applied sciences

MDPI

Review

Antifungal Activity against Human and Plant Mycopathogens, and Green Synthesis of Silver Nanoparticles Exhibiting Such Activity

Kamila Górka and Konrad Kubiński *

Department of Molecular Biology, Faculty of Medicine, The John Paul II Catholic University of Lublin, Konstantynów 1h, 20-708 Lublin, Poland; kamilagorka@kul.pl
* Correspondence: kubin@kul.pl

Abstract: Silver nanoparticles have long been known for their antibacterial properties. Recently, increasing numbers of studies confirm that they have antifungal properties as well. Due to the increasing number of these studies, this review was performed, summarizing most of the research conducted so far in this field and presenting the results of the activity of silver nanoparticles against fungal pathogens of humans and plants, green synthesis of silver nanoparticles, and the mechanism of action. The combined activity with antifungal drugs and toxicity assessment is also presented. The review describes the antifungal activity of silver nanoparticles against pathogens such as *F. oxysporum*, *F. graminearum*, *T. asahii*, *B. cinerea*, *P. concavum*, and *Pestalotia* sp. as well as many species of the genus *Candida*. The green synthesis of these nanoparticles has been carried out from many species of plants and microorganisms. The research cited in this review confirms the fact that silver nanoparticles obtained using green synthesis exhibit antifungal activity and can therefore be an excellent alternative to the chemical synthesis of these particles. All this proves that silver nanoparticles have a great potential to be used as a potential antifungal agent in the future.

Keywords: silver nanoparticles; antifungal activity; antifungal properties; green synthesis; *Candida*

Citation: Górka, K.; Kubiński, K. Antifungal Activity against Human and Plant Mycopathogens, and Green Synthesis of Silver Nanoparticles Exhibiting Such Activity. *Appl. Sci.* **2024**, *14*, 115. https://doi.org/10.3390/app14010115

Academic Editor: Antonio Valero

Received: 7 December 2023
Revised: 18 December 2023
Accepted: 20 December 2023
Published: 22 December 2023

1. Introduction

Nanoparticles are generally considered to be particles whose size is in the range of 1–100 nm. They are an interesting and desirable object of modern research because they very often show various unique properties compared to their macro-scale counterparts [1]. They arouse constantly growing interest due to the discovery of new applications in many fields of science and industry. The main direction in recent times is medicine, where nanoparticles are used for diagnostic and therapeutic purposes. This is mainly related to the large active surface-to-mass ratio of nanoparticles. In addition, the active surface is able to bind and transfer other compounds; hence, nanoparticles are considered good carriers of proteins or drugs, as they can deliver these compounds directly to the target site [2]. In addition, nanoparticles, mainly of such metals as gold (Au), silver (Ag), and platinum (Pt), are used as catalysts for chemical reactions or in optical biosensors and chemosensors. Considering their biological activities, silver nanoparticles are a matter of special interest in biology and medicine. Depending on their physicochemical properties, e.g., dimensions, formulation, and high reactivity, metal nanoparticles show different biological activities [3–6]. They can act as antibacterial, anticancer, antioxidant, and anti-inflammatory agents [7–10]. Taking into account the medical applications of silver nanoparticles (AgNPs), the most popular is their antibacterial activity. Colloidal silver has long been a popular antibacterial agent. In the history of the use of silver in medicine, 1884 was a breakthrough year, when Carl Crede used a solution of silver nitrate to treat gonococcal conjunctivitis in newborns. Silver nitrate was also used in dentistry to treat caries. Currently, silver can be found in many antibacterial cosmetics, such as soaps, deodorants, shampoos, and mouthwashes [1,11]. Data indicate

that, in 2023, over 1000 consumer products containing nanosilver were identified (approved and not by the FDA in the USA), which are mainly used in the medical, textile, and cosmetics sectors [12]. Silver nanoparticles exhibit a broad spectrum of anticancer activity, making them highly promising for application as novel therapeutic agents or drug carriers. However, in order to develop a safe and effective anticancer agent based on AgNPs in the future, it is essential to investigate more mechanisms of the anticancer action of these nanoparticles. AgNPs also demonstrate potential as a new therapeutic strategy for wound healing. Studies have shown that the action of AgNPs in this context involves the regulation of the production of various cytokines and proteins participating in the wound-healing process. They also promote early adhesion, contraction, and closure of the wound. Silver nanoparticles also exhibit favorable properties in bone healing. They can be used as osteoconductive material or as a doping material for synthetic bone scaffolds, providing protection against potential bacterial infections, which are common and risky in bone grafts. Another biomedical application involves incorporating AgNPs into dental biomaterials due to their antibacterial and anti-biofilm effectiveness. Additionally, research indicates that AgNPs also have the potential for use as adjuvants in vaccines, antidiabetic agents, or as biosensors [13].

Silver nanoparticles are also widely used in food processing and packaging designed to protect food against microorganisms [14].

As a feed additive, it has been shown that they reduce the occurrence of pathogenic microorganisms, so they could reduce the use of antibiotics in livestock. Additionally, their potential use in water treatment has been demonstrated by incorporating them into foam filters or by the impregnation of ultrafiltration membranes. Moreover, AgNPs are good candidates for use in food packaging due to their good stability and slow release of silver ions in stored food. In the context of food safety, another approach is emerging to use AgNPs as biosensors. This approach involves creating smart packaging to detect pathogens and transforming this information into a detectable signal that would allow for the early detection of food contamination. Due to the fact that there is insufficient research on the safety of AgNPs in food, the EU does not allow their use in dietary supplements or food packaging [15]. However, in 2021, the EFSA published information in which it was concluded that the use of AgNPs as an additive in an amount of up to 0.025% w/w in polymers such as polyolefins, polyesters, and styrenes that do not swell in contact with hydrated food does not raise concerns regarding their use. A summary of the most important applications of AgNPs is shown in Figure 1.

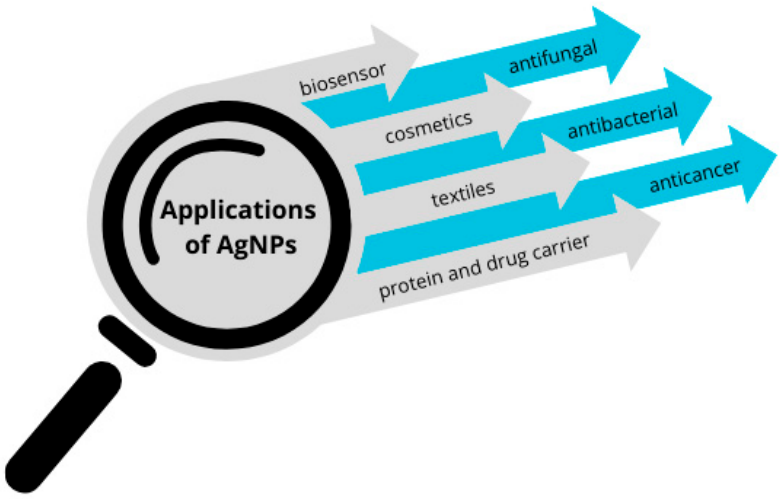

Figure 1. Applications of AgNPs.

The antibacterial properties of silver nanoparticles are well known and have been confirmed by numerous studies [7,16]. AgNPs have been shown to inhibit the growth and multiplication of such bacteria as *Escherichia coli*, *Bacillus cereus*, *Staphylococcus aureus*,

Pseudomonas aeruginosa, *Citrobacter koseri*, *Salmonella typhi*, *Klebsiella pneumoniae*, and *Vibrio parahaemolyticus* [14]. However, especially recently, a lot of research has been published on the antifungal activity of silver nanoparticles against many species of fungi. Nanoparticles synthesized by chemical, physical, and green synthesis methods are active (Figure 2). Testing the activity of AgNPs against fungi is particularly important due to the enormous resistance of pathogenic strains to systemic drugs.

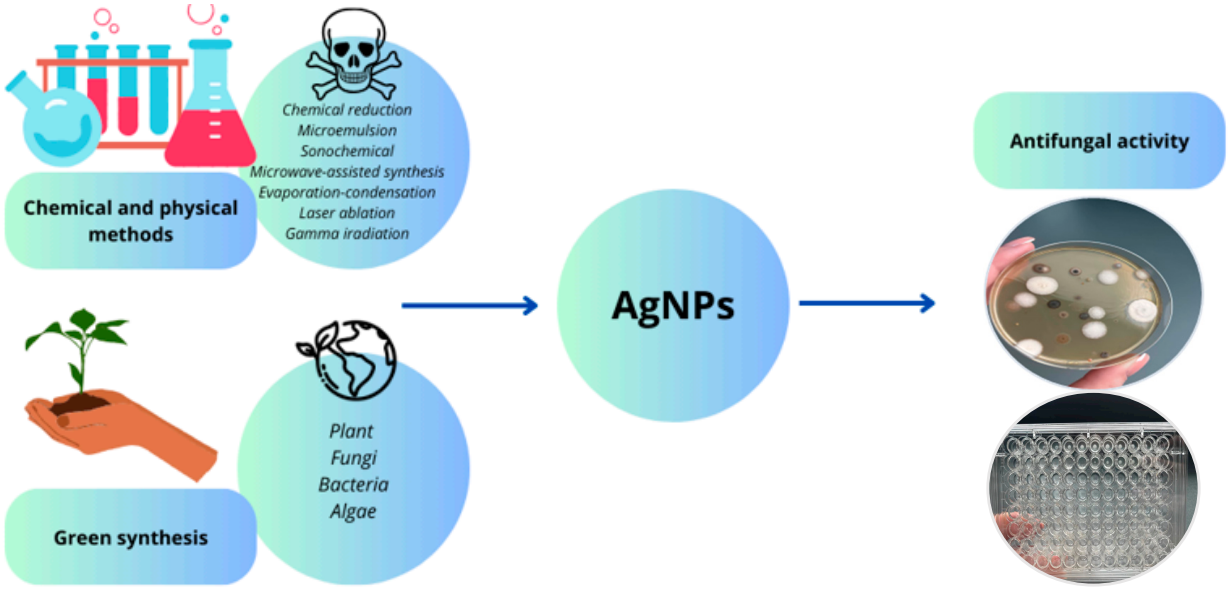

Figure 2. AgNPs' synthesis methods and testing their antifungal activity.

