated with antioxidant metabolites, their antioxidant activities are enhanced; products with antioxidant potentials from such integration are referred to as nanoantioxidants [7]. Antioxidants that are usually contained in diets are the most well-known antioxidants, which are plant-derived. Plant phytochemicals have antioxidant qualities, and plants with antioxidant properties improve the innate antioxidant system in organisms [6,8].

Some nanoparticle oxides naturally have physicochemical features that confer active nitrogen and oxygen species scavenging effects and treat a range of ailments caused by oxidative stress [9]. For example, cerium oxide nanoparticles have been reported to demonstrate remarkable antioxidant capabilities with auto-regenerative radical scavenging activity, which allows for sustained efficacy [10,11].

The use of nanoparticles as antioxidant agents has been investigated for several years, with researchers studying their potential to avoid oxidative stress and inflammation. Nanoparticles as antioxidants are a very significant topic because diseases like cancer, heart disease, and neurological disorders are becoming more widespread because of oxidative stress [12,13].

Nanoparticles have been compared to standard antioxidants, such as vitamins C and E, and have shown encouraging results in terms of antioxidant efficacy as well as safety. Studies have demonstrated that nanoparticles can effectively scavenge reactive oxygen species and reduce oxidative stress *in vitro* and *in vivo* [14,15]. Using nanoparticles as antioxidant could completely change the field of antioxidant therapy, opening the door to new and creative ways to stop and treat diseases linked to oxidative stress [16].

Nanoparticles as antioxidant agents have received significant attention in recent years due to their unique features and potential applications in a variety of domains. Understanding the role of nanoparticles as antioxidant agents is vital for creating innovative and effective antioxidant therapies that can antagonize oxidative stress and inflammation, which are triggers of numerous disease conditions. Studies have demonstrated that nanoparticles can serve as antioxidants by scavenging free radicals, reducing lipid peroxidation, and modulating enzymes involved in oxidative stress [17,18].

2. Oxidative stress and antioxidants

Oxidative stress is the disturbance in the balance by which free radicals and reactive oxygen species (ROS) are produced, reactive nitrogen species (RNS), and reactive sulfur species (RSS), and the body's capacity to neutralize their harmful impact, which includes damage to cells, mitochondria, DNA, and lipids. Normal metabolic processes or contacts with xenobiotics or pollutants generate free radicals [19].

Reactive oxygen species play a crucial role in controlling several physiological systems. ROS, or reactive oxygen species, are chemical compounds that possess unpaired oxygen electrons and act as oxidizing agents. They undergo rapid conversion into free radicals. When the pace at which production occurs exceeds the rate at which clearance takes place, an excess of reactive oxygen species (ROS) builds up in the body, resulting in increased production of oxidative compounds and specific proteases [20,21]. Oxidative stress can generate reactive oxygen species, which may cause the release of mitochondrial contents due to damage to the mitochondrial membrane. Additionally, it can induce alterations in the nucleotide sequences of DNA molecules, such as deletion, addition, frame shift, or point mutation (Fig. 1). A variety of pathological ailments, including cancer, diabetes, atherosclerosis, arthritis, cardiovascular diseases, and neurological diseases, arise as a consequence of these repercussions.

Antioxidants have the ability to regulate the process of autoxidation by impeding the spread of free radicals or preventing the formation of free radicals (as shown in Fig. 2). This helps reduce oxidative stress, enhance immune function, and promote long-term health and longevity [19,22]. *In vitro* use of antioxidants often causes numerous problems, such as auto-oxidation and polymerization. As [23] reported, artificial nanoantioxidants can be produced by attaching an antioxidant to the surface of a nanoparticle. The antioxidant prepared in this manner, which could be natural or synthetic, could perform like the natural antioxidant system. In this direction, researchers have extensively incorporated state-of-the-art nanotechnology to overcome intrinsic disadvantages found in the *in vitro* usage of antioxidants, such as being out of their biomatrix, and facilitate the synthesis and use of antioxidants on a wider scale. Biomimetic nano engineering has been utilized to make biomedical antioxidant systems more stable, with improved targeting, and

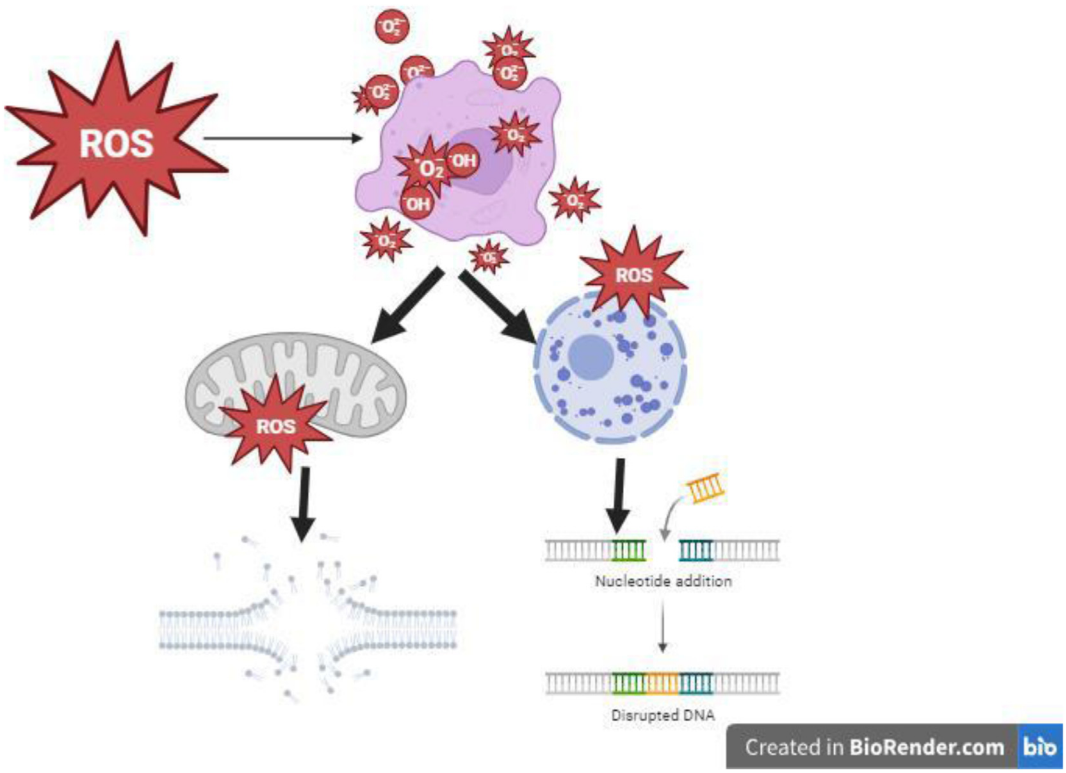

Fig. 1. Mitochondrial membrane and genetic material damage of ROS.

