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Marine Algae Derived Nanoparticles in Medicine: Clinical Applications and Future Prospective – A review

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ABSTRACT

Marine algae exhibit as an ideal bioresource within the marine ecology with the characteristics of renewability, presence of unique primary and secondary metabolites, ability to harvest throughout the year, easy to cultivate in a large scale, etc. When running back to ten years past, it is proved that the synthesis of drugs from natural extracts are more effective and less toxic for a wide variety of clinical applications including cancer, and diabetic therapies. As marine algae play the role of the most unexplored natural bioresource among other sea organisms, they act as a potential candidate in the field of therapeutic discoveries and pharmaceuticals. Hence, the prerequisite of novel perspectives has risen up for the synthesis of desired primary and secondary metabolites via marine algae for drug discoveries recently. As marine algae enriched with medicinally potent chemicals including nanomaterials like silver, copper, gold, and zinc which are responsible for vast variety of biological functions including immunostimulatory, anti-tumor, antioxidant, anti-diabetic, anti-obesity, skin whitening, anti-aging, and anti-cancer activities, it is founded to be composed with the ability of playing a vital role in therapeutic discoveries. In this review, it tends to deal with the application of marine algae-derived nanoparticles in medicine, its clinical applications, and future prospects in advance.

1. Introduction

At the nanoscale, nanotechnology is a thriving and growing field of science, engineering, and technology [1]. Nanoparticles or nanomaterials (NPs), with diameters between 1 and 100 nm and concentrations between 10-9 m, are the end result of nanotechnology [2], [1]. According to the classifications, NPs are categorized into three types: natural nanoparticles, incidental nanoparticles, and engineered nanoparticles [3]. NPs are extensively used in biotechnological, medicinal, cosmetic, and electrical uses. The effective physiochemical and structural characteristics of NPs make nanotechnology a great field to concentrate on [4]. Nanotechnology allows scientists to manipulate the characteristics of materials by altering their scale, which has sparked interest in a wide range of nanomaterial applications [3]. In there, the optical, chemical, thermal, and physicochemical parameters of metallic nanoparticles are peculiar [4]. The physical properties of materials that have been reduced in size can change dramatically from those of the bulk counterparts' material. Nanomaterials have physical features such as being composed of large surface atoms, enormous surface energies, spatial confinement, and reduced defects [5]. Hence, scientists are currently working to develop a wide range of nanotechnology-enabled manufacturing procedures that reduce waste, eventually leading to atomically accurate molecular production with zero waste [5]. Nanoparticles as catalysts for higher effectiveness in prevailing manufacturing techniques by reducing or eliminating the use of poisonous chemicals, the discovery of nanomedicine, nanoparticles, and nanodevices for water and air pollution reduction, and nanoparticles for more efficient power generation are some examples of nanotechnology applications in recent era [2], [1], [6].

