International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 326-334 www.ijprajournal.com ISSN: 2249-7781

Anticancer Activity of Silver Nanoparticles

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Submitted: 02-01-2023 Accepted: 10-01-2023

ABSTRACT: The pharmaceutical role of silver nanoparticles has increased over the last decades, especially those synthesized through herbal medicinal plants, due to their variety of pharmacological importance. Panax ginseng Meyer (P. ginseng) has been widely used as a therapeutic herbal medicine for a long time in cancer treatment. In this study, the cytotoxic and oxidative effect of novel silver nanoparticles synthesized from P. ginseng fresh leaves (P.gAgNPs) were evaluated in different human cancer cell lines. An eco-friendly, easy, one-step, non-toxic and inexpensive approach is used, where aqueous plant extract acts as a reducing as well as the stabilizing agent of Silver Nanoparticles. The Silver Nanoparticles were characterized by UV-Vis spectroscopy, Fourier Transform Infrared Spectroscopy, Energy-Dispersive X-ray, Scanning Electron and Transmission Electron Microscopy and spectroscopy analysis.

Keywords: Silver nanoparticles, anticancer activity, eco-friendly, pathogenic microorganisms, algal biomass.

I. INTRODUCTION:

Pathogenic microorganisms and cancer are major causes of human fatality worldwide. Developing resistance to commercial antibiotics is another dilemma associated with most human pathogens [Abdel-Aziz, M. M., et al 2020]. Staphylococcus aureus is a gram-positive bacterium and a member of the normal microbiota in the human body; however, it is one of the most important pathogenic bacteria, acting on a wide range of infections [Kim S-H, et al 2011] (Ahmad et al 2020). One of the leading causes of death globally is cancer. The search for treatments that may be applied against various tumours has grown throughout time. Current medicines which demonstrate capabilities to regulate and/or inhibit the growth of cancer cells or tumours, however, might generate a serious adverse effect on the patient diminishing its life quality. Nanotechnology has attracted attention in the field of biological applications to its application in the production of the agent with varied qualities. Due to its capacity to connect with the microbial membrane and stimulate the generation of reactive oxygen species, silver nanoparticles (AgNPs) have been employed as an anti-microbial agent (ROS). (Siegel, R. et al 2014;Rajeswaran, A et al 2008; Wang Z. et al 2014; Conde J. et al 2011; Chaloupka K. et al 2010; Singh P. et al 2015; castro-aceituno2016).

Nanoparticles (NP) are particles found in natural, unintentional, or synthetic materials, 50% or more of which fall within this size range of 1-100 nm. In general, there are two types of nanoparticles: (i) inorganic and (ii) organic. Organic nanoparticles include fullerenes, quantum dots, and carbon nanotubes, whereas inorganic nanoparticles involve metallic nanoparticles (like Au, Ag, Cu, and Al) and semiconductor nanoparticles (like ZnO, ZnS, and CdS) (mathur et al 2017).

Researchers are interested only in nanotechnology whichmight be created in various sizes and forms and used in modern biotechnology (Goodsell 2004). Nanoparticles are particularly interesting for a variety of applications including chemical sensors, catalysts, electronic components, pharmaceutical goods, and medical diagnostic imaging due to their distinct optoelectronic and physicochemical characteristics. (Choi et al. 2015; Coccia et al. 2012; Cavanagh et al. 2010), and antimicrobial activity (Nam et al. 2015; Beyth et al. 2015) (patil et al 2016).

II. ANTICANCER ACTIVITY OF SILVER NANOPARTICLES:

Silvernanoparticles (AgNPs) have been demonstrated to be efficient in suppressing tumour growth by limiting angiogenesis, a fundamental stage in the development and pathophysiology of cancer. In many human cell lines, including endothelium cells, glioblastoma cells, and breast cancer cells, promising anticancer effects of AgNPs are being studied. (Chugh et al 2021; Dawadi S. et al 2021; Gomathi AC et al 2019; Thapa RK et al

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 326-334 www.ijprajournal.com ISSN: 2249-7781

2017; Rajeshkumar S. et al 2016; Gopu M. et al 2021).

