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Review Article

Green synthesized seaweeds-based metal nanoparticles: therapeutic prospective for anticancer activity

Ali ZEYTÜNLÜOĞLU[1*]

[1] *Pamukkale University, Denizli Vocational School of Technical Sciences, Department of Chemical and Chemical Processing Technologies, 20160, Denizli, Turkiye*

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*****Corresponding author e-mail: azeytun@pau.edu.tr

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ABSTRACT

Nanoparticles containing metals such as silver, gold, copper, zinc, iron and magnesium are prepared via green synthesis by numerous prokaryotic and eukaryotic organisms used in medical and various industrial applications. Nanoparticles in medical applications play an important role in the diagnosis of diseases by bioimaging, and in the treatment of diseases by gene and drug delivery, tissue engineering and implant applications. In the last ten years, numerous studies reported on the biosynthesis of metal nanoparticles and their effect on cancer cell lines utilizing seaweed extracts. Seaweeds is preferred because it has more advantages over other bio-sources in production via green synthesis of nanoparticles. Our findings clearly show that metal nanoparticles prepared by green synthesis using different seaweed species extracts damage cancer cells at the concentration range of 0.40-344 ug/mL and cause their deaths in laboratory experiments carried out in vivo. In this work, we provide details on the use of seaweed in metal nanoparticle synthesis, characterization methods, its advantages, and the applications of synthesised nanoparticles in cancer treatments.

Keywords: Green synthesis, metal nanoparticles, seaweeds, anticancer effect, cytotoxic activity.

1. INTRODUCTION

Cancer is a disease with the highest number of cases worldwide and is the cause of many deaths. It is predicted that 27.5 million new cancer cases will be recorded worldwide each year by 2040. According to the statistics reports of the World Health Organization; One in every 5 people in the world has a case of cancer. 1 in 9 of men and 1 in 12 women are dying from cancer disease. The most common types of this disease, among more than 100 types are lung, female breast, bowel, and prostate cancer. Radiotherapy, chemotherapy, surgery, immunotherapy, stem cell transplant and hormone therapy are the most commonly used treatment methods in cancer treatment today.[1-2] It is expected that the expenditures for cancer treatment on a global scale will increase by 9-12 % and the market share will reach 245 million dollars by 2030.[3]

One of the problems encountered with cancer treatment methods is creating undesirable side effects from the treatment regime. Advances in nanobiotechnological studies have been an important step in overcoming this problem.[4] The new diagnostic and therapeutic materials for the treatment and diagnosis at an early stage of cancer can be synthesized in nanosized (between 1 and 100 nm) by using physical and chemical methods. However, the use of hazardous toxic chemicals in these methods has negative effects on living things and the environment. The synthesis is carried out at high temperatures implying higher process costs and time-consuming in addition to intense labor spent on their production. All these results necessitated the development of new approaches. Green synthesis is carried out using extracts obtained from various natural resources such as plants, seaweeds, fungi and bateria is the most accepted among these approaches. Nanoparticle synthesis can be performed in single-step by this method. The natural extracts could work as a reducing and capping agent in nanoparticle synthesis. In recent decades, there have been a tremendous explosion in the synthesis of silver, gold and other metallic nanoparticles using algal extracts because of its environment-friendly and low-cost productions. In addition, advantages such as no toxic waste during production, use of biomolecules as reducing agents, providing a larger surface area for effectiveness and being able to be produced in the desired size and

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shape by changing the growth conditions are reasons for the increasing interest in the production of algae-based nanoparticles.[5] Algae-based synthesized nanoparticles are used in the treatment of various bacterial[6], viral[7], and fungal[8] diseases.