Our planet "The earth" is mainly covered with 71% of seawater which is encountered with a rich diversity of unique marine ecology in its bulk portion [7]. When considering marine ecology, marine organisms can be considered a rich source of marine natural products that can be used to cure and eliminate lifethreatening disorders such as cancer and acquired immunodeficiency syndrome (AIDS) [8], [9]. Apart from that, these marine algae are enriched with natural bioactive constituents such as sterols, sulfated polysaccharides, carotenoids, peptides, and chitin-derived compounds which are responsible for the valuable biological functions related to those disorders [10]. Out of other marine organisms including marine crustaceans, fishes, Mollusca and oysters, marine algae considered to be composed of less exploration and less popular on an economic basis among humans [8]. As marine algae are discovered with ideal renewable capabilities, they are considered a renewable energy resource where we have difficulties in accession when compared to other terrestrial flora [11]. The ability of algae to accumulate metals and reduce metal ions makes them the superior contender for the biosynthesis of nanoparticles. Furthermore, algae are relatively convenient and easy to handle, along with several other advantages such as synthesis at low temperature with greater energy efficiency, less toxicity, and risk to the environment flora [11]. In the physical and chemical methods, different commercially available surfactants were used as templates and capping agents in NPs synthesis with different morphologies. Therefore, exploration of their applications and phytochemical compositions are highly required in advance for the efficient and appropriate utilization of marine algae [12]. Previous research evidenced that phenols, ascorbic acid, flavonoids, citric acid, terpenes, polyphenolics, alkaloids, and reductase-like algal secondary metabolites can play the role of reducing agents [11]. So, these secondary metabolites are responsible for numerous biological functions in living organisms including antioxidant, wound healing, anti-coagulant, insecticidal, anti-diabetic, and anti-hypertensive activities [13]. It is also founded that these algal bioactive constituents can eliminate the disorders related to the digestive tract as they are an ideal functional food in the nutraceutical industry as well [13]. It is discovered that the bioactivity of marine algae can be enhanced with the proven safety via the deployment of metal mediated algal nanoparticle synthesis. When considering nanoparticles, biologically synthesized silver, gold, copper and zinc are founded to be cause zero hazard during and after the utilization in biological experiments [14].

With the advancement of the popularity related to natural compounds, novel drugs, drug leads and chemical entities derived from natural products represent valuable effects with compared to synthetic ones [15], [16]. In addition to that, more than 50% of the drugs from all existing drugs and 80% of the chemotherapeutics drugs which are approved recently are developed with the aid of bioactive constituents derived from natural sources [17]. Apart from that, seaweed-derived carrageenan, agar and alginate have a wide range of applications in the culinary, pharmaceutical, and biotechnology industries [18]. Many forms of sulfated polysaccharides derived from marine macro and micro algae have been demonstrated to be useful in the fight against some deadly disorders like cancer and AIDS as well [8]. In addition to that, marine seaweeds synthesize carotenoids with the capability of fighting against some chronic disorders like cancers and cardiovascular diseases [18]. Even more, some marine algal varieties have the ability to cure more than 80% of human diseases including chronic diseases like cancer. Some of the algal derived bioactive compounds exhibit effects of cytotoxicity by fighting against macromolecules represent by tumor cells as they are related to the oncogenic transduction pathway [19]. Moreover, almost all of the discovered marine algae represent significant number of metabolites which have the ability to fight against tumors by inhibiting the growth of human cancer cells both in vivo and in vitro models [17]. Hence, extensive researches and novel technology related to marine algae derived nanoparticles have open the way to discover therapeutics in this generation and upcoming future as well.

2. Synthesis of algal nanoparticles

The term algal nanotechnology referred to the synthesis of nanoparticles from marine algae like gold, silver, copper and zinc [3]. When considering marine algae in nanotechnology, they are known as Bio-Nano factories where they are having high capacity for metallic nanoparticle biosynthesis with the aid of either wet form or dry form pathways [14]. This algal derived nanoparticle synthesis mainly relies on three pathways including wet, dry and computational nanotechnologies [20]. Among them, dry nanotechnology deals with the principle of physiochemical generation of inorganic nanoparticles like carbon and silicon whilst wet nanotechnology deals with the nanoparticle synthesis using a biological liquid medium. In addition to that, modeling and simulation-based nanomaterial synthesis is related to the computational nanotechnology [14]. Moreover, physical aspects of those synthesized nanoparticles like shape and size also can be changed with the alteration of numerous cultivation parameters like temperature, pH, algal species and incubation time [21]. Anyway, with the help of biomolecules secreted by marine algae, they have the ability to reduce metal salts to metallic nanoparticles as well [22]. In general, marine algae biosynthesize their nanoparticles via three steps as preparation of algae extract in organic solvent or water by increasing temperature, preparation of ionic

