RESEARCH ARTICLE

Metallic nanoformulations: Green synthetic approach for advanced drug delivery

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Abstract: An important reason for investigation using plants for nanotechnological research is due to their easy availability as well as applications in various ailments. Silver nanoformulation can be synthesized using whole plant extract or bioactive of that particular plant. In addition, plant extracts or bioactive of the plant may act both as reducing agents and stabilizing agents in the synthesis process of nanoformulation. The therapeutic effect of plant extract is hindered because of its instability, poor solubility, and low bioavailability. So, nowadays, researches have been carried out for improving all these properties including sustainability through silver nanotechnological approach. The major advantage of green synthesis using plant extracts is that, organic solvents and other excipients are not used because the plant phytochemicals are involved directly in the reduction of the ions and formation of silver nanoparticles. The present review provides an updated knowledge on mechanism of green synthesis of silver nanoparticle and their mechanism of action as antibacterial and anticancer activities.

Keywords: Nanotechnological; Silver nanoparticles; Reduction; Green synthesis; Antibacterial; Anticancer.

1. Introduction

Nanoparticles of metals (silver, gold, palladium, and platinum) are one of the recent active nanotechnological research areas due to their miraculous electronic, optical, and chemical properties[1]. Conventionally nanoparticles were formulated only by chemical and physical methods. The chemical synthesis method of NPs leads to involvement of some of the toxic chemical, polymer, surfactant, co-surfactant, etc that may have adverse effect on the therapeutic applications. Nowadays, the nanoparticles are synthesized via green synthesis, in this method the microorganisms (bacteria, fungi, algae), and plants extract are used for reducing metallic compounds[2]. The green synthesis of nanoparticles is very cost-effective, eco-friendly, simple procedure because there is no need of pressure, temperature maintenance, furthermore, it doesn't need any type of stabilizer, and easily scaled up for large scale synthesis compared with other methods[3]. Numbers of researches reveal that metallic nanoparticles can be synthesized with different sizes and shapes by changing in the concentration of the plant extract as well as concentration of metal ions[4].

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According to the Pubmed data, green synthesis of silver nanoparticles (AgNPs) was reported since 2003, the number of publications on AgNPs is steadily being increased from 2009 and the maximum number of publications in 2016 and 2017 with 18, 194 and 196 papers, respectively. Same as green synthesis of gold nanoparticles was first reported in 2004 and being increased from 2009 to 2016 and 2017 with 27, 103 and 100 publications, respectively (**Figure 1**).

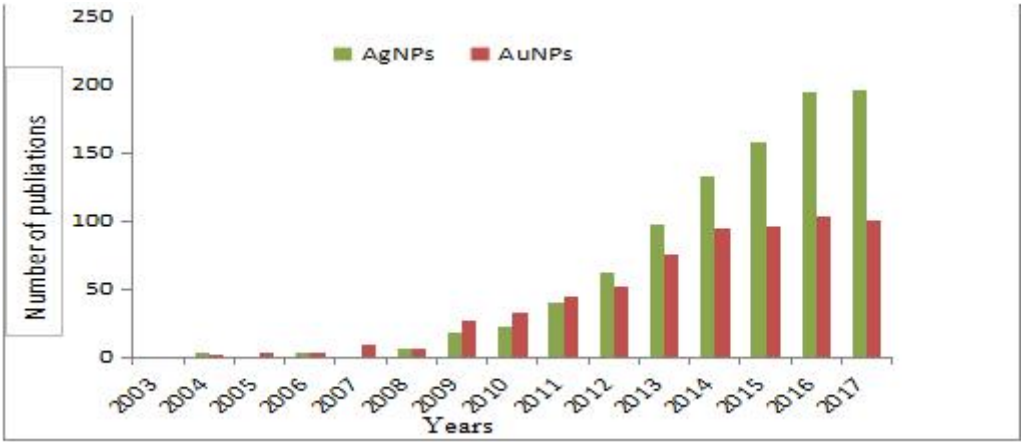

Figure 1. Articles published on green synthesized silver and gold nanoparticles

2. Mechanism of silver nanoparticles synthesis

The green synthesis of AgNPs by biological methods is due to the presence of phytochemicals like flavonoids, alkaloids, glycosides, terpenoids, phenols, carbohydrates, proteins, enzymes and coenzymes etc are donating electron for the reduction of Ag^{+} ions to Ag^{0} ions (**Figure 2**)[5,6]. Various parameters such as concentration of metal ions, composition of plant extract, pH of the reaction mixture, and reaction period are basically affect the size and shape of the silver nanoparticles. Most of the researches reveal that basic medium is more suitable for synthesis of AgNPs due to mono dispersity, better stability, good yield and more reduction of silver ions compared to acidic and neutral medium[7–9]. However, the drawback was also associated with formation of AgNPs in very high pH (>11) due to agglomeration and unstable nanoparticles[3].