The efficacy of metal nanoparticles synthesized using extracts of green, brown and red algae in different cancer treatments was evaluated (Table 1). The cytotoxic actions against cancer cells of metal nanoparticles promote oxidative stress in cells by inducing the overproduction of ROS and as a result, mitochondrial damage occurs in cancer cells. Mitochondrial damage causes disruption of cell membrane integrity and arrest of cell cycles. This cascade of events leads to apoptotic cancer cell deaths. Thus, metal nanoparticles play an active role in reducing the percentage of viable cancer cells.[9-10]

2. MATERIALS AND METHODS

2.1. Mechanism of NPs formation

Metal nanoparticles can be synthesized via physical, chemical, and biological methods. The chemical reducing agents, inorganic and organic solvents that are potentially hazardous to human health and environment are used in the synthesis of nanoparticles by chemical method. Most of the synthesis of nanoparticles by chemical method is carried out at room temperature. Moreover; The unpredictable changes in nanoparticle structures are other disadvantages of chemical-mediated nanoparticle synthesis.[11] The green synthesis of metal nanoparticles are generally done via a bottom-up approach.[12]

Synthesis of inorganic NPs can be performed by two different mechanisms as intracellular or extracellular. In extracellular mechanism the bioreduction of metal ion to its nanoparticle occurs on the surface of the algal cell while in intracellular mechanism the enzymatic bioreduction process occurs inside the cell wall and cell membrane.[13] The intracellular formation can be observed with naked eye and after visualized by electron microscopes. *Ulva intestinalis* promoted AuNPs formation since the plant turned purple.[14] In the intracellular synthesis, the NPs are mostly found to get released into the culture media and stabilized there.[15] Generally, the extracellular synthesis is more common. Nanomaterials produced by this method possess some unique and important features, while NPs obtained intracellularly show very narrow size distribution.[16] In addition, while making their way from the cells to outlying medium, the NPs interact with the polysaccharides-based organic matrix.[17,18] Two ways of the NPs separation can be described as follows:
1 -The NPs colloidally stable and further change in their size and shape is prevented by the biopolymers, which act as the capping agent.
2 - Stable NPs inside the cells affect their weight and lead to their settling.[15]

In addition, the remnant cells can stay viable and continue the cycle of biosynthesis.[19]

The first study on the application of algae *Chlorella vulgaris* in the synthesis of AuNPs was presented in 2007. Thus, it is a new and developing field. Seaweeds or macroalgae recently called as bio-nano factories are one of the commercially important marine livingresources.[20] They comprise of more than 30 000 species which are classified into three groups based on their distribution and pigmentation[21] as green algae (Chlorophyta), red algae (Rhodophyta), and brown algae (Phaeophyta). Metal nanoparticles derived from seaweeds can be an appropriate alternative for nanoparticles obtained from plants.[22] The general process steps applied in seaweed-mediated metal nanoparticle synthesis are given in Figure 1.

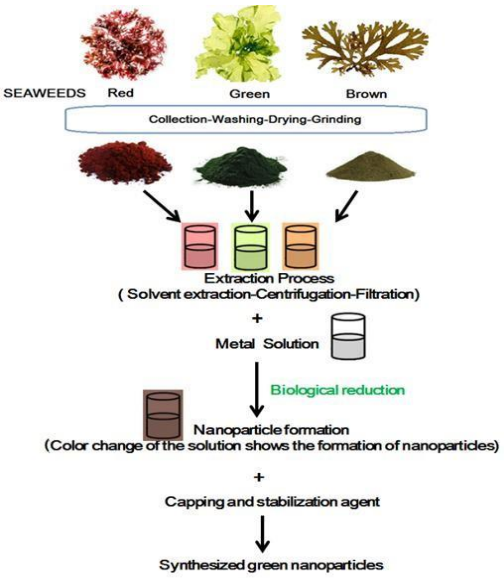

Figure 1. Flowchat represent the seaweeds-mediated nanoparticle synthesis.

