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Research Article

SYNTHESIS OF SILVER NANO PARTICLES USING A MARINE ALGA, ZONARIA CRENATA J. AGARDH AND ITS ANTICANCER ACTIVITY

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ABSTRACT

In this study, *Zonariacrenata* J. Agardh was selected for the preparation of silver nanoparticles based on the presence of bioactive secondary metabolites. Freshly collected marine alga was used for the preparation of aqueous extract as the reducing and capping agent. Various concentration of extract (1%-5%) was added to silver nitrate solution. Brownish black color change was observed which indicates the formation of silver nanoparticles. Silver NPs was then isolated from the solution by evaporating and overnight drying on dryer. The synthesized silver NPs were subjected to FT-I R analysis and TEM analysis. FT-IR analysis revealed the role of functional groups in the formation of AgNPs. A shift from 1209 cm^{-1} to 1211 cm^{-1} was due to the involvement of the ether linkages of flavanone that are absorbed on the surface of metal NPs. A strong intense band at 1354 cm^{-1} was shifted to 1361 cm^{-1} which indicates the interactions of ester group. Shift from 1629 $cm^{-1}$to 1631 cm^{-1}reveals the participation of carbonyl group. TEM analysis of silver nanoparticles shows spherical and quasi- spherical shape in the dimensions ranging from 10nm to 40nm. Antioxidant properties were observed in green synthesized silver nanoparticles. A549 cell line treated with silver nanoparticles decreased cell viability. 35% cell death was determined at 50 µg/ml nanoparticles concentrations. The silver nanoparticles were incubated with MCF-7 at various concentrations, and the nanoparticles decreased MCF-7 cell viability. At 6.25 µg/ml, 94.8% viability was observed and it decreased to 52.6% at 25 µg/ml concentration.

INTRODUCTION

Nanotechnology is one of the emerging fields used to produce inter-atomic structural particles. Nanoparticles are small in size (1–100 nm) and these particles exhibited wide application in medical, agriculture, chemical, electronic and pharmaceutical fields. The synthesis of NPs with pre-determined morphology is the important objective in the fields of chemistry that can be used for the preparation of biosensor, biomedical, catalysis and lower-cost electrode. Nanoparticles (NPs) have unique functional properties which is different from that of bulk materials of bulk materials. Hence NPs are the ideal materials for various uses in biotechnology, medicine, waste water treatment and preparation of health care products. Many methods have been applied for the fabrication of NPs with predetermined properties. To prepare NPs, two basic approaches are bottom-ups and top- down.

Green synthesis methods of NPs preparation had attained much more attention in recenty ears and are widely used in research and development on materials science. These green synthesized NPs reduce environmental pollution by reducing the usage of toxic-solvents, prevention of waste and eco-friendly. Biosynthesis is one of the important approaches to use biological materials and avoid toxic by-products using sustainable and eco-friendly method. Green synthesis of metal and metal oxide NPs has been adopted to accommodate many sources, including, bacteria, algae and plant extract (Helan*et al.*, 2016). The application of plant extract is a simple, rapid and easy method to obtain NPs in large quantities than bacteria, plant and fungi-based NPs synthesis. Biosynthesized NPs have several applications in the pharmaceutical industries such as synthesis of functional nanodevices, drug delivery etc. (El Shafey, 2020; Haritha *et al.*, 2016).

Plants, fungi, bacteria, *Actinomycetes* and algal samples are commonly applied for the biosynthesis of NPs. These extracts/samples have novel therapeutic properties and are applied for the biosynthesis of NPs with desired biological properties. In biological synthesis, both unicellular and

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multicellular organisms are used (Mohanpuria *et al.,* 2008). Among various natural sources, plants are one of the major bioresource that are eco-friendly and inexpensive.

Algae extract is widely used as the natural capping agent for the biosynthesis of NPs production. These natural capping agents are applied to maintain the functional properties and to stabilize NPs. Capping agents are used to produce NPs with desired morphology. Plant Phyto-components such as, terpenoids, flavonoids, phenolic compound, protein and amino acid are used for the biosynthesis of NPs. Isoprenoids or terpenoidshavebeen used for the biosynthesis of iron NPs. These terpenoids are important secondary metabolites of the terrestrial plants. (Vilas *et al.,* 2014).