2.1Anticancer properties of microalgae-derived Biocompounds:

Because of the multi-stage process of uncontrolled cell development, malignancies can develop everywhere in the body. There are more than 200 different varieties of cancer that can be caused by several things, such as genetic changes, radiation, toxic chemicals, and viruses. The most accurate way to diagnose cancer and determine its kind and stage is by tissue biopsy. In a small-scale, handmade glass photobioreactor, Sayegh et al. (2016) identified the PUFA component in the fungus Thamnidium elegans and the microalga Nannochloropsis. They discovered that the percentage of cell viability in the breast and lung malignant cells was 31.5% and 62.56%, respectively, at the maximum concentration (150 g/ mL).Additionally, it has been suggested that DHA induces its anti-tumour effects via extending the cell cycle (Khaligh, S. F., &Asoodeh, A. 2022).

Enhanced ROS generation and increased lipid peroxidations in n-3 PUFA-treated cancer cells significantly contribute to the development of anticancer characteristics (Kang et al. 2010). Lipid raft structures, which are mostly composed of saturated fatty acids, create PUFA-rich, cholesterol-poor non-raft domains that prevent the growth of cancer cells. This is because the lipid rafts are necessary for effective CXCR4-mediated signalling. T. suecica heterotrophic culture provides advantages over autotrophic culture, including an increase in algal biomass and improved lipid, protein, and carbohydrate accumulation (Khaligh, S. F., &Asoodeh, A. 2022).

The use of heterotrophic microalgae for biological activities is not advised since the extraction of EPS from them had cytotoxic effects on the gingival fibroblast cell line (HGF 1). The capacity of peptides derived from Chlorella to reduce the UVB-induced level that causes premature ageing under UV exposure is one of these alluring qualities. Polypeptides produced from P. lutheri may be used in cosmetics. Cancerous cells are protected by spirulina extract. Changes in kidney function indicators, inflammatory markers, and markers of stress were linked to changes in induced nephrotoxicity (Khaligh, S. F., &Asoodeh, A. 2022).

A summary of the anticancer action of biochemical compounds derived from different algal species is given in Table 1.

Table 1: Types of Biocompounds derived from different microalgae and their biological activity (Khaligh, S. F., &Asoodeh, A. 2022).

Bioactive compounds	Microalgae	Target cell	Mechanism of action	References
n-3 PUFAs (Polyunsaturated fatty acid)	Chlorella sp. S14	MCF-7 breast cancer cell/A549 human lung epithelial cells	Growth inhibitory effect of tumour cells	Vilakazi et al. (2021)
EPA (Eicosapentaenoic acid)	Nannochloropsis salina	MCF-7 breast cancer cell	Dose-dependent lethal effect	Sayegh et al. (2016)
DHA (Docosahexaenoic acid)	Crypthecodiniumcohnii	MCF-7 breast cancer cell	Induction of sub-G1 cells/ down-regulation of Bcl-2 gene expression	Chiu et al. (2004)
GA3P(D- galactan sulphate associated with L-(+)- lactic acid	Gymnodiniumsp. A3	Human myeloid leukemia K562 cells	Induction of apoptosis	Umemura et al. (2003)
Polysaccharide	Phaeophyceae (Sargassum)	MCF-7 breast cancer cell	Cell growth inhibition by activating the JNK	Xie et al. (2018)

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Volume 8, Issue 1 Jan-Feb 2023, pp: 326-334 www.ijprajournal.com ISSN: 2249-7781

			signal pathway	
Exopolysaccharide	Tetraselmissuecica (Kylin)	HL-60 myeloid leukemia cells, MCF-7 breast cancer cell & NCL-H460 lung cancer cell line	Antiproliferative effects	Parra-Riofrío et al. (2020)
Peptide	Chlorella	Human skin fibroblasts	Suppressing expressionof transcription factorAP-1& cysteine-rich 61/ MCP-1 production	Chen et al. (2011)
Peptide (Met- Gly-Arg-Tyr)	Pavlova lutheri	B16F10 melanoma cells	Suppressing microphthalmia-associated transcription factor (MITF) & tyrosinase (TYR) protein expression	Oh et al. (2015)
Peptide (YGFVMPRSGL-WFR)	Spirulina platensis	A549 cancer cells	Antiproliferative action	Wang and Zhang. (2016)
Carotenoids	Chlorella ellipsoidea	Colon carcinoma (HCT-116)	Dose-dependent cytotoxic activity	Cha et al. (2008)
C-Phycocyanin	Spirulina platensis	MDA-MB-231 cells	Antiproliferative effect through the MAPK signalling pathway	Jiang et al. (2018)
Fucoidan (polysaccharide)	Fucus vesiculosus	Lewis lung carcinoma (LLC) cell line	Triggers of TNF production and phagocytic activities	Alekseyenko et al. (2007)