The study of algae-mediated biosynthesis of metal nanoparticles are known under term of phyco-nanotechnology.[23] Biomolecules are generally extracted by disrupting the algal cells obtained from their living cultures. As an example, biomolecules from *C. vulgaris* were extracted to synthesize AuNPs.[24] In a different study, proteins of high molecular weights from the biomass of the same algae were successful in promoting AgNPs. Apart from these methods, biosynthesis of nanoparticles using whole cells or cell free supernatant has also been reported.[19]

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2.2. Factors Affecting Nanoparticles Produced by Green Synthesis

Nanomaterial structural properties (such as size, shape, composition, surface structure) are responsible for its toxicity. Nanoparticles can be produced such as spheres, cubes, hallows, ellipsoids, dumbbells, rods, stars, urchins, prisms, hexagonal in different shapes (Figure 2). The physical, chemical and biological parameters during the synthesis determines the structural properties. These parameters are pH of the solution, temperature, reaction time, stirring speed, incubation time, metal ion concentration, extract concentration, capping agents and green material type used. In addition, many of these factors also affect the stability of the nanoparticles.[25,26]

The *pH* of the media has an effect on the size and texture of the nanoparticle. *The temperature* of the reaction medium is an important parameter in nanoparticle synthesis. The temperature value varies according to the nature of the nanoparticle and the method used for synthesis. The p*ressure* is an effective parameter in reducing metal ions and determining the size and shape of nanoparticles. However, if a biological agent is used for the reduction of metal ions, the reaction takes place faster than in a pressurized environment. *The incubation time* during synthesis plays an important role in the quality of the nanoparticle. Especially; long-term light exposure during synthesis changes the properties of the nanoparticle. In addition, changes in nanoparticle structure are observed after long-term storage. Various organisms such as plants, seaweeds and microorganisms as biological agents are used in the production of nanoparticles by green synthesis.

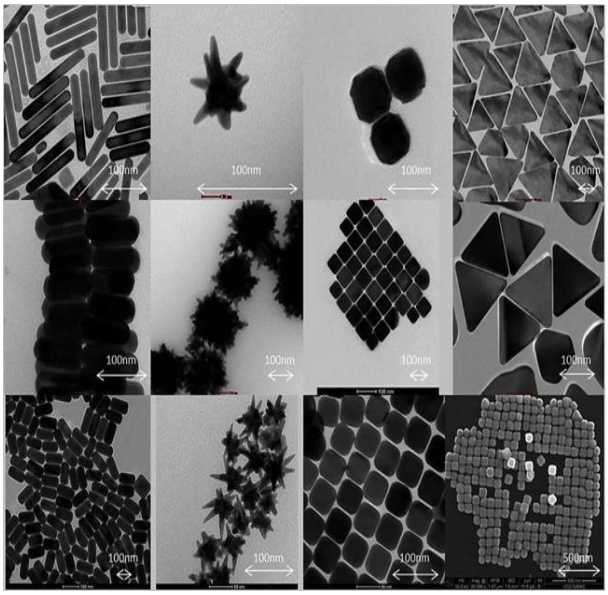

Figure 2: Electron microscopy images of nanoparticle shapes [permission from Ref[72] Copyright, 2016; IGI Global]

These living systems produces secondary metabolites and enzymes that act as reducing and stabilizing agents for the synthesis of nanoparticles. The organism to be used in metabolite or enzyme extraction, the selected extraction method, the obtained and applied extract concentration are factors that determine the efficiency of the synthesis.[25]

2.3. Advantages of Using Seaweeds in Green Synthesis

Green synthesis of nanoparticles has several advantages compared with conventional methods as it is a simple, cost-effective and eco-friendly method which does not require toxic chemicals, high temperature and energy.[27] The natural sources are not harmful when comparing with the synthetic ones. The marine renewable sources such as algae or seaweeds are important naturalorganisms used in various applications. They play a critical role in the development of novel molecules and have high potential for production of NPs.[28] In addition, they are available throughout the year and grows much faster than terrestrial plants.[29] Besides that, oceans whichaccount for more than 70% of the Earth's surface are a large reservoir of these natural resources.[30] Algae are rich in bioactive compounds, such as polysaccharides, polyphenols, carotenoids, proteins, amino acids, vitamins and minerals.[31] The algal phytochemicals have hydroxyl, carboxyl and amino functional groups, which show an effective metal-reducing and capping ability in one step synthesis of the metal NPs.[32,33] An algal species synthesizes NPs by accumulating the cations within its cellular matrix and subsequently reducing them.[19] Metal nanoparticles show reactivity, requiring more stabilization after or during their synthesis to prevent aggregation and oxidation over time. Even though many stabilizing agents are reported, the presence of polysaccharides and gum in algae play an important role in controlling the size of nanoparticles.[27] Their stabilization is based on the existence of several binding sites throughout the polysaccharide chain which promote attachment to the metal's surface, effectively "trapping" the metal nanoparticle and providing strong protection against aggregation and chemical modification.[34]