Polysaccharides are also used as the reducing agents. These polysaccharides modify the shape, size, and structure of TiO_2 and also induces various phases. For example, rutile phase is obtained in the presence of chitosan in the medium and starch is used to generate anatase phase. Green synthesis offerstheuseofnon-toxic substances for the extraction of phytochemicals (Duan*etal.,* 2015). Natural polysaccharides improve the kinetics of sol-gel methods because of their potent catalytic properties and has been reported previously (Boury and Plumejeau, 2015). Amino cellulose is used for the synthesis of gold nanoparticles and acted as reducing and capping agent. L-histidineis used for the preparation of gold NPs and the concentration of amino acid decides the particle sizes (Maruyama *et al.,* 2015).

Silver NPs have antibacterial activities and caused ROS-mediated cellular toxicity and membrane damage. They are active against drug resistant bacteria, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus megaterium*, *Bacillus subtilis*, *Sarcinalutea*, *Aspergillus niger* and *Candida albicans* (Martinez-Carmona *et al.,* 2018; Jin *et al.,* 2019; Siddiqi*et al.,* 2018). *Arthrospira platensis* leaves extracted with fabricated ZnO was found to be effective against bacterial strains such as, *S. aureus*, *B. subtilis* and the increased activity was observed at higher concentrations. At lower concentrations of ZnO antibacterial activity decreased (El-Belely *et al.,* 2021).

Cancer cells are characterized by unrestricted cell division of cells with abnormal characters. The number of cancer cases increased in recent years (Barabadi *et al.,* 2017). Nanomedicine is one of the emerging fields which is very useful in treatment and diagnosis of cancers. Nanomedicine shows potential characteristics based on phytochemicals involved in the formulations of metal nanoparticles. Metallic NPs have applications in the synthesis of nano-platform drugs because of its unique physicochemical activities. Moreover, the biogenic metallic nanoparticles have potential applications in the treatment ofcancer.

Medicinal plant extract has been applied for the preparation of NPs with anticancer properties (Khan, *et al.,* 2018). Metallic NPs also have fluorescent properties when exposed to X-rays. It can be used to diagnose cancer cells in the human body. Anticancer properties of NPs (10 nm) in Hela cell lines were studied at various NPs concentrations. ZnONPs showed dose-dependent anticancer activity and the cell viability was 5 - 50% in HeLa cells. Fe-doped ZnONPs are quasi-spherical in shape. The particle size was approximately 10-20 nm which shows anticancer activities (Pandurangan *et al.,* 2016). The chitosan-coated NPs are spherical shaped and 100 nm in diameter. This chitosan coated and uncoated materials were tested against Helacells at various concentrations (Chen *et al.,* 2013). The chitosan coated Helacells improved cytotoxicity through cellular internalization, formation of ROS, apoptosis and cell death at 75 µg/mL concentrations. The green synthesized ZnONPs mediated by the aqueous extract of *Gracilaria edulis* showed cytotoxicity (Fakhroueian *et al.,* 2018). The aim of the present study is to green synthesize silver nanoparticles using algal extract and to analyze its antioxidant and anticancer activity.

MATERIALS ANDMETHODS

Macroalgae

In this study, macro algae were collected from Kanyakumari, South west coast of India. This sample site is located between 77°15' and 77°36' east longitude and 8°03' and 8°35' north latitude. Algae were collected manually from the detached portion of the exposed rock surfaces of coast (Plate1). Macro algae samples were collected between January 2022 and February 2022 and all the samples were transported to the laboratory for further analysis. The materials were cleaned and debris was removed. All the collected macroalgae were photographed using a digital camera.

Plate 1 Rocky sea shore of Kanyakumari coast, West coast of India

Selection of macroalgae

Zonariacrenata J. Agardh was selected based on availability throughout the season and based on the presence of secondary metabolites (Duraisamy and Selvaraju, 2020).

Distribution of *Zonariacrenata* J. Agardh

Zonaria is a brown alga comprising about 12 species. Specimens can reach around 25 cm in size, all of which exhibit a characteristic semi-circular growth pattern. It produces distinct alternating patterns of darker and lighter tissue. *Zonaria* is widespread with some species being locally abundant on shallow sub tidal of rock reefs (Plate2).

Plate 2 Z *crenata*Agardh, 1817 collected from Kanniyakumari coast, Tamilnadu, India.

