Hindawi
Journal of Nanomaterials
Volume 2022, Article ID 2271278, 22 pages
https://doi.org/10.1155/2022/2271278

Review Article

Biogenic Metallic Nanoparticles from Seed Extracts: Characteristics, Properties, and Applications

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Received 3 July 2022; Revised 12 September 2022; Accepted 14 September 2022; Published 14 October 2022

Academic Editor: Zhengwei Huang

Metal nanoparticles (MNPs) are popular in different research fields due to their unique physical and chemical properties and superior antimicrobial, anticancer, antioxidant, larvicidal, and catalytic potentials. Although conventional wet methods like colloidal synthesis, calcination, and spark ablation for synthesizing MNPs are effective, their synthesis uses an array of reducing and stabilizing agents and gases, making the process tedious. Additionally, metal nanoparticles induce oxidative stress through reactive oxygen species (ROS), showing high toxicity. Research and development in green chemistry have gained momentum and massive attention because of being efficient, clean, economical, environment-friendly, and free of hazardous byproducts. Recently, seed extracts in-lieu of chemical stabilizers and reducing agents have become popular because of the single-step green synthesis of MNPs. Seeds provide the researchers with a cost-effective alternate to other biological methods due to low maintenance costs, culture/growth independence for biomass, and diversity of phytochemicals as reducing and capping agents. Thus, effective green synthesis approaches are considered sustainable for MNP synthesis. This review depicts the literature on the challenges associated with metal and metal oxide nanoparticles and discusses their synthesis using seed extracts. The application section of the review discusses the antimicrobial, anticancer, and larvicidal activities of seed extracted-synthesized metallic nanoparticles. Furthermore, insights into the different biological potentials of the synthesized green MNPs have also been discussed.

1. Introduction

The continued growth in nanotechnology and its broad spectrum of applications have led to fundamental changes in research, i.e., materials science and engineering, such as quantum dots (QD), nanobiotechnology, applied microbiology, and surface-enhanced Raman scattering (SERS) [1, 2]. Indeed, nanotechnology has demonstrated to have a critical role in the field of technologies using nanoscale structures (nanoparticles) in electronics, optics, optoelectronic devices, biomedical science, chemical industry, mechanics, nonlinear optical devices, drug-gene delivery, space industries, energy science, catalysis, and photoelectrochemical applications [3]. Nanoparticles (NPs) exhibit excessive interest due to their large surface-to-volume ratio and extremely small size (nm), conferring both chemical and physical properties compared to their chemical composition and structure [4, 5]. Specifically, for NPs, a wide spectrum of applications has been listed in different fields, also revealing an immense interest due to their unique features shown by multiple researchers. Nanoparticles are used in industries such as biomedical, electronics, food, and material. They are also used in the oil and gas industry and play a vital role during oil recovery [6]. However, the chemically synthesized nanoparticles have toxicity concerns against various cell types. The primary reason for the toxicity of chemically synthesized nanoparticles occurs due to their curvature, functional groups, free energy, shape, particle size, and surface characteristics which result in fibrillation, loss of enzymatic activity, thiol cross-linking, and protein unfolding [7]. Despite the nanoscale size, they have shown toxic effects. Different studies have reported the toxicity associated with nanoparticle use [8]. Consequently, nanotechnology was combined with green chemistry to produce nature friendly NPs via microbes, plants, and others to overcome such problems [9]. In this approach, pure metal and metal oxide NPs are generated via a biomimetic approach, where the biological system executes the role of biological laboratories [10]. To synthesize biogenic NPs, the bottom-up approach is followed, where compounds and atoms act as the building block and self-accumulate themselves to form the final product [11].

Recently, for synthesizing NPs, various herbal plant species and their extracts have been used as reductants and capping agents [12]. Several bacterial cells and their extracts have been used for synthesizing different types of NPs of gold (Au), silver oxide (AgO), silver (Ag), titanium dioxide (TiO_2), and cadmium sulfide (CdS) [13]. In addition, some fungi species have been used to synthesize TiO_2, CdS, and Ag NPs. Other biological resources, including honey, have been especially used to synthesize NPs from Au, platinum (Pt), Ag, lead (Pd), and carbon [13]. On a comprehensive analysis, NPs obtained from plants are more stable and monodispersed than microbial species. The processes involved in the synthesis of metallic nanoparticles have advanced considerably. Reports are available on the DNA-guided nanoparticle formation on the graphene oxide surface. In this study, the metal-graphene oxide nanostructures were built using DNA molecules as templates. Such nanoparticles can find applications in detecting specific nucleotide sequences [14]. DNA-directed nanoparticles are also finding applications in the management of plant infections. Per the research done by Ocsoy et al., DNA-directed AgNPs were synthesized on graphene oxide substratum. These NPs reduced the *Xanthomonas perforans* population in vitro and on the plants. *Xanthomonas perforans* is known to cause bacterial spot disease in tomatoes, which makes these nanocomposites an effective biocontrol agent [15, 16]. Besides biocontrol, NPs can serve the application of detection of human pathogens. Turek et al. report the synthesis of gold-DNA aptamer composites to detect methicillin-resistant *Staphylococcus aureus* (MRSA). Reports are available on the protein-based nanoparticle synthesis wherein phosphorescent manganese-doped ZnS QDs were synthesized with biosensing applications for protein detection [17]. These applications and many others reflect well on the potential of biosynthesized nanoparticles.

Seeds are a well-known repertoire of interesting and highly valuable phytochemicals such as caffeic acid, chlorogenic acid, cinnamic acid, coumaric acid, (epi)catechin, (epi)gallocatechin, epicatechin gallate, essential amino acids, ferulic acid, naringenin, syringic acid, polyunsaturated fatty acids (PUFA), and vanillic acid [18–23]. Seed extracts contain a variety of bioactivities with industrial potentials, such as antibacterial, anticancerous, antimutagenic, antiviral, and cardioprotective activities [24]. Compared to generic plant extracts, seed extracts have certain advantages, such as convenient availability and processing; they do not require particular growth conditions or reactors to extract the bioactive constituents from them.

Moreover, there are distinct advantages of plant-based nanoparticles. The most notable ones are as follows: (1) they consume less time to synthesize from metal ions and (2) they can be used to synthesize NPs using green chemistry and selecting the solvent medium and environment-friendly reductant and nonhazardous materials for synthesis [13]. In this way, a wide range of compounds, like amides, amines, alkaloids, flavonoids, phenolics, and terpenoids in the plant-based extract, assist in reducing and stabilizing metal ions [25]. Additionally, other compounds, such as peptides, sugars, water, and vitamins from coffee and tea extracts, have been successfully used for synthesis [26–31]. Hence, this review is aimed at drawing attention to the challenges associated with metal nanoparticles and highlight the importance of seed extracts for generating metallic NPs. Finally, various metallic NPs synthesized from seed extracts, the methods used for synthesis, and their applications have been emphasized.

2. Problems Associated with Metallic Nanoparticles

2.1. Oxidative Stress-Mediated Toxicity. Ahamed et al. found that in human pulmonary epithelial cells (A549), the Cu_2ONP-induced genotoxic reaction via the p53 pathway also increases the checkpoint protein p53 of the cell cycle and enhances the DNA damage repair proteins MSH2 and Rad51. Cu_2ONPs are also reported to generate oxidative

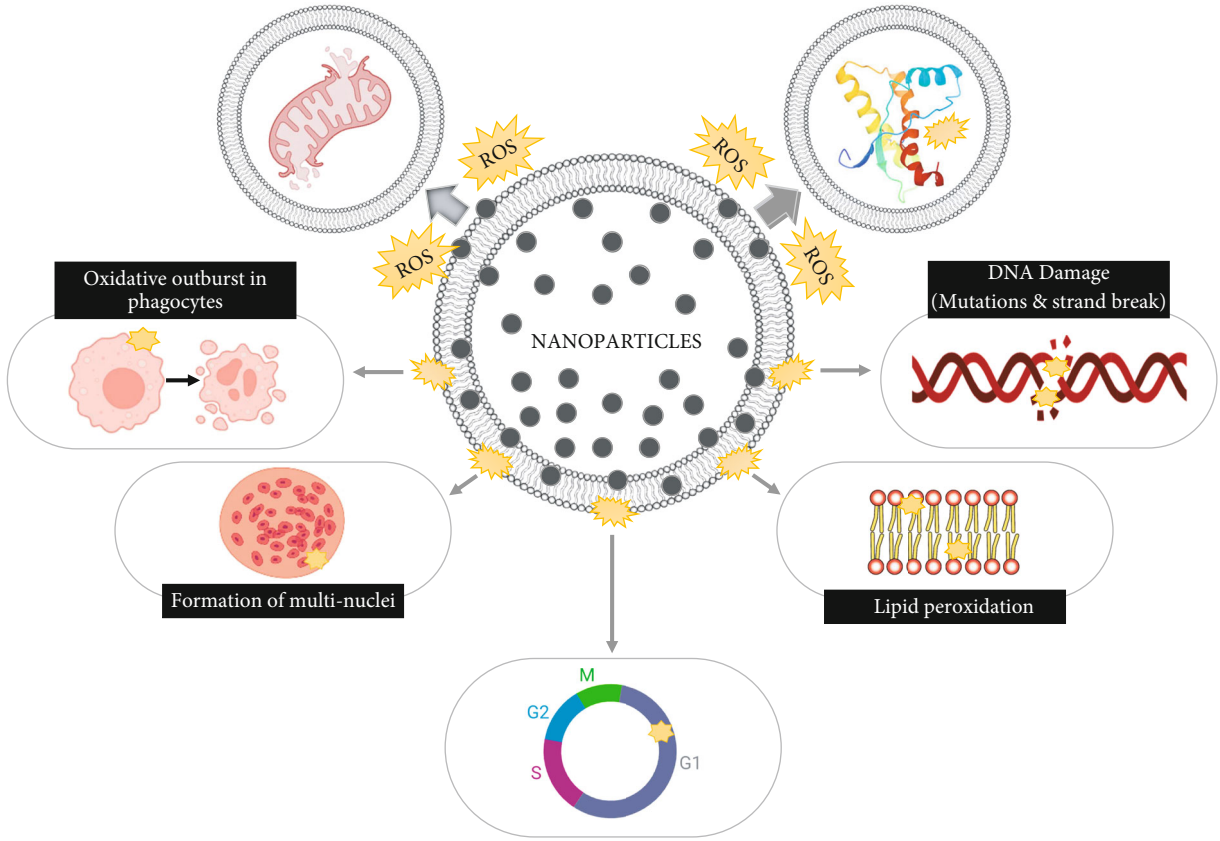

Figure 1: Graphical representation of oxidative stress-mediated metallic nanoparticles toxicity.

stress at various concentrations (10, 25, and 50 μg/ml), as evidenced by the depletion of superoxide dismutase (SOD), catalase (CAT), and glutathione also stimulate peroxidation of lipids. These studies revealed that Cu_2ONPs induce genotoxicity in A549 cells, possibly due to the generation of oxidative stress [32] (Figure 1).