2.4. Methods of Characterization of NPs

The term "characterization" refers to the processes through which the properties and structure of the material are explored.[35] In the synthesis of NPs, it is important to be sure that the prepared particles are at a nanoscale. NPs obtained by green synthesis are characterized by several analytic techniques from the most basic to the most advanced devices. The morphology of the nanoparticles, in particular, particle size, shape, pore size, and surface area can be determined by transmission or scanning electron microscopy (TEM or SEM), atomic force microscopy (AFM), and dynamic light scattering (DLS). In the SEM micrographs 3D images of particles could be seen in the dispersion, while by TEM two dimensional

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images with greater resolution could be obtained. DLS and ZP (zeta potential) measurements have gained popularity as simple, easy, and reproducible devices to assess particle size and surface charge. The stability of the obtained NPs is also determined by zeta potential analysis.[36]

The crystalline structure of nano-metals can be identified by a powerful nondestructive technique as X-ray diffraction (XRD).[26] To provide the crystalline nature and fractal dimensions, the diffraction patterns obtained from the penetration of X-rays into the NPs is compared with standards.[32] Energy-dispersive spectroscopy (EDS) is a widely used tool to assess the presence of metals.[37] High resolution transmission electron microscopy (HRTEM) can be used to provide information related to the crystalline nature of the nanoparticles as well.[38]

Biomolecules such as polysaccharides, peptides, and pigments, which hold an important place in the biosynthesis of the NPs are present in algal extracts. The structure or functional groups involved in the bioreduction, stabilization, and capping of metal nanoparticles can be unraveled by Fourier transform infrared (FTIR) spectroscopy. In addition, by using the FTIR spectra, it can be determined that functional groups such as the -C = O-, -NH_2, and -SH- groups adjust to the surface of the biosynthesis non-metals .[39]

The change in color of a mixture formed during the biosynthesis of NPs can be monitored by UV-Vis absorption spectroscopy. A change of color to brownish violet indicates the presence of Ag nanoparticles, and a change to purple or pink shows the presence of Au nanoparticles. The spectral range was reported to be 190–1,100 nm since nanometals have striking optical properties due to surface plasmon resonance (SPR).[40] SPR frequency of NPs is dependent on size, shape, aspect ratio, and the dielectric constant of the metals.[38] The SPR of Ag and AuNPs ranges from 400–450 nm and 500–550 nm, respectively.[32]

UV-Vis spectrophotometer was also used to detect the particle size of the metal NPs in solution, since blue and green light rays, with lower intensity and higher diffusion, are displayed in a broad-spectrum band (between 320 and 580 nm).[41] Using all the above-mentioned methods, scientists can characterize the structural features of NPs.[23]

3. Anticancer studies on Seeweeds

Nanoparticles play an important role in the diagnosis and treatment of diseases with successful bioimaging, gene-drug delivery, tissue engineering and implant applications.[42] The discovery of their ability to destroy cancer cells without damaging healthy cells and tissues has caused them to be seen as a new ray of hope in cancer treatments.

In the last ten years, many studies report on the biosynthesis nanoparticles utilizing seaweed extracts and various metals (Ag, Au, Cu, Zn, Mg, Fe etc.) and their affect on cancer cell lines (Table 1). It has been observed to reduces cancer cell proliferation depending on using different concentrations and types of seaweed-derived nanoparticles in this studies.