Synthesis of silver nanoparticles

Preparation of extracts and synthesis of silver nanoparticles

Five grams of fresh sea weed was weighed and ground using a pestle and mortar were packed down into the beaker containing 100 ml of double – distilled water (DDW). The extraction was done using domestic microwave oven at a power of 800 W and with 2450 MHz frequency for 5 min for enhanced polyphenol extraction. Then, the extract formed was vacuum-filtered using Whatman Grade 1 filter paper and the extract was separated. The aqueous extract was further stored at 4ºC and were used for the biosynthesis of AgNPs. Further every glassware used were completely washed with distilled water and then rewashed with Mill-Q water and air dried. Different concentrations of silver nitrate (1–10mM) were dissolved in 100ml of DDW, and the beaker was placed on the magnetic stirrer. To that, different concentrations of aqueous extract (1% - 5%) were added in drop wise manner, and continuous stirring was given. Reactions was stopped after 30 ml of different extract concentration were emptied in to the reaction mixture and the colloidal solution turns brownish black. The reaction mixture was incubated at room temperature (29 ± 2 °C) and at different incubation times. Silver NPs was then isolated from the solution by evaporating water on hotplate, and by overnight drying on dryer. They were further purified by refluxing them three times with Milli Q water followed by ethanol.

Characterization of silver nanoparticles

The synthesized silver NPs were subjected to UV-spectroscopy analysis. The colour change from yellowish-brown to dark black was a confirmatory sign for silver NP formation. A defined amount NPs were dispersed in double distilled water and analyzed by UV-Vis spectroscopy (Shimadzu UV-2450) to determine the surface plasmon vibration at wavelength of 200-800 nm with 1 nm resolution. The functional groups were studied by using Thermo Nicolet FTIR Nexus spectrometer coupled with DTGS detector. The green synthesized silver NPs morphology were analyzed using TEM.

Antioxidant activity of silver nanoparticles

DPPH free-radical scavenging activity assay was performed. 0.25 mg/ml of 2, 2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) (Sigma Aldrich, U.S.A) solution was used to determine the antioxidant capacity. Stock solutions were prepared at the sample concentration of 10 mg/ml. Reaction mixtures consisted of stock solution, 2 ml DPPH working solution, and methanol as a solvent to have a sample concentration from 0.1 to0.5mg/ml. The negative controls had only the solvent instead of the testing solution. The mixtures were incubated for 30 minutes at 37 °C in the dark. The decrease in the absorbance at 517 nm was measured (Sethiya *et al*., 2013). The experiment was carried out in triplicate. Samples and positive control (ascorbic acid) were tested in triplicate over the same range of sample concentrations. Radical scavenging activity was calculated using the following formula:

$$SC\% = 100\% x \frac{(A_B - A_E)}{A_B} (\%),$$

Where A_B is absorbance of the blank sample and A_E is absorbance of the seaweed extract. The antioxidant activity was expressed as the IC50 value. This value was determined from the plotted graphs of scavenging activity against the concentration of the sample.

Anti-cancer activity of silver nanoparticles

Anticancer effect of silver nanoparticles was studied. The cell lines such as, MCF-7 breast cancer cells, and A549 lung carcinoma cell lines were collected from NCCS, Pune. These cells were further maintained in Dulbecco's modified eagles' media (HIMEDIA, Mumbai, India) and 10% FBS (Invitrogen). These cells were grown at 37 °C in the presence of 5% CO_2 in CO_2 incubator in humidified chamber (NBS, EPPENDORF, GERMANY). The selected cells were trypsinated with the use of 500µl of 0.025% Trypsin in phosphate buffered saline containing 0.5m MEDTA for about 2 minutes (HIMEDIA, MUMBAI, INDIA). Then it was passed into T flasks in sterile condition. Purified silver nanoparticles were incubated at various concentrations (6.25 µg/ml, 12.5 µg/ml, 25 µg/ml, 50 µg/ml and 100 µg/ml) and for 24 h. The percentage viability was evaluated by standard MTT assay after 24 hours of incubation.

