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#### 2 Review

# Applications of biosynthesized metallic nanoparticles – A review

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ABSTRACT

We present a comprehensive review of the applications of biosynthesized metallic nanoparticles (NPs). The biosynthesis of metallic NPs is the subject of a number of recent reviews, which focus on the various "bottom-up" biofabrication methods and characterization of the final products. Numerous applications exploit the advantages of biosynthesis over chemical or physical NP syntheses, including lower capital and operating expenses, reduced environmental impacts, and superior biocompatibility and stability of the NP products. The key applications reviewed here include biomedical applications, especially antimicrobial applications, but also imaging applications, catalytic applications such as reduction of environmental contaminants, and electrochemical applications including sensing. The discussion of each application is augmented with a critical review of the potential for continued development.

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#### 1. Introduction 43

The unique properties of nanoscale materials have given rise to 44 45 tremendous research activity directed towards nanoparticle (NP) fabrication, characterization and applications. In order to reveal 46 ever more favorable NP functionality, some researchers look to 47 nature for methods to produce NPs with novel properties or 48 49 enhanced function. Many organisms are known to form inorganic materials either intra- or extracellularly. For example, iron-reduc-50 ing bacteria have been known to reduce labile and/or toxic metals 51 52 into their zero-valent form [1]. The same or similar metal-reducing capability used as an NP production method is called biosynthesis 53 [2]. As reviewed recently, many different prokaryotic and eukary-54 55 otic organisms have been used to produce metallic NPs [3], and biosynthesis of NPs has attracted increasing attention in the past 56 57 10 years [4].

Among the key advantages that the biological approach has over 58 59 traditional chemical and physical NP synthesis methods is the bio-60 logical capacity to catalyze reactions in aqueous media at standard 61 temperature and pressure. Production in aqueous media under 62 standard conditions leads to many cost advantages, in terms of both 63 capital equipment and operating expenses, especially in the

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purchase and disposal of solvents and other consumable reagents. Biosynthesis can be implemented in nearly any setting and at any scale [3]. In addition, extensive investment in biotechnology know-how for optimized production of food, pharmaceuticals and fuels also informs NP biosynthesis techniques. One important drawback of NP biosynthesis methods is the requirement in some applications to purify the sample or to separate the NPs from the biological material used in their synthesis (See Figs. 1-6). Q3 71

The properties of biosynthesized materials may differ from materials prepared by other methods. Biosynthesis can result in forms that are difficult to make using other techniques, such as alloys and wires. Biosynthesized NPs can also have enhanced stability and biocompatibility and reduced toxicity, mainly due to coating them with biogenic surfactants or capping agents. The potential range of sizes, shapes and compositions of biosynthesized NPs translates into a broad domain of existing and new nanomaterial applications.

Applications of biosynthesized metal-based NPs range from various biomedical purposes (e.g. antimicrobial coatings, medical imaging and drug delivery) to catalytic water treatment and environmental sensors. We have organized this review according to the applications that use biosynthesized NPs. The chemical composition, form and organism used for the biosynthesis are also described.

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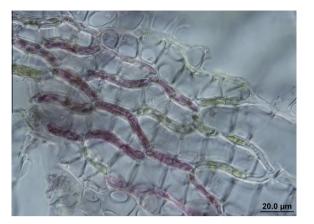
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**Fig. 1.** Light microscopy of gold nanoparticle biosynthesis inside the moss leaf. The purple color indicates the presence of gold nanoparticles inside the cells (picture taken and kindly provided by Markéta Bohunická).

## 88 **2. Biomedical applications**

Applications of metallic NPs in the biomedical fields are numer-89 90 ous, and there is strong potential for continued growth in this area. 91 Metallic NPs are widely used for their antimicrobial functionality; 92 for example, silver NPs (AgNPs) have been incorporated into 93 wound dressings, bone cements and implants [5]. Gold NPs (AuN-94 Ps) have medically relevant optical and anticancer properties. For 95 example, Alanazi et al. [6] describe how surface plasmon absorp-96 tion and surface plasmon light scattering can be used for diagnostic 97 and therapeutic applications, and Patra et al. [7] describe the fab-98 rication and application of AuNPs for targeted cancer therapy. As 99 described by Pankhurst et al. [8,9], magnetic NPs appear promising 100 for targeted drug delivery and hyperthermia applications.

## 101 2.1. Antimicrobial applications

The ongoing development of antimicrobial agents is important due to the continuous selection of antibiotic resistance traits in bacteria and other pathogens. Different metallic NPs, including titanium, copper, magnesium and particularly silver and gold, are known for their antimicrobial, antiviral and antifungal capabilities [10]. These metallic NPs are actively investigated as disinfectants, in food processing, and for use as additives in clothing and in medical devices [11].

The following sections describe the key antibacterial, antiviral and antifungal properties described in the literature for biosynthesized NPs (Tables 1 and 2). However, due to the large number of papers describing antimicrobial activity using slightly different materials, endpoints or methods, in some cases only representative examples are provided.

## 2.1.1. Antibacterial activity

AgNP exposure causes toxicity to bacteria, primarily from Ag ions released into aqueous solution following partial oxidation [5]. Ag ions and small NPs interact with the plasma membrane, disturbing cellular functions, including permeability and respiration, and ultimately leading to lysis. AgNP exposure can prevent DNA replication and protein synthesis by binding to DNA or by denaturizing ribosomes [5].

The detailed mechanisms of AuNP antibacterial functionality against *Escherichia coli* is described by Cui et al. [12]. AuNPs were shown to collapse membrane potential, strongly inhibiting ATPase activity and resulting in a decrease in cellular ATP levels. Another consequence of AuNP exposure was inhibited binding of tRNA to the ribosome subunit.

Bacterial susceptibility to antimicrobial agents can depend on the cell wall structure. Bacteria are classified into two categories, based on their cell wall structure: Gram-negative (G-) bacteria have a multi-layer cell wall and Gram-positive (G+) bacteria have a single-layer cell wall. Antibacterial activity of biosynthesized NPs has been studied for both types of bacteria.

A variety of biological materials have been used for the biosyn-136 thesis of NPs with demonstrable antibacterial effects. These mate-137 rials include fungal, bacterial and algal biomass, as well as extracts 138 of botanical materials, including leaves, bark, roots and tubers. One 139 of the first reports of antibacterial effects of biosynthesized NPs 140 was published by Vigneshwaran et al. [13]. These authors used 141 the edible mushroom Pleurotus sajor-caju for the synthesis of 142 AgNPs and performed successful antimicrobial testing against 143

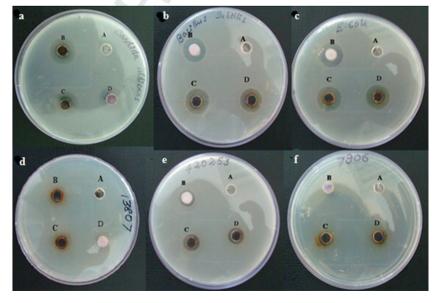


Fig. 2. Antimicrobial activity of AgNPs synthesized by S. hygroscopicus. (a) Candida albicans; (b) Bacillus subtilis; (c) Escherichia coli; (d) Enterococcus faecalis; (e) Salmonella typhimurium; (f) Saccharomyces cerevisiae. Each plate shows (A) culture supernatant; (B) AgNO<sub>3</sub> control; (C, D) synthesized AgNPs, respectively. Reprinted from Ref. [15] with permission from Elsevier.

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