3.1. Gold Nanoparticles

The use of gold nanoparticles in invitro assays, imaging methods and therapeutic drug delivery systems employed in diagnosis and treatment of cancer are investigated.[1] Particularly, their unique properties such as high performance in imaging methods and reducing the side effects of drugs in drug delivery have increased the interest in gold nanoparticles.[43] The green synthesis of AuNPs was performed using extracts of plant, bacteria, seaweeds, etc. The literature studies on the cytotoxic activities against various cancer cell lines of gold nanoparticles synthesized using seaweed are shared below:

AuNPs prepared utillizating *Gelidium pusillum* (Red algae) extracts by Jeyarani et al showed a significant cytotoxic activity at a concentration of 43.09 µg/mL against breast cancer cell line (MDA-MB-231).[44] Ajdari and colleagues found that significant cytotoxic effect to the various cancer cell lines (HeLa, HepG2, CEM-ss and MDA-MB-231) as dose- and time-dependent manner of AuNPs synthesized using water extracts of the brown seaweed *Sargassum glaucescens*.[45] Chellapandian and friends observed that the gold nanoparticles they biosynthesized had little effect against Human embryonic kidney tumorigenic cells (HEK-293) even at high concentration (100 µg/mL).[46] Algotiml et al synthesized gold nanoparticles (AuNPs) with *Gracilaria foliifera* extracts showed potent anticancer activity against human breast adenocarcinoma cell lines (MCF-7) at 188 µg/mL concentrations.[47] Gold nanoparticles (AuNPs) prepared against human colon adenocarcinoma (HT-29) cell from *Acanthophora spicifera* (Red alga) extracts by Babu et al. caused cytomorphological changes on HT-29 cells and notable increases in the number of apoptosis, at an IC_{50} value of 21.86 µg/mL.[48] Also, Dhas et al. synthesized gold nanoparticles exhibited concentration-dependent cytotoxic effect on HeLa cells using marine brown alga *Sargassum swartzii*. Synthesized AuNPs nanoparticles reduced the mitochondrial activity of HeLa cells by 50% within 24 hours at a concentration of 41.10 µg/mL.[49] González-Ballesteros et al. examined the potent cytotoxic effect of gold nanoparticles prepared with three species *Chondrus crispus* (Brown algae), *Gelidium corneum* (Red algae), *Porphyra linearis* (Red algae) of seaweeds against lung cancer cell line (A549) and humanleukemia monocytic cell line (THP-1). They emphasized the usability of gold nanoparticles prepared with these three seaweed species as an immunotherapeutic agent

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from the results they obtained.[50] González-Ballesteros et al. in two other studies determined that gold nanoparticles prepared with brown (*Cystoseira baccata*) and a green algae (*Ulva lactuca*) showed a stronger cytotoxic effect against Colorectal cancer cell lines (Caco-2 and HT-29).[51,52]

3.2.Silver Nanoparticles

It has been observed to have significant effects on the growth and viability of HEPG2 cells of AgNPs nanoparticles prepared with 3 different types of seaweeds *G. elongata, T. ornata* and *E. flexuosa* by Azeem et al. Similar results have been obtained in the effect on the HEPG2 cell line for all three species. It has been determined that time and nanoparticle concentration affect anticancer activity.[53] Kassas and Attia synthesized AgNPs with an extract of the red seaweed *Pterocladiella capillacea* showed potent cytotoxic activity against the human hepatocellular carcinoma (HepG2) cell line at 5.0µg/mL concentrations.[54] In another study, El-Kassas and El-Sheekh tested the cytotoxic effects of silver nanoparticles biosynthesized with an extract of the Red seaweed *Corallina officinalis* against the human breast cancer cell line (MCF-7). They showed that, in 1.5 µl/mL concentration of the biosynthesized AgNPs, the MCF-7 cell's growth was significantly inhibited.[55] AgNPs synthesized with *Gracilaria edulis* extracts exhibited cytotoxicity against breast carcinoma cells (MDA-MB-231) in concentration at 344.27 µg/mL.[10] Moshfegh et al. prepared AgNPs which showed the best inhibitory activity at 100 µg/mL against MCF-7 breast cell lines.[56] The AgNPs synthesized with *Sargassum wightii* extracts exhibited a time-dependent cytotoxic effect on Human cervical carcinoma (HeLa) cells as reported by Suganya et al. The best inhibition concentration that decreased cell viability at the end of 48 h was 6.84 µg/mL.[57] AgNPs synthesized using *Spyridia filamentosa* extracts exhibited strong citotoxicity against Breast cancer cell line (MCF-7).[58]