2.2Inhibition of autophagy enhances the anticancer activity of Silver Nanoparticles:

AgNPs, or silver nanoparticles, have the potential to be used as an anticancer agent since they are cytotoxic to cancer cells. Ag NPs triggered autophagy in cancer cells via activating the PtdIns3K signalling pathway. Inhibiting autophagy, a crucial cellular degradative process, maybe a beneficial tactic for enhancing the effectiveness of AgNPs in anticancer treatment. AgNP's impact on cancer cells in a melanoma model was considerably improved by wortmannin, a popular autophagic inhibitor (lin2014).

In B16 melanoma cells, Ag NPs promoted autophagy, which was cytoprotective in nature since wortmannin reduced cell viability by 28.54% and increased cell killing by 23.66%. The tumour model was subsequently produced by subcutaneously injecting B16 cells into the right flank of C57BL/6 mice. All of the animals were killed after 8 days of therapy, and the subcutaneous

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melanoma tumours were photographed and weighed (lin2014).

2.3AgNPs in cancer control:

Caspase-mediatedsynthesis, as well as other morphological alterations such as membrane integrity impairment, cell growth decreased, cytoplasmic condensation, and so on. AgNPs with IC50 values of 63.37, 27.54, and 23.84 µg/mL against normal African monkey kidney (Vero), HeLa (cervical), and MCF-7 (breast) cells, respectively, were synthesized by G. mangiferae extracts, which are biocompatible and encompass promising candidates for a range of biopharmaceutical as well as agricultural applications.(Chung IM et al 2016; Mathur et al. 2017).

2.4AgNPs induce cytotoxicity and ROS production in cancer cells

P. ginseng is frequently utilized in the treatment of several disorders [Leung K W and Wong A. S 2010]. Several pharmacological properties are reported in compounds produced from leaves, including anti-cancer properties [Chen s et al 2014; Wang H et al 2009; Jung, C. H. et al 2005; Ma, H. Y. et al 2012]. In this investigation, we discovered that P.g.AgNPs were more hazardous to the MCF7 cell line than the A549 or the HepG2 cell lines. These findings imply that the decrease in cell viability may result from ROS (Reactive Oxygen Species)production (Castro et al 2016).

2.5AgNPs reduce cell proliferation in A549 lung cancer cells

Previous studies have shown that ginseng-derived substances, namely ginsenoside Rg1, can suppress cell growth. The freshly generated DNA strands of actively proliferating A549 cells were examined in this work using bromodeoxyuridine (BrdU) in the presence or absence of P.gAgNPs therapy. We discovered that the DNA synthesis of A549 lung cancer cells was dramatically decreased by 75% and 60% at dosages of 5 and 10 mg/mL and 20 mg/L, respectively. The information points to 10 mg/L as the ideal concentration for more research to determine the substance's anti-cancer effects (Castro et al 2016).

2.6AgNPs reduce cell migration and EGFR phosphorylation in EGF-enhanced A549 cells

P. gAgNPs inhibited cell migration in EGF-enhanced A549 cells after 24 hours of treatment at 10mg/mL.The impact on EGFR's mRNA and protein levels was assessed using PCR and Western blot, respectively. Following a 48-hour P.gAgNPs therapy, mRNA levels for EGFR and ELK1 were also lowered. VEGF-induced migratory cells are affected by silver nanoparticles, according to prior work (Kalishwaralal, K. et al. 2009; Castro et al 2016).