Li et al. reported oxidative damage in MRC-5 human lung fibroblasts proteins and lipids after exposure to AuNPs in vitro [33]. Additionally, cells treated with AuNPs produced significantly more lipid hydroperoxides, indicating peroxidation of lipids. Moreover, the western blot study confirmed oxidative damage by verifying malondialdehyde (MDA) protein adducts [33]. The oxidative stress impact was investigated on the genotoxic and cytotoxic potential of AgNPs against human glioma (U251) and human lung fibroblasts (IMR-90) cell lines. It has been found that AgNPs cause malfunction of mitochondria and generation of reactive oxygen species (ROS), which results in DNA damage and chromosome abnormalities. The disruption of the mitochondrial respiratory chain by AgNPs resulted in ROS generation and the termination of ATP synthesis, leading to DNA damage [34]. Chairuangkitti et al. revealed the mechanisms behind AgNP (<100 nm) toxicity related to ROS generation in A549 cells. Surprisingly, ROS-independent (cell cycle arrest) and ROS-dependent (cytotoxicity) mechanisms are involved in AgNP toxicity in A549 cells [35].

In human liver cells (HepG2), the genotoxic and apoptotic capacities of ZnONPs were investigated. Their cellular toxicity was also observed at the molecular level. On exposure to ZnONPs at a dose of 14-20 μg/ml for 12 h, HepG2 viability decreased, and apoptosis occurred. Also, they caused DNA damage, as demonstrated by an upsurge in formamidopyrimidine DNA glycosylase- (Fpg-) sensitive regions mediated by oxidative stress. ROS also caused mitochondrial membrane damage and increased the Bax/Bcl2 ratio, leading to a mitochondria-mediated apoptosis pathway [36]. Likewise, the toxicity of ZnONPs against human skin melanoma (A375) cells and oxidative stress impact was studied. It has been noted that exposure to ZnONPs leads to oxidative stress, as supported by antioxidant enzyme depletion and lipid peroxidation. The supported study also revealed DNA damage in cells on exposing the ZnONPs, mediated by oxidative stress [37]. Iron/iron oxide nanoparticles have been reported to induce oxidative stress leading to cellular damage and toxicity. Imam et al. showed the dopaminergic damage in neuronal cells induced by the iron nanoparticles having a size of 10 nm in a dose-dependent manner [38]. Wu et al. also showed the toxic effects of ultrasmall iron oxide nanoparticles on multiple organs. In their study, the team showed that the iron oxide nanoparticles bearing size of less than 4.2 nm had toxic effects on the cardiac tissues of mice. Further analysis revealed the formation of hydroxyl free radicals in the heart tissue and serum. Additionally, treatment with these NPs also elevated liver enzymes alanine amino transferase and aspartate aminotransferase, indicating significant liver toxicity [39].

2.2. Metal and Metal Oxide-Mediated Toxicity. Lei et al. assessed the biochemical composition of extracts of the liver, serum, urine, and rat kidney tissues by treating them with various doses of Cu_2ONPs for five days. The results revealed that toxic effects were found maximum at higher doses of Cu_2ONPs (200 mg/kg/d). The observed toxic effects were hepatocytic necrosis and caused proximal renal tube necrosis [40]. Song et al. analyzed the toxicity of four Cu_2ONPs with average sizes of 25, 50, 78, and 100 nm against two fish cell lines (RTH-149 and PLHC-1) and two mammalian cell lines (HepG2 and H4IIE). They observed that exposure of Cu_2ONPs to cell lines has a clear dose-effect relationship. On exposure to smaller Cu_2ONPs (25 nm), the cell lines of mammals were highly sensitive compared to the cell lines of fish. The minimum IC_{50} was observed after introducing the H4IIE cell line to Cu_2ONPs. The strain of RTH-149 demonstrated the highest resistance against Cu_2ONP suspensions [41].

Van der Zande et al. studied the chemical nature of AgNPs' coating surfaces and their toxic effects on organisms. For AgNPs coated with polyvinyl pyrrolidone (PVP) and AgNPs, oral doses were given to rats, and experimental studies were performed for 28 days. The presence of AgNPs in each organ was detected through dissection in rats, and the maximum concentrations were found in the spleen and liver [42]. In coated and uncoated AgNPs with polyethylene glycol (PEG), Pinzaru et al. determined the toxic effects of sodium dodecyl sulfate and sodium citrate. *In vitro* studies were carried out with mice and human keratinocyte (SKH-1 and HaCat) cell lines and found that the viable cell number was not affected up to 72 h at dose ranges from 0.1 to 3.0 μmol/l. While concentrations varying from 10 to 50 μmol/l displayed a cytotoxic effect [43].

Park et al. studied the toxicity effect of AgNPs with varying sizes in mice. The daily dose received by each mouse was 1 mg/kg (for 14 days) with various sizes of AgNPs. They found that smaller AgNPs of size 20 to 70 nm tend to be accumulated in multiple organs (the testis, liver, brain, kidneys, and lung), which was not the case with larger particles (>300 nm). Moreover, introducing AgNPs at variable doses of a mean size of 42 nm for 28 days revealed an adverse effect on the liver and kidneys at higher doses (from 1.00 mg/kg) [44]. Kim et al. reported AgNPs' oral toxicity in rats exposed for 90 days (0 to 500 mg/kg) and a decrease in the body mass in male rats, and storage of AgNPs was noted in the liver [45]. Toxicity concerns have been raised for iron/iron oxide nanoparticles as well. One of the major considerations of nanoparticle synthesis is the size. Iron oxide nanoparticles larger than 200 nanometers can accumulate in speel due to entrapment, while the smaller particles are excreted by the kidneys [46]. One study on mice showed that the magnetic nanoparticles crossed the blood-brain barrier and the blood-testis barrier, causing an accumulation of the inhaled nanoparticles in the brain, testis, lung, liver and spleen [47]. In vivo studies on female CD® IGS rats showed that the ferric oxide nanoparticles caused apoptotic death of erythrocytes at 12 mg/kg/day. Besides red cell apoptosis, there were notable alterations in the cell membrane, cytoplasmic calcium levels, and oxidative stress-induced cell death [48].

2.3. Environmental Hazards of Metallic Nanoparticles. There are numerous applications of green-synthesized metallic nanoparticles in various industries. The harmful effects of chemically and physically synthesized nanoparticles are multiple folds higher than the green synthesized nanoparticles. However, the biogenic nanoparticles have an inherent issue of stability. Despite using biomolecules and cellular compounds as stabilizing or capping agents, these capping agents tend to dissociate when such NPs are released into the environment. However, because of their small size, the NPs are invasive to most biological membranes and can impart cytotoxic and neurotoxic effects on humans.

3. Advantages of Seed Extracts for NP Synthesis

Formed by complex matrices on the outer layer and the germ, seeds are affluent in bioactive phytochemicals, vitamins, and minerals that save the DNA of plants from oxidative stress, thus facilitating the species perpetuation [18]. Also, the seeds' endosperm accumulates nutritional components to maintain the future seedling with a variable mixture of complex carbohydrates, high-quality proteins, and fat, depending on the type of seed [18].

The "speciality" term has been newly applied to seeds to express high-value and unique food products [49]. Also, some seeds have been represented as "*super seeds*" for marketing purposes, owing to their health-related benefits. Even though "*super fruit*" has been described in scientific reports, "*super seeds*" require acceptance and better sensitization of the general public to describing their health benefits [50, 51]. The most accepted speciality seeds comprise chia (*Salvia hispanica* L.), black cumin (*Nigella sativa* L.), hemp (*Cannabis sativa* L.), flax (*Linum usitatissimum* L.), perilla (*Perilla frutescens* L.), sesame (*Sesamum incidicum* L.), quinoa (*Chenopodium quinoa* Willd.), and pumpkin (*Cucurbita* spp.). The reason behind the selection of quinoa, chia, pumpkin, and flax seeds and their use as speciality seeds is that they have been recommended as part of the healthy food choice as per dietary guidelines of the United States Department of Agriculture (USDA) [49]. Some seeds and their derived oils (perilla, sesame, hemp, and black cumin) have been used in recipes, health-promoting ingredients, and nutraceuticals formulation worldwide and have received significant attention from consumers.

On the other hand, some seeds have generally been considered waste products generated from vegetable/fruit processing industries and households [24]. Apples (*Malus domestica*) led to the production of 10.91% of seed as byproducts, while the same from papaya (*Carica papaya*) was around 6.5%, and mangoes (*Mangifera indica*) around 13.5% [52, 53]. However, seeds contain high amounts of bioactive components and have thus been studied for their content in dietary fibers, phenolic, and other natural compounds [54]. In most vegetables and fruits, only the pulp or flesh is edible. Still, studies have shown that large quantities of essential nutrients and phytochemicals are found in peels, seeds, and other vegetables and fruit components that are not usually consumed [55]. For example, the seeds of mangoes (*Mangifera indica*), jackfruits (*Artocarpus*

Table 1: Phytochemicals of some seeds and their function as capping agents in NPs for the benefit of human beings.