Viswanathan et al. synthesized AgNPs using the red seaweed *Hypnea valentiae* extracts, which were cytotoxic against the HT-29 human colon cancer and A549 lung cancer cell lines with IC_{50} values of 24.6 and 5.91 µg/mL.[59] The anti-cancer efficiency of biosynthesized AgNPs with *Caulerpa taxifolia* extracts against A549 lung cancer cells were evaluated by Zhang et al. had the best concentration for cytotoxicity at 40 µg/mL.[60] AgNPs synthesized using *Padina tetrastromatica* extracts exhibited effective cytotoxic activity against Breast cancer cell line (MCF-7) at 86.7 ug/mL concentration.[61] An inhibitory concentration (IC_{50}) of 95.35 µg/mL was recorded against Ehlrich *Ascites Carcinoma* (EAC) cell lines upon treatement with AgNPs prepared using *Enteromorpha compressa*extracts by Ramkumar et al. Thus, AgNPs play an effective role against the growth of EAC cells.[33]

3.3.Copper Nanoparticles

Ramaswamy et al. synthesized CuO NPs using brown algae (*Sargassum polycystum*) extracts. The synthesized CuO NPs showed significant anticancer activity at 61.25 µg/mL against breast cancer cell line (MCF-7).[62] Aboeita and friends observed greatly increased effectiveness of the anticancer drug if used together with chemotherapeutic drugs such as Nedaplatin of CuO NPs instead of using CuO nanoparticles alone for cancer treatment. In their study, the highest cell deaths were recorded in breast cancer cell lines at (IC_{50}=0.40 ug/mL).[63]

3.4. Zinc Nanoparticles

The synthesis of ZnO nanoparticles using *U. lactuca* (Ul) and *S. marginatum* (Sm) extracts was carried out by Anjali. The synthesized nanoparticles showed effective cytotoxic activity on MCF-7 cell lines With IC_{50} values and maximum cell death ratio calculated as 91.18 -104.78 µg/mL and 97.34-96.03% for Ul-ZnO and Sm-ZnO.[64] Priyadharshini et al synthesized silver and zinc oxide nanoparticles with *Gracilaria edulis* extracts showed cytotoxic activity against the Human prostate cancer cell line (PC3).[65] Sanaeimehr et al evaluated the cytotoxic effects on human liver cancer cell line (HepG2) of green-synthesized ZnONPs with *Sargassum muticum* extracts. They showed that cell growth inhibition by ZnO nanoparticles was both time and dose-dependent.[66]

3.5 Magnesium Nanoparticles

The synthesis of MgO nanoparticles with brown algae (*Cystoseira crinita*) extracts was carried out by Fauda et al and tested against the Colorectal cancer cell line (Caco-2). The IC_{50} value of MgO-NPs against cancer was found to be 113.4 µg/mL.[6] Pugazhendhia et al. prepared MgONPs with *Sargassum wightii* extracts and showed that it had a potent inhibitory activity at 37.5 µg/mL against lung cancer cell line (A549).[67]

