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Mini Review

On the anti-cancer activities of silver nanoparticles

Abstract

In the present mini-review silver nanoparticles (AgNPs) due to their superior physicochemical, and biological properties are intensively dealt with. The proper knowledge of these characteristics is essential to maximize their potential applications in many areas while minimizing their hazards to humans and the environment. This manuscript aims to critically review AgNPs synthesized via different approaches, its utilization in cancer treatment and future challenges.

Keywords: anti-cancer activities, AgNPs, IC50, Plasmon, HepG2, MCF-7, MDAMB231, SKBR3, rosa indica

Volume 5 Issue 1 - 2018

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Received: December 20, 2017 | **Published:** February 09, 2018

Introduction

Silver nanoparticles (AgNPs) constitute a class of materials with sizes in the range 1-100nm. The interest in the study of AgNPs concerning their various behaviours has recently increased because of their unique and attractive physical, chemical, and biological properties.[1–7] AgNPs are also known to have particular functions regarding toxicity, surface plasmon resonance, and electrical resistance. Based on these, intensive research works have been conducted to investigate their properties and potential applications for several purposes such as antimicrobial agents in wound dressings, anticancer agents, electronic devices, and water treatment as well.[8–15]

Cancer is a group of diseases, generating various pathological and metabolic changes in cellular environments. It is developed through diverse signaling mechanisms including cell proliferation, angiogenesis, and metastasis.[16,17] Cancer cells have abnormal metabolic activities in aerobic glycolysis, mitochondrial DNA depletion, and alterations in respiratory chains and genomic expressions. The physical and chemical treatments of cancer are limited at different stages. However, currently available therapies have an adverse effect and affect normal cell functions while giving excess drug and radiation exposures.[18,19]

A marginal increase in cancer cases within the last few years ends up mostly, with death.[20] In several cancer types, we have to manipulate satisfactory medicine carriers similar to drug delivery to be applied as adequate chemotherapeutic agents.[21,22] Recently, AgNPs are reported to modulate the Pgp activity and therefore enhance the chemotherapeutic efficacy against multi-drug resistant cancer cells, thus, further emphasizing their excellent potential as combinational partners.[23] Moreover, the genotoxicity of AgNPs is supported by the generation of double-stranded DNA breaks along with chromosomal instability that drives the initiation of apoptotic execution.[24,25] This acting mechanism implies that AgNPs can be mutually associated with a great many DNA-targeting anticancer drugs (Figure 1).

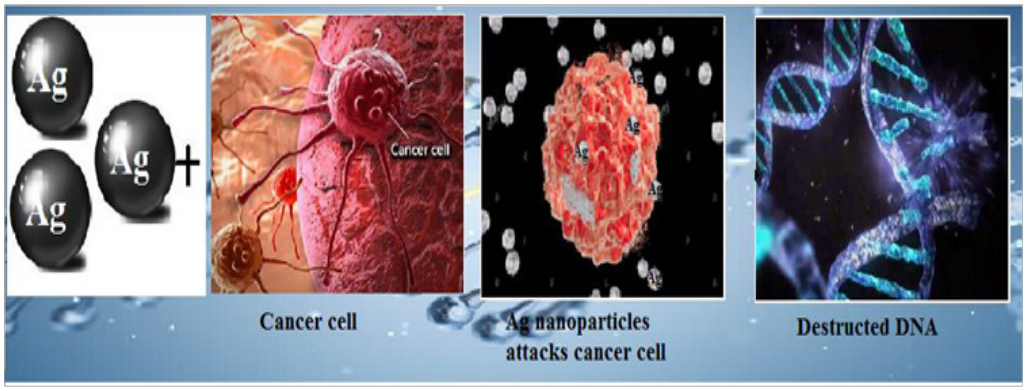

Figure 1 Mechanism of action of silver nanoparticles against cancer cells.

There is several review papers published to address the issues associated with AgNPs regarding their toxicology properties during their use as antimicrobial agents for textiles, dental biomaterials, and bio-detectors, as well as during their syntheses.[26–34] For instance, toxicity properties including cytotoxicity and genotoxicity of capped or uncapped AgNPs have been reviewed in detail.[35] Their toxicity mechanisms after oral exposure were also thoroughly discussed.[36] Also, a recent review of AgNPs had focused on their synthesis using plant extracts for antimicrobial applications.[37] Most of the above studies concentrate chiefly on the different synthesis methods and their bactericidal activities. The reviews on the anticancer activity are somewhat seldom. Therefore, this review aims to present the anticancer activities for silver nano-particles synthesized from different sources.

Anticancer activity of silver nanoparticles

The Metallo-pharmaceuticals were included within the research field that was previously dominated by organic compounds and natural products. Many platinum and platinum-based compounds including carboplatin and oxaliplatin were approved as antitumor agents.[38] However, numerous drawbacks of platinum-based pharmaceuticals were reported proving, therefore, their curative effects.