Seed varieties	Phytochemicals	Role	Types of metallic NPs	Phytochemicals as capping agents	References
Avocado, pomegranate	Caffeic acid, cinnamic acid, syringic acid, chlorogenic acid, coumaric acid, (epi)catechin, (epi)gallocatechin, ferulic acid, naringenin, epicatechin gallate, and vanillic acid; hydroxybenzoic acids, ellagic acid, 3,3′-di-o-methylellagic acid, 3,3′.4′-tri-o-methylellagic acid, β-sitosterol, genistein, and daidzein	Antioxidant, antidiabetic, anticardiovascular, and anticancer	Copper oxide	Alkaloids, flavonoids, polyphenols, alkanes, and alkenes	[19–23]
Fennel, mango, thymol	α-Pinene, limonene, eucalyptol, carveol, quinic acid, protocatechuic acid, catechin (+), caffeic acid, syringic acid, naringin, and kaempferol; gallic acid, coumarin, caffeic acid, vanillin, mangiferin, ferulic acid, and cinnamic acid; thymol, limonene, p-cymene, and γ-terpinene	Antioxidant, antidiarrheal, and anti-inflammatory	Gold	Flavonoids, terpenoids, tannins, and thymol	[69–75]
Custard apple, date palm, grape	Cyclic peptides, cyclic octapeptides, and annonaceous acetogenins; p-hydroxy-hydrocinnamic acid, myristic acid, oleic acid, and lauric acid; catechin, epicatechin, epicatechin gallate, protocatechuic acid, procyanidin B1, B2, B3, and B4	Anticancer, antimicrobial, antioxidant, antidiabetic, and antiaging	Silver	Amino acids and proteins	[76–81]
Green cardamom	1, 8-cineole, α-terpinyl acetate, α-terpineol, sabinene, nerol, and α-pinene	Anticancer	Zinc oxide	Phenolic compounds	[82, 83]
Fenugreek, drumstick	Polyphenols, lysine, L-tryptophan, alkaloids, vitamin C, niacin, potassium, and diosgenin; amino acids, alkaloids, flavonoids, and phenolic compounds	Dye degradation, antibacterial, nitrate removal	Iron	Amino acids	[84, 85]

heterophyllus), avocados (*Persea Americana*), and longans (*Dimocarpus longan*) contain phenolic compounds at a concentration 15% higher compared to the fruit pulp [56, 57]. Dhingra and Kapoor revealed that the crude fiber content in the mango seed kernel is 1.75% [58]. In comparison, Sagar et al. reported 3.96% [59]. Likewise, Ashoush and Gadallah reported in their study that the crude fiber content in mango kernel powder is 0.26 ± 0.07 g/100 g, with seeds, peel, and rind of vegetables and fruits possessing the largest amounts of phenolic compounds [60]. Al-Farsi and Lee found that date (*Phoenix dactylifera*) seeds are a good source of phenolic compounds and antioxidants [61]. Except for the olives oil, the oils obtained from seeds have a maximum phenolic concentration than other edible oils [62]. Five vegetable seed extracts, viz. summer squash (*Cucurbita pepo*), bottle gourd (*Lagenaria siceraria*), cucumbers (*Cucumis sativus*), tinda (*Praecitrullus fistulosus*), and bitter melon (*Momordica charantia*), have been reported to be very effective against various microbes, including *Trichoderma reesei*, *Fusarium oxysporum*, *Escherichia coli*, *Serratia marcescens*, and *Streptococcus thermophilus*, which may be due, at least in part, to their high content of phenolic compounds [63, 64].

In folk medicine, seeds comprise the most often used plant parts for therapeutic uses, containing an inflated capsule that arises from the united follicles holding a substantial amount of oil with a pungent smell and bitter taste [24]. For example, fennel (*Foeniculum vulgare)* essential oil is used in the food industry as a flavouring agent in pickles, bread, beverages, cheese, and pastries. In addition, it can be used as an essential component in the pharmaceutical and cosmetic industry, presenting excellent antispasmodic, hepatoprotective, antioxidant, analgesic, inflammatory, diuretic, and anticancer effects [65–68]. In short, many seeds-derived phytochemicals are used to synthesize NPs, presenting excellent biological applications in humans, as shown in Table 1.

4. Green Synthesis of Metallic Nanoparticles Mediated by Seed Extracts

Seed extracts are recognized for having good amounts of reducing agents. For example, seeds of custard apple (*Annona squamosa* L.), cardamom (*Elettaria cardamomum*), jackfruit (*Artocarpus heterophyllus*), kalnoji (*Nigella sativa*), fenugreek (*Trigonella foenum-graecum*), and jamun (*Syzygiumcumini*) contain very rich amounts of phenolic acids, flavonoids, terpenoids, and proteins and thiamine [76, 83, 86–89]. Thus, NPs synthesized from such seeds present an added value as compared to NPs synthesized through biological methods, including the synthesis of NPs through microbial action (pure strains), which is quite a tricky process and consumes more time to convert the soluble metallic salts into elemental NPs/elemental oxide [8, 10]. The broad-spectrum mechanism known in the diverse NP biosynthesis using seed extracts is displayed in Figure 2 and summarized in Table 2.

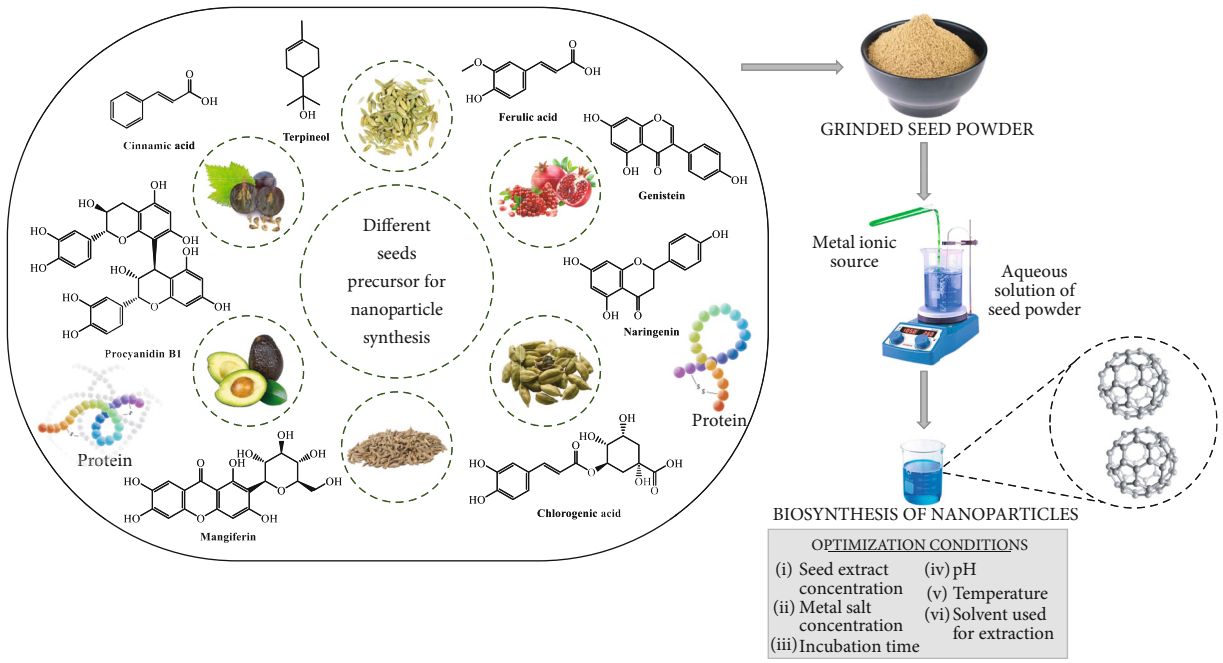

Figure 2: A general mechanism illustrates the formation of NPs using seed extracts.

For the synthesis of metallic nanoparticles from seed extracts, typically, three major components are essential, *viz.* a precursor (salt(s) of the metal whose nanoparticle is desired), a reducing agent (present in the seed extract) and a capping agent (works as a stabilizer of the nanoparticle by preventing further reactions or modifications of NPs). Major reducing and capping agents in seed extracts include polyol compounds, phenolic compounds, and flavonoids. The basic mechanism of synthesising nanoparticles by seed extracts is the reduction of metal ions by the reducing agents present in seeds. These agents include alkaloids, terpenoids, phenolic compounds, and organic aldehydes. Besides these small molecules, enzymes belonging to the class of dehydrogenases are also involved in NP synthesis. However, elucidating the exact mechanism of NP synthesis is difficult due to the variety of phytochemicals in the seed extracts. Typically, for silver nanoparticles, the Ag^+ ions present in the aqueous solution of silver nitrate are acted upon by the reducing agents in seed extracts to form Ag. The Ag precipitates then undergo a process of nucleation in which the synthesized nanoparticles agglomerate in the absence (primary nucleation) or presence (secondary nucleation) of crystalline precursors. In the case of plant extracts, the extracellular synthesis of metallic nanoparticles takes place.

4.1. Reaction Parameters in NP Synthesis. In nanoparticle synthesis, different physicochemical parameters play a vital role. These parameters include temperature, pH, and incubation time. Typically, the nanoparticle size and shape are more uniform at lower temperatures. Lower temperatures reduce the average particle size, whereas higher temperatures increase the rate of synthesis of nanoparticles [111]. During nanoparticle synthesis, the time and temperature are modulated to adjust the desired size and shape of the nanoparticles. The various time and temperature combinations for NP synthesis are summarized in Table 2. pH also significantly affects the size and shape of the nanoparticles. Whereas the microorganisms accumulate metal ions at acidic pH (between 2 and 6), the accumulation of metal ions requires alkaline pH. In the case of iron oxide nanoparticle synthesis from *Carica papaya* extract, the reaction pH was adjusted to 11 [112]. On the other hand, Buarki et al. synthesized iron oxide nanoparticles at pH 7.0 from *Hibiscus rosa sinensis* [113].

5. Characterization Techniques for Analyzing NPs

The characterization of NPs is essential to know and boost advances in the NP synthesis and obtain a deeper knowledge of their value. Scanning electron microscopy (SEM), ultraviolet-visible spectroscopy (UV-vis spectroscopy), transmission electron microscopy (TEM), atomic force microscopy (AFM), XRD (X-ray diffraction), Fourier-transform infrared spectroscopy (FTIR), and dynamic light scattering (DLS) are the most commonly used techniques for the characterization of NPs [114]. The SEM technique identifies the size, shape, and morphology of the synthesized NPs, where the image produced is in considerably high resolution [115]. The SEM micrographs are beneficial to understanding the three-dimensional structure of the specimens. SEM possesses enormous field depth due to a thin beam of electrons [116]. TEM shows higher resolving power than SEM, a widespread technique for characterising NPs. It can resolve materials having a distance of only 0.2 nm to present information regarding cell anatomy, interaction with the membrane, and state of NPs accumulation in the cell. TEM is considered one of the gold standards for NP

Table 2: Synthesis and characterization of metallic NPs obtained from different seed varieties.