% viability = (OD of Test/ OD of Control) × 100

RESULTS

Characterization of silvernanoparticles

The FTIR spectral data shown in Fig. 1a and b revealed the functional groups involved in the formation of AgNPs. A shift from 1209 cm^{-1} to 1211 $cm^{-1}$was due to the involvement of the ether linkages of flavanone that are absorbed on the surface of metal NPs. A strong intense band at 1354 cm^{-1} was shifted to 1361cm^{-1} which indicates the interactions of ester group. Shift from 1629 cm^{-1} to 1631 cm^{-1}reveals the participation of carbonyl group of amides of proteins. The presence of hydroxyl group was revealed by the shift from 3309 cm^{-1} to 3318 cm^{-1}. Hetero compounds such as, carbohydrates, flavonoids and proteins in algal extract were responsible for the instant reduction and capping of silver ion intoAgNPs.

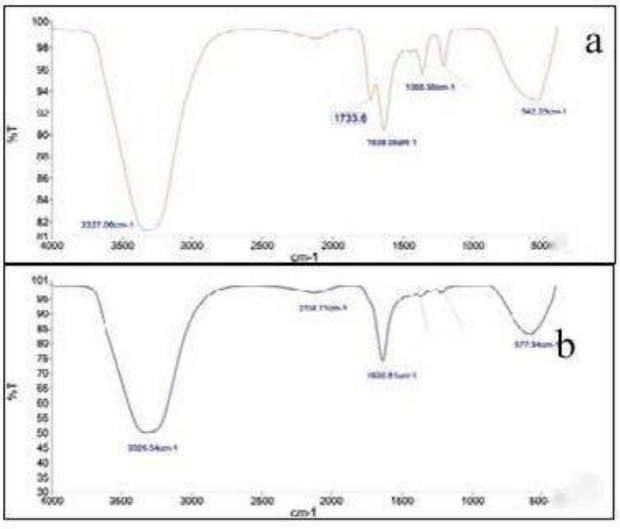

Fig. 1 FTIR spectral data of algal extract (a) and the development of silver nanoparticles (b).

Morphology of silver nanoparticles

Figure 2 shows the distributions of particle size of AgNPs from 10 nm to 40 nm with an average diameter of 14 nm. The complete structural dimension of green synthesized AgNPs was provided by TEM (Fig. 2). The surface morphology of silver nanoparticles showed spherical and quasi- spherical shape with the particle size dimensions ranging from 10 nm to 40nm.

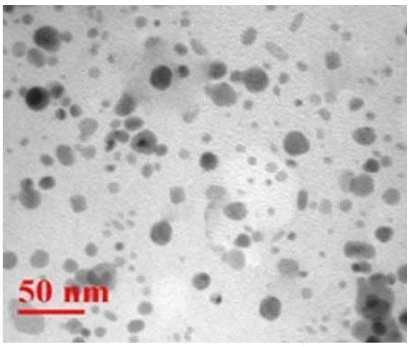

Fig. 2 Transmission electron microscopy image of silver nanoparticles green synthesized using algal extract.

Antioxidant activity of silver nanoparticles

Antioxidation properties of silver nanoparticles revealed maximum activity at higher concentrations. The rate of oxidation increased with increasing concentration of the sample. Silver nanoparticles showed the highest antioxidant activity at 100 mg/ml sample concentration and DPPH activity was 837%.

Anti-Cancer Activity

In the present investigation, the percentage difference in viability of Cell Lines-A549, and MCF-7 were analyzed by standard MTT assay after 24 hours of incubation and the result was depicted in Table1.

Table 1 Viability of A549 cell line treated with silver nanoparticles

Nanoparticles (µg/ml)	Absorbance@ 540nm	Viability (%)
Control	0.2429	100
6.25	0.1927	79.33306
12.5	0.1782	73.36352
25	0.1644	67.68217
50	0.1581	65.08851
100	0.1028	42.32194

A549 cell line treated with silver nanoparticles decreased cell viability and the result was described in Figure 4. At 12.5 µg/ml concentration about 26% cell viability decreased. At 50 µg/ml concentration, 35% cell death was determined. However, at maximum concentration (100 µg/ml), about 58% cell death was observed.