Many cancer types are not susceptible to platinum drugs, and there are many toxic side effects, including gastrointestinal and haematological toxicity.[39] Moreover, several cancer cells have either intrinsic or acquired resistance to other platinating agents and cisplatin.[40] Consequently, current anticancer research has been devoted to the discovery of novel transition metal compounds. While silver was initially investigated because of its advantageous antimicrobial activity, there has been a recent interest in its anticancer functions (Table 1).

Table 1 Silver nanoparticles from different sources against several cancer cells

AgNPs synthesis route	Tested cancer cell	Reference
plant dandelion- *Taraxacum officinale*	human liver cancer cells (HepG2)	41
Plant Extract-*Commelina nudiflora L*	HCT- 116 colon cancer cells	42
plant extracts of guava and clove	human colorectal adenocarcinoma, the human kidney, human chronic myelogenous, leukaemia, bone marrow, and human cervix	43
Plant Extract- Nostoc linckia	MCF-7	31
Chemical synthesis	A549 (Human lung carcinoma), HeLa (Human cervical adenocarcinoma), MCF7 (Human breast adenocarcinoma), MDAMB231 (Human breast adenocarcinoma), and SKBR3 (Human breast adenocarcinoma) cells	44
Plant Egtract-ethanolic extract of rose (Rosa indica) petals	human colon adenocarcinoma cancer cell line HCT 15	42

Saratale et al.[41] developed AgNPs from common medicinal plant dandelion, *Taraxacum officinale* and showed their high cytotoxic effect against human liver cancer cells (HepG2).[41] The AgNPs Synthesized by Kuppusamy et al.[42] Using *Commelina nudiflora L*[42] aqueous extract showed a reduced cell viability and increased cytotoxicity against HCT-116 colon cancer cells. Biofunctionalized silver nanoparticles synthesized within different plant extracts of guava and clove showed the satisfactory anti-cancer effect against four different cancer cell lines; human colorectal adenocarcinoma, the human kidney, human chronic myelogenous, leukaemia, bone marrow, and human cervix.[43] The developed silver nanoparticles using a proteinaceous pigment phycocyanin extracted from Nostoc linckia as reducing agent exhibited effective cytotoxic activity against MCF-7. The inhibitory concentration (IC50) was 27.79±2.3µg/mL.[31] Moreover, the chemically synthesized AgNPs composites possessed promising anticancer activity against the A549 (Human lung carcinoma), HeLa (Human cervical adenocarcinoma), MCF7 (Human breast adenocarcinoma), MDAMB231 (Human breast adenocarcinoma), and SKBR3 (Human breast adenocarcinoma) cells.[44] Kuppusamy et al.[42] successfully bio-synthesized silver nanoparticles using the ethanolic extract of rose (Rosa indica) petals. The Ag functionalized extract proved potential anticancer activity against human colon adenocarcinoma cancer cell line HCT 15.[42]

Effect of silver nanoparticles size on their anticancer activity

The biological effects of various metal nanoparticles in p53-deficient tumor cells as well as *in vitro* tumor stroma and *in vivo* metastasis models were investigated.[45] A higher cytotoxicity was recorded for the smaller, 5 nm sized silver nanoparticles compared to their larger counterparts. Additionally, it was concluded that silver nanoparticles could induce apoptosis-dependent programmed cell death in the absence of the tumor suppressor p53. Conventional cancer therapy often fails to cause cell death in p53-deficient cancer cells. The unique chemotherapeutic potential of such developed AgNPs was proved. Moreover, it was concluded that nanoparticles of size 5-35nm primarily induced cell death through the mitochondrial structure and function targeting. Although the smaller Ag nanoparticles are more cytotoxic, the apoptotic action mechanism of both 5 and 35nm was identical.[46] Interestingly, the cytotoxic features of silver and silver hybrid nanoparticles are cell-type dependent. In this domain, a higher cytotoxicity was recorded against cancer cells compared to non-cancerous fibroblasts. Conclusively, the stimulation of tumor-associated fibroblast cells with metal nanoparticles represents a typical therapeutic strategy. Since the treatment by Ag and Ag hybrids suppress the cancer cell promoting the activity of a tumor associated fibroblasts. Additionally, the *in vivo* results proved the ability of Ag/hybrids to inhibit the 4T1 tumor metastatic spreading in mice. Impressively, Ag hybrids can enhance the therapeutic efficacy of intravenous doxorubicin treatment.[47]

Conclusion

The silver nanoparticles proved unique anticancer activity against different types of cancer cells. The several syntheses approaches significantly affect the cytotoxic activity of the achieved Ag nanoparticles. Future challenges on AgNPs synthesis and their release into the environment other than scaling up production, assess several potential avenues for future works are to promote a safer and more efficient utilization of these nanoparticles.

Citation: Abdel-Fattah WI, Ali GW. On the anti-cancer activities of silver nanoparticles. *J Appl Biotechnol Bioeng.* 2018;5(1):43–46.
DOI: 10.15406/jabb.2018.05.00116

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

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Citation: Abdel-Fattah WI, Ali GW. On the anti-cancer activities of silver nanoparticles. *J Appl Biotechnol Bioeng.* 2018;5(1):43–46.
DOI: 10.15406/jabb.2018.05.00116