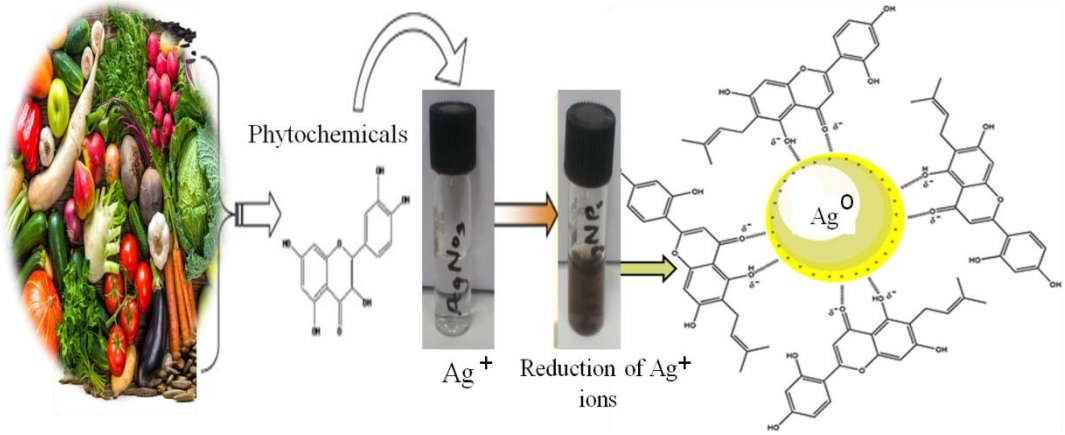

Figure 2. Mechanism of green synthesis of silver nanoparticles

3. Applications of green synthesized AgNPs

Nowadays, synthesis of AgNPs is among the most interesting scientific areas of research using green chemistry method. The major advantage of green synthesis using plant extracts is that, organic solvents and other excipients are not used because the plant phytochemicals are involved directly in the reduction of the ions and formation of silver nanoparticles. Moreover, the reducing and capping agents are usually phenolic derivatives identified by IR spectroscopy, consequently, the antioxidant, antimicrobial and anticancer activities of silver nanoparticles are increased significantly[10]. Many researchers have been reported that AgNPs of plant extract possess broad spectrum antibacterial

activity including multi drug resistant human pathogens[10–13]. Furthermore, AgNPs were also showed significant effect against fungal and yeast pathogens[14]. Recently, the anticancer activity of silver nanoparticles has been raising as one of the major trust areas of nanotechnology because AgNPs initiated cell death by reducing cell proliferation, enhancing intracellular reactive oxygen species, DNA damage and apoptosis[15,16]. Considerably, Jeyaraj *et al*. (2013) reported that AgNPs showed significantly better anticancer activity compared to cisplatin a standard drug for cancer[17]. Interestingly, the AgNPs of Rhododendron dauricum flower extract has shown potent free radical scavenger compared to the Trolox[18]. The antibacterial and anticancer mechanism of silver nanoparticles is described in **Figure 3.**

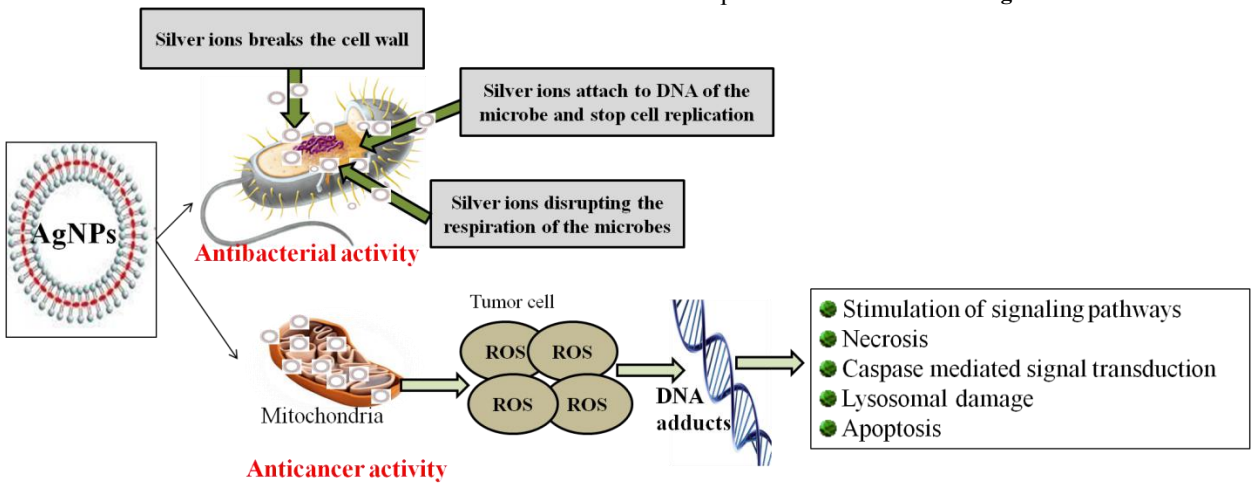

Figure 3. Antibacterial and anticancer mechanism of silver nanoparticles

4. Conclusions

The present review focused on the mechanism of green synthesis of silver nanoparticles, mechanism of AgNPs in cancer and as antibacterial, and application of AgNPs. AgNPs synthesized using plant extracts show better tumor specificity, promising antioxidant, antibacterial, and anticancer activity, and also reduced toxic effects to healthy cells. The efficacy of nanoparticles is mostly due to their large surface area which is responsible for efficient drug delivery. Up to now, only a few researches have been reported regarding green synthesis of AgNPs using pure compounds. Hence more researches must be made using pure compounds and the exact mechanism of reduction and capping through plant metabolites is still remains indefinable and challenging.

Author Contributions

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Anuradha Mishra, M. Pharm. Ph.D.(Pharmacology), is currently working as Associate Professor, Faculty of Pharmacy, Integral University, Lucknow, Uttar Pradesh. Her main interest area of research is Ethanopharmacology, and nanotechnology applications in the treatment of cancer and other associated phsysiological conditions.

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Afreen Usmani as first author wrote this manuscript under Dr. Anuradha Mishra (corresponding author) instruction. Pragyandip P Dash as one co-author made some necessary revision in the manuscript. All three authors who meet authorship criteria certify that they have participated sufficiently in the work to take public responsibility for the content.

Conflict of Interest

All authors have approved the final manuscript and no potential conflict of interest was reported by the authors.

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