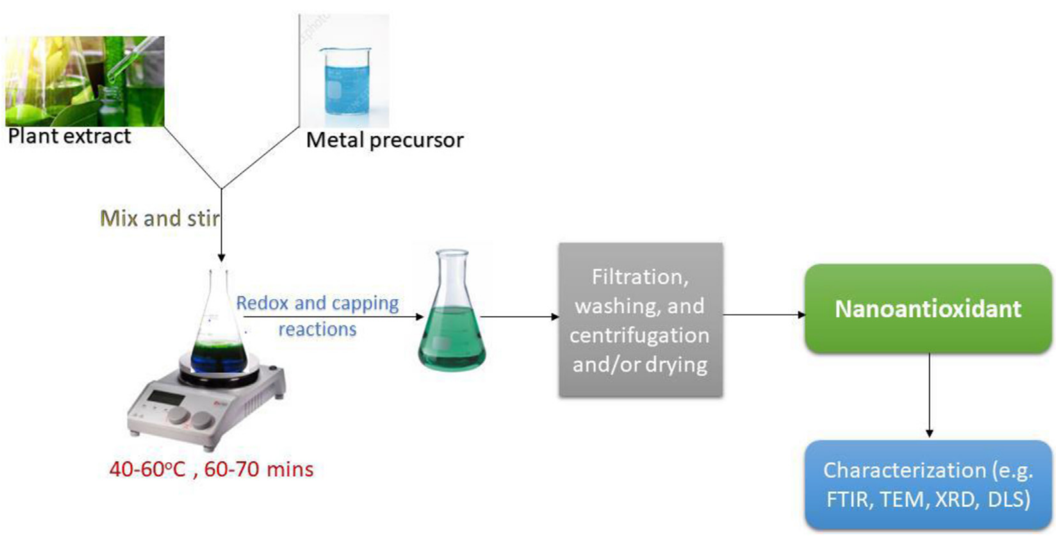

Fig. 2. Schematic representation of nanoantioxidant synthesis.

reduced toxicity, which sometimes do not perform optimally *in vivo* [23,24].

3. Nanoantioxidants

Nanoantioxidants are a unique class of antioxidants since they can be designed to stay longer than tiny molecules, get beyond metabolic clearance quickly, and target specific locations [25]. Synthetic nanoantioxidants are produced through a series of sequential processes and characterization procedures to validate their integrity and reproducibility (Fig. 2).

Currently, advanced nanotechnology is being investigated to address the inherent drawbacks of using antioxidants in laboratory settings, while also enabling the production and use of antioxidants on a larger scale [24,26]. Nanoengineering based on biomimetic principles is being used to increase the stability and targeted distribution of biomedical antioxidant systems, as well as to tackle difficulties associated with toxicity and biocompatibility [23]. Depending on the mode of application of nanoparticles, they can be synthesized in different forms as organic, inorganic, or hybrid nanoparticles (Fig. 3) (see Fig. 4).

Inorganic nanoparticles have inherent antioxidant capabilities and have been effectively investigated for their antioxidant properties. They display many advantages, such as good pharmacokinetics, stable anti-oxidative action, and intrinsic ROS-scavenging capabilities [16].

Nano systems utilized in pharmaceutical formulations have demonstrated promising results in increasing the delivery of medications in challenging formulations. Porous silica nanoparticles have demonstrated favorable characteristics for utilization in biological systems. However, some challenges persist in the development of more efficient and environmentally sustainable materials. The development of nanoantioxidant carriers has emerged as a unique technique for enhancing these nano materials [27]. Several authors have constructed and described nanoantioxidant carriers that are based on porous nanoplatforms that exhibit antioxidant potential [28–30].

Over the past few decades, the field of nanotechnology has experienced significant growth, resulting in the development of a diverse range of nanomaterials. Many of these materials are classified as "synthetic" and are often perceived with a certain degree of skepticism by the general population. Scientific understanding supports many of these materials, the term "nano" does not always imply

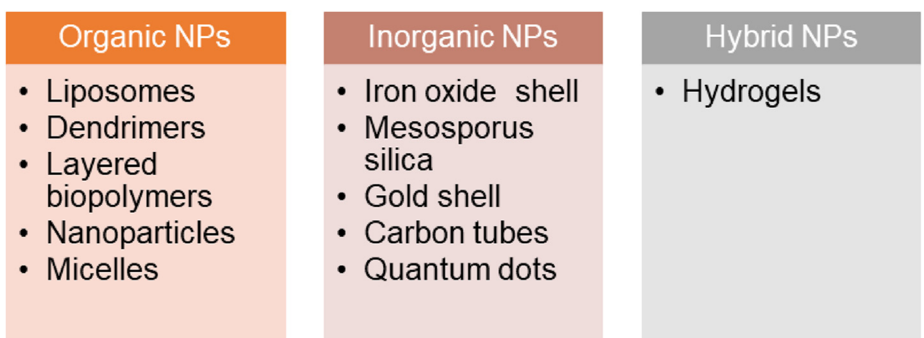

Fig. 3. Types of nanoparticles.

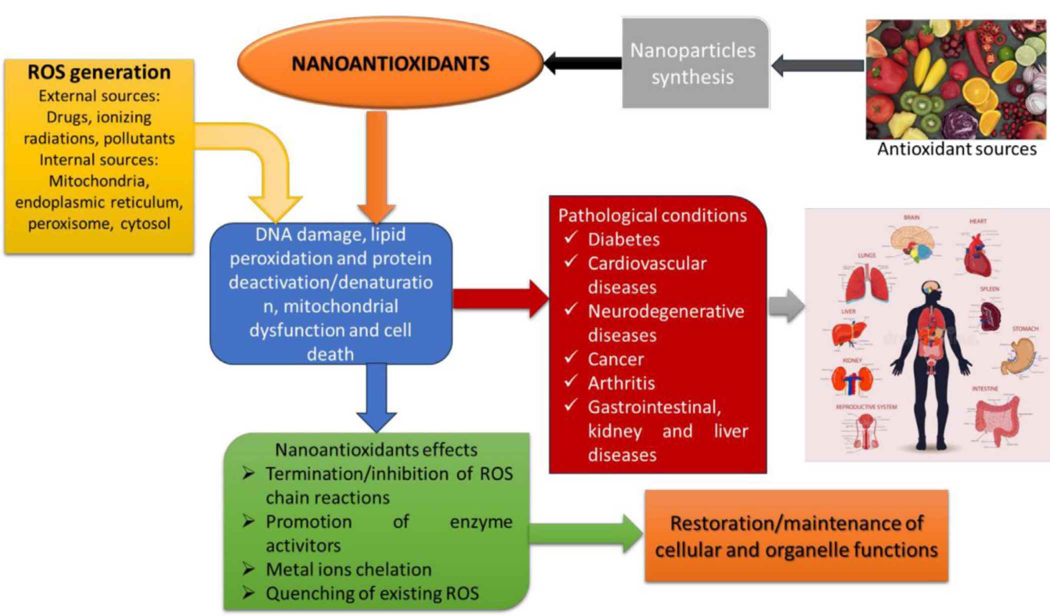

Fig. 4. Biological roles of nanoantioxidants.