We can observe that silver nanoparticles accompany us in everyday life in household and biomedical products and possess significant positive properties, including the ability to eliminate pathogenic microorganisms. However, it should be noted that their use also raises concerns about their potential threat to human health and the environment. The major routes of entry of AgNPs are ingestion, inhalation, and dermal contact. Their toxicity is due to the fact that AgNPs are able to induce inflammation and oxidative stress at the site of exposure. Despite numerous toxicological studies, long-term toxicity data are still lacking. However, an occupational respiratory exposure limit value of 0.19 $\mu g/m^3$ for AgNPs has recently been proposed based on a subchronic inhalation toxicity study in rats [17]. Research using in vitro cell cultures indicates that AgNPs are toxic to several human cell lines (human bronchial epithelial cells, human umbilical vein endothelial cells, red blood cells, human peripheral blood mononuclear cells, immortal human keratinocytes, liver cells). Furthermore, tests conducted in vivo using mice, rats, and zebrafish have demonstrated that AgNPs can penetrate the blood–brain barrier and accumulate in organs such as the liver, kidneys, and spleen. The induced cytotoxicity, however, largely depends on the size of the nanoparticles, dosage, and duration of exposure [17,18].

2. Materials and Methods

Since, in addition to antibacterial properties, AgNPs show antimycotic effects, which are less widely known, the aim of this mini-review was to survey the current literature, both original papers and reviews, on the antifungal properties of silver nanoparticles against plant and human mycopathogens with particular emphasis on the action on *Candida* species. The review was based on scientific publications in English mainly from 2015–2023 available in the largest biomedical databases, i.e., PubMed, ScienceDirect, and Wiley Library. The databases were searched with such keywords as silver nanoparticles, fungi, antifungal properties, and *Candida*. Keywords were entered in various combinations. The selection of publications was made in two stages. In the first one, the selection was made based on titles and abstracts. In the second stage, the full text was analyzed. Studies that were considered

unrelated to the topic discussed in the review were rejected. The individual steps taken during the development of this review are outlined in the scheme below (Figure 3).

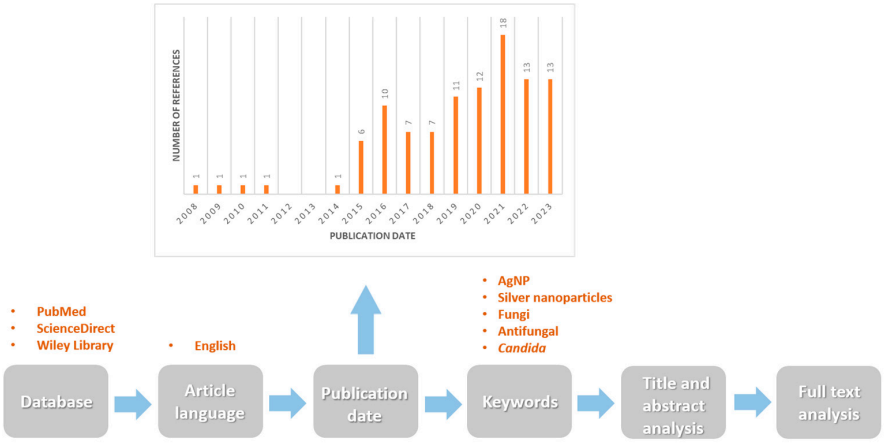

Figure 3. Diagram illustrating the approach to collecting and analyzing information.

3. Description of the State of Knowledge

3.1. Antifungal Activity of Silver Nanoparticles against Candida Species

Silver nanoparticles are regarded to have antifungal properties, but the number of studies confirming this feature is currently insufficient. Although fungal infections are not as widespread as bacterial infections, the incidence of fungal infections has been increasing in recent years. An especially alarming phenomenon is the increasing drug resistance, which is an even more serious problem due to the small arsenal of antifungal agents available on the market. Currently, the most commonly used systemic drugs are amphotericin B, nystatin, fluconazole, and itraconazole, but their solubility and bioavailability are not satisfactory [19–21]. In addition, their use is associated with the risk of side effects, such as allergic and severe skin reactions. Fungal infections often affect and pose a serious threat to immunocompromised patients [22–24]. Yeasts of the genus *Candida* are considered to be the most common cause of invasive fungal disease in such individuals. They can lead to bloodstream infections, which are associated with high mortality despite treatment [25]. The most common representative of this species is *Candida* albicans. It is part of the healthy human microflora, where it exists as a harmless commensal. However, if the natural balance in the microbiome is disturbed, e.g., in subjects with reduced immunity, it can become the cause of life-threatening infections. In addition, *C. albicans* has the ability to form a biofilm. It is a tightly packed community of cells that can grow on biotic and abiotic surfaces. This form is very difficult to combat with the use of traditional drugs [26].

Studies have shown that AgNPs have good activity against *Candida* spp. They can both inhibit the growth of yeast cells and influence various virulence factors, e.g., biofilm formation. The antifungal activity of AgNPs against *C. albicans* was investigated by Alshaikh et al. [27]. AgNPs were coated with polyvinylpyrrolidone (PVP) for water dispersion. Five isolates of *C. albicans* were used in the study and the minimum inhibitory concentration (MIC) was determined. The MIC values of AgNPs against *C. albicans* isolates ranged between 24 and 12 µg/mL. They were compared to fluconazole, which had an MIC value of 20 µg/mL. In this study, AgNPs were even more potent than fluconazole against some strains of *C. albicans*. In another study, AgNPs were synthesized using ribose sugars as reducing agents and sodium dodecyl sulfate (SDS) as a blocking agent. The antifungal activity of these nanoparticles was evaluated against 30 strains of *Candida* spp. (14 *C. albicans* and 16 *C. tropicalis*) isolated from blood samples from hospitalized patients. The tested strains showed a strong sensitivity to the nanoparticles used [28]. It was shown that silver nanoparticles are also effective against *C. albicans* biofilm with the half maximal inhibitory concentration (IC_{50}) of 0.089 ppm [29]. Recent studies conducted using an iturin–AgNPs complex also showed excellent antifungal activity of the synthesized

molecules (MIC = 1.25–5 μg/mL) against *C. albicans*. Moreover, the mechanism of the antifungal activity of the tested complex was revealed. Iturin–AgNPs caused damage to the integrity of the cell membrane, which in turn increased its permeability and the leakage of intracellular proteins and nucleic acids outside the cell [30]. In a study conducted by Dorgham et al. [31], silver nanoparticles were synthesized using the sugarcane process by-product (molasses) and named Mo-capped AgNPs. The synthesized molecules showed promising activity against *C. albicans* DAY185 with an MIC of 16 μg/mL. With the use of a scanning electron microscope and through the determination of the minimal biofilm eradication concentration (MBEC), it was also confirmed that the nanoparticles penetrated the preformed biofilm and eliminated the microbial cells. Moreover, the activity of AgNPs against *Candida* species was tested in vivo in a mouse model of oral candidiasis. In this study, nanoparticles synthesized with the use of the green synthesis method using Erodium glaucophyllum extract were used. The effect of the treatment was a significant reduction in candidal tissue invasion, fewer inflammatory changes, and no tissue modification [32]. Another in vivo study concerned AgNPs individually and combined with fluconazole. Activity was tested in a murine model of systemic candidiasis against *C. albicans*. The best results were obtained for combined treatment with AgNPs and fluconazole. This treatment reduced the fungal burden and increased the survival rate of infected mice [33]. Although the body of evidence for the anti-*Candida* activity of AgNPs is limited, the nanoparticles show promising potential to be developed as antimycotic agents.

3.2. Antifungal Activity of Silver Nanoparticles against Fungal Plant Pathogens and Other Species of Fungi

Silver nanoparticles are also commonly tested against plant mycopathogens. Various fungi can cause crop destruction and, thus, large economic losses for farmers. They also reduce the quality of agricultural products used in everyday life, i.e., fruits, vegetables, and cereals. An obvious method for combating these pathogens is the use of various types of agrochemicals; however, they have a number of adverse side effects, i.e., environmental pollution, emergence of resistant pathogens, or impact on other organisms that are not the direct target of combating fungal contamination. *Fusarium* species are one of the most widespread mycopathogens. These filamentous fungi from the *Ascomycota* family, commonly found in the soil, can attack various plant species. Silver nanoparticles have been identified as potential antifungal agents against *F. oxysporum*, which attacks plant roots and causes widespread losses in tomato cultivation, and *F. graminearum*, which causes fusarium head blight (FHB) in cereal crops [34–37]. FHB manifests itself as the partial or complete bleaching of a spikelet combined with glume discoloration. FHB, in addition to infecting plant parts, is associated with the production of the deoxynivalenol mycotoxin by *Fusarium* spp. Therefore, firstly, it causes large quantitative and qualitative losses in crops and, secondly, it poses a threat to human and animal health after consuming grain containing this mycotoxin [38]. Another fungal pathogen used in tests of the antifungal activity of silver nanoparticles is *Trichosporon asahii*, in which a significant growth-inhibiting effect was observed. The MIC concentration in this case was 0.5 μg/mL, which was lower than that of the known antifungal agents, amphotericin B, 5-flucytosine, caspofungin, terbinafine, fluconazole, and itraconazole; they used the pathogenic fungi *Botrytis cinerea*, *Pilidium concavum*, and *Pestalotia* sp. to assess the antifungal activity of AgNPs [39,40]. They observed that the presence of nanoparticles inhibited the growth of the fungi and spore germination. For example, in the case of *B. cinerea* spores, germination was completely inhibited in a culture containing 100 ppm of AgNPs. In turn, AgNPs synthesized by Elgorban et al. [41] were analyzed against Rhizoctonia solani, which is a pathogen for several hundred plant species. Their results showed that AgNPs caused a reduction in the growth of R. solani. Moreover, Żarowska et al. [42] reported that AgNPs inhibited the growth of *Aspergillus brasiliensis*, *Chaetomium globosum*, *Penicillium pinophilum*, *Paecilomyces variotii*, and *Trichoderma virens*.