Seed plant common name	Scientific name	Type of synthesized NPs	Characterization methods										Reaction temperature/time/solvent used	Morphology	Size (nm)	Stability	References
			UV-vis	TEM	SEM	FT-IR	XRD	EDX	DLS	Zeta potential	HRTEM	AFM					
Avocado	*Persea americana*	Copper oxide	√	√	√	√	√	—	—	—	—	√	40-50°C/6-7 h/copper sulfate	Spherical	42-90	NS	[21]
Pomegranate	*Punica granatum*	Copper oxide	√		√	√	√	√	—	—	—	√	60°C/1-2 h/copper chloride	Spherical	40-80	ND	[20]
Wheat	*Triticum aestivum*	Copper oxide	√	√	√	√	√	—	—	—	—	—	RT/1 h/copper (II) sulfate	Crystal	20.76	3 months	[90]
Black beans	*Phaseolus vulgaris*	Copper oxide	—	√	√	√	√	√	√	—	—	—	120°C/7-8 h/copper sulfate	Spherical	26.6	ND	[91]
Black pepper	*Piper nigrum*	Copper oxide	√	—	—	—	√	—	—	—	—	—	RT/3 h/copper sulfate pentahydrate	NS	>40	ND	[92]
Mango	*Mangifera indica*	Gold	√	√	√	√	√	√	√	—	√	—	RT/NS/chloroauric acid tetrahydrate	Spherical	46.8	ND	[73]
Mango	*Mangifera indica*	Gold	√	√	—	√	√	—	—	√	—	—	RT/24 h/gold (III) chloride trihydrate	Triangle and irregular	19.45	ND	[93]
Fennel	*Foeniculum vulgare*	Gold	√	√	—	√	√	—	—	—	—	—	RT/NS/tetrachloroauric(III) acid trihydrate	Spherical	10-30	ND	[72]
Thymol	*Trachyspermum ammi*	Gold	√	√	—	—	√	√	—	—	—	—	300W/2 min/chloroauric acid	Crystal	16.63	ND	[75]
Avocado	*Persea americana*	Silver	√	√	—	√	—	—	—	—	—	—	RT/5 h/silver nitrate	Semispherical and oblongated	NS	ND	[94]
Longan	*Dimocarpus longan*	Silver	√	√	—	√	√	√	√	√	—	—	25°C/40 min/silver nitrate	Cubic	40	ND	[95]
Grape	*Vitis vinifera* L.	Silver	√	√	√	—	—	—	√	—	—	—	95°C/10 min/silver nitrate	Colloidal	91.89	ND	[80]
Custard apple	*Annona squamosa* L.	Silver	√	√	—	√	√	—	—	—	—	—	Sunlight/30 min/silver nitrate	Spherical	22	ND	[81]
Date palm	*Phoenix dactylifera*	Silver	√	√	√	√	√	—	—	—	—	—	RT/30 min/silver nitrate	Spherical	17-19	ND	[79]
Durian	*Durio zibethinus*	Silver	√	√	√	√	√	√		√	—	—	Sunlight/30 min/silver nitrate	Spherical and rod	20-75	120 days	[96]
African star apple	*Chrysophyllum albidum*	Silver	√	—	—	√	—	—	—	—	—	—	95°C/15 min/silver trioxonitrate	NS	NS	ND	[97]
Noni	*Morinda citrifolia* L.	Silver	√	—	—	√	—	—	—	—	—	—	RT/24 h/silver nitrate	Spherical	3	Six months	[98]
Jackfruit		Silver	√	√	√	√	√	—	—	—	—	—		Irregular	10.78	ND	[99]

Table 2: Continued.

Seed plant common name	Scientific name	Type of synthesized NPs	Characterization methods										Reaction temperature/time/solvent used	Morphology	Size (nm)	Stability	References
			UV-vis	TEM	SEM	FT-IR	XRD	EDX	DLS	Zeta potential	HRTEM	AFM					
	Artocarpus heterophyllus lam												121°C/5 min/silver nitrate				
Green gram	*Vigna radiata*	Silver	√	√		√	√	—	—	—	—	—	RT/3 h/silver nitrate	Spherical	18	Five months	[100]
Cumin	*Cuminum cyminum*	Silver	√	—	√	√	√	—	√	—	—	—	90°C/5 h/silver nitrate	Spherical	111-125	ND	[101]
Fenugreek	*Trigonella foenum-graecum*	Silver	√	—	—	√	—	—	√	—	—	—	RT/NS/silver nitrate	Spherical	95-110	30 days	[102]
Green cardamom	*Elettaria cardamomum*	Silver	√	—	√	—	√	—	—	—	—	—	75°C/30 min/silver nitrate	Spherical	40-70	ND	[103]
Kalonji	*Nigella sativa*	Silver	√	—	—	√	√		√	—	—	—	NS/silver nitrate	Spherical	8-80	ND	[104]
Kalonji	*Nigella sativa*	Silver	√	√	√	√	√		√	√	—	—	80°C/2 h/silver nitrate/	Spherical	10-12	ND	[89]
Quince	*Cydonia oblonga*	Zinc oxide	√	—	—	√	√	√	—	—	—	—	80°C/5 h/zinc nitrate hexahydrate	Crystal	25	ND	[105]
Jamun	*Syzygium cumini*	Zinc oxide	√	√	√	√	√	—	—	—	—	—	60°C/45 min/zinc acetate	Spherical	50-60	ND	[106]
Longan	*Dimocarpus longan*	Zinc oxide	√	√		√	√	—	—	—	—	—	450-800 W/1 min/zinc diacetate	Irregular	10-100	ND	[107]
Fennel	*Foeniculum vulgare*	Zinc oxide	√	—	√	√	√	√	—	—	—	—	99°C/1 h/zinc oxide in water	Spherical	23-51	ND	[108]
Coriander	*Coriandrum sativum* L.	Zinc oxide	—	—	√	—	—	—	—	—	—	—	75-80°C/3 h/zinc acetate	NS	128.1	ND	[109]
Green cardamom	*Elettaria cardamomum*	Zinc oxide	√	√	√	√	√	—	—	—	—	—	60°C/3 h/zinc acetae	Spherical	18.72	ND	[82]
Fenugreek	*Trigonella foenum-graecum*	Iron	√	√	—	√	√	—	—	—	—	—	300°C/15 min/iron chlordie	NS	11	ND	[84]
Drumstick	*Moringa oleifera*	Iron	√	√	—	√	√	—	√	—	—	—	NS/30 min/ferric chloride	Spherical	2.6	ND	[85]
Pomegranate	*Punica granatum*	Iron	√	—	√	—	√	√	—	—	—	√	70°C/15 min/iron chlordie	Seimi-spherical	25-55	ND	[110]

NS: not specified; ND: not done; AFM: atomic force microscopy; TEM: transmission electron microscopy; UV-vis: ultraviolet-visible spectroscopy; FT-IR: Fourier transform infrared spectroscopy; EDX: energy-dispersive X-ray spectroscopy; SEM: scanning electron microscopy; DLS: dynamic light scattering; XRD: X-ray powder diffraction; HRTEM: high-resolution transmission electron microscopy; RT: room temperature.

Table 3: Applications of copper oxide NPs synthesized from various seed varieties.

Seed plant family	Reducing agent	Seed variety	Applications	References
Lauraceae	Carboxylic acid, alkanes, and carbolic acid	*Persea americana*	Antibacterial activity against *Escherichia coli*, *streptococcus* sp., *Klebsiella* sp., and *Rhizobacterium*; antifungal activity against *Aspergillus flavus*, *Aspergillus fumigates*, and *Fusarium oxysporum*; antioxidant activity	[21]
Lythraceae	Polyphenolic, aromatic in phenolic, alcohols, and carboxylic groups	*Punica granatum*	Photocatalytic activity against methylene blue (MB)	[20]
Poaceae	Hydroxyls, carbonyl, and alcohols	*Triticum aestivum*	Catalytic activity against 4-nitrophenol	[90]
Fabaceae	Proteins, amino acids, oligosaccharides, complex carbohydrates, alkaloids, phenols, saponins, and flavonoids	*Phaseolus vulgaris*	Induced apoptosis and suppressed the proliferation of HeLa cell line	[91]

Table 4: Applications of gold NPs synthesized from various seed varieties.

Seed plant family	Reducing agent	Seed variety	Applications	References
Anacardiaceae	Flavanoids, terpenoids, and tannins	*Mangifera indica*	Antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus cereus* (ATCC11778), *Bacillus subtilis* (ATCC6633), *Staphylococcus aureus* (ATCC29737), *Escherichia coli* (NCIM2931), *Pseudomonas aeruginosa* (ATCC9027), *Klebsiella pneumonia* (NCIM2719), and *Salmonella typhimurium* (ATCC23564); antifungal activity against *Cryptococcus neoformans* (ATCC34664), *Candida albicans* (ATCC2091), and *Candida glabrata* (NCIM3438); antioxidant activity; anticancer activity against human gastric cancer cell line (AGS), human cervical cancer cell line (HeLa cells), and breast cancer cell line (MCF-7); antiangiogenic properties	[73, 93]
Apiaceae	Carboxyl, alkoxy, alcohols, hydroxyl, and carboxylate	*Foeniculum vulgare*	Catalytic activity against rhodamine B (RhB) and methylene blue (MB)	[72]
Apiaceae	Thymol	*Trachyspermum ammi*	Antibacterial activity against *Listeria monocytogenes* (ATCC19114) and *Serratia marcescens* (ATCC13880); biofilm inhibition activity; anticancer activity against liver hepatocellular (HepG2) cell line	[75]

characterization, as it provides a clear image through diffraction and gives the specimens investigative, morphological, and structural information [117, 118]. AFM presents a clear, higher-resolution image, i.e., 100-fold more than the optical diffraction limit [119]. UV-vis spectroscopy provides the absorption or transmission measurement of aqueous medium and transparent or opaque substances. This technique is mainly used with microgels to characterize NPs. It plays a significant role in examining the catalytic activities of hybrid NPs and their functional role in photonic and sensing techniques [120, 121].

XRD determines lattice arrangements such as chemical composition, unit cell arrangement, bond angles, crystalline nature of phases, and lattice plane spacing of NPs [114]. DLS is an extensively employed technique to provide the size of NPs in colloidal suspensions in the submicrometer and nano ranges [122]. FTIR technique shows the vibrational stretching frequency of bonds between metal and oxygen [123].

The DLS, FTIR, SEM, TEM, UV-vis spectroscopy, and XRD methods are commonly used for characterizing seed extract-derived nanoparticles [89, 124].