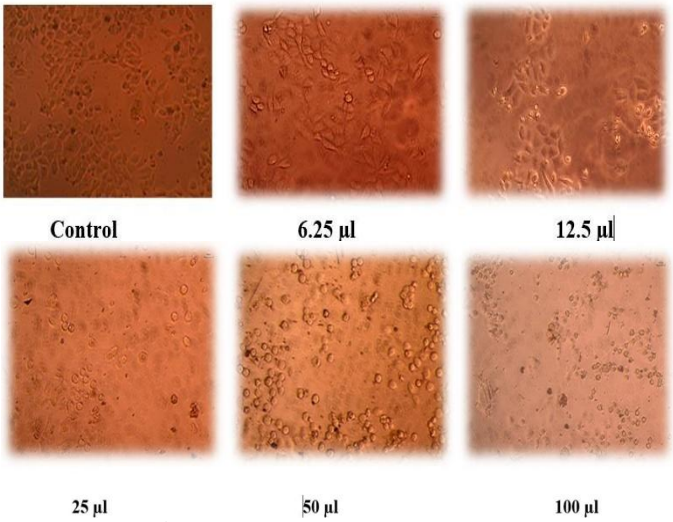

Fig. 4 Viability of A549 cell line treated with silver nanoparticles at various concentrations.

The silver nanoparticles were incubated with MCF-7 at various concentrations, and the nanoparticles decreased MCF-7 cell viability. At 6.25 µg/ml,94.8% viability was observed and it decreased as 52.6% at 25 µg/ml concentration (Table 2).

Table 2 Viability of MCF7 cell line treated with silver nanoparticles

Sample (µg/ml)	Absorbance @ 540 nm	Viability (%)
Control	0.8525	100
6.25	0.8085	94.83871
12.5	0.5895	69.14956
25	0.4486	52.6217
50	0.4015	47.09677
100	0.3784	44.3871

MCF7 cell line treated with silver nanoparticles decreased cell viability and induced morphological changes (Fig. 5). At 12.5 µg/ml concentration about 30% cell viability decreased. At 50 µg/ml concentration, 63% cell death was determined. However, at maximum concentration (100 µg/ml), 55% cell death was observed.

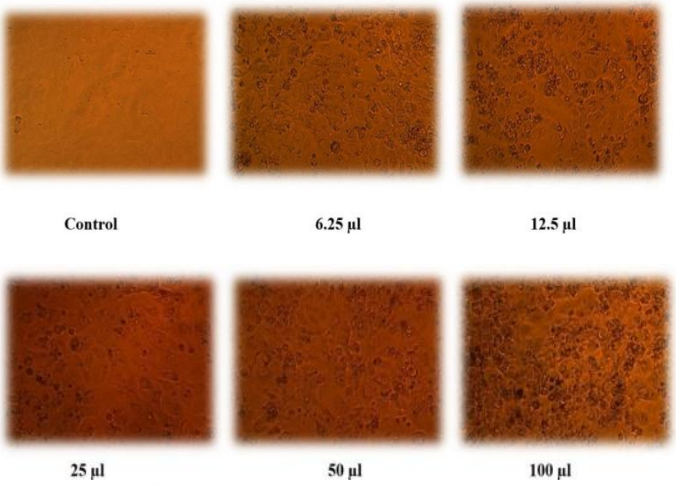

Fig. 5 Viability of MCF7 cell line treated with silver nanoparticles at various concentrations

DISCUSSION

The type, morphology, stability, and aggregation of nanoparticles are the main properties determining their biological activity (Auria-Soro*et al.*, 2019). In the present study, analysisof the physical properties of green synthesized AgNPs confirmed their crystalline nature (Oves*etal.*, 2019), reveales their small size (meansize = 20nm), good stability, and coating with biological functional groups. The size of nanomaterials is an important feature that affects their physical properties, penetration into cells, and interactions with cell molecules. Smaller nanoparticles have a relatively larger surface area when compared to the same volume of material made up of bigger particles thus such nanoparticles have higher surface activity (Navya and Daima, 2016). Smaller nanoparticles easily penetrate through biological membranes (Jeevanandam*et al.*, 2018). They can also easily pass through the blood-brain barrier if their diameter is under 12 nm (Sonavane*et al.*, 2008). Moreover, the nanoparticles also cause a dose-dependent increase in oxidation and DNA damage (Donaldson and Stone, 2003).