"artificial." Undoubtedly, nature exhibits remarkable capabilities as a nanotechnologist. The spectrum of tiny particles encompasses a range of substances, including inorganic ash, soot, sulfur, and mineral particles found in the atmosphere or in wells, as well as sulfur and selenium nanoparticles generated by various bacteria and yeasts. Given that these nanoparticles are entirely derived from natural sources, it is not surprising that there is a growing inclination towards the development of natural nanoproducts. This is particularly evident in the emerging domains of phyto- and phyco-nanotechnology [31].

4. Emerging trends in the synthesis of nano antioxidants

Current research trends have made it rather difficult to discriminate between the different groups of nanoantioxidants. Almost all metallic nanoantioxidants are coupled with organic compounds. Three major themes are dominating the research pool: metallic nano antioxidants, functionalized nano antioxidants, and greenly manufactured nano antioxidants with plant extracts.

In normal circumstances, the self-antioxidant defense mechanism of the human body is capable of quantitatively controlling free radicals. However, in certain circumstances, which are at the threshold of developing disorders, the human body calls for an external source of antioxidants [21,32]. Due to the quick degradation of orally administered antioxidants by acids and enzymes in the human body, only a fraction of the consumed amount is effectively absorbed [33].Therefore, it is widely acknowledged and imperative to formulate efficacious approaches for the efficient transportation of stable antioxidants to critical regions [32].

Metallic nanoparticles (NPs) possess significant antioxidative properties as a result of their ability to transition between various oxidation states. Notable antioxidant characteristics encompass superoxide dismutase, catalase, oxidase, and peroxidase-mimicking activity [6].

The thermal stability and chemical inertness of inorganic nanoparticles allow the exploration of their potential and the immobilization of natural antioxidants. In addition, the use of nanoparticle-conjugated natural antioxidants improves the chemical stability of these antioxidants under physiological conditions. This approach allows the products to be delivered in its intact molecular form across a broader concentration range. Moreover, it is noteworthy that this approach provides a steady and continuous release of the antioxidants [34,35].

Metal oxide nanozymes have been identified as highly effective and prospective contenders for the replication of antioxidant enzymes in the treatment of oxidative stress-induced pathological conditions. Nevertheless, their current efficacy is limited due to weak catalytic activity [36].

Metal nanoparticles, transition metal oxides, and nanocomposites that have been functionalized with antioxidants have been recognized as potent nanoantioxidants. Chemical and green synthesis processes can be employed to produce them in monometallic, bimetallic, and multi-metallic combinations [24].The antioxidant properties of nano materials are influenced by various factors, including their adjustable structure, physicochemical properties, crystallinity, surface charge, particle size, surface-to-volume ratio, and surface coating. Nanoantioxidants possess numerous benefits compared to traditional antioxidants. The aforementioned factors encompass improved bioavailability, regulated release, and precise localization [17].

Drug-loaded antioxidant nanoparticles constitute another fascinating field of research. These nanoparticles can be loaded with specific medications that have antioxidant capabilities, hence boosting their therapeutic efficacy. They possess numerous benefits, including favorable pharmacokinetics, consistent anti-oxidative activity, and the inherent ability to scavenge reactive oxygen species (ROS) [36,37].

In recent times, there has been a growing proposal to utilize engineered nanostructured particles as an innovative approach for the delivery of novel antioxidants that possess increased characteristics. Nanoparticles that have been modified with natural antioxidants or antioxidant enzymes, using nanoparticles as the carrier or delivery vehicle, have been shown to effectively enhance antioxidant activity and deliver specific antioxidants that have limited ability to pass through cell membranes and be absorbed by cells [38,39].

Nano materials that have been functionalized with surface antioxidants have demonstrated enhanced antioxidant activity and bioavailability [40]. The utilization of biodegradable nanoparticles has been employed to enhance the bioavailability of natural antioxidants, mitigate leaching and volatility, and replicate potential enzyme functions in biological systems [41].

Silica nanoparticles, also known as SiO_2, have garnered significant attention in various fields such as chemistry, medicine, pharmaceuticals, and biomedical applications. Their optical transparency, chemical inertness, mechanical stability, biocompatibility, the ease and scalability of their synthesis techniques largely contributed to this. Furthermore, the meticulous manipulation of SiO_2 nanoparticles (SiO_2 NPs) with regards to their particle size, porosity, crystallinity, shape, and surface chemistry enables the modification of various molecules of interest through diverse coating techniques, catering to a wide range of applications [42,43].

The antioxidant activity of mesoporous SiO_2 nanoparticles (MSN) functionalized with morin, a flavonoid consisting of 2′,3,4′,5,7 pentahydroxyflavone, was investigated in terms of their ability to scavenge $HO^{\bullet}$ and quench O_2. The nanoantioxidant composite was less effective at deactivating O_2 than morin in both homogeneous liquids and lipid membranes. However, it was more effective at working jointly to defend against $HO^{\bullet}$ [43].

Gold nanoparticles (Au NPs) derived from varied synthesis processes have also been confirmed as an efficient antioxidant agent [44]. However, to enhance antioxidant and antiradical properties, Researchers have connected Au NPs natural compounds or manufactured to work with both natural antioxidants and other man-made compounds [45].

The DPPH radical scavenging capabilities of AuNPs immobilized on cellulose fiber were investigated under both light and dark conditions. The DPPH radical scavenging performance of AuNPs composites was shown to be much higher compared to pure fiber composites, owing to the catalytic activity of AuNPs. Interestingly, the composite exhibited a somewhat greater scavenging rate when there was light (86.05% $\pm$ 0.009) than when it was dark (77.86% $\pm$ 0.006). In the same way, AuNPs mixed with 3,6-dihydroxyflavone demonstrated 72.04% suppression of DPPH, 70.01% OH, 71.08% H_2O_2, and 69.01% of NO, which was considerably greater than their natural 3,6-dihydroxyflavone (64.21%, 62.11%, 60.11%, and 61.24%, respectively) [46].