3.3. Combined Action of AgNPs and Known Antifungal Drugs

So far, studies have shown that nanoparticles improve the activity of known antifungal drugs. The synergism between AgNPs and fluconazole was confirmed in several papers [27,33,43]. In turn, other studies tested the antifungal activity of AgNPs in combination with ketoconazole against Malassezia furfur. It is a representative of yeast, which naturally inhabits the human skin microbiota and is associated with several skin diseases, e.g., folliculitis, seborrheic dermatitis, and dandruff versicolor. The observations showed no antagonistic effect, and synergism was observed in 17.08% of the 40 tested M. furfur isolates [44]. Synergism between AgNPs and amphotericin B against *C. albicans* and *C. tropicalis* was demonstrated as well. An aqueous extract of Maytenus royleanus was used for the synthesis of these nanoparticles. The conjugation of amphotericin B with silver nanoparticles enhanced the antifungal activity of the systemic drug with an MIC value of 1.5 and 5 µg/mL, respectively [45]. The study by Jia and Sun attempted to identify the mechanisms of synergistic action between AgNPs and fluconazole. The results of this study showed that AgNPs can promote fluconazole accumulation in resistant *C. albicans*. Increased ROS production was identified as the probable cause of the synergy between AgNPs and fluconazole [33].

3.4. Green Biosynthesis of Silver Nanoparticles with Antifungal Properties

Of great interest is the green synthesis of nanoparticles, a technique based on the use of plants and their components as reducing agents (Figure 4). The possibility of their use results from the fact that many plants are rich in antioxidant compounds, such as polyphenols, flavonoids, and amide compounds. They have reducing hydroxyl groups that have the ability to reduce silver ions to elemental silver [46]. These methods are usually simple, convenient, cost-effective, and, most importantly, environmentally friendly, as they eliminate the need for toxic chemicals and solvents. Various species of microorganisms can also be used for the synthesis of nanoparticles; however, a necessary condition in this method is to maintain the asepticity of the entire process [47,48].

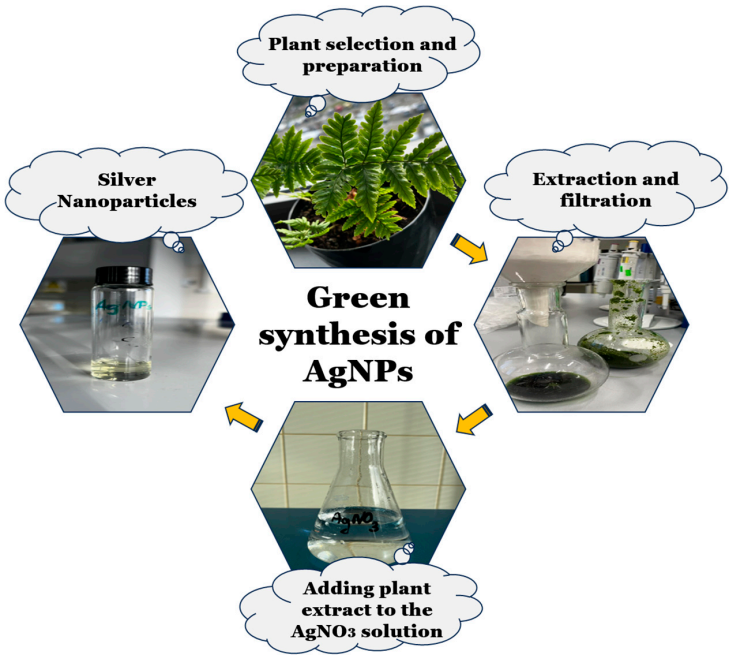

Figure 4. Green synthesis scheme based on the example of the synthesis of silver nanoparticles using plant extracts. The first step includes the selection and appropriate preparation of the plant, followed by the extraction process and obtaining the plant extract, which, in the next stage, is mixed with a solution of silver salts under the appropriate set of conditions. Then, the phytochemical compotes from the plant extract act as reducing agents and cause the conversion of Ag^{+} ions to Ag^{0} nanoparticles.

AgNPs synthesized by *Artemisia annua*, plants from the Asteraceae family, were evaluated against three species of *Candida*: *C. albicans*, *C. tropicalis*, and *C. glabrata*. The particles showed activity against all the species used in the study with an MIC value in the range of 80–120 μg/mL [49]. Silver nanoparticles synthesized using beech bark extracts (BBE), silver acetate, and nitrate salts (AgNPs Acetate BBE and AgNPs Nitrate BBE) were tested as well. The antifungal activity of the compounds was tested against *Candida* reference strains (*C. albicans*, *C. parapsilosis*, *C. krusei*, *C. auris*, and *C. guilliermondii*). Growth inhibition was observed in all the tested strains in the presence of both AgNP BBEs, with the exception of *C. auris*. The tested compounds also inhibited biofilm formation but only against *C. albicans* and *C. guilliermondii*. In addition, synergistic activity of the nanoparticles was observed in combination with fluconazole against *C. parapsilosis* and *C. guilliermondii* [43]. Spruce bark extracts (SBE) were also used for AgNP biosynthesis. Acetate and nitrate silver salts (AgNPs SBE acetate, AgNPs SBE nitrate) against the same five *Candida* strains were tested as above. AgNP SBEs inhibited the growth of *C. parapsilosis*, *C. krusei*, and *C. guilliermondii*; moreover, they showed a synergistic effect with fluconazole against *C. parapsilosis* and *C. guilliermondii* and inhibited biofilm formation by *C. albicans*, *C. auris*, and *C. guilliermondii* [50]. Other research focused on AgNPs produced by the callus extract from *Solanum incanum* L., a plant from the nightshade family. Plant pathogenic fungi *F. oxysporum*, *Alternaria alternata*, *Aspergillus niger*, and *Pythium ultimum* were used. At a concentration of 25 μg/mL, AgNPs inhibited the growth of these fungi in the range of approximately 30–50% depending on the strain, while these values at a concentration of 200 μg/mL ranged between 65 and 90% [51]. Salem et al. carried out an environmentally friendly synthesis of silver nanoparticles using *Pseudomonas indica* S. Azhar [52]. The studies of the antifungal activity of these molecules focused on fungi that cause mucormycosis, a dangerous disease that affects mainly people with diabetes or cancer or after transplants. The Rhizopus microsporus, Mucor racemosus, and Syncephalastrum racemosum species were used in the study. The results showed antifungal activity of nanoparticles against all the tested fungi at a concentration of 400 μg/mL, with the MIC values of 50, 50, and 100 μg/mL against *R. microsporus*, *S. racemosum*, and *M. racemosus*, respectively. Another study was focused on the synthesis of AgNPs using an aqueous extract of the red seaweed *Gelidiella* acerosa as a reducing agent. The antifungal activity of these nanoparticles was tested against *Humicola insolens*, *Fusarium dimerum*, *Mucor indicus*, and *Trichoderma reesei*. The antifungal assay was performed with the agar well diffusion method. The results showed higher antifungal activity against *M. indicus* and *T. reesei*, whereas moderate activity was revealed against *F. dimerum* and *H. insolens*, compared with the standard antifungal agent clotrimazole [53]. Dried grass was also used for the synthesis of AgNPs. The antifungal effects of the synthesized AgNPs on *Fusarium solani* and *Rhizoctonia solani* were evaluated using the agar dilution method. The results showed that the effect of these nanoparticles was similar to that of amphotericin B and much stronger than that of fluconazole [54]. AgNPs were also successfully synthesized using an aqueous callus extract from *Gymnema sylvestre*. The synthesized AgNPs exhibited effective antifungal activity against both *C. albicans* and non-albicans *Candida* species [55]. Another example is nanoparticles biosynthesized using a cell-free extract of Bacillus thuringiensis MAE 6. The nanoparticles showed activity against the four most common *Aspergillus* species, i.e., *A. niger*, *A. terreus*, *A. flavus*, and *A. fumigatus*, at concentrations of 0.5 mg/mL [56]. Silver nanoparticles were also synthesized using *A. terreus* and tested against *A. niger* and *C. albicans*. In this study, *A. niger* showed the highest susceptibility to AgNPs (MIC = 0.312 μg/mL), whereas *C. albicans* showed the highest resistance (MIC = 1.25 μg/mL) [57]. Another example is the AgNP synthesis using Nigrospora oryzae. These nanoparticles displayed strong antifungal activity against *Fusarium* spp. [58]. Using an Amaranthus retroflexus extract, it was also possible to synthesize AgNPs that showed antifungal activity. The MIC_{50} against *Macrophomina phaseolina*, *A. alternata*, and *F. oxysporum* was 159.80, 337.09, and 328.05 μg/mL, respectively. However, these types of nanoparticles turned out to be inactive against *Trichoderma harzianum* and *Geotrichum candidum* [59]. In the study of Riberio et al., seven biogenic AgNPs were obtained using the

fungi species *Aspergillus tubingensis*, *Aspergillus* spp., *Bionectria ochroleuca*, Cladosporium pini-ponderosae, *Fusarium proliferatum*, *Epicoccum nigrum*, and *Exerohilum rostratum*. AgNPs showed antifungal activity against clinical strains of *Candida*: *C. albicans*, *C. krusei*, *C. glabrata*, *C. guillermondii*, *C. parapsilosis*, and *C. tropicalis*. All of the tested AgNPs were more effective than amphotericin B, which was used as the positive control in this study [60]. One recent study on antifungal activity against *C. albicans* involved AgNPs synthesized by green synthesis using glucose as a reducing agent and incorporated into an agar matrix to form a film (AgFilm). The AgFilm showed a high antifungal activity with an inhibition zone of 19 ± 2 mm [61]. Corn cob xylan was also used as a green reducing and stabilizing agent in the synthesis of AgNPs. Antifungal activity was demonstrated against *C. albicans*, *C. parapsilosis*, and Cryptococcus neoformans with an MIC value of 7.5 µg/mL [62]. Other publications where information about the green synthesis of silver nanoparticles and their antifungal properties can be found are listed in the table below [Table 1].