Toxic effect on cells increases with an increase in the nanoparticle surface charge. Therefore, higher positively charged nanoparticles interact strongly with negatively charged cell surface thus more easily penetrate into cells and consequently may generate higher cytotoxic effect than negatively charged ones (Aura-Soro *et al.*, 2019). Moreover, positively charged nanoparticles tend to accumulate more in

tumor cells (Hoshyar *et al.,* 2016). Small in sized (1.7-50 nm) and negatively charged AgNPs with moderate, good (zeta potential from −14.7 to −18.0 mV) and high stability (−35.3 to −81.5 mV) synthesized by filamentous Actinobacteria have been reported by many authors (Bakhtiari-Sardari *et al.,* 2020). Therefore, our findings are in line with these previously published results.

The FTIR bands observed in region 3,318 cm^{-1} is characteristic for vibrations of hydroxyl and amino groups (Oves *et al.,* 2019). The peak at 2,900cm^{-1} is due to the C–Hand peak at 2,820 cm^{-1} can be associated with CH_3-symmetric stretching vibration (Qayyum *et al.,* 2017; Raj *et al.,* 2015). The strong band at 1,631 cm^{-1}be assigned to stretching of carbonyl groups (C=O), where as bands inspectrum 1,350–1,405cm^{-1} correspond to C–N stretching and NH bending, indicating the presence of aliphatic groups of amide II (Zaki *et al.,* 2011). The peak at 1,020 cm^{-1}can be assigned to C–O stretching vibration whereas this one at 536 cm^{-1} corresponds to C–Cl stretching in the alkyl group (Gurunathan *et al*., 2018). Similar FT-IR absorption bands from the AgNP simplies that aqueous extract of macro alga could act as capping agents as well as reducing agents for the formation of stable AgNPs. Based on obtained results it is concluded that AgNPs synthesized from algal extract were capped with molecules with amino bonds. Capping agents are responsible for the reduction of Ag ions to AgNPs and stability of formed nanostructures (Oves *et al.,* 2019).

Antioxidant activity of biosynthesized AgNPs was evaluated by 1, 1-diphenyl- 2-picrylhydrazyl (DPPH) radical scavenging assay. Free radical scavenging activity of AgNPs was determined by a decrease in absorbance of DPPH solution at 517nm. When DPPH solution was mixed with various concentrations of biosynthesized AgNPs, DPPH radical scavenging activities of biosynthesized AgNPs were increased at the higher concentrations. High antioxidant activity of nanoparticles is possibly due to polyphenolic compounds, as previously reported (Athukorala *et al.,* 2006). This result indicates that strong antioxidant activity of biosynthesized AgNPsis highly related to the Algal extract remained on the surface of the AgNPs. Due to the efficient antioxidant activities of nanoparticles, it can be a good candidate as pharmaceutical and nutraceutical products.

In recent years, search on anticancer drugs from marine resources is increasing due to their lower side effects (Kim, 2015a; Kim 2015b). A similar anticancer capability of biosynthesized AgNPs against various cell lines was found in other recent studies (Jeyaraj *et al.,* 2013). High cytotoxic effect of biosynthesized AgNPs using marine algal extract wasreported (Chanthini *et al.,* 2015). In this study, the cell viability of tested cell lines was remarkably inhibited in the presence of AgNPs at a concentration of 25µg/ml or higher. AgNP concentration in a range of 6.25 µg/ml – 100 µg/ml decreased the viability of MCF7 cell. In A549 the viability of measured cells was from 78.3% to 42.3%. Morphologies of MCF7 and A549 cells after treatment with biosynthesized AgNPs from 6.25 - 100 µg/mL of concentration were observed. The cells treated with green synthesized nanoparticles showed dramatic morphological changes, attributed to the rupture of the membrane.

The natural algal extracts are considered as both reducing and capping agents of biosynthesized nanoparticles (Akhtar *et al.,* 2013). Recently, Shu *et al.* (2020) applied various natural sources for the synthesis of AgNPs and reported that amino acids, alpha-linolenic acid, and aminobutyric acid are responsible for reducing of silver ions and capping of AgNPs. They reported that due to capping by biomolecules, the stability of monodispersed AgNPs perpetuates for more than 1 year. These capping agents protect AgNPs from aggregation and oxidation of Ag^0 to Ag+ ions. Moreover, the protein coating of AgNPs can be used as drug delivery systems for the human cells (Rodriguez *et al.,* 2013). However, available reports on capping agents of biogenic nanoparticles, especially ones of the macro algal origins, show that the current knowledge on this subject is still less.