In a study conducted by researchers [47,48], it was shown that seabuckthorn (SBT) leaf extracts, which were modified with silver nanoparticles (SBT@AgNPs) and poly (vinyl alcohol) embedded silver nanoparticles (PVA-AgNPs), exhibited superior efficacy in combating free radicals compared to the conventional medication, fluconazole [49]. In contrast, the biofunctionalized silver nanoparticles (AgNPs) exhibited heightened antioxidant efficacy in relation to their ability to reduce power and scavenge free radicals. According to the findings of this investigation, it was observed that AgNPs exhibited a higher efficacy in reducing phospho molybdate and ferric ions, as well as eliminating superoxide and DPPH radicals, compared to both the extract and the standard [50].

The SBT@AgNPs exhibited much more DPPH radical-scavenging activity compared to the plant extract. The heightened degree of activity can be attributed to the existence of phytochemicals derived from SBT leaf extracts, which serve as capping agents within the nanoparticles.

As stated in the reported work of [47], the synergistic interaction between phytochemicals and Ag ions leads to the production of antioxidant properties via concurrent processes of hydrogen atom transfer (HAT) and single electron transfer.

The use of natural nanoantioxidants shows significant promise in the mitigation and management of disorders linked to oxidative stress. The ability to administer antioxidants in a controlled and focused manner has the potential to greatly enhance therapeutic results. Furthermore, because they originate from natural sources, these substances exhibit biocompatibility and biodegradability, thereby mitigating the potential for negative consequences [51].

The utilization of flavonoids and phenol-rich plant phytochemicals in a nanoparticulate system has emerged as a prominent strategy for enhancing the biopharmaceutical performance and therapeutic efficacy of phytopharmaceuticals. This method is increasingly recognized and employed within the scientific community. Numerous studies have documented the anticancer properties of flavonoids in relation to several forms of cancer, including solid tumors [52]. Flavonoids possess the ability to impede the metastasis of cancer through various mechanisms, including modulation of autophagy, inhibition of the cell cycle, induction of apoptosis, and enhancement of antioxidant defense. The utilization of flavonoids in clinical settings, despite their notable anticancer properties, is constrained by their unfavorable biopharmaceutical characteristics.

These include inadequate solubility in water, restricted ability to traverse biological membranes such as in the intestinal and blood–brain barriers, and instability within biological systems [4,53].

According to [54], There has been an observation that nano particulate systems offer a potential approach for enhancing the nanoantioxidant and pharmacological properties of promising flavonoids. This, in turn, enhances anticancer activity that loaded flavonoids display.

Naturally occurring nanomaterials, artificially produced nanomaterials derived from natural sources, and nanomaterials that are either naturally occurring or produced from natural sources possess unique chemical and physical characteristics, biological functions, and potential uses, particularly in the fields of medicine, nutrition, cosmetics, and agriculture [31,55].

In forthcoming times, these naturally occurring nanoparticles will not solely serve as catalysts for scientific investigation while enhancing environmental sustainability in a conventionally advanced domain, but also offer resolutions, exemptions, and temporary halts to a diverse array of challenges. In this context, one can anticipate the emergence of distinct biogenic manufacturing facilities, the development of valuable novel materials derived from waste, the effective removal of contaminants using nano-bioremediation, as well as the transformation of chemicals and materials with low solubility into biologically viable forms [31].

Abdellatif, Mohammed [56] conducted a study aimed at enhancing the therapeutic potential of nanoparticles for cancer cell treatment. In this study, the researchers manufactured silver nanoparticles using an extract derived from the *Matricaria chamomilla* plant, with the aim of establishing a safe and natural approach. The synthesized nanoparticles exhibited notable antioxidant properties and effectively inhibited the proliferation of SW620 and HT-29 cancer cell lines when administered at a dose of 20 μM. The nanoparticles exhibit a significant upregulation of the apoptotic gene BAX, accompanied by a substantial down regulation of the anti-apoptotic genes BCL2 and BCL-Xl. It is postulated that this phenomenon contributes to the proliferation of colorectal cancer cells. SN-CHM has been recognized for its significant anticancer properties against the SW620 and HT-29 cell lines.

Aguilar, Jiménez [57] conducted a study wherein doped silver and gold organic nanoparticles (ONPs) of lipoic acid were synthesized and found to have superior antibacterial properties compared to other types of nanoparticles.

The primary deficiencies appear to be in adequately clarifying the structural characteristics of the organically produced chemicals that are responsible for the observed exceptional antioxidant and pharmacological actions. Often, researchers fail to specifically identify flavonoids, phenolics, or phytochemicals that form bonds with metallic components.

Furthermore, differentiating the participation of many phytochemicals leads to the creation of unique nano-moieties, which in turn contribute to the reproducibility of the observed enhancements in activity. It has been hard to reproduce the results of many studies that used botanical extracts because they didn't give enough information about the final structure of the nanoantioxidant. We recommend initially isolating and characterizing the phytochemicals present in plant extracts to optimize the production of nanoantioxidants for widespread application. This preliminary step will provide a comprehensive understanding of the chemical composition and structure of the phytochemicals.

Subsequently, the process of green synthesis of nanoantioxidants can be conducted, utilizing the identified phytochemicals. By following this approach, it is possible to achieve large-scale production of effective nano antioxidants, thereby facilitating their utilization for the benefit of a broad population.

5. Mode of action of nanoantioxidants

Nanoantioxidants represent a new and innovative area of study within antioxidant research, providing numerous benefits compared to traditional antioxidants [24]. The primary method by which nanoantioxidants function involves two pathways: scavenging reactive oxygen and nitrogen species (RONS) or preventing the formation of RONS [58–60].

Regular metabolic activities and contact with environmental contaminants produce free radicals, highly reactive entities. These radicals cause damaged to cells and are associated to a range of diseases and disorders related to oxidative stress [61,62]. Antioxidants, especially nanoantioxidants, function by reacting with free radicals and transforming them into non-toxic substances, thus impeding the advancement of potentially dangerous chain reactions [16].

Metal nanoparticles, transition metal oxides, and nanocomposites that have been functionalized with antioxidants are examples of highly effective nanoantioxidants. Chemical and green synthesis approaches can be used to synthesize monometallic, bimetallic, and multi-metallic combinations [24]. The underlying antioxidant properties of these nanostructures rely on their adjustable arrangement, physicochemical characteristics, crystalline structure, surface charge, particle dimensions, surface-to-volume proportion, and surface coating [63].