Table 1. Biogenic AgNPs with antifungal activity.

Organism Used for Synthesis	Target Fungi	Antifungal Activity MIC [µg/mL] or Inhibition Zone [mm] or Inhibition Rate [%]	Reference
Agave americana, *Mentha spicata*, *Mangifera indica*	*Verticillium dahliae*, *Aspergillus niger*, *Aspergillus parasitica*, *Fusarium oxysporum*, *Penicillium notatum*	12–89%	[63]
Aspergillus kambarensis	*Candida albicans*, *Candida tropicalis*, *Fusarium oxysporum*, *Aspergillus niger*	13.1–44.2 mm	[64]
Cinnamomum camphora	*Fusarium oxysporum*	154.39 µg/mL	[65]
Marinobacter lipolyticus	*Candida albicans*	16 ± 2 mm	[66]
Navicula cincta	*Aspergillus flavus*, *Aspergillus niger*, *Aspergillus fumigatus*, *Rhizopus stolonifer*	3.01–6.02 mg/µL	[67]
Sidr honey	*Candida albicans*	9.70 ± 0.09–15.20 ± 0.29 mm	[68]
Zea mays	*Fusarium* sp., *Rhizopus oryzae*, *Candida albicans*	12 ± 1.0–14.6 ± 0.57 mm	[69]
Parrotiopsis jacquemontiana	*Aspergillus flavus*, *Aspergillus niger*, *Fusarium solani*, *Mucor piriformis*, *Aspergillus fumigatus*, *Candida albicans*	10–20 µg/mL	[70]
Trichoderma asperellum	*Fusarium oxysporum*, *Fusarium graminearum*, *Pythium ultimum*	20.0 ± 2.0–28.67 ± 3.05 mm	[71]
Artemisia afra	*Candida albicans*	200 µg/mL	[72]
Phoma gardeniae	*Candida albicans*	5.95 µg/mL	[73]
Cassia fistula	*Candida krusei*, *Trichophyton mentagrophytes*	21.6 ± 1.1–23.3 ± 1.1 mm	[74]
Trifolium resupinatum	*Rhizoctonia solani*, *Neofusicoccum Parvum*	84–91%	[75]
Bipolaris maydis	*Exserohilum turcicum*	5.0 ± 0.84–10.7 ± 1.26 mm	[76]
Trichoderma atroviride	*Phomopsis theae*	75.7–80.3%	[77]
Helminthosporium sp., *Chaetomium* sp.	*Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Curvularia* sp., *Bipolaris* sp., *Fusarium* sp.	30–70 µg/mL	[78]
Phoma capsulatum, *Phoma putaminum*, *Phoma citri*	*Aspergillus niger*, *Candida albicans*	5.95 µg/mL	[79]

Table 1. *Cont.*

Organism Used for Synthesis	Target Fungi	Antifungal Activity MIC [μg/mL] or Inhibition Zone [mm] or Inhibition Rate [%]	Reference
Ginkgo biloba	*Setosphaeria turcica*	7.0 ± 1.41–13.0 ± 1.79 mm	[80]
Mentha pulegium	*Candida albicans*	100 μg/mL	[81]
Phoenix dactylifera	*Rhizoctonia solani*	22–80%	[82,83]
Zingiber officinale, *Thymus vulgaris*	*Candida albicans*	0.5–0.7 μg/mL	[83]
Tagetes patula	*Colletotrichum chlorophyti*	24.88 ± 0.85–63.01 ± 0.97%	[84]
Hyptis suaveolens	*Candida albicans*	0.27 ± 0.03–0.97 ± 0.13 μg/mL	[85]
Elettaria cardamomum	*Alternaria alternata*, *Aspergillus niger*, *Botrytis cinerea*, *Fusarium oxysporum*, *Penicillium expansum*	8–64 μg/mL	[86]
Arthroderma fulvum	*Candida albicans*, *Candida parapsilosis*, *Candida krusei*, *Candida tropicalis*, *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus terrrus*, *Fusarium solani*, *Fusarium moniliforme*, *Fusarium oxysporum*	0.125–4.00 μg/mL	[87,88]
Justicia spicigera	*Colletotrichum* sp., *Fusarium solani*, *Alternaria alternata*, *Macrophomina phaseolina*	35.60 ± 3.55–80.95 ± 1.35%	[88]
Jasminum nudiflorum	*Amanita longipes*	32 μg/mL	[89]

Recently, there has been growing interest in synthesis methods that utilize templates such as viruses' DNA, membranes, or diatoms [90,91]. A representative example is the method by Kora et al., where gum kondagogu, a non-toxic and renewable natural plant polymer, was used as a template. The synthesized silver nanoparticles had a significant antibacterial effect [92]. To illustrate the use of a matrix for the synthesis of nanoparticles, it is worth mentioning the research by Kucełow et al. [93], where dextran-graft-polyacrylamide served as a template, and the study by Matos and Courrol, where the synthesis utilized an aqueous saliva solution and irradiation with light from a mercury metal halide lamp [94]. Another eco-friendly reducing factor during the synthesis of silver nanoparticles can be exposure to sunlight. Binaymotlagh et al. utilized this method in their research. Additionally, they developed a one-pot process for the synthesis of AgNPs inside peptide hydrogels [95]. Such hydrogels with silver nanoparticles have great potential for use in medicine as dressings that improve the healing of wounds, including burns, and at the same time inhibit the development of infection in the treated area [96].

3.5. Mechanisms of Antifungal Activity of Silver Nanoparticles

The mechanism of action of silver nanoparticles on cells has not yet been thoroughly investigated, but several most likely mechanisms have been identified (Figure 5). These include the ability to attach AgNPs to the cell wall and the ability to penetrate the cell interior, induction of oxidative stress, and interference with signal transduction and protein synthesis [97]. Researchers suggest that the ability of AgNPs to connect with the cell wall occurs as a result of the electrostatic interaction between positively charged silver ions and the negatively charged surface of the cell membrane and to then penetrate it, thus causing structural changes in the cell membrane, which in turn increases its permeability. Other researchers suggest that silver nanoparticles lead to the inactivation of enzymes and proteins associated with the membrane or change the composition of the lipid bilayer, which translates into a change in its integrity. Another example is the interaction of silver ions with the disulfide bonds of enzymes involved in cellular metabolism, causing their

inactivation. It was also found that silver ions bind to the 30S ribosomal subunit, deactivate the ribosome complex, and stop protein synthesis [98]. Generally, the main mechanism of activity of AgNPs is the ability to produce reactive oxygen species that cause oxidative stress in the cell. Free radicals can cause, among other things, lipid peroxidation, damage to the integrity of cell membranes, and DNA damage, which leads to cell apoptosis. The mechanisms mentioned here were confirmed in the studies of Xia et al. on the action of AgNPs on *Trichosporon asahii*. Analysis under an electron microscope showed that silver nanoparticles caused damage to the cell wall and membrane and then penetrated the cells and damaged mitochondria and ribosomes. They also caused condensation and marginalization of chromatin [39]. In the study by Wen et al. using the plant pathogen *Ustilaginoidea virens*, it was also confirmed that AgNPs disrupt the integrity of the cell wall and cell membrane and also affect the transcription process [99]. An increase in the permeability of the cell membrane was also identified in the case of studies on the influence of AgNPs on the cells of four pathogens causing rot of kiwi fruit: *Alternaria alternata*, *Pestalotiopsis microspora*, *Diaporthe actinidiae*, and *Botryosphaeria dothidea* [100].

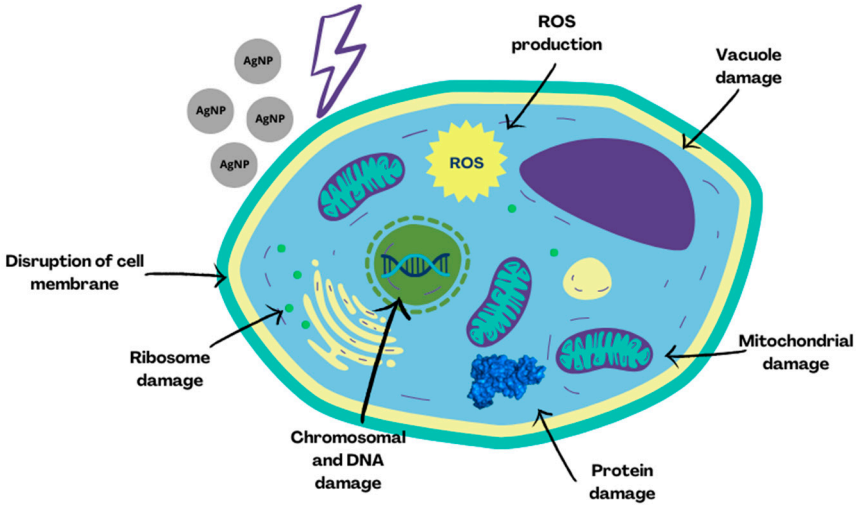

Figure 5. Antifungal mechanisms of silver nanoparticles, based on [35].