6. Types of Green Synthesized Metallic NPs

6.1. Copper Oxide Nanoparticles (Cu_2ONPs). Copper oxide (Cu_2O), a transition metal oxide, shows a narrow bandgap (~2.0 eV) and displays various properties, including high specific surface area, improved redox potential, significant electrochemical activity, and incomparable stability in solutions [11, 125]. NPs produced with noble metals have promising applications in various fields, such as sensors/biosensors, biocidal agents, antifouling coatings, energy storage, electrochemistry, and catalyst [11]. In addition, these NPs are broadly used in clinical analytes for nonenzymatic sensing owing to their ability to support electron transfer [11]. The seed-mediated Cu_2ONPs and their applications are listed in Table 3.

6.2. Gold Nanoparticles (AuNPs). Recently, AuNPs have received ample attention due to their physical (shape and size) and optical biocompatibility [125]. For example, AuNPs with distinct morphological features have been broadly used in medicine for multiple purposes, such as drug carrier and tumor exposure [11]. The seed-mediated AuNPs and their applications are listed in Table 4.

6.3. Silver Nanoparticles (AgNPs). AgNPs have received considerable attention because of their catalytic and biochemical activities due to their massive surface area compared to particles with analogous structures [11]. The synthesis of AgNPs follows two steps: in the initial step, Ag^+ ions are reduced to Ag°, and in the next step, colloidal AgNPs clustering occurs to form oligomeric clusters, which in the later stage get stabilized [11]. The reduction in Ag^+ ions needs biological catalysts, like enzymes, acquired from various biological sources, e.g., plants, fruit extracts, and microbes. Furthermore, varieties of seed extracts have been well-known for AgNP synthesis due to their biological effect, as listed in Table 5.

6.4. Zinc Oxide Nanoparticles (ZnONPs). Recently, researchers in nanotechnology have underlined that ZnONPs have diverse applications in various areas, e.g., biomedical, optical, and electronic sectors [11, 125]. It is believed that synthesized ZnONPs are safe, easy, and cost-effective. Also, the Food and Drug Administration (FDA) has approved such NPs' generally recognized safe (GRAS) status [126, 127]. Majorly known for their wound healing and anti-inflammatory potential, ZnONPs have also been used to formulate facial cosmetic products, e.g., sunscreen lotions, as they demonstrate intrinsic UV filtering potential [128]. Moreover, ZnONPs are used for drug delivery systems due to their anticancer, antimicrobial, antifungal, and antidiabetic effects [128]. The seed-mediated ZnONPs and their applications are listed in Table 6.

6.5. Iron Oxide Nanoparticles (FeONPs). Iron oxide (hematite) is the most common ecofriendly and natural nanoparticles among different types of nanoparticles [110]. As iron is known to have a significant role in biogeochemical cycle of the environment. Therefore, the influence of ecofriendly nature of iron oxide nanoparticles is being evaluated in the biological system. Concerning this, various researchers are now attempting to explore their biological potential. In fact for the past four decades, the antiferromagnetic and magnetic iron oxide nanoparticles are being used in biomedical sciences [110]. In biomedical sciences, iron nanoparticles are used as antibacterial agents to cease the activity of bacterial species without harming the host cells. Lately, iron oxide nanoparticles have been used in fabrication of sensor for biomolecules, hyperthermia, metabolites, and magnetic toxicology [110].

A study reported the iron nanoparticles synthesized using fenugreek (*Trigonella foenum-graecum)* seed have been reported effective degradation activity for methyl orange dye in the presence of UV light with rate constant k_{app} of $0.025\,min^{-1}$ and pseudofirst-order kinetics [84]. Another study reported about antiabacterial activity of FeNPs against Gram-negative *E. coli* and Gram-positive *S. aureus.* The result obrtained from the study showed the minimum inhibitory concentration (MIC) of 32 μg/ml and 64 μg/ml for *E. coli* and *S. aureus*, respectively. Katata-Seru and his colleagues developed iron nanoparticles using *Moringa oleifera* seed extract which showed an effective removal of nitrate ion (NO_3^-) from ground and surface water by 85% [85]. The result obtained from the study showed the maximum zone of inhibition (i.e., 6 mm) against *Escherichia coli.* In 2019, Bibi and his teammates fabricated Fe_2O_3NPs using seed extract of pomegranate(*Punica granatum*), which were evaluated for photocatalytic activity against reactive blue under UV light irradiation. The result obtained from the study showed the 95.08% of degradation of reactive blue with reaction time of 56 min [110].

7. Antimicrobial Activity of Seed Extract-Mediated NPs

Among the broad spectrum of biological effects, NPs demonstrate good antimicrobial activity, as NPs can pass through the bacterial membrane, ultimately influencing cellular activity and metabolic activity [129, 130]. After entering the bacterial cells, NPs obstruct the metabolic activity of cells, with NPs adhering to the basic cell components, including liposomes, DNA, ribosomes, and enzymes (Figure 3). The basic components associated with NPs result in oxidative stress, heterogeneous alterations, gene expression alterations, protein deactivation, enzyme inhibition, cell membrane permeability changes, and electrolyte imbalance [129]. Cell walls, including membranes used as protective checkpoints, also cause resistance in bacteria from the outer environment.

Various pathways exist in the NP absorption in Gram-negative and Gram-positive bacteria through the cell membrane [131]. Lipopolysaccharides (LPS) found in Gram-negative bacteria present a negative charge for NPs attraction. However, in Gram-positive bacteria, teichoic acid carries out the same function. NPs flow via the molecular phosphate chain and avoid accretion. Additionally, NPs are reported for their efficacy against Gram-positive compared to Gram-negative bacteria. LPS, lipoproteins, and phospholipids are barriers and only allow the movement of macromolecules. While damaged cell membranes and cellular death are found in Gram-positive bacteria as the cell wall contains a thin peptidoglycan layer, teichoic acid with enough pores helps to allow the passage of foreign substances [129].

Avocado seed-mediated Cu_2ONPs demonstrated excellent antibacterial activity against Gram-negative and Gram-positive bacteria strains. A maximum inhibition zone was found in *Streptococcus,* a Gram-positive bacterium, at a concentration of 75 μl with a zone diameter of 22.23 ± 0.15 mm, and a minimum inhibition zone was determined in *Rhizobacterium* at a concentration of 25 μl with a zone diameter 9.27 ± 0.15 mm. Due to the maximum inhibition zone in *Streptococcus*, it has been proved that the avocado seed-mediated Cu_2ONPs illustrated efficacy in controlling

Table 5: Applications of silver NPs synthesized from various seed varieties.

Seed plant family	Reducing agent	Seed variety	Applications	References
Lauraceae	Polyphenols	*Persea americana*	Antibacterial activity against *Escherichia coli*	[94]
Sapindaceae	Phenolic, flavonoids, alkane, and alkyl halide	*Dimocarpus longan*	Photocatalytic activity against methylene blue (MB); catalytic activity against 4-nitrophenol; antioxidant activity	[95]
Vitaceae	Alcohol, alkyne, carbonyl, and alkene	*Vitis vinifera* L.	Antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*; antifungal activity against *Fusarium solani, Fusarium oxysporum, Helminthosporium rostratum*, and *Alternaria alternata*	[80]
Annonaceae	Amide, alkynic, and alcohol	*Annona squamosa* L.	Photocatalytic activity against coomassie brilliant blue; antibacterial activity against *staphylococcus aureus* (MTCC96) and *Klebsiella pnuemoniae* (MTCC109); larvicidal action against *Anopheles stephensi*	[81]
Arecaceae	Carbonyl and proteins	*Phoenix dactylifera*	Antioxidant activity; anticancer activity against breast cancer cell line (MCF-7)	[79]
Malvaceae	Galacturonic acid, galactose, and arabinose	*Durio zibethinus*	Antibacterial activity against *Staphylococcus aureus* (ATCC 43300), *Staphylococcus haemolyticus* (ATCC 29970), *Bacillus subtilis* (ATCC 6633), *Escherichia coli* (ATCC 25922), and *Salmonella typhimurium* (14028); photocatalytic activity against methylene blue (MB); cytotoxicity against brine shrimp	[96]
Rubiaceae	Alcohols and phenols	*Morinda citrifolia* L.	Antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*	[98]
Moraceae	Hydroxyl, and carbonyl	*Artocarpus heterophyllus* Lam	Antibacterial activity against *Staphylococcus aureus* (NCIM 2654), *Bacillus cereus* (NCIM 2703), *Bacillus subtilis* (NCIM 2635), and *Pseudomonas aeruginosa* (NCIM 5032)	[97]
Fabaceae	Proteins and phenolics	*Vigna radiata*	Antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*	[100]
Apiaceae	Phenol, alcohols and aldehyde	*Cuminum cyminum*	Anticancer activity against breast cancer cell line (MCF-7) and breast adenocarcinoma metastatic cell line (AU565)	[101]
Fabaceae	Carboxylic acids, primary amines, aliphatic amines and alkyl halides	*Trigonella foenum-graecum*	Antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus vulgaris*; antioxidant activity; anticancer activity against skin cancer cell line (A431)	[102]
Ranunculaceae	Phenol, alkanes, amide, alcohols ether, carboxylic acids, and anhydrides	*Nigella sativa*	Antibacterial activity against microorganisms *Klebsiella pnuemoniae* (MTCC618), *Escherichia coli* (MTCC40), *Staphylococcus aureus* (MTCC3160), *Pseudomonas aeruginosa* (MTCC1688), *enterococcus faecalis* (MTCC439); antibiofilm activity; anticancer activity against breast cancer cell line (HCC712); photocatalytic activity against Congo red	[89, 104]
Zingiberaceae	Flavones	*Elettaria cardamomum*	Antibacterial activity against *Bacillus subtilis*	[103]

Streptococcus infections like endocarditis, sepsis, and wound and skin infection [21]. It has been revealed that rice-grain-shaped *Caesalpinia bonducella* seed extract-mediated Cu_2ONPs displayed good antimicrobial potential by inhibiting bacterial growth. This study found that Cu_2ONPs have good antibacterial properties against *S. aureus* compared to *Aeromonas*. The antibacterial properties of Cu_2ONPs could be due to their interaction with the bacterial surface, which can easily damage the cell by ripping the bacterial cell wall [132].

The study displayed that both antifungal and antibacterial activities were dose-dependent. Mango seed-mediated AuNPs showed antibacterial activity against *S. aureus*, and *E. coli* was dose-dependent [73]. AuNPs at a concentration of 10 μg/ml were unaffected in *the replication of E. coli and S. aureus cells*. But, as the concentration increased to 25 μg/ml and more than 100 μg/ml, significant growth inhibition was observed in Gram-positive *S. aureus* and Gram-negative *E. coli* bacteria. The study also revealed that AuNPs induced antibacterial activity due to producing reactive oxygen species (ROS) and damaging

Table 6: Applications of zinc oxide NPs synthesized from various seed varieties.