Researchers have effectively investigated the inherent antioxidant capabilities of inorganic nanoparticles. They exhibit many advantages, such as good pharmacokinetics, stable anti-oxidative action, and intrinsic ROS-scavenging capabilities [28]. Over the past few decades, the development of inorganic nanoparticles capable of scavenging reactive oxygen species (ROS) has made significant progress. These advancements have resulted in the creation of more efficient and precise medications for numerous inflammatory diseases [64]. Certain nanomaterials, such as organic substances like melanin and lignin, metal oxides like cerium oxide, or metal nanoparticles like gold and platinum, possess inherent redox activity.

This particular activity is commonly associated with the capture of radicals and/or the manifestation of features resembling those of superoxide dismutase and catalase [65].

Nanoantioxidants possess many benefits compared to traditional antioxidants, such as enhanced bioavailability, regulated release, and precise transport to the intended location of action. Nevertheless, the progress in nanoantioxidant advancement is impeded by inadequate characterization of the characteristic of ‘antioxidant activity’ and the utilization of overly simplistic chemical techniques [17].

The mechanism via which nanoantioxidants exert their effects is complex and characterized by several aspects. A series of reactions transform a particular reactive form of oxygen into a different reactive form. The nanoantioxidants have the ability to penetrate cells or organelles, be released, and exert their biological impact by eliminating unwanted free radicals (Figs. 5 and 6).

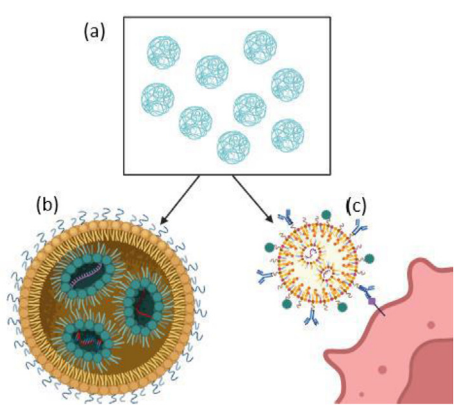

Fig. 5. (a) Lipid nano-antioxidant scaffold in the (b) nucleus (c) getting attached to a cell membrane.

6. Advancements in nanotherapies targeting antioxidants

Recent scientific research has confirmed the significance of nanoparticles in therapeutic interventions for various diseases and medical conditions. Numerous researchers have persistently explored diverse strategies to augment the pharmacological capabilities of nanosubstances, hence expanding the scope of their practical utility. Green synthesis has emerged as the predominant method for producing nanoparticles. The compatibility between plant phytochemicals and therapeutic metal salts, the body's ability to metabolize organic compounds, the somewhat lower toxicity of plant-derived components, and the environmental advantages of synthetic and organic moieties over purely synthetic alternatives mostly contribute to the observed efficacy [55].

This piece offers an in-depth assessment of recent advancements in antioxidant nanotherapies, encompassing various types of nano particles. These include inorganic nanoparticles designed to effectively eliminate reactive oxygen species (ROS), organic nanoparticles with innate antioxidant characteristics, and drug-loaded antioxidant nano particles. In their study [66], developed a nanoformulation utilizing Prussian blue (PTCN) for the purpose of addressing Alzheimer's disease (AD) through the inhibition of central nervous system (CNS) neurons associated with the pathogenesis of AD.

The efficacy of this intervention was evaluated for both its preventive and therapeutic applications. The results indicate that PTCN has demonstrated efficacy in attenuating cognitive decline, inhibiting Alzheimer's disease (AD)-related pathogenic mechanisms, and preventing hippocampal atrophy in individuals with amyloid precursor protein (APP) and human presenilin 1 (PS1). Both amyloid precursor protein (APP) and presenilin 1 (PS1) are present in neurons of the central nervous system (CNS) and have been identified as early indicators of Alzheimer's disease (AD) in both mice and humans.

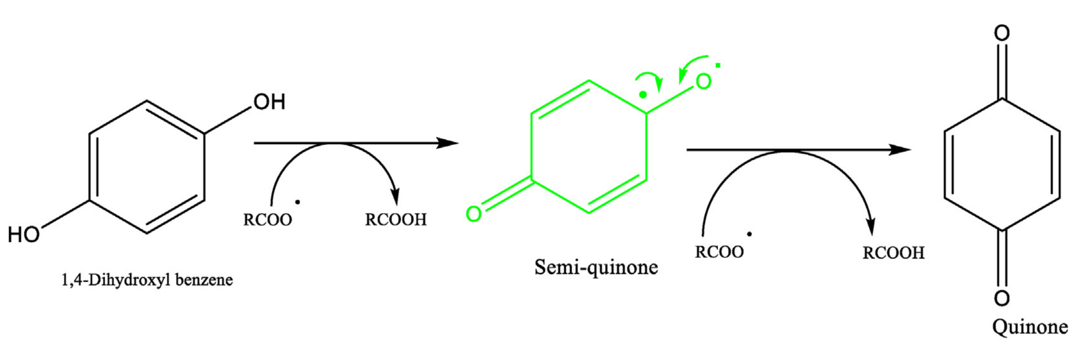

Fig. 6. Mode of action of phenols against ROS.

A recent investigation by [67], the focus was directed towards the examination of a naturally occurring nano-antioxidant termed DSNP, which was synthesized and evaluated utilizing date seeds as the primary source material. The researchers employed the DPPH assay to evaluate the antioxidant potential of the substance against free radicals, the FRAP assay to assess its ferric ion reduction capacity, and the ABTS assay to determine its efficacy in scavenging free radicals. The acid hydrolysis approach was discovered to be effective in producing potent natural nano-antioxidants derived from date seeds, which exhibited a multitude of bioactive qualities. Nevertheless, the outcome was contingent upon other factors such as temperature, duration of hydrolysis, concentration of acid, and the ratio of solid to liquid.

The study conducted by [68] investigated the antioxidant capacity of CMC/Gel/TiO2−Ag, a composite material composed of carboxymethyl cellulose and gelatin with embedded TiO2−Ag nanoparticles. The overall antioxidant capacity exhibited enhancement, which can be attributed to the synergistic antioxidant efficacy of the different constituents within the composites.

Similarly [69], employs the inherent antioxidant characteristics of melanin, a naturally derived substance, in conjunction with cerium oxide to enhance the overall efficacy of the therapy for age-related macular degeneration (AMD). The results of their study demonstrated that CMNP nano-antioxidants effectively alleviated pathology resembling age-related macular degeneration (AMD), leading to big improvement.

The combined utilization of nanoparticles demonstrated enhanced efficacy in the elimination of reactive oxygen and nitrogen species (RONS) compared to the individual application of a single nano-antioxidant.