3.6. Toxicity of Silver Nanoparticles

We can observe that silver nanoparticles accompany us in everyday life in household and biomedical products and possess significant positive properties, including the ability to eliminate pathogenic microorganisms. However, it should be noted that their use also raises concerns about their potential threat to human health and the environment. The toxicity of nanoparticles depends on their size, shape, coating/capping agent, and method of synthesis. Interestingly, it was also noticed that nanoparticles synthesized using the green synthesis method are often more toxic than those synthesized with traditional methods. Toxicity is demonstrated at both the cellular and molecular levels. The major routes of entry of AgNPs are ingestion, inhalation, and dermal contact. Their toxicity is due to the fact that AgNPs are able to induce inflammation and oxidative stress at the site of exposure. In addition to causing oxidative stress, AgNPs also cause a decrease in glutathione levels (GSH) and lipid peroxidation, which in turn leads to DNA damage, apoptosis, and necrosis. Despite numerous toxicological studies, long-term toxicity data are still lacking. However, an occupational respiratory exposure limit value of 0.19 $\mu g/m^3$ for AgNPs was recently proposed based on a subchronic inhalation toxicity study in rats [17]. Research using in vitro cell cultures indicates that AgNPs are toxic to several human cell lines (human bronchial epithelial cells, human umbilical vein endothelial cells, red blood cells, human peripheral blood mononuclear cells, immortal human keratinocytes, liver cells). For example, studies on human skin cancer cells (A431) and fibrosarcoma cells (HT-1080) showed that AgNPs (7–20 nm; 6.25 ug/mL; after 24 h of exposure) induced oxidative

stress in these cells, manifested by a reduced level of GSH and superoxide dismutase (SOD) activity and increased lipid peroxidation. Moreover, they caused the induction of caspase 3 activity and DNA breaks. However, in the case of human colon cancer cells (HT29), hepatoma cells (HepG2), colon cancer cells (HCT116), lung adenocarcinoma cells (A549), lung fibroblasts (IMR-90), and glioma cells (U251), the main cause of toxicity was the generation of reactive oxygen species (ROS). In turn, in the case of mouse embryonic stem cells and mouse embryonic fibroblasts (25 nm; 50 ug/mL; after 72 h of exposure, coated), the increased expression of p53 (cell cycle checkpoint protein), γ-H2AX (biomarker for DNA double-strand breaks), and Rad 51 (DNA repair protein) was identified. Furthermore, tests conducted in vivo using mice and rats demonstrated that AgNPs can penetrate the blood–brain barrier and accumulate in organs such as the liver, kidneys, and spleen. The induced cytotoxicity, however, largely depends on the size of the nanoparticles, dosage, and duration of exposure [17,18]. During studies on Sprague–Dawley rats, a negative impact on the liver was observed after the ingestion of AgNPs (60 nm, 300 mg), while prolonged inhalation exposure to AgNPs resulted in lung damage. Additionally, an increased level of silver was found in the offsprings' tissues exposed during the prenatal period. Another consequence of exposure (10 days) was lung inflammation in mice. In in vivo studies on AgNPs in zebrafish, a reduction in the embryo hatching success rate, abnormal dorsal chord, damaged eyes, and curved tail in larvae were observed. The acute toxicity dose for zebrafish was determined to be 40 μg/L for 48 h. AgNPs exhibited cytotoxicity for rainbow trout cell lines and their hepatocytes, and exposure to AgNPs in catfish embryos resulted in mortality, DNA fragmentation, and malformations. Jasmine rice was used as a plant model for studying the toxicity of AgNPs. It was demonstrated that AgNPs, depending on their concentration, can inhibit germination and restrict root growth [101].

4. Conclusions

The presented review highlights the importance of silver nanoparticles as an antifungal agent against both plant and human fungal pathogens. Silver is well known for its antibacterial properties, which are confirmed by numerous studies; but, currently, attention is increasingly being paid to its antifungal properties. There are far fewer scientific publications on the antifungal activity of silver nanoparticles than those presenting their antibacterial activity, but they all confirm the antifungal potential of silver nanoparticles against a wide range of fungal species, including *Candida* sp., *Fusarium* sp., and *Aspergillus* sp. It was also confirmed that silver nanoparticles are effective against fungal biofilm, which is extremely resistant to treatment. In the discussion of the antifungal properties of silver nanoparticles, it is impossible not to mention the green synthesis of these nanoparticles. This is currently a common method of synthesis due to its significant environmental benefits compared to the traditional chemical synthesis. Both plants and microorganisms are used for this purpose. Silver nanoparticles synthesized in this way show excellent antifungal properties against the tested species of fungi. In addition, research confirms that silver nanoparticles can be successfully combined with antifungal drugs used so far, enhancing their effect on fungal cells. All the studies presented in this review lead to the conclusion that silver nanoparticles are a good candidate for antifungal treatment, both as an alternative to the currently used antifungal drugs and in combination with these medicines. Therefore, they can be used in the treatment of fungal diseases of plants, including crops, and in the treatment of problematic human infections caused by resistant fungi. Moreover, many articles indicate the potential of using AgNPs for anticancer treatment, as research shows that AgNPs inhibit the proliferation of various cancer lines, including breast, prostate, and lung cancer. Another possible medical application is the treatment of wounds or use as a doping material for synthetic bone scaffolds or dental biomaterials, providing protection against potential bacterial infections. Apart from medical applications, other possible uses of AgNPs include the disinfection of surfaces, water, and air, as well as food processing and storage. Despite the efforts of many researchers, and although more is increasingly known about the mechanisms of action of AgNPs on cells, this knowledge is

still not sufficient and further research is needed to understand the exact processes. The factor limiting the use of AgNPs is their toxicity to humans, which, however, largely depends on the size of the particles, shape, method of synthesis, and the route and time of exposure. The next challenge concerns the method of green synthesis of AgNPs. Although this is a common, environmentally friendly method, it requires further development, including, in order to obtain the homogeneity of nanoparticles, investigating how the substances present in the plant extract affect the structure and stability of nanoparticles and the technological innovations that are necessary to enable the use of these methods on a larger scale. Moreover, there are many plants and microorganisms in the environment whose synthesis has not yet been tested; therefore, further searches are necessary to identify the most efficient biological agent for this process. To conclude, AgNPs open a new path towards the development of new drugs and therapies for many plant and human diseases, even those with high mortality, such as cancer or treatment-resistant fungal infections. However, nanotechnology is a constantly developing field, so further research is necessary to make AgNPs not only effective but also safe, firstly, for ourselves and, secondly, for the environment around us.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Burdușel, A.C.; Gherasim, O.; Grumezescu, A.M.; Mogoantă, L.; Ficai, A.; Andronescu, E. Biomedical Applications of Silver Nanoparticles: An Up-to-Date Overview. *Nanomaterials* **2018**, *8*, 681. [CrossRef] [PubMed]
2. Altammar, K.A. A review on nanoparticles: Characteristics, synthesis, applications, and challenges. *Front. Microbiol.* **2023**, *14*, 1155622. [CrossRef] [PubMed]
3. Pucelik, B.; Sułek, A.; Borkowski, M.; Barzowska, A.; Kobielusz, M.; Dąbrowski, J.M. Synthesis and Characterization of Size- and Charge-Tunable Silver Nanoparticles for Selective Anticancer and Antibacterial Treatment. *ACS Appl. Mater. Interfaces* **2022**, *14*, 14981–14996. [CrossRef]
4. Kubiński, K.; Górka, K.; Janeczko, M.; Martyna, A.; Kwaśnik, M.; Masłyk, M.; Zięba, E.; Kowalczuk, J.; Kuśtrowski, P.; Borkowski, M.; et al. Silver Is Not Equal to Silver: Synthesis and Evaluation of Silver Nanoparticles with Low Biological Activity, and Their Incorporation into C_{12}Alanine-Based Hydrogel. *Molecules* **2023**, *28*, 1194. [CrossRef] [PubMed]
5. Verkhovskii, R.; Kozlova, A.; Atkin, V.; Kamyshinsky, R.; Shulgina, T.; Nechaeva, O. Physical properties and cytotoxicity of silver nanoparticles under different polymeric stabilizers. *Heliyon* **2019**, *5*, e01305. [CrossRef]
6. Yunusov, K.E.; Sarymsakov, A.A.; Jalilov, J.Z.O.; Atakhanov, A.A.O. Physicochemical properties and antimicrobial activity of nanocomposite films based on carboxymethylcellulose and silver nanoparticles. *Polym. Adv. Technol.* **2021**, *32*, 1822–1830. [CrossRef]
7. Bruna, T.; Maldonado-Bravo, F.; Jara, P.; Caro, N. Silver Nanoparticles and Their Antibacterial Applications. *Int. J. Mol. Sci.* **2021**, *22*, 7202. [CrossRef]
8. Al-Khedhairy, A.A.; Wahab, R. Silver Nanoparticles: An Instantaneous Solution for Anticancer Activity against Human Liver (HepG2) and Breast (MCF-7) Cancer Cells. *Metals* **2022**, *12*, 148. [CrossRef]
9. Salari, S.; Bahabadi, S.E.; Samzadeh-Kermani, A.; Yosefzaei, F. Evaluation of Antioxidant and Antibacterial Potential of GreenSynthesized Silver Nanoparticles Using *Prosopis farcta* Fruit Extract. *Iran J. Pharm. Res.* **2019**, *18*, 430–455.
10. Tyavambiza, C.; Elbagory, A.M.; Madiehe, A.M.; Meyer, M.; Meyer, S. The Antimicrobial and Anti-Inflammatory Effects of Silver Nanoparticles Synthesised from *Cotyledon orbiculata* Aqueous Extract. *Nanomaterials* **2021**, *11*, 1343. [CrossRef]
11. Verma, P.; Maheshwari, S.K. Preparation of Sliver and Selenium Nanoparticles and Its Characterization by Dynamic Light Scattering and Scanning Electron Microscopy. *J. Microsc. Ultrastruct.* **2018**, *6*, 182–187. [CrossRef] [PubMed]
12. Kaiser, K.G.; Delattre, V.; Frost, V.J.; Buck, G.W.; Phu, J.V.; Fernandez, T.G.; Pavel, I.E. Nanosilver: An Old Antibacterial Agent with Great Promise in the Fight against Antibiotic Resistance. *Antibiotics* **2023**, *12*, 1264. [CrossRef] [PubMed]
13. Xu, L.; Wang, Y.-Y.; Huang, J.; Chen, C.-Y.; Wang, Z.-X.; Xie, H. Silver nanoparticles: Synthesis, medical applications and biosafety. *Theranostics* **2020**, *10*, 8996–9031. [CrossRef] [PubMed]
14. Siddiqi, K.S.; Husen, A.; Rao, R.A.K. A review on biosynthesis of silver nanoparticles and their biocidal properties. *J. Nanobiotechnol.* **2018**, *16*, 14. [CrossRef] [PubMed]
15. Zorraquín-Peña, I.; Cueva, C.; Bartolomé, B.; Moreno-Arribas, M.V. Silver Nanoparticles against Foodborne Bacteria. Effects at Intestinal Level and Health Limitations. *Microorganisms* **2020**, *8*, 132. [CrossRef]
16. Ahmad, S.A.; Das, S.S.; Khatoon, A.; Ansari, M.T.; Afzal, M.; Hasnain, S.; Nayak, A.K. Bactericidal activity of silver nanoparticles: A mechanistic review. *Mater. Sci. Energy Technol.* **2020**, *3*, 756–769. [CrossRef]