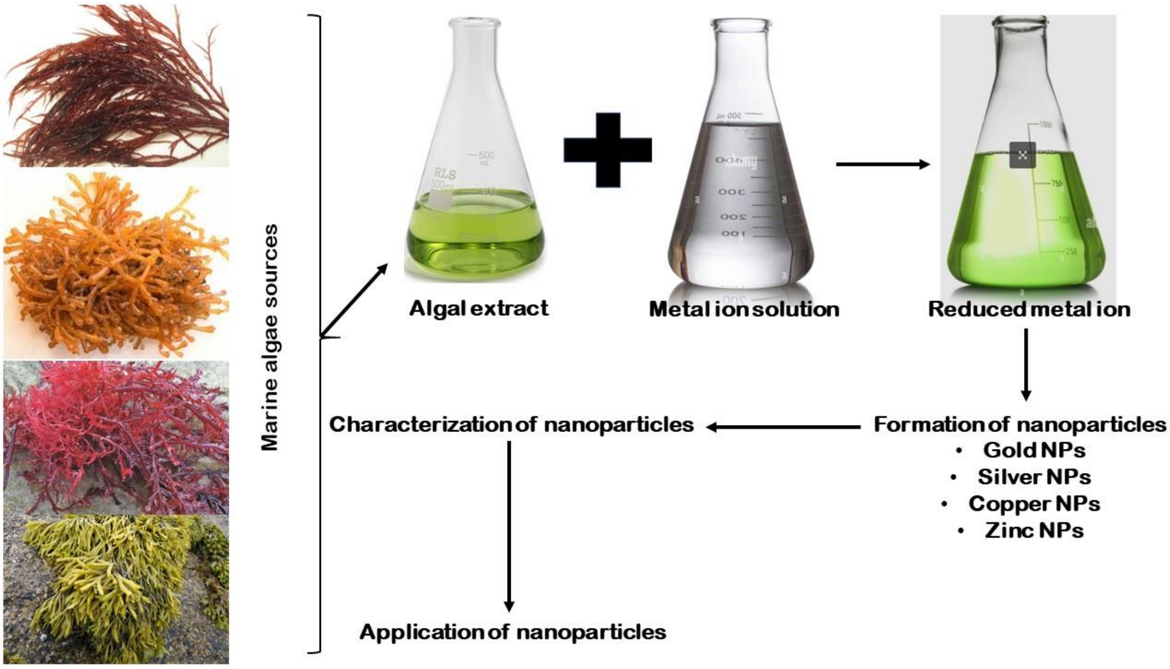

Figure 1: Common steps involved in the algal-derived nanoparticle synthesis

metal compounds using molar solutions and incubation of all these two solutions with or without stirring at certain manipulated atmosphere respectively [23] (Figure 1). Previous studies revealed that, marine algae synthesized nanoparticles either via extracellularly or intracellularly based on the algal species and the amount of metal extract doses [4]. The presence of reducing substances like pigments, peptides, polysaccharides, proteins and reducing sugars, which reduce metal ions and precipitate to metal nanoparticles within the neighboring fluid, is credited with the extracellular nanoparticle formation [24]. Moreover, blue and green algal related photosynthetic electron transport chain founded to be encompassed NADPH dependent reductase and NADPH like reducing agents in addition to the redox reactions [25]. These redox reactions are happened in the thylakoid membrane, cell membrane and inside of the cytoplasm which are identified as major participants in metallic ion reduction. For the stabilization and capping of the metal nanoparticles, contribution of the amino acid derived proteins and sulfated polysaccharides are very important [24].