The study by [13] reported that the addition of gallic, caffeic, and ferulic acids increased the antioxidant capability of plant phenolic phytochemicals. The experiment resulted in the production of pseudo boehmite-phenol hydrosols that exhibit enhanced antioxidant and radical scavenging capabilities. In addition, these hydrosols demonstrated significant membrane-protecting and antioxidant activities when tested *in vitro* using both cells and non-cells models. The utilization of synthesized nano-antioxidants has been described as a viable approach for the formulation of drug delivery systems targeting a wide range of therapeutic agents.

Ramos, Jiménez [70] utilized thymol, a chemical known for its addictive properties, in the synthesis of a nanocomposite by incorporating it into modified montmorillonite. The nanocomposite were developed specifically for the purpose of enhancing packaging materials. The analysis of DPPH antioxidants indicates that the nano-bio composites have favorable qualities as packaging materials. The impact of curcumin nanosupplements on preventing lipid peroxidation resulting from exercise was investigated in a randomized experiment conducted by [71].

The findings of the study provided confirmation that the use of curcumin nanosupplements may be beneficial in preventing lipid peroxidation in individuals who are overweight.

In a brief communication published in 2011 [72], investigated the impact of inorganic, organic, and elemental nano-selenium on the growth, selenium content, and antioxidant status of juvenile male goats. Resultantly, samples of blood collected from a total of 40 weaning Taihang black goats, were divided into four distinct groups. The samples were subjected to measurement for serum glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), catalase (CAT), malondialdehyde (MDA) activity, and selenium (Se) content. The utilization of nano-Se with enhanced antioxidant capacity was noticed to be more efficient when compared to inorganic or organic Se. In another study, researchers [73] conducted a comprehensive analysis to assess the relative importance of nano-copper in relation to antioxidant activities in Guizhou black goats. By analyzing blood parameters, it has been noted that the utilization of nano-copper not only leads to a substantial increase in blood copper levels but also greatly enhances the antioxidant capacity.

A study conducted by [74], it was observed that the exposure of medaka (*Oryzias latipes*) fish embryos to nano-iron resulted in oxidative damage. This damage was evidenced by an elevation in the levels of malondialdehyde (MDA). The absence of oxidative damage in adult fish was ascribed to the inherent capacity of these individuals to undergo self-repair. In their study, Yang, Huang [75] investigated the potential of selenium-doped carbon nanodots to penetrate the endoplasmic reticulum and mitigate the presence of reactive oxygen species. The se-doped carbon nanodots exhibited a notable reduction in both cytotoxicity and elimination. Oxygen (O_2) is a chemical element. The present study investigates the impact of radical and alleviated-induced inflammatory action in live mice.

Du, Wang [76] synthesized a functionalized gold nanoparticle with the aim of enhancing the bioavailability and biocompatibility of antioxidants. The findings indicated a notable increase in

Table 1. Recent Advances in Antioxidant Potencies of some Nanoparticles.

Nanoparticles	Application	Mechanism of Action	Key Findings	Reference
Prussian Blue nanoformulation (PTCN)	Alzheimer's disease (AD)	Antioxidation and Adjustable Treatment Strategies	The findings demonstrate that, in both preventative and therapeutic trials, PTCN could successfully mitigate AD-related pathological processes, enhance cognitive decline, and rescue hippocampus shrinkage in APP/PS1 mice.	[66]
Date seed nanoparticles (DSNPs)	Food and Industries	DPPH, FRAP, ABTS	Their findings demonstrated how temperature, hydrolysis duration, acid concentration, and the solid-to-liquid ratio affect the acid hydrolysis method's capacity to yield strong natural nano-antioxidants from date seeds with high bioactive properties.	[67]
Carboxylic methyl cellulose/ Gelatin were impregnated with TiO_2–Ag (CMC/Gel/TiO_2–Ag)	Food Packaging	DPPH	The synergistic antioxidant power of each individual composite component was credited with improving the total antioxidant potential.	[68]
γ-AlOOH (pseudo boehmite)	Nanotherapeutic	FRAP, DPPH	due to their increased radical scavenging capacity, the produced nano-antioxidants were suggested for use in designing drug delivery systems of different therapeutic agents.	[77]
Cerium oxide (Ceria) coated melanin-PEG nanoparticles (CMNPs)	Nanotherapeutic	RONS detection kit (Enzo chemical, ENZ-51011)	In comparison to the delivery of a single nano-antioxidant, the nanoparticle demonstrated a synergistic impact in scavenging against numerous reactive oxygen and nitrogen species (RONS).	[69,78–80]
Cerium oxide NPs (CNPs)	Antioxidant potential/Antitumor	SROS	Reactive oxygen species (ROS) are scavenged by CNPs.	[81–84]
AuNP-modified CeO_2 NPs	Antioxidant potential	Methyl Violet (MV) -Fenton reagent	Au/CeO2 nanorods and nanoparticles showed reduced antioxidant activity at increasing concentrations, while Au/CeO2 nanocubes showed increased antioxidant activity.	[85]
Thymol Modified Montmorillonite (D43B)	Packaging material	DPPH	The nano-biocomposites' DPPH antioxidant characterization indicates that they would be a great choice for packaging material.	[70]
Nano-Curcumin supplement	Prevention of Lipid Peroxidation	Malondialdehyde, Catalase, Glutathione Peroxidase, and Superoxide Dismutase enzymes	According to the study, using a curcumin nano supplement boosts the body's antioxidant system.	[71]
Inorganic, organic, and elemental Nano-selenium	Growth performance	Glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA)	Compared to inorganic or organic Se, nano-Se with enhanced antioxidant capability was found to be more efficiently used.	[72]
nano-copper	Antioxidant functions	Automated hematology analyzer (SF-3000, Sysmex-Toa Medical Electronic, Kobe, Japan)	Not only did nano-copper dramatically increase blood copper levels, but it also dramatically improves antioxidant capability.	[73]