This study revealed the significant antiproliferative activity of biosynthesized silver nanoparticles against the selected cancer cell lines. However, such increased activity may be due to the synergetic effect of both nanosized silver and the bioactive phytocompounds from the marine alga attached on the surface of the nanoparticles. In a previous study, Shejawal *et al.* (2021) synthesized silver nanoparticles with the help of 1% aqueous extract of the Carotenoid phytopigment ‘‘Lycopene”, isolated from tomato, extracted in benzene and observed their anticancer activity against various cell lines. The Lycopene AgNPs were tested on Hella, COLO320 DM, H29 cancer cell lines, and it was reported through MTT assay the percent inhibition of 40.9 ± 0.69, 41.41 ± 0.41, and 35.43 ± 0.67 against Hella, COLO320DM and H29 cancer cell lines respectively. Lin *et al.* (2014) reported that silver nanoparticles act as anticancer agents by induction of autophagy of cancer cells through activation of the ptdlns3K pathway. Furthermore, they observed that inhibition of autophagy by autophagic inhibitor like wortmannin results in enhanced cancer cell killing efficacy in the mouse melanoma cell model (B16 cell lines). Shejawal *et al.* (2020) synthesized iron and silver nanoparticles ranging in size from 50 to 100 nm by a green synthesis method from a polyphenolic bioactive phytocompound ‘‘proanthocyanidin”, isolated from grape seed and successfully evaluated various biological activities of synthesized nanoparticles. They reported significant anticancer activity against different colon cancer cell lines (COLO320 DM and H29) through SRB and MTT assays. According to the SRB assay, proanthocyanidin-AgNPs inhibited the growth of COLO320DM (inhibition: 71.61.97%) and H29 (inhibition: 69.211.86%) cell lines. The MTT assay reveals that proanthocyanidin-AgNPs showed 64.27 ± 1.63 and 63.34 ± 1.64 percent inhibition against COLO320DM and H29 cell lines respectively.

Gomathi *et al.* (2020) synthesized AgNPs by using the fruit shell of *Tamarindusindica*, and the resulting biosynthesized nanoparticles proved effective in a dose dependent manner against the MCF-7 cell line (human breast cancer). The biosynthesis of AgNPs from the latex of *Euphorbia antiquorum*L., which was successful in controlling the *in-vitro* growth of the human cervical carcinoma cell line (Hela). The green synthesis approach of nanoparticles adds a double benefit owing to the presence of a diversity of medicinal plants with known anticancer properties to be employed in the therapeutics of cancer.

Silver nanoparticles or composites have a dual role, that is, they act as the ragnostic agents. They absorb and scatter particular wavelengths of visible light, commonly known as surface Plasmon resonance (SPR), and also possess an enhanced SERS. These properties of silver nanomaterials enable them to act as diagnostic probes and contrast agents for several imaging

technologies (Soica *et al.,* 2018). Some research works suggest the activation of p53, caspase-3, and p-Er K1/2 by silver nanomaterials eventually leads to apoptosis and regulates cell division through a series of events taking place in the cells (Murali *et al.,* 2018).

It is also evident from research work that cancer cells have an enhanced permeation and retention (EPR) effect, which leads to the intake of more and more Nano silver and generating more cytotoxic silver ions. Silver nanomaterials act as carrier vehicles for carrying the therapeutic anticancer payload (drugs), resulting in the increased efficiency and potency of anticancer drugs. It also facilitating targeted delivery of anticancer drugs to lessen the cytotoxic effects of chemotherapy on normal healthy tissues (Patra *et al.,* 2015). Silver nanoparticles act as anticancer agents by induction of autophagy of cancer cells through activation of the ptdlns3K pathway. Furthermore, they observed that inhibition of autophagy by autophagic inhibitor like wortmann in results in enhanced cancer cell killing efficacy in the mouse melanoma cell model (B16 cell lines) (Lin *et al*., 2014).

CONCLUSION

There needs to be more research and management strategies on systemic toxicity and its affect humans, other animals, aquatic ecosystems, soil, and the atmosphere. The usage and demand of nanosilver-based products in the commercial markets are increasing. Moreover, the antiviral activity of silver nanoparticles also needs more clarification. Thus, the production of nanoparticles in well-controlled morphological and physicochemical characteristics for use in human bodies and other areas still remains an active field of interdisciplinary study.

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