17. Ferdous, Z.; Nemmar, A. Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure. *Int. J. Mol. Sci.* **2020**, *21*, 2375. [CrossRef]
18. Liao, C.; Li, Y.; Tjong, S.C. Bactericidal and Cytotoxic Properties of Silver Nanoparticles. *Int. J. Mol. Sci.* **2019**, *20*, 449. [CrossRef]
19. Yang, W.; Wiederhold, N.P.; O Williams, R. Drug delivery strategies for improved azole antifungal action. *Expert Opin. Drug Deliv.* **2008**, *5*, 1199–1216. [CrossRef]
20. Yu, H.; Zhang, L.; Liu, M.; Yang, D.; He, G.; Zhang, B.; Gong, N.; Lu, Y.; Du, G. Enhancing Solubility and Dissolution Rate of Antifungal Drug Ketoconazole through Crystal Engineering. *Pharmaceuticals* **2023**, *16*, 1349. [CrossRef]
21. Wasan, E.K.; Bartlett, K.; Gershkovich, P.; Sivak, O.; Banno, B.; Wong, Z.; Gagnon, J.; Gates, B.; Leon, C.G.; Wasan, K.M. Development and characterization of oral lipid-based Amphotericin B formulations with enhanced drug solubility, stability and antifungal activity in rats infected with Aspergillus fumigatus or *Candida albicans*. *Int. J. Pharm.* **2009**, *372*, 76–84. [CrossRef] [PubMed]
22. Ma, Z.; Wang, X.; Li, C. Strategies of Drug Delivery for Deep Fungal Infection: A Review. *Pharm. Nanotechnol.* **2020**, *8*, 372–390. [CrossRef] [PubMed]
23. Renzi, D.F.; Campos, L.d.A.; Miranda, E.H.; Mainardes, R.M.; Abraham, W.-R.; Grigoletto, D.F.; Khalil, N.M. Nanoparticles as a Tool for Broadening Antifungal Activities. *Curr. Med. Chem.* **2021**, *28*, 1841–1873. [CrossRef] [PubMed]
24. Trombino, S.; Mellace, S.; Cassano, R.; Rockich-Winston, N.; Gillette, C.; Train, B.; Tippens, A.S.; Flesher, S.; Shepherd, M.; Ali, H.; et al. Solid lipid nanoparticles for antifungal drugs delivery for topical applications. *Ther. Deliv.* **2016**, *7*, 639–647. [CrossRef]
25. Lee, Y.; Puumala, E.; Robbins, N.; Cowen, L.E. Antifungal Drug Resistance: Molecular Mechanisms in *Candida albicans* and Beyond. *Chem. Rev.* **2021**, *121*, 3390–3411. [CrossRef]
26. Ponde, N.O.; Lortal, L.; Ramage, G.; Naglik, J.R.; Richardson, J.P. *Candida albicans* biofilms and polymicrobial interactions. *Crit. Rev. Microbiol.* **2021**, *47*, 91–111. [CrossRef]
27. Alshaikh, N.A.; Perveen, K.; Bahkali, A.H. Effect of silver nanoparticles alone and in combination with fluconazole on *Candida albicans*. *J. King Saud Univ.-Sci.* **2023**, *35*, 102399. [CrossRef]
28. Mallmann, E.J.J.; Cunha, F.A.; Castro, B.N.M.F.; Maciel, A.M.; Menezes, E.A.; Fechine, P.B.A. Antifungal activity of silver nanoparticles obtained by green synthesis. *Rev. Inst. Med. Trop. Sao Paulo* **2015**, *57*, 165–167. [CrossRef]
29. Lara, H.H.; Romero-Urbina, D.G.; Pierce, C.; Lopez-Ribot, J.L.; Arellano-Jiménez, M.J.; Jose-Yacaman, M. Effect of silver nanoparticles on *Candida albicans* biofilms: An ultrastructural study. *J. Nanobiotechnol.* **2015**, *13*, 91. [CrossRef]
30. Zhou, L.; Zhao, X.; Li, M.; Lu, Y.; Ai, C.; Jiang, C.; Liu, Y.; Pan, Z.; Shi, J. Antifungal activity of silver nanoparticles synthesized by iturin against *Candida albicans* in vitro and in vivo. *Appl. Microbiol. Biotechnol.* **2021**, *105*, 3759–3770. [CrossRef]
31. Dorgham, R.A.; Al Moaty, M.N.A.; Chong, K.P.; Elwakil, B.H. Molasses-Silver Nanoparticles: Synthesis, Optimization, Characterization, and Antibiofilm Activity. *Int. J. Mol. Sci.* **2022**, *23*, 10243. [CrossRef] [PubMed]
32. Abdallah, B.M.; Ali, E.M. Therapeutic Effect of Green Synthesized Silver Nanoparticles Using *Erodium glaucophyllum* Extract against Oral Candidiasis: In Vitro and In Vivo Study. *Molecules* **2022**, *27*, 4221. [CrossRef]
33. Jia, D.; Sun, W. Silver nanoparticles offer a synergistic effect with fluconazole against fluconazole-resistant *Candida albicans* by abrogating drug efflux pumps and increasing endogenous ROS. *Infect. Genet. Evol.* **2021**, *93*, 104937. [CrossRef] [PubMed]
34. Akpinar, I.; Unal, M.; Sar, T. Potential antifungal effects of silver nanoparticles (AgNPs) of different sizes against phytopathogenic *Fusarium oxysporum* f. sp. radicis-lycopersici (FORL) strains. *SN Appl. Sci.* **2021**, *3*, 506. [CrossRef]
35. Jian, Y.; Chen, X.; Ahmed, T.; Shang, Q.; Zhang, S.; Ma, Z.; Yin, Y. Toxicity and action mechanisms of silver nanoparticles against the mycotoxin-producing fungus *Fusarium graminearum*. *J. Adv. Res.* **2021**, *38*, 1–12. [CrossRef] [PubMed]
36. Alvarez-Carvajal, F.; Gonzalez-Soto, T.; Armenta-Calderón, A.; Ibarra, R.; Esquer-Miranda, E.; Juarez, J.; Encinas-Basurto, D. Silver nanoparticles coated with chitosan against *Fusarium oxysporum* causing the tomato wilt. *Biotecnia* **2020**, *22*, 73–80.
37. Dutta, P.; Kumari, J.; Borah, P.; Baruah, P.; Kaman, P.K.; Das, G.; Kumari, A.; Saikia, B. Synthesis of fungus mediate silver nanoparticles (AgNP) its characterization and study the efficacy against inoculam, biomass and protein content of *Fusarium oxysporum*. *Int. J. Chem. Stud.* **2020**, *8*, 2619–2625. [CrossRef]
38. Teli, B.; Purohit, J.; Rashid, M.; Jailani, A.A.K.; Chattopadhyay, A. Omics Insight on Fusarium Head Blight of Wheat for Translational Research Perspective. *Curr. Genom.* **2020**, *21*, 411–428. [CrossRef]
39. Xia, Z.-K.; Ma, Q.-H.; Li, S.-Y.; Zhang, D.-Q.; Cong, L.; Tian, Y.-L.; Yang, R.-Y. The antifungal effect of silver nanoparticles on *Trichosporon asahii*. *J. Microbiol. Immunol. Infect.* **2016**, *49*, 182–188. [CrossRef]
40. Bayat, M.; Zargar, M.; Chudinova, E.; Astarkhanova, T.; Pakina, E. In Vitro Evaluation of Antibacterial and Antifungal Activity of Biogenic Silver and Copper Nanoparticles: The First Report of Applying Biogenic Nanoparticles against *Pilidium concavum* and *Pestalotia* sp. *Fungi. Molecules* **2021**, *26*, 5402. [CrossRef]
41. Elgorban, A.M.; El-Samawaty, A.E.-R.M.; Yassin, M.A.; Sayed, S.R.; Adil, S.F.; Elhindi, K.M.; Bakri, M.; Khan, M. Antifungal silver nanoparticles: Synthesis, characterization and biological evaluation. *Biotechnol. Biotechnol. Equip.* **2015**, *30*, 56–62. [CrossRef]
42. Żarowska, B.; Koźlecki, T.; Piegza, M.; Jaros-Koźlecka, K.; Robak, M. New Look on Antifungal Activity of Silver Nanoparticles (AgNPs). *Pol. J. Microbiol.* **2019**, *68*, 515–525. [CrossRef]
43. Mare, A.D.; Ciurea, C.N.; Man, A.; Mareș, M.; Toma, F.; Berța, L.; Tanase, C. In Vitro Antifungal Activity of Silver Nanoparticles Biosynthesized with Beech Bark Extract. *Plants* **2021**, *10*, 2153. [CrossRef]
44. Mussin, J.E.; Roldán, M.V.; Rojas, F.; de los Ángeles Sosa, M.; Pellegri, N.; Giusiano, G. Antifungal activity of silver nanoparticles in combination with ketoconazole against *Malassezia furfur*. *AMB Express* **2019**, *9*, 131. [CrossRef] [PubMed]