3.6. Iron Nanoparticles

Namvar et al tested the anticancer activity of magnetic iron oxide and gold nanoparticles synthesized using brown seaweed extract (*Sargassum muticum*) against various cancer cell lines (Jurkat, MCF-7, HeLa, HepG2, K562, CEM-ss and HL-60) *in vitro*. In their results; magnetic iron and gold nanoparticles were observed to induce apoptosis and also activate caspase3 and 9.[68,69] Salehzadeh et al evaluated cytotoxic effects of Fe_3O_4/Ag nanocomposite biosynthesised by *Spirulina platensis* extract against MCF-7 (human breast cancer cells). It showed important reduction in cell proliferation at 135 µg/mL.[70]

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Table 1: Anti-tumoral activity in different cancer lines of synthesized nanoparticles using various seaweed species

Seaweed name	Algae types	Cancer types	NPs types	IC_{50} (µg/mL)	NPs size/shape	References
Galaxaura elongata	Red			104.15	30 to 90 nm/ Spherical	
Turbinaria ornata	Brown	Liver cell line (HepG2)	Ag	104.81	20 to60 nm/ Spherical	53
Enteromorpha fexuosa	Green			104.91	30 to 90 nm/ Spherical	
Gracilaria edulis	Red	Breast cancer cell line (MDA-MB-231)	Ag	344.27 ± 2.56	62.72 ± 0.25 nm/ Spherical	10
Hypnea valentiae	Red	Lung cancer cell line (A549) Human colon adenocarcinoma cells (HT-29)	Ag	5.917 24.6	10-45 nm/ Spherical	59
Caulerpa taxifolia	Green	Lung cancer cell line (A549)	Ag	40	10-100 nm/ Spherical	60
Sargassum wightii	Brown	Human cervical carcinoma (HeLa) cells	Ag	6.84(24 h) 47.48 (48 h)	80-100 nm/ Spherical	57
Spyridia filamentosa	Red	Breast cancer cell line (MCF-7)	Ag	Data not shown	20-30 nm/ Spherical	58
Ulva lactuca	Green	Colorectal cancer cell line (HT-29)	Ag	13	31 ± 8 nm/ Spherical	52
Polysiphonia alga	Red	Breast cancer cell line (MCF-7)	Ag	4.19	5-25 nm/ Spherical	56
Sargassum muticum	Brown	Breast cancer cell line (MCF-7)	Ag	25-50	40-65 nm/ Spherical- hexagonal	71
Enteromorpha compressa	Green	Ehlrich Ascites Carcinoma (EAC) cell lines	Ag	95.35	4-24 nm/ Spherical	33
Padina tetrastromatica	Brown	Breast cancer cell line (MCF-7)	Ag	86.7	40–50 nm/ Round-shaped	61
Gracilaria edulis	Red	Human prostate cancer cell line (PC3)	Ag		55-99 nm/ Spherical	65
Pterocladiella capillacea	Red	Liver cancercell line (HepG2)	Ag	3.7µl/mL	11.4±3.52 nm	54