Seed plant family	Reducing agent	Seed variety	Applications	References
Rosaceae	Hydroxyl	*Cydonia oblonga*	Photocatalytic activity against methylene blue (MB)	[105]
Myrtaceae	Carboxylic acid	*Syzygium cumini*	Larvicidal and ovicidal activity against *Aedes aegypti*	[106]
Sapindaceae	Aldehydes	*Dimocarpus longan*	Photocatalytic activity against methylene blue (MB), malachite green (MG), methyl orange (MO), and orange II (OII)	[107]
Apiaceae	Hydroxyl and alkaline	*Foeniculum vulgare*	Antibacterial activity against *Staphylococcus aureus* (ATCC 43300), ESBL-producing *Escherichia coli* (ATCC 9637), *Bacillus subtilis* (WS15), *Salmonella typhimurium* (ATCC 14028), *Pseudomonas aeruginosa* (ATCC 27584), *Enterococcus faecium* VRE, and *Klebsiella pneumoniae* (ATCC 13883); antifungal activity against *Candida albicans* (ATCC 8436), *C. parapsilosis* (ATCC 22019) and *Cryptococcus* sp.; anticancer activity against breast cancer cell line (MCF-7)	[108]
Apiaceae	Phenolics and flavonoids	*Coriandrum sativum* L.	Antioxidant activity	[109]
Zingiberaceae	Amine and aromatic compounds	*Elettaria Cardamomum*	Antioxidant activity; antibiofilm activity; antibacterial activity against *Enterococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Proteus vulgaris*; larvicidal activities against *Aedes aegypti*, and *Culex tritaeniorhynchus*	[82]

ESBL: extended spectrum beta-lactamases.

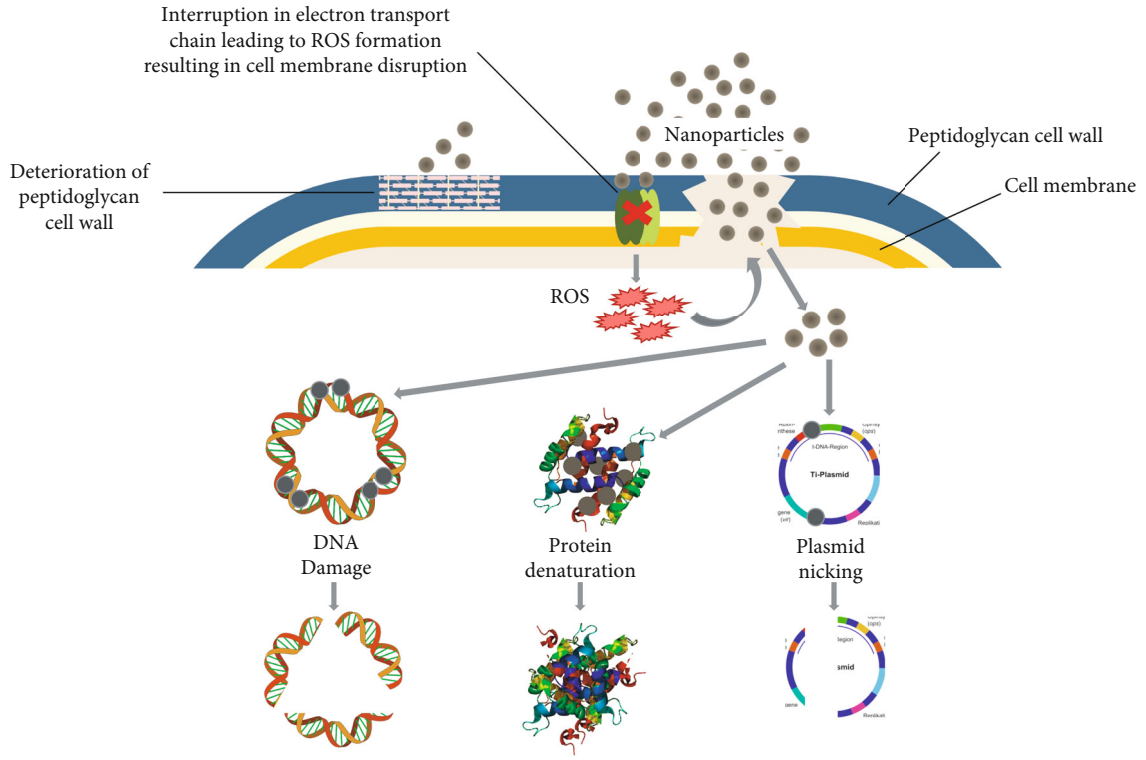

Figure 3: Graphical representation of the antimicrobial mechanism of biogenic NPs.

bacterial cells [73]. Donga et al. observed mango seed-mediated AuNPs. It noted their antifungal and antibacterial activities against *B. subtilis* (ATCC6633), *B. cereus* (ATCC11778), *S. aureus* (ATCC29737), *E. coli* (NCIM2931), *C. rubrum* (ATCC14898), *K. pneumoniae* (NCIM2719), *S. typhimurium* (ATCC23564), *P. aeruginosa* (ATCC9027), *C. albicans* (ATCC2091), *C. neoformans* (ATCC34664), and *C. glabrata* (NCIM3438) [93].

Al-Otibi et al. found that grape seed extract-mediated AgNPs showed stronger antibacterial potential against *S.*

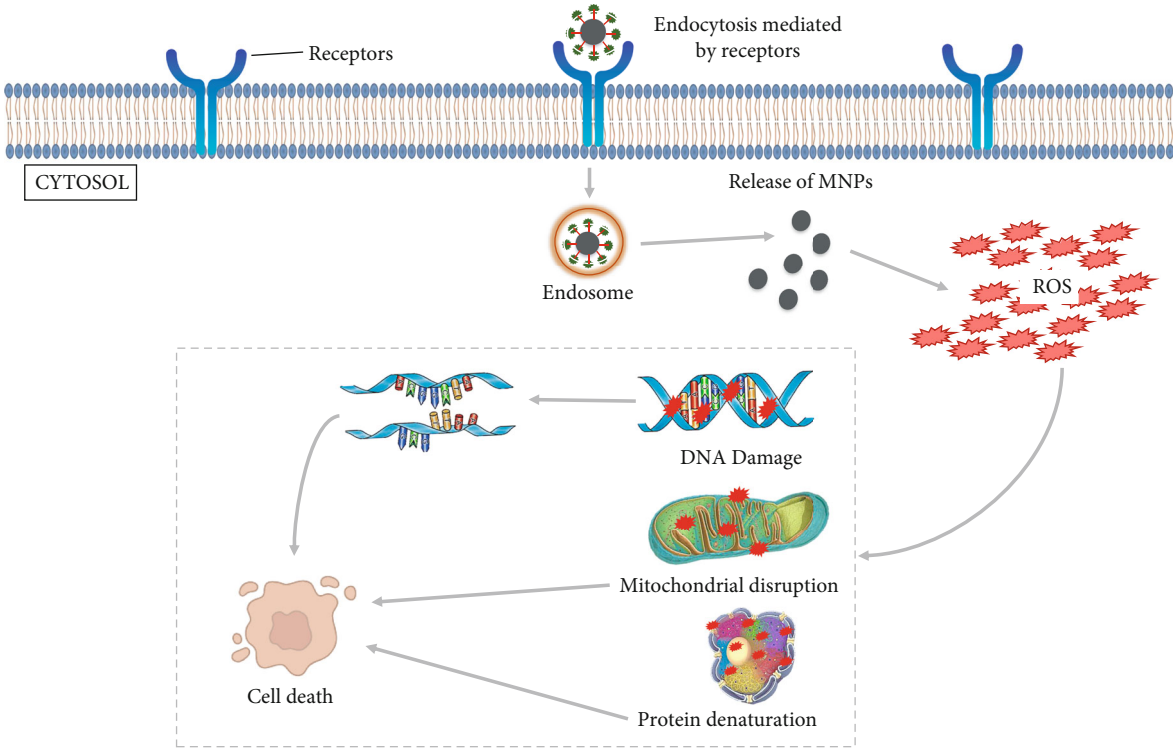

Figure 4: Graphical image of the anticancer mechanism of biogenic NPs.

aureus, *B. subtilis*, *P. aeruginosa*, and *E. coli* than only the seed extract [80]. Related studies were done against different fungal species, viz. *Fusarium oxysporum*, *F. solani*, *Alternaria alternate*, and *Helminthosporium rostratum*. Similarly, the seed of *Durio zibethinus*-mediated AgNPs demonstrated moderate antibacterial action against *S. typhimurium*, *B. subtilis*, *E. coli*, and *S. aureus* [96]. Alsalhi et al. revealed in their study that fennel seed-mediated ZnONPs showed minimum inhibitory concentration (MIC) values against bacterial, and yeast strains were 16.00 μg/ml for *C. albicans* (ATCC 8436) and 32.00 μg/ml for *E. faecium* VRE; in the case of *Cryptococcus* sp., *S. typhimurium* (ATCC 14028), and *S. aureus* (ATCC 43300), *P. aeruginosa* were 64.00 μg/ml, and for *C. parapsilosis* (ATCC 22019), it was 128 μg/ml [108]. The seed of green cardamom-mediated ZnONPs illustrated better antibiofilm activity at 100 μg/ml against several bacteria such as *P. vulgaris*, *E. faecalis*, *P. aeruginosa*, and *S. aureus* [82].