45. Ahmad, A.; Wei, Y.; Syed, F.; Tahir, K.; Taj, R.; Khan, A.U.; Hameed, M.U.; Yuan, Q. Amphotericin B-conjugated biogenic silver nanoparticles as an innovative strategy for fungal infections. *Microb. Pathog.* **2016**, *99*, 271–281. [CrossRef] [PubMed]
46. Zhu, J.; Li, H.; Wang, Y.; Wang, Y.; Yan, J. Preparation of Ag NPs and Its Multifunctional Finishing for Cotton Fabric. *Polymers* **2021**, *13*, 1338. [CrossRef] [PubMed]
47. Rautela, A.; Rani, J.; Debnath, M. Green synthesis of silver nanoparticles from Tectona grandis seeds extract: Characterization and mechanism of antimicrobial action on different microorganisms. *J. Anal. Sci. Technol.* **2019**, *10*, 5. [CrossRef]
48. Roy, A.; Bulut, O.; Some, S.; Mandal, A.K.; Yilmaz, M.D. Green synthesis of silver nanoparticles: Biomolecule-nanoparticle organizations targeting antimicrobial activity. *RSC Adv.* **2019**, *9*, 2673–2702. [CrossRef]
49. Khatoon, N.; Sharma, Y.; Sardar, M.; Manzoor, N. Mode of action and anti-Candida activity of *Artemisia annua* mediated-synthesized silver nanoparticles. *J. Med. Mycol.* **2019**, *29*, 201–209. [CrossRef]
50. Mare, A.D.; Man, A.; Ciurea, C.N.; Toma, F.; Cighir, A.; Mareș, M.; Berța, L.; Tanase, C. Silver Nanoparticles Biosynthesized with Spruce Bark Extract—A Molecular Aggregate with Antifungal Activity against. *Antibiotics* **2021**, *10*, 1261. [CrossRef]
51. Lashin, I.; Fouda, A.; Gobouri, A.A.; Azab, E.; Mohammedsaleh, Z.M.; Makharita, R.R. Antimicrobial and In Vitro Cytotoxic Efficacy of Biogenic Silver Nanoparticles (Ag-NPs) Fabricated by Callus Extract of *Solanum incanum* L. *Biomolecules* **2021**, *11*, 341. [CrossRef] [PubMed]
52. Salem, S.S.; Ali, O.M.; Reyad, A.M.; Abd-Elsalam, K.A.; Hashem, A.H. *Pseudomonas indica*-Mediated Silver Nanoparticles: Antifungal and Antioxidant Biogenic Tool for Suppressing Mucormycosis Fungi. *J. Fungi* **2022**, *8*, 126. [CrossRef] [PubMed]
53. Vivek, M.; Kumar, P.S.; Steffi, S.; Sudha, S. Biogenic Silver Nanoparticles by *Gelidiella acerosa* Extract and their Antifungal Effects. *Avicenna J. Med. Biotechnol.* **2011**, *3*, 143–148. [PubMed]
54. Khatami, M.; Sharifi, I.; Nobre, M.A.L.; Zafarnia, N.; Aflatoonian, M.R. Waste-grass-mediated green synthesis of silver nanoparticles and evaluation of their anticancer, antifungal and antibacterial activity. *Green Chem. Lett. Rev.* **2018**, *11*, 125–134. [CrossRef]
55. Netala, V.R.; Kotakadi, V.S.; Domdi, L.; Gaddam, S.A.; Bobbu, P.; Venkata, S.K.; Ghosh, S.B.; Tartte, V. Biogenic silver nanoparticles: Efficient and effective antifungal agents. *Appl. Nanosci.* **2016**, *6*, 475–484. [CrossRef]
56. Hashem, A.H.; Saied, E.; Amin, B.H.; Alotibi, F.O.; Al-Askar, A.A.; Arishi, A.A.; Elkady, F.M.; Elbahnasawy, M.A. Antifungal Activity of Biosynthesized Silver Nanoparticles (AgNPs) against *Aspergilli* Causing Aspergillosis: Ultrastructure Study. *J. Funct. Biomater.* **2022**, *13*, 242. [CrossRef]
57. Lotfy, W.A.; Alkersh, B.M.; Sabry, S.A.; Ghozlan, H.A. Biosynthesis of Silver Nanoparticles by *Aspergillus terreus*: Characterization, Optimization, and Biological Activities. *Front. Bioeng. Biotechnol.* **2021**, *9*, 633468. [CrossRef]
58. Dawoud, T.M.; Yassin, M.A.; El-Samawaty, A.R.M.; Elgorban, A.M. Silver nanoparticles synthesized by *Nigrospora oryzae* showed antifungal activity. *Saudi J. Biol. Sci.* **2020**, *28*, 1847–1852. [CrossRef]
59. Bahrami-Teimoori, B.; Nikparast, Y.; Hojatianfar, M.; Akhlaghi, M.; Ghorbani, R.; Pourianfar, H.R. Characterisation and antifungal activity of silver nanoparticles biologically synthesised by *Amaranthus retroflexus* leaf extract. *J. Exp. Nanosci.* **2017**, *12*, 129–139. [CrossRef]
60. Ribeiro, L.G.; Roque, G.S.C.; Conrado, R.; De Souza, A.O. Antifungal Activity of Mycogenic Silver Nanoparticles on Clinical Yeasts and Phytopathogens. *Antibiotics* **2023**, *12*, 91. [CrossRef]
61. Mallmann, E.J.J.; Cunha, F.A.; Agressott, E.V.H.; de Menezes, F.L.; Barbosa, R.d.C.C.; Martins, R.T.; Cunha, M.d.C.d.S.O.; Queiroz, M.V.O.; Coutinho, H.D.M.; de Vasconcelos, J.E.L.; et al. Antifungal Activity of Nanobiocomposite Films Based on Silver Nanoparticles Obtained Through Green Synthesis. *Curr. Microbiol.* **2023**, *80*, 251. [CrossRef] [PubMed]
62. Silva Viana, R.L.; Pereira Fidelis, G.; Jane Campos Medeiros, M.; Antonio Morgano, M.; Gabriela Chagas Faustino Alves, M.; Domingues Passero, L.F.; Lima Pontes, D.; Cordeiro Theodoro, R.; Domingos Arantes, T.; Araujo Sabry, D.; et al. Green Synthesis of Antileishmanial and Antifungal Silver Nanoparticles Using Corn Cob Xylan as a Reducing and Stabilizing Agent. *Biomolecules* **2020**, *10*, 1235. [CrossRef] [PubMed]
63. Ahmad, B.; Shireen, F.; Bashir, S.; Khan, I.; Azam, S. Green synthesis, characterisation and biological evaluation of AgNPs using *Agave americana*, *Mentha spicata* and *Mangifera indica* aqueous leaves extract. *IET Nanobiotechnol.* **2016**, *10*, 281–287. [CrossRef] [PubMed]
64. Gholami-Shabani, M.; Sotoodehnejadnematalahi, F.; Shams-Ghahfarokhi, M.; Eslamifar, A.; Razzaghi-Abyaneh, M. Physicochemical properties, anticancer and antimicrobial activities of metallic nanoparticles green synthesized by *Aspergillus kambarensis*. *IET Nanobiotechnol.* **2022**, *16*, 1–13. [CrossRef] [PubMed]
65. Huang, W.; Xu, M.; Duan, H.; Bi, Y.; Yu, H. Inhibition of *Fusarium oxysporum* by AgNPs biosynthesised using *Cinnamomum camphora* fruit extract. *IET Nanobiotechnol.* **2019**, *13*, 42–45. [CrossRef]
66. Oves, M.; Qari, H.A.; Felemban, N.M.; Khan, M.Z.; Rehan, Z.A.; Ismail, I.M.I. Marinobacter lipolyticus from Red Sea for lipase production and modulation of silver nanomaterials for anti-candidal activities. *IET Nanobiotechnol.* **2017**, *11*, 403–410. [CrossRef]
67. Boobalakrishnan, S.; Mani, P.; Pottail, L.; Sundararajan, S.K. Synthesis of nano-silver from *Navicula cincta* and the evaluation of its antimicrobial activity. *Micro Nano Lett.* **2020**, *15*, 119–124. [CrossRef]
68. Ghramh, H.A.; Ibrahim, E.H.; Kilany, M. Study of anticancer, antimicrobial, immunomodulatory, and silver nanoparticles production by Sidr honey from three different sources. *Food Sci. Nutr.* **2020**, *8*, 445–455. [CrossRef]
69. Hema, J.A.; Malaka, R.; Muthukumarasamy, N.P.; Sambandam, A.; Subramanian, S.; Sevanan, M. Green synthesis of silver nanoparticles using *Zea mays* and exploration of its biological applications. *IET Nanobiotechnol.* **2016**, *10*, 288–294. [CrossRef]