Physical sizes and shapes of synthesized nanoparticles can be altered with the aid of physical and chemical parameters like pH, reducing agent concentration, temperature, exposing duration, metal type, and type of metal in the medium [25]. Alterations of these physical and chemical parameters also reduce the nanomaterial aggregation and agglomeration [20]. Moreover, extracellular nanoparticle biosynthesis also can be increased by changing pH parameters. With the enhancement of pH of the liquid medium, reducing ability of functional groups increases and thus lead to stablilize the synthesis of nanoparticles [5]. Although at much lower pH values, H+ concentrations are somewhat high. Because of that reason, the reducing power of functional groups becomes very low at that time [14]. When biosynthesis of algal nanoparticles takes place in a liquid medium, we can observe it via an indicator which shows a slight color change. Change of color into the pink, ruby red or purple represent the production of gold nanoparticles while color change to brown indicate the biosynthesis of silver nanoparticles [5]. Nanoparticle biosynthesis from marine algae, particularly algal derived metallic nanoparticles provides a sustainable and safer platform with respect to conventional agents on the basis of cytotoxicity levels. Proteins available within these algae can be used as template for the enhancement of the stability of synthesized nanoparticles which in turn lead to the enhancement of their potent to use in nanomedicine [4]. In addition to that, these seaweeds are relentlessly exposed to metal salts available in the marine water and owned a natural tendency in metal salt reduction. This ability provides significances in the synthesis of algal derived mono dispersed metal nanoparticles with respect to the synthetic surfactants [26]. When it's come to the field of algal Nano chemistry, the ease of growing and cultivation of these algae year-round in large scales is attracting its attention recently [27].

Most popular algae varieties including macro and micro algae, red algae, green algae and brown algae are able to synthesize nanoparticles naturally [28], [29]. Among them, some microalgae species like Chlorella and Chlamydomonas are discovered as ideal silver nanoparticle synthesizers after exposing to AgNO3 for about 14 days. For another type of alga Chlamydomonas sp. their nanoparticles are embedded in the outside of the cell cytoplasm because they have oxidative stress on cells and proteins during photosynthesis [11]. Apart from that, some green algae Ulva fasciata and Ulva reticulata are founded as ideal spherical silver nanoparticle synthesizers while brown algae Ulva compressa and Sargassum plagiophyllum are able to biosynthesize silver nanoparticles after exposing to AgNO3 for 15 minutes at 60 ◦C [30]. In addition to that, green alga Chlorococcum sp. is identified as a good spherical monodispersed ferrous ion nanoparticle synthesizer after exposing to FeCl2 at dark conditions for about two days [31]. Nanoparticles of hexagonal zinc oxides are synthesized by brown alga S. muticulum after the incubation of their extract with the dehydrate of zinc acetate for 3 to 4 hours at 70 ◦C [32], [3]. Some previous studies also revealed that the algal synthesized nanomaterials have the potent to utilized in enzyme immobilization processes as well. Hence, algal derived natural nanoparticles grab bulk portion in nanomedicine in recent era [33]. So, it is important to discuss different types of nanoparticles in detail to find their significant roles in the medical field.

2. 1 Metal oxide nanoparticles

Metal oxide nanoparticles are a popular type of nanoparticles that can be used in antibacterial, medicinal, and other applications [34], [35]. They exist as many types of nanoparticles like zinc nanoparticles, copper nanoparticles, silver nanoparticles and gold nanoparticles [3], [36]. They are available in a wide range of green, chemical and physical ways and the most important stockpiling in chemical or physical technology is the delicate and virulent discharge that causes environmental crises [37], [38]. The bulk of researchers focus on the science or bio elimination of metal - flecks to excite this stockpile [39], [40].

2.1.1. Zinc nanoparticles

The variety of applications for zinc oxide nanoparticles is much broader and they can act as antibacterial and antifungal assistant [39]. For instance, unique alga Sargassum muticum was used to harvest zinc oxide nanoparticles, which were found to inhibit angiogenesis in HepG2 cells when compared to apoptotic analysis [39]. The nanoparticles' compromise will be more significantly altered as a result of either active or passive shipment of medication or medication for future use. The most important and widely accepted of the three key eradication procedures for nanoparticles are unaccomplished eradication [39]. First, microbes will gradually increase the eradication, and the task should be accomplished. Following that, zinc oxide nanoparticles are obtained as a result