nano-iron	Antioxidant functions	Superoxide dismutase (SOD) and Malondialdehyde (MDA) assay	Oxidative damage caused by nano-iron on *Oryzias latipes* (medaka) fish embryo	[74]
Se-doped carbon nanodots	Antioxidant/Anti-inflammatory function	Fe^{2+}/H_2O_2	Carbon nanodots doped with selenium greatly remove both O^{2-} and OH. radical and reduced the inflammatory response that was generated in living mice	[75]
Solanum lycopersicu carbon nanodots	Antioxidant potential	DPPH	Tomato-derived carbon dots possess a greater antioxidant capacity compared to other carbon dots that have been previously published.	[86]
Gold Nanoparticles	Antioxidant	DPPH	Compared to antioxidant monomer, antioxidant activity of the Nano-antioxidant was much higher.	[58,76]
Curcuma pseudomontana - Gold (CurAuNPs) NPs	Antioxidant potential	DPPH, NO, FRAP, ABTS	CUR-AuNPs demonstrated strong antioxidant and radical scavenging properties.	[87]
Gold – (,6-dihydroxyflavone, lutein and selenium methyl selenocysteine)	Antioxidant potential	DPPH, H2O2, NO	The individual dietary phytochemical nano composite was found to be less than ascorbic acid used as standard	
Kaempferol – Gold (KAuNPs) NPs	Antioxidant/Anticancer potential	DPPH	The NPs demonstrated strong free radical scavenging capabilities *in vitro*.	[88]
Selenium nanoparticles (SeNPs)	Fertilizer/Food packaging	Foliar Application, FRAP, DPPH	Plant tolerance to sandy soil conditions is improved by the action of nanoselenium as a stressor and/or stimulant, which strengthened the antioxidant defense systems in tested groundnut cultivars. The package can shield the product from oxidation	[89,90]
Cassia fistula (Cafi-AgNPs)	Reactive chemical Specie detector	ABTS, DPPH˙, NO˙	The suggested sensor showed good analytical performance, linearity of 10–200 μM, 3.0 μM H_2O_2 detection limit, and was effectively used to detect H_2O_2 in human plasma.	[91]
Morus alba – Silver (MaAgNPs) NPs	Antioxidant Potential	DPPH, ABTS, H_2O_2, (SROS)	The resulting nanoparticles exhibited antioxidant activity against free radicals that was dose dependent.	[92]
Calophyllum tomentosum – Silver (CtAgNPs) NPs	Antioxidant Potential	DPPH, H_2O_2, NO, FRAP	The functional groups in the extract were thought to be the reason behind the CtAgNPs' significant antioxidant activity.	[93]
(*Allium cepa* (Alce-AuNPs)	Antioxidant Potential	DPPH, FRAP, ABTS	The resulting nano-bioconjugates were discovered to be more active than the extract alone and to function as strong antioxidants and anti-inflammatory agents.	[94]
Nano-Zinc Oxide	Immune Response and Antioxidant Defense	DPPH, Antioxidant enzyme activities and malondialdehyde Concentration	Applying ZnONP to broiler chickens' diets up to 80 mg/kg is safe and may enhance their cellular immunity and antioxidant defense.	[95,96]
Tecoma castanifolia – ZnO NPS	Antioxidant Activities	DPPH	The antioxidant activity shown that the radical scavenging activity rises with ZnO nanoparticle concentration.	[97]

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Table 1. (continued)

Nanoparticles	Application	Mechanism of Action	Key Findings	Reference
Knoxia sumatrensis − ZnO NPS	Antioxidant Activities	DPPH, H_2O_2, ABTS	Dosed dependent improved antioxidant activities	[98]
Rutin-loaded poly (lactic co-glycolic acid) (PLGA) nanoparticles	Nano-antioxidant Therapy (hepatocellular carcinoma)	antioxidant enzyme	decreased occurrence of blood vascular inflammation, hepatic nodule formation, inflammatory cell infiltration, and cell swelling	[99]
PDA-Zn-BAI NPs (Dopamine, Zinc and baicalein)	Prevent Hepatic Oxidative Stress	Scavenging Reactive Oxygen Species (SROS)	Within five days, the damage caused by acetaminophen to the liver was reversed by using PDA-Zn-BAI NPs nanoparticles that efficiently scavenge reactive oxygen species.	[100]
Manganese disulfide-silicon dioxide (MnS_2−SiO_2) NPs	Antioxidant Potential	DPPH	The capacity of MnS_2−SiO_2 to scavenge radicals was improved.	[101]
Eucalyptus globulus − Zirconia oxide NPs (ZrO2 NPs)	Colon cancer	DPPH	ZrO2 NPs shown potent anti-cancer and robust antioxidant properties against the examined cell types.	[102]
Quercetin-Titanium Oxide ($QTiO_2$)	Antioxidant Stability	Scavenging Reactive Oxygen Species (SROS)	In cells exposed to superoxide and ROS, the antioxidant potency of the $QTiO_2$ nano-antioxidant was effectively assessed.	[103]
Quercetin-Silica (QSi) NPs	Antioxidant Potential	Scavenging Reactive Oxygen Species (SROS)	Both the free and quercetin-loaded silica nanoparticles demonstrated superoxide radical scavenging properties.	[104]
Poly lactide-co-glycolic acid/Quercetin NPs	Antioxidant Potential	DPPH	Improved solubility and antioxidant ability	[105]
Platinum-Nano antioxidant	Multiple Organ Failure	Scavenging Reactive Oxygen Species (SROS)	The research demonstrated the viability of multifunctional nanotherapeutics in preventing ischemia-reperfusion harm.	[29]
Zirconia Oxide (ZrO_2) and Titania Oxide (TiO_2) NPs	Nanotherapies	DPPH	The study unequivocally demonstrates that, *in vitro*, dose- and size-dependent, nanoparticles exhibit improved biocompatibility and strong antioxidant capacity.	[106]
AgO2 NPs	Biomedical Applications	DPPH	Good Nano-antioxidant for biomedical applications	[107]
Nano-complexes of Zn(II), Cu(II), Ni(II) and Co(II)	Antioxidant Potential	DPPH	The structure of Cu (II) Nano complex and reduction potential of Cu (II) were shown to be responsible for its remarkable antioxidant activity.	[108]
Guava Silver NPs (GVE-SNP)	Antioxidant Potential	DPPH, ABTS	Strong radical scavenging activity was demonstrated by the nanoparticles against DPPH and ABTS.	[109]
Caffeic acid Zinc oxide (ZnO@CA)	Antioxidant Potential	ABTS	Strong antioxidant activity was demonstrated by ZnO@CA nanoparticles.	[110]
Caffeic acid Silica/Rutin nanoparticles (MSN-CAF, MSN-RUT)		Oxygen Radical Absorbance Capacity (ORAC)	There is a noticeable decline in the antiradical capacity of caffeic acid (98.7%), whereas rutin (33%) shows a slight decrease, which may account for the high ORAC values found with MSN-RUT.	[111]
Poly (tannic acid)−Silica NPs	Antioxidant Potential	ABTS	Significant antioxidant ability	[112]