8. Anticancer Activity of Seed-Mediated NPs

According to the World Health Organization (WHO) 2019 reports, cancer is growing worldwide and is a significant cause of death, around 70 [133, 134]. Chemotherapy, surgery, radiation therapy, and hormone replacement therapy are the prime approaches to tackle them. Various medicinal plants have been recorded for their cytotoxic and anticancer potential, where polyphenols, like phenolic acids, flavonoids, other nonphenolic compounds, alkaloids, and terpenes, have been reported for promising biological effects [135–138]. For example, triterpenoids, like fomitellic, avicins, oleanolic, boswellic acid, ursolic, and pomolic acids, displayed cytotoxic effects [139]. Flavonoids like kaempferol, rutin, and quercetin have been underlined for their anticancer potential [136]. Thus, the application of nanotechnology for disease management has boosted new interdisciplinary research in different streams, including engineering, chemistry, biology, and medicine for detection, diagnosis, and treatment [140] (Figure 4). For instance, Doxil® (Johnson and Johnson, New Brunswick, NJ, USA), Myocet (Perrigo, Dublin, Ireland), and Abraxane® (Celgene, Summit, NJ, USA) are the nanobased anticancer drugs recommended for clinical use by the Food and Drug Administration (FDA, USA) [141]. Doxil formulation is a liposome-encapsulated form of doxorubicin, an anthracycline antibiotic extracted initially from streptomyces. Myocet is nanoencapsulated cyclophosphamide, and Abraxane is an albumin-bound nanoparticle formulation of paclitaxel. In addition, several studies have been done which evaluate the effectiveness of several NPs in distinct types of cancer. These studies and drugs indicate the potential of nanotechnology in developing anticancer pharmaceuticals [141].

Several research groups have reported seed-mediated nanoparticle synthesis and their anticancer activities by looking at the immense potential of nanotechnology for anticancer drug development and the medicinal potential of seed metabolites [142–144]. Nagajyothi et al., in their study, evaluated the *in vitro* anticancer activity and revealed that black bean seed-mediated Cu_2ONPs were efficient against human cervical carcinoma cells because of the enhancement of mitochondria-derived reactive oxygen species (ROS), which leads to liposomal membrane lipid

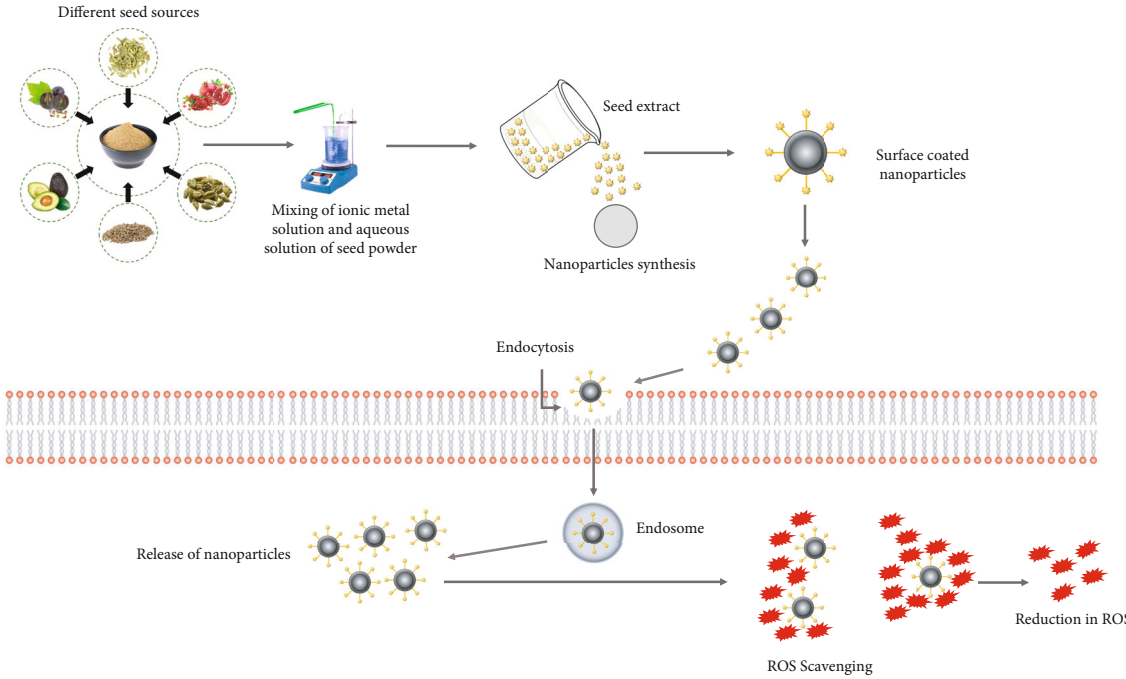

Figure 5: Schematic diagram presents the antioxidant mechanism of biogenic NPs.

peroxidation, controlling many signaling pathways and affecting the cellular cytokinetic movements [91]. The fragmentation of mitochondrial disruption assay proved the structural modification of mitochondria after association with NPs. A clonogenic assay also confirmed the inability of NPs to incubate cancer cells to proliferate well [91]. Black bean seeds are known to contain considerable concentrations of anthocyanin and polyphenols. Polyphenolic compounds can reduce the risk of developing cancers through induction of apoptosis, modulation of signal transduction, and induction of cell cycle arrest [145, 146]. Mango seed-mediated AuNPs resulted in cancer cell growth inhibition [73].[61] The study revealed that AuNPs at a concentration of 25 μg/ml were considered a biologically safe dose to inhibit the growth of cancerous cells. Also, these NPs had no other cytotoxic effects on normal cells. Also, it has been reported that mango seed-mediated AuNPs have dose-dependent cytotoxicity potential against the MCF-7 cell line [93]. The *Mangifera indica* extracts contain considerable amounts of polyphenols, flavonoids, and quercetin, which can work as reducing agents in gold NP synthesis. One plausible mechanism of the anticancer potential of these AuNPs is their antiangiogenic potential. Enabling angiogenesis is one of the hallmarks of cancer, and if a metallic nanoparticle formulation inhibits angiogenesis, there is a potential application of such an extract as a therapeutic [93]. At 400 mg/ml, AuNP-treated HeLa cells demonstrated cell viability of 67%, whereas the MCF-7 cell line showed 58% cell viability. Thymol (*Trachyspermum ammi)* seed-mediated AuNPs showed anticancer activity in HepG2 cancer cells in a concentration- and time-dependent manner. The IC_{50} of TA-AuNP-treated HepG2 was 92.453 μg/ml. A study reported that the treatment of TA-AuNPs significantly lowered the HepG2 cancer cells' glutathione (GSH) levels, suggesting that TA-AuNPs might be considered for anticancer therapy [75].

Mohammadi et al. reported that date palm-mediated AgNPs were effective against 7,12-dimethylbenz[a] anthracene- (DMBA-) induced breast cancer in male Sprague Dawley rats. In the study, the group showed anticachexic effects of the AgNPs as the nanoparticle formulation increased the mean body weight in the rats compared to the untreated set. The onset of cachexia is considered life-threatening as it leads to substantial loss of muscle mass. There was also reduced breast cancer metastasis to other organs like the spleen, kidney, and liver [79]. Devanesan et al. revealed that the seed extract of *Pimpinella anisum*-mediated AgNPs displayed cytotoxic anticancerous potential on colorectal cancer (CRC) cell lines HCT8 and SW620. The team reported selective killing of cancer cells was seen using proliferation assay, apoptosis assay, and cell cycle analysis [147]. While against A549 lung cancer cell lines, *Derris trifoliate* seed extract-mediated AgNPs illustrated moderate activity with an adequate concentration of 86.23 ± 0.22 μg/ml [148].

Fennel seed-mediated ZnONPs also displayed cytotoxicity against the MCF-7 cell line in a dose-dependent manner. The highest cytotoxicity was found at 100 μg/ml. Confocal microscopy revealed an alteration in the morphology of the nuclei and the actin filaments through DAPI and Phalloidin-Alexa fluor 594 stainings. The alteration in the nuclei and cytoskeletal filaments is a visual indicator of programmed cell death. The study concluded that the cytotoxicity of ZnONPs could be due to intracellular liberation of dissolved Zn metal ions in combination with ROS induction. This process included induced binary response, with the proinflammatory cell's reaction against ZnONPs [108].

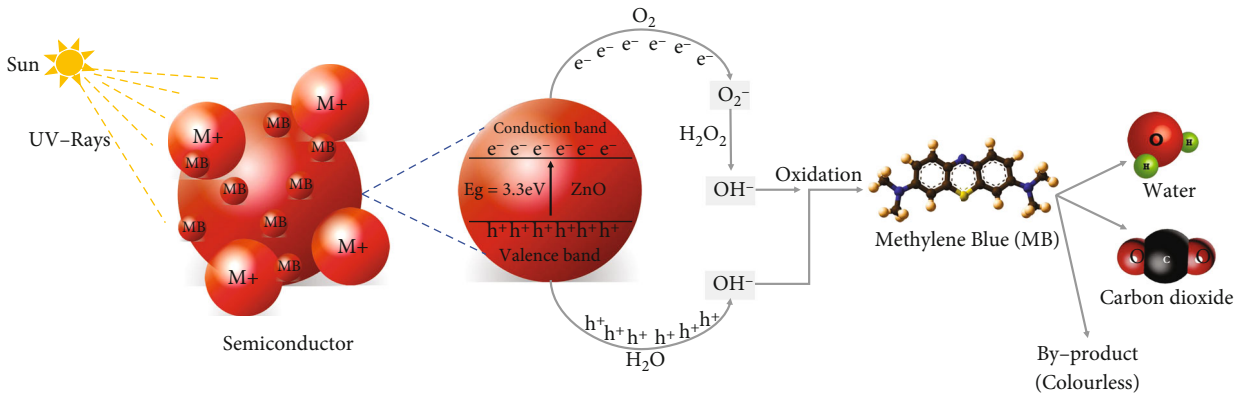

Figure 6: Photocatalytic mechanism of biogenic NPs.

9. Antioxidant Activity of Seed Extract-Mediated NPs

Oxidative stress has been increasingly pointed out as being a cause of many diseases [149]. Indeed, at a molecular level (DNA, proteins, unsaturated bonds of lipids, etc.), a high load of oxidants leads to oxidative alteration of the biological system, finally leading to damage and accelerating cell death [150, 151]. This phenomenon occurs typically where oxidative matter is formed, and the defense mechanisms fail. Reactive oxygen species (ROS) comprise the vital group of oxidants, including radicals such as the superoxide ion ($O_2^{\bullet-}$), hydroxyl (·OH), and nonradicals, e.g., organic peroxides and hydrogen peroxide. All of them have been characterized by exerting severe damage at both cell and tissue levels, culminating in the onset of multiple disorders [149, 152–155].