70. Ali, S.; Sulaiman, S.; Khan, A.; Khan, M.R.; Khan, R. Green synthesized silver nanoparticles (AgNPs) from *Parrotiopsis jacquemontiana* (Decne) Rehder leaf extract and its biological activities. *Microsc. Res. Tech.* **2022**, *85*, 28–43. [CrossRef]
71. Zhao, L.; Gong, K.; Wang, Y.; Kong, S. Rapid and environment-friendly preparation of silver nanoparticles and their inhibition against phytopathogenic fungi. *Micro Nano Lett.* **2021**, *16*, 213–220. [CrossRef]
72. Elemike, E.E.; Onwudiwe, D.C.; Ekennia, A.C.; Jordaan, A. Synthesis and characterisation of silver nanoparticles using leaf extract of *Artemisia afra* and their in vitro antimicrobial and antioxidant activities. *IET Nanobiotechnol.* **2018**, *12*, 722–726. [CrossRef] [PubMed]
73. Rai, M.; Ingle, A.P.; Gade, A.; Duran, N. Synthesis of silver nanoparticles by *Phoma gardeniae* and *in vitro* evaluation of their efficacy against human disease-causing bacteria and fungi. *IET Nanobiotechnol.* **2015**, *9*, 71–75. [CrossRef] [PubMed]
74. Mohanta, Y.K.; Panda, S.K.; Biswas, K.; Tamang, A.; Bandyopadhyay, J.; De, D.; Mohanta, D.; Bastia, A.K. Biogenic synthesis of silver nanoparticles from *Cassia fistula* (Linn.): In vitro assessment of their antioxidant, antimicrobial and cytotoxic activities. *IET Nanobiotechnol.* **2016**, *10*, 438–444. [CrossRef] [PubMed]
75. Khatami, M.; Nejad, M.S.; Salari, S.; Almani, P.G.N. Plant-mediated green synthesis of silver nanoparticles using *Trifolium resupinatum* seed exudate and their antifungal efficacy on *Neofusicoccum parvum* and *Rhizoctonia solani*. *IET Nanobiotechnol.* **2016**, *10*, 237–243. [CrossRef]
76. Huang, W.; Fang, X.; Wang, H.; Chen, F.; Duan, H.; Bi, Y.; Yu, H. Biosynthesis of AgNPs by B. maydis and its antifungal effect against *Exserohilum turcicum*. *IET Nanobiotechnol.* **2018**, *12*, 585–590. [CrossRef]
77. Ponmurugan, P. Biosynthesis of silver and gold nanoparticles using Trichoderma atroviride for the biological control of Phomopsis canker disease in tea plants. *IET Nanobiotechnol.* **2017**, *11*, 261–267. [CrossRef]
78. Lachmapure, M.; Paralikar, P.; Palanisamy, M.; Alves, M.; Rai, M. Efficacy of biogenic silver nanoparticles against clinical isolates of fungi causing mycotic keratitis in humans. *IET Nanobiotechnol.* **2017**, *11*, 809–814. [CrossRef]
79. Rai, M.; Ingle, A.P.; Gade, A.K.; Duarte, M.C.T.; Duran, N. Three *Phoma* spp. synthesised novel silver nanoparticles that possess excellent antimicrobial efficacy. *IET Nanobiotechnol.* **2015**, *9*, 280–287. [CrossRef]
80. Huang, W.; Bao, Y.; Duan, H.; Bi, Y.; Yu, H. Antifungal effect of green synthesised silver nanoparticles against *Setosphaeria turcica*. *IET Nanobiotechnol.* **2017**, *11*, 803–808. [CrossRef]
81. Kelkawi, A.H.A.; Abbasi Kajani, A.; Bordbar, A.K. Green synthesis of silver nanoparticles using Mentha pulegium and investigation of their antibacterial, antifungal and anticancer activity. *IET Nanobiotechnol.* **2017**, *11*, 370–376. [CrossRef] [PubMed]
82. Khatami, M.; Pourseyedi, S. *Phoenix dactylifera* (date palm) pit aqueous extract mediated novel route for synthesis high stable silver nanoparticles with high antifungal and antibacterial activity. *IET Nanobiotechnol.* **2015**, *9*, 184–190. [CrossRef] [PubMed]
83. Mohammadi, M.; Shahisaraee, S.A.; Tavajjohi, A.; Pournoori, N.; Muhammadnejad, S.; Mohammadi, S.R.; Poursalehi, R.; Delavari, H. Green synthesis of silver nanoparticles using *Zingiber officinale* and *Thymus vulgaris* extracts: Characterisation, cell cytotoxicity, and its antifungal activity against Candida albicans in comparison to fluconazole. *IET Nanobiotechnol.* **2019**, *13*, 114–119. [CrossRef] [PubMed]
84. Sukhwal, A.; Jain, D.; Joshi, A.; Rawal, P.; Kushwaha, H.S. Biosynthesised silver nanoparticles using aqueous leaf extract of *Tagetes patula* L. and evaluation of their antifungal activity against phytopathogenic fungi. *IET Nanobiotechnol.* **2017**, *11*, 531–537. [CrossRef] [PubMed]
85. Malathi, S.; Manikandan, D.; Nishanthi, R.; Jagan, E.; Riyaz, S.; Palani, P.; Simal-Gandara, J. Silver Nanoparticles, Synthesized using *Hyptis suaveolens* (L) Poit and their Antifungal Activity against *Candida* spp. *Chemistryselect* **2022**, *7*, e202203050. [CrossRef]
86. Jamdagni, P.; Rana, J.; Khatri, P. Comparative study of antifungal effect of green and chemically synthesised silver nanoparticles in combination with carbendazim, mancozeb, and thiram. *IET Nanobiotechnol.* **2018**, *12*, 1102–1107. [CrossRef] [PubMed]
87. Xue, B.; He, D.; Gao, S.; Wang, D.; Yokoyama, K.; Wang, L. Biosynthesis of silver nanoparticles by the fungus *Arthroderma fulvum* and its antifungal activity against genera of *Candida*, *Aspergillus* and *Fusarium*. *Int. J. Nanomed.* **2016**, *11*, 1899–1906. Available online: https://www.dovepress.com/biosynthesis-of-silver-nanoparticles-by-the-fungus-arthroderma-fulvum-peer-reviewed-fulltext-article-IJN (accessed on 6 December 2023).
88. Bernardo-Mazariegos, E.; Valdez-Salas, B.; González-Mendoza, D.; Abdelmoteleb, A.; Camacho, O.T.; Duran, C.C.; Gutiérrez-Miceli, F. Silver nanoparticles from *Justicia spicigera* and their antimicrobial potentialities in the biocontrol of foodborne bacteria and phytopathogenic fungi. *Rev. Argent. Microbiol.* **2019**, *51*, 103–109. [CrossRef]
89. Yang, Q.; Guo, J.; Long, X.; Pan, C.; Liu, G.; Peng, J. Green Synthesis of Silver Nanoparticles Using *Jasminum nudiflorum* Flower Extract and Their Antifungal and Antioxidant Activity. *Nanomaterials* **2023**, *13*, 2558. [CrossRef]
90. Govindaraj, A.; Ramakrishnan, M.; Shanmugam, R.; Sp, S.D. Green synthesis, characterization, and antibacterial activity of *Citrus lanatus* based silver nanoparticles. *Bioinformation* **2023**, *19*, 403–406. [CrossRef]
91. Kulkarni, D.; Sherkar, R.; Shirsathe, C.; Sonwane, R.; Varpe, N.; Shelke, S.; More, M.P.; Pardeshi, S.R.; Dhaneshwar, G.; Junnuthula, V.; et al. Biofabrication of nanoparticles: Sources, synthesis, and biomedical applications. *Front. Bioeng. Biotechnol.* **2023**, *11*, 1159193. [CrossRef] [PubMed]
92. Kora, A.J.; Sashidhar, R.; Arunachalam, J. Gum kondagogu (*Cochlospermum gossypium*): A template for the green synthesis and stabilization of silver nanoparticles with antibacterial application. *Carbohydr. Polym.* **2010**, *82*, 670–679. [CrossRef]
93. Kutsevol, N.; Chumachenko, V.; Rawiso, M.; Shyichuk, A. Green synthesis of silver nanoparticles using dextran-graft-polyacrylamide as template. *Micro. Nano. Lett.* **2016**, *11*, 256–259. [CrossRef]

94. Matos, R.A.d.; Courrol, L.C. Saliva and light as templates for the green synthesis of silver nanoparticles. *Colloids Surf. A Physicochem. Eng. Asp.* **2014**, *441*, 539–543. [CrossRef]
95. Binaymotlagh, R.; Del Giudice, A.; Mignardi, S.; Amato, F.; Marrani, A.G.; Sivori, F.; Cavallo, I.; Di Domenico, E.G.; Palocci, C.; Chronopoulou, L. Green In Situ Synthesis of Silver Nanoparticles-Peptide Hydrogel Composites: Investigation of Their Antibacterial Activities. *Gels* **2022**, *8*, 700. [CrossRef] [PubMed]
96. Martínez-Higuera, A.; Rodríguez-Beas, C.; Villalobos-Noriega, J.M.A.; Arizmendi-Grijalva, A.; Ochoa-Sánchez, C.; Larios-Rodríguez, E.; Martínez-Soto, J.M.; Rodríguez-León, E.; Ibarra-Zazueta, C.; Mora-Monroy, R.; et al. Hydrogel with silver nanoparticles synthesized by *Mimosa tenuiflora* for second-degree burns treatment. *Sci. Rep.* **2021**, *11*, 11312. [CrossRef]
97. Mukherjee, K.; Bhagat, N.; Kumari, M.; Choudhury, A.R.; Sarkar, B.; Ghosh, B.D. Insight study on synthesis and antibacterial mechanism of silver nanoparticles prepared from indigenous plant source of Jharkhand. *J. Genet. Eng. Biotechnol.* **2023**, *21*, 30. [CrossRef]
98. Mikhailova, E.O. Silver Nanoparticles: Mechanism of Action and Probable Bio-Application. *J. Funct. Biomater.* **2020**, *11*, 84. [CrossRef]
99. Wen, H.; Shi, H.; Jiang, N.; Qiu, J.; Lin, F.; Kou, Y. Antifungal mechanisms of silver nanoparticles on mycotoxin producing rice false smut fungus. *iScience* **2023**, *26*, 105763. [CrossRef]
100. Li, L.; Pan, H.; Deng, L.; Qian, G.; Wang, Z.; Li, W.; Zhong, C. The antifungal activity and mechanism of silver nanoparticles against four pathogens causing kiwifruit post-harvest rot. *Front. Microbiol.* **2022**, *13*, 988633. [CrossRef]
101. Noga, M.; Milan, J.; Frydrych, A.; Jurowski, K. Toxicological Aspects, Safety Assessment, and Green Toxicology of Silver Nanoparticles (AgNPs)-Critical Review: State of the Art. *Int. J. Mol. Sci.* **2023**, *24*, 5133. [CrossRef] [PubMed]