Carminic acid − Silica NPs	Pharmaceutical Emulsions	DPPH	Vitamin E consumption was shown to have decreased up to 9.26% of the initial amount, indicating a significant antioxidant effect of the produced nanomaterial.	[27]
Gallic acid − Silica NPs	Antioxidant Potential	DPPH	Fast decolorization of the DPPH solution was the outcome of the SiO_2-GA NPs' interaction with DPPH radicals, suggesting strong antioxidant activity.	[113,114]
Chitosan-Ag NPs	Nanotherapies	DPPH, H_2O_2, FRAP, NO	Chitosan-coated nanoformulations may have therapeutic potential against breast cancer, according to the preliminary research.	[115]
Clerodendrum phlomidis − Ag NPs	Antioxidant/Anticancer	DPPH, FRAP, SRCA	Using the DPPH assay, ferric reducing power, superoxide radical scavenging activity, and phosphomolybdate assay, biosynthesised AgNPs show much higher antioxidant activity than the crude extract.	[50]
Lippia nodiflora − Ag NPs	Antioxidant Potential	DPPH, H2O2, SRCA	AgNPs and the standard both demonstrated a strong inhibitory effect on the DPPH radical, indicating a potential source of antioxidants.	[116]
4-N-methyl benzoic acid − Ag NPs	Antioxidant/Antitumor	DPPH, SRCA	The product can be further investigated to construct a good lead ingredient for biomedical applications. The investigation confirmed that the nanoparticles manufactured using 4-N-methyl benzoic acid, sourced from a medicinal plant, had good antioxidant and anticancer activity.	[117]
Asphodelus aestivus − Ag NPs	Antioxidant Potential	DPPH, H_2O_2	Both biologically produced silver nanoparticles and plant aerial extract shown enhanced shifts in the percentage of their ability to scavenge free radicals when tested for antioxidant activity.	[118]
Chitosan/iron oxide NPs	Biomedical Applications	DPPH, H_2O_2	A promising bio-nanomaterial for a variety of biological applications is the CS-FeO nanocomposite.	[119]
Graphene - TiO2 NPs	Antioxidant Potential	DPPH, H_2O_2, ABTS	The NPs lessen the undesirable photooxidative damage to neighboring organic target molecules, indicating that graphene encapsulation may be a novel strategy for controlling the detrimental effects of redox-active nanomaterials on the environment or human health.	[120]
Eumelanins − melanin (MeDHICA-melanin)	Dermo-Cosmetic Applications	H_2O_2	Their findings suggest that MeDHICA-melanin may be used as an antioxidant to treat skin damage, photoaging, and skin cancer.	[121]

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Table 1. (continued)

Nanoparticles	Application	Mechanism of Action	Key Findings	Reference
Superparamagnetic iron oxide nanoparticles (SPION)	Antioxidant Potential	DPPH	Their findings suggest that the release of phenol capped SPION into a solution containing weakly bound phenols may be the source of its antioxidant activity.	[122]
Poly (lactic acid) - Ursolic acid (PLA - UA)	Antioxidant/Anticancer	Hypochlorous acid (HOCl) scavenging activity	PLA nanoparticles demonstrated promise as UA carriers, preserving the antioxidant and anticancer properties of the UA.	[123]
Poly (vinyl alcohol)- Silver NPs (PVS−Ag)	Antioxidant Measurement	Gallic acid	The created sensor was effectively used to evaluate the Total Antioxidant Capacity of commercial ginger products.	[48]
Tragiainvolucrate − Platinum (Ti-PtNPs) NPs	Antioxidant Potential	DPPH	Ti-PtNPs exhibited dose dependent antioxidant effect	[124]
Falcaria vulgaris − Copper (Fv-CuNPs) NPs	Antioxidant Potential	DPPH	Comparable antioxidant effect relative to that of the standard used	[125]
*Borreriahispida*Copper (Bh-CuNPs) NPs	Antioxidant Potential	DPPH	Exhibit potent antioxidant potential	[126]
Cissus vitiginea - Copper (Cv-CuNPs) NPs	Antioxidant Potential	DPPH	DPPH activity was significantly inhibited by the CuONPs in a dose-dependent manner.	[127]
Ag/Cu and Cu/Zn bimetallic NPs	Antioxidant Potential	DPPH, FRAP, H_2O_2	At all doses, Ag/Cu bimetallic nanoparticles demonstrated more antioxidant activity against ascorbic acid than Cu/Zn bimetallic nanoparticles.	[128]
Vernonia mespilifolia - - bimetallic silver-platinum nanoparticles (AgPtNPs)	Antioxidant Potential	DPPH, FRAP, ABTS	AgPtNPs shown improved capacity to scavenge free radicals, particularly against DPPH and ABTS.	[129]
Clove bud - Au/Ag bimetallic nanoparticles	Antioxidant Potential	DPPH, ABTS, H_2O_2	When compared to Mono Metallic NPs (MMNPs), Au/Ag BMNPs had superior antioxidant and catalytic activity, which might be explained by the phytochemicals' coating and synergistic effect.	[130]

DPPH - 2,2-diphenyl-1-picrylhydrazyl, FRAP - Ferric Reducing Potential, ABTS - 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid, H_2O_2 - Hydrogen Peroxide, NO - Nitric Oxide, SROS - Scavenging Reactive Oxygen Species, SOD - Superoxide dismutase, MDA − Malondialdehyde, GSH-Px - serum glutathione peroxidase, NPs − Nanoparticles.

antioxidant activity when comparing it to that of the antioxidant monomer. The experimental outcomes were shown to be comparable when salvianic acid A was employed as the functional group. The past decades have witnessed notable advancements in the field of nanoantioxidants, as shown in Table 1 below.

7. Conclusion

Though developing rapidly, research on nanoantioxidants is still in its infancy, and there are plenty of chances for advancement. Based on the most recent studies, it is possible to draw the conclusion that antioxidants play an unquestionable role in the treatment and prevention of diseases caused by reactive chemical species based on the results of the most current studies. This is especially crucial for suppressing oxidative stress. Numerous nanoparticles have had their antioxidant qualities successfully assessed during the past few decades. Nonetheless, there is an urgent need to address the main areas of concern regarding the structural elucidation of organically formed compounds responsible for their extraordinary pharmacological and antioxidant capabilities, as well as the associated elimination and toxicities.

Consent for publication

All authors consent for the manuscripts to be published.

Availability of data and materials

Data are available on request.

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Abbreviations

ABTS	2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid
AD	Alzheimer's disease
AMD	age-related macular degeneration
APP	amyloid precursor protein
CAT	catalase
CNS	Central Nervous System
DPPH	2,2-diphenyl-1-picrylhydrazyl
DSNP	Date seed Nanoantioxidant
FRAP	Ferric Reducing Potential
FT-IR	fourier-transform Infrared
GSH-Px	serum glutathione peroxidase
H_2O_2	Hydrogen Peroxide
MDA	malondialdehyde
NO	Nitric Oxide
NPs	Nanoparticles
ONPs	Organic Nanoparicles
PTCN	Prussian blue
RNS	reactive nitrogen species
ROS	reactive oxygen species
RSS	reactive sulfur species
SEM	scanning electron microscope
SOD	superoxide dismutase
XRD	X-ray diffraction analysis

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