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Table 1. *Cont.*

Seaweed name	Algae types	Cancer types	NPs types	IC_{50} (µg/mL)	NPs size/shape	References
Chondrus crispus	Brown	Lung cancer cell line (A549)				
Gelidium corneum	Red	Human leukemia monocytic cell line (THP-1)	Au	20-25	30-200 nm/ spherical, triangular, and hexagonal	53
Porphyra linearis	Red					
Cystoseira myrica	Brown				9-11nm/ Spherical	
Gracilaria foliifera	Red	Breast cancer cell line (MCF-7)	Au	188		47
Ulva rigida	Green				13nm/ Spherical	
Gelidium pusillum	Red	Breast cancer cell line (MDA-MB-231)	Au	43.09 ± 1.6	12 ± 4.2 nm/ Spherical	44
Acanthophora spicifera	Red	Human colon adenocarcinoma cells (HT-29)	Au	21.86	<20 nm/ Spherical	48
Gracilaria verrucosa	Red	Human embryonic kidney tumorigenic cells (HEK-293)	Au	100	20-80 nm/ Spherical	46
Ulva lactuca	Green	Colorectal cancer cell lines (HT-29)	Au	23	7.9 ± 1.7 nm/ Spherical	52
Cystoseira baccata	Brown	Colorectal cancer cell lines (Caco-2 and HT-29)	Au	79.03 and 49.61	8.4 ± 2.2 nm/ Spherical	51
Sargassum glaucescens	Brown	Human cervical carcinoma (HeLa) cells liver cancercell line (HepG2) Breast cancer cell line (MDA-MB-231) Leukemia cell line (CEM-ss)	Au	4.75 ±1.23 7.14 ± 1.45 10.32 ±1.5 11.82 ± 0.9	3.65 ± 1.69 nm/ Spherical	45
Sargassum muticum	Brown	Human leukemia cell lines: K562 Jurkat CEM-ss HL-60	Au	4.22 ± 1.12 5.71 ± 1.4 6.55 ± 0.9 7.29 ± 1.7	<10 nm/ Spherical	69
Corallina officinalis	Red	Breast cancer cell line (MCF-7)	Au	1.5 µl/mL	14.6 ± 1 nm	55
Sargassum swartzii	Brown	Human cervical carcinoma (HeLa) cells	Au	41.10	35 nm/ Spherical	49

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Table 1. *Cont.*

Seaweed name	Algae types	Cancer types	NPs types	IC_{50} (µg/mL)	NPs size/shape	References
Pterocladia capillacea	Red	Breast cancer cell line (MCF-7) Liver cancercell line (HepG2) Ovarian cancer cell line (SKOV-3)	CuO	0.40 ± 0.08 1.50 ± 0.12 0.70 ± 0.09	62 ± 17.7 nm/	63
Sargassum polycystum	Brown	Breast cancer cell line (MCF-7)	CuO	61.25		62
Spirulina platensis		Breast cancer cell line (MCF-7)	Fe_3O_4	135	30-50 nm/ Spherical	70
Sargassum muticum	Brown	Breast cancer cell line (MCF-7) Leukemia cell line (Jurkat cells) Human cervical carcinoma (HeLa) cells Liver cancercell line (HepG2)	Fe_3O_4	18.75±2.1 6.4±2.3 12.5±1.7 23.83±1.1		68
Cystoseira crinita	Brown	Colorectal cancer cell line (Caco-2)	MgO	113.4	3-18 nm/ Spherical	6
Sargassum wightii	Brown	Lung cancer cell line (A549)	MgO	37.5 ± 0.34	68.06 nm/ Flower-shaped	67
Ulva lactuca	Green	Breast cancer cell line (MCF-7)	ZnO	91.18	12–17 nm spherical	64
Stoechospermum marginatum	Brown			104.78	6–11 nm round-shaped	
Sargassum muticum	Brown	Human liver cancer cell line (HepG2)	ZnO	175		66
Gracilaria edulis	Red	Human prostate cancer cell lines (PC3)	ZnO		66-95 nm/Rod-shaped	65

4. CONCLUSIONS AND FUTURE PROSPECTS

Cancer is still one of the leading causes of death all over the world despite advances in science and technology. In this chapter, information about the use of seaweed in metal nanoparticle synthesis, characterization methods, its advantages and the applications of the nanoparticles prepared in cancer treatments are given. The eco-friendly nanoparticles produced by green synthesis and their usability in versatile applications will increase the interest in this field day by day. However, there are still questions to be answered regarding the administration route, dose amount, toxicity in-vivo applications, biodegradability and stability statutes. Because most of the studies are carried out in cell culture media under in vitro conditions. There is the need to evaluate these metal nanoparticles both on animal models in vivo and in terms of pharmacokinetics, pharmacodynamics and genotoxicity.

The synthesis of metal nanoparticles using Seaweeds which have rich secondary metabolite content and investigation of their efficacy in industrial applications such as health, food and the environment are still in their infancy. Further research in this area is required to better understand the potential roles of Seaweeds in various industrial applications.

Conflict of interests

I declare that there is not a conflict of interest with any person, institute, company, etc.

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