Table 2: The different algal species show Anticancer activity (Xu et al 2017)

Species	Polysaccharide Type	Molecular Weight (Da)	Monosaccharide	Backbone	Biological Activities	Reference
Alaria marginata	Galactofucan	-	Fuc: Gal: Xyl = 47.5:47.3 :5.2	→3)-α-L-Fuc-(2,4-SO3 −)-(1→	Anticancer	Usoltseva, R.V., et al 2016
Coccophoralangsdorfii	Fucoidan	-	Fuc	α-1,3 and α-1,4-Fuc	Anticancer	Imbs, T.I., et al. 2016
Eisenia bicyclis	Laminaran	19–27 k	Glc	β-1,3 and β-1,6-Glc	Anticancer	Menshova, R.V., et al 2014

Gal, galactose; Glc, glucose; Xyl, xylose; Fuc, fucose.

2.7Anticancer activity of Silver Nanoparticles in MCF-7 human breast cancer cell line:

Silver nanoparticles have become a significant class of nanomaterials with several commercial and medicinal uses. One of the cutting-

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edge methods in the treatment of cancer is the development of biocompatible molecules utilizing nanotechnology. Tamarindus indica (Tamarind) fruit shell extract is a straightforward, inexpensive, environmentally friendly, and mass-produced product (GomathiA.C. et al 2019).

2.8Anticancer activity against human lung cancer cells by Silver Nanoparticles:

Lung cancer is the top major cause of cancer death in the globe (Maasomi ZJ. et al 2017; Javidfar S. et al 2017). Cancer is one of the leading causes of mortality worldwide (Amirsaadat S. et al 2017; Mellatyar H. et al 2018). 85% of instances of lung cancer are caused by smoking cigarettes and being around tobacco smoke (Vineis P. et al 2014; Sheervalilou R. et al 2016). Due to their significant side effects and toxicity on non-cancerous tissues, the current therapeutic medicines used to treat lung cancer are both expensive and ineffective (Dadashpour M. et al 2018).

2.9Anticancer Activity of Silver Nanoparticles on Human Cervical Cancer Cells:

Due to its very complicated character, cancer is one of the major causes of medically recognized mortality. Females are most likely to get cervical cancer. According to L. M. Alvarez-Salas et al. (2007), human papillomavirus infections of types 16 and 18 are the cause of cervical cancer. Utilizing an aqueous extract of S. japonica for the biosynthesis of AgNPs. Brown algae called S. japonica are mostly eaten as a delicacy [M. D. Guiry 2008]. Although it is indigenous to Japan, it has been grown in China, Russia, France, and Korea. Here, we describe the environmentally friendly manufacture of AgNPs utilizing an aqueous S. japonica extract and assess their anticancer potential against the HeLa cervical cancer cell line (Sreekanth2016).

III. CONCLUSION:

The most accurate way to diagnose cancer and determine its kind and stage is by tissue biopsy. Lipid raft structures, mostly composed of saturated fatty acids, create PUFA-rich, cholesterol-poor non-raft domains that prevent the growth of cancer cells. In a small-scale, handmade glass photobioreactor, Sayegh et al. (2016) identified the PUFA component in the fungus Thamnidium elegans and the microalga Nannochloropsis. They discovered that the percentage of cell viability in the breast and lung malignant cells was 31.5% and 62.56% at the maximum concentration (150 g/ mL). Polypeptides produced from P. lutheri may be used in cosmetics.Ag NPs, or silver nanoparticles, have the potential to be used as an anticancer agent since they are cytotoxic to cancer cells. Inhibiting autophagy, a crucial cellular degradative process, maybe a beneficial tactic for enhancing the effectiveness of AgNPs in anticancer treatment.They showed that the uniform, monodisperse, and stable biosynthesized AgNPs had potent anti-cancer effects on A549 lung cancer cells.P. gAgNPs reduced cell viability and stimulated the generation of reactive oxygen species in A549, MCF7, and HepG2 cell lines. In P. gAgNPs-treated A549 cells, the p38 MAPK/p53-mitochondrial caspase-3 pathway is activated, causing cell death.Silver nanoparticles have become a significant class of nanomaterials with several commercial and medicinal uses. One of the cutting-edge methods in the treatment of cancer is the development of biocompatible molecules utilizing nanotechnology.The aqueous S. japonica extract has been effectively used to create straightforward, affordable, and environmentally friendly AgNPs. In human cervical cancer cells, AgNPs had a cytotoxic impact.

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