In previous decades, a new type of inorganic NPs functionalized with natural antioxidants has been formulated based on metal, carbon, and metal-organic frameworks (MOFs) to reduce the damage caused by ROS in biomedical areas (Figure 5). For example, mango seed-mediated AuNPs exhibited dose-dependent antioxidant activity [93]. The IC_{50} value was recorded at 256 mg/ml, 555 mg/m,l and 62 mg/ml for 2,2-diphenyl-1-picrylhydrazyl (DPPH), superoxide anion (SO), and 2,2-Azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) activity, respectively. The DPPH and ABTS assays are free radical-based methods for assessing the radical-scavenging abilities of different compounds and nanoparticles. While the DPPH assay is done in a methanol-water mixture, the ABTS assay is performed in an aqueous solution. In biochemistry, this translates to the suitability of the DPPH assay for compounds soluble in a methanol-water mixture instead of just water [93]. In another study, fenugreek seeds-mediated AgNPs showed dose-dependent antioxidant activity [99]. Also, Longan-mediated AgNPs exhibited better antiradical activity than commercial AgNPs using the DPPH assay [95]. Similarly, *Derris trifoliate* seed-mediated AgNPs showed an IC_{50} value of 8.25 μg/ml by DPPH [148].

10. The Catalytic Activity of Seed Extract-Mediated NPs

Several compounds, including 4-nitrophenol and its derivatives, are widely used in insecticides, herbicides, and dyes, and they are organic pollutants that harm ecosystems [156]. Specifically, 4-nitrophenol is toxic and considered an enormous risk, and its degradation is currently a matter of concern. Even though 4-nitrophenol-reduced products are used as intermediaries in white/black film developers, paracetamol, rubber antioxidants, corrosion inhibition, and sulfur dyes are also precursors in antipyretic and analgesic drugs [157]. $NaBH_4$ is conventionally used as a metal catalyst and reducing agent for AgNPs, Cu_2ONPs, PdNPs, and AuNPs and is believed to be a highly effective way to reduce 4-nitrophenol [158–161] (Figure 6). Methylene blue (MB) is an aromatic pollutant, heterocyclic in nature, discharged from the dye industries [162]. $NaBH_4$ is used as a reductant in NPs and MB, whose primary purpose is to be used as an absorbent [163].

Buazar et al. used wheat seeds to synthesize Cu_2ONPs. They observed that by adding biogenic NPs, the UV-vis absorption peak intensity of 4-nitrophenol at 315 nm disappeared in 20 min, specifying the quick adsorptive removal of 4-nitrophenol pollutant from its aqueous solution. 4-Nitrophenol is a potential carcinogenic agent, and its degradation using the biogenic nanoparticles implies the remediation potential of these nanoparticles. The study also reported considerable recyclability of these nanoparticles, strengthening the potential of their use as a catalytic agent. The team showed up to 95.5% recycling of the nanoparticle catalysts after five days of use [90]. Choudhary et al. revealed that the deep blue solution color disappeared fast by adding fennel seed extract synthesized AuNPs in MB dye and $NaBH_4$ solution. Within two minutes, the blue color of MB disappeared completely [72]. This may be attributed to using a seed extract instead of a chemical surfactant during nanoparticle formulation. The molecules in the seed extract do not interfere with the surface area available for catalysis, whereas a surfactant can form a layer masking the catalytic surface. At room temperature, the catalytic efficiency of

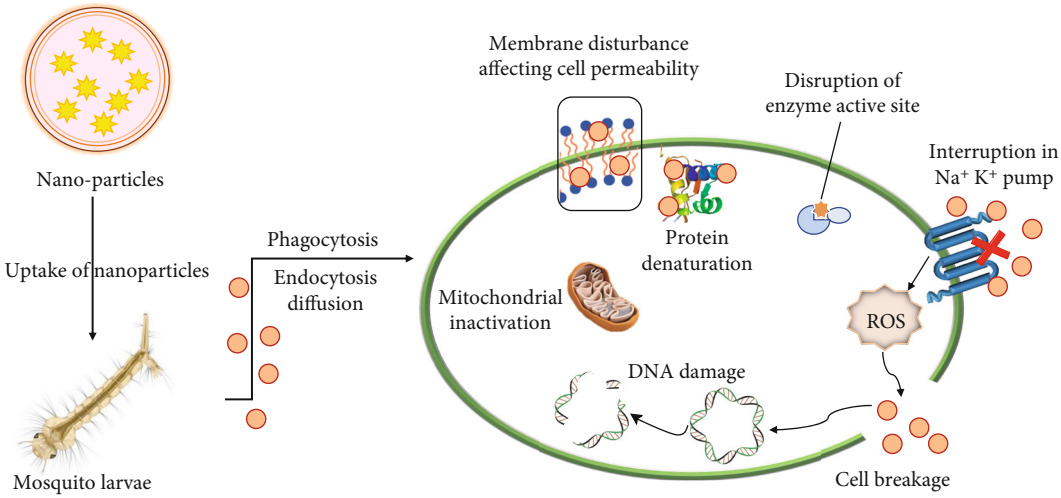

Figure 7: Graphical illustration of antimosquito activity of biogenic NPs.

AuNPs was also studied to reduce rhodamine B (RhB) by $NaBH_4$. The characteristic absorption peak of RhB was observed at 554 nm, which disappeared in 2 min using Au nanocatalyst and $NaBH_4$ [72]. Khan et al. reported that *Dimocarpus longan*-based AgNPs showed photo and chemocatalytic activities. The AgNPs generated 4-aminophenol (4-AP) from 4-nitrophenol within twelve minutes. Also, the catalytic activity of commercial AgNPs was comparatively lesser than the biogenic AgNPs. The photocatalytic activity of these NPs was tested against methylene blue and considerable degradation of methylene blue [95]. This potential is due to the small size of the nanoparticles. As a result, the capping agents occupy more sites, and the overall surface area is higher. Because the biogenic NPs show higher activity than commercial ones, the biopotential for dye degradation significantly contributes to the catalytic activity. Most likely, the phytochemicals in the seed extracts provided an adsorptive surface for the dye molecules, thereby providing the required proximity between the electron donor and acceptor molecules [95]. It was reported that custard apple seeds synthesized AgNPs reduced the coomassie brilliant blue dye within 30 min [81]. In sunlight exposure, with durian-mediated AgNPs, MB was reduced within three hours [96]. ZnO NPs derived from quince seed displayed reduced MB better under UV radiation exposure for 120 min vis-à-vis dark or low light conditions [105]. Microwave synthesized longan seed-mediated ZnONPs showed high MB removal of up to 70% within half an hour [107]. However, the particles were less efficient for decolorizing MG, MO, and OII. Such difference is easily accounted for by varying accessibility of these dyes onto the ZnONPs surface, which is well acknowledged as crucial in determining the catalyst's efficiency.

11. Larvicidal Activity of Seed Extract-Mediated NPs

Several compounds have been investigated to assess their antimosquito activity, as natural products have been targeted and attracted intense interest. In this area, NPs have also been developed to improve the general effectiveness of such compounds, among other effects. In particular, custard apple-mediated AgNPs have demonstrated larvicidal activity in *Anopheles stephensi* III and IV instars [81] (Figure 7). Third instar stage mosquito larvae led to 100% mortality in bioassays using AgNPs at a 60 μg/ml dose. The LC_{50} and LC_{90} of the third instars were 22.44 μg/ml and 40.65 μg/ml, respectively, whereas, for the 4^{th}instars, it was 27.83 μg/ml and 48.92 μg/ml. The study concluded that the larvicidal activity of AgNPs could be attributed to the penetration of AgNPs into the insect gut wall followed by binding to sulfur and a phosphorous group of deoxyribonucleic acid, eventually leading to cell death by affecting cellular function [81]. Saini et al. revealed that after 72 h of exposure, *Cullen corylifolium* (L.) seed extract-mediated AgNPs demonstrated high bioefficacy against the *Anopheles stephensi* 3^{rd} instar larvae (LC_{50}, 6.03; LC_{90}, 10.86 ppm), *Culex quinquefasciatus* (LC_{50}, 16.55; LC_{90}, 36.81 ppm) and *Aedes aegypti* (LC_{50}, 8.29; LC_{90}, 13.75ppm) [164].

Roopan et al. utilized Jamun seed-mediated ZnONPs and revealed that these NPs exhibited both ovicidal and larvicidal activity against *A. aegypti* with LC_{50} and LC_{90} of 51.94 ppm and 119.99ppm, respectively [106]. ZnONPs synthesized from cardamom-wrapped (*Elettaria cardamomum*) showed high potential for *A. aegypti* (LC_{50} = 13.27 μg/ml, L C_{90} = 25.36 μg/ml) and *Culex tritaeniorhynchus* (LC_{50} = 15.09 μg/ml, LC_{90} = 29.70 μg/ml). Compared to *Cx. tritaeniorhynchus*, *Ae. aegypti* was more susceptible to *Ec*-ZnONPs [82].

12. Conclusion and Future Prospects

The remarkable advances in developing new approaches in nanotechnology and green chemistry have led to the possibility of exploring innovative approaches, such as synthesizing nanoparticles with natural matrices, thus promoting sustainability. Specifically, the possibility of using seed extracts to synthesize metal nanoparticles (MNPs) leads to

a substantial and easy increase in the production scale, being environment friendly, low cost, and free from toxicity, making this approach favorable to the sustainable development of nanoscience. Furthermore, these synthesized MNPs have more comprehensive applications, for example, anticancer, antimicrobial, antimosquito, antioxidant, and catalytic agents. However, this approach requires further exploration, even given the significant progress in this field. For example, different MNPs have been synthesized using seed extracts, but various parameters in the synthetic process need to be optimized. In addition, the mechanism involved in synthesizing MNPs needs to be further elucidated. The lack of understanding of different chemical constituents involved in the stabilization and synthesis of MNPs remains a challenge for researchers. Also, and not least important, is that the extensive use of MNPs raises concern about the accumulation of nanoparticles in the environment, making this of huge importance to assess their *in vivo* toxicity and study their long-term effects on animals, the environment, and humans. Therefore, it is hoped that further exploration in this direction will provide and allow us to gain a better insight into utilizing this green synthesis approach for the progress and development of human civilization.

Data Availability

All data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors have no conflicts of interest associated with this work or the publication.

Authors' Contributions

RS (Rohit Sharma), KK, and SM contributed to the conceptualization and design of the paper outline. KB, CC, DSD, RS (Reena Singh), PB, and SS collected data, performed the literature review, and prepared the manuscript. AN, NCM, RS (Rohit Sharma), KK, and SM critically reviewed and edited the manuscript. All the authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit it to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. Kanchan Bhardwaj and Chirag Chopra contributed equally to this work.

Acknowledgments

The authors would like to thank the Shoolini University for allowing the current review to be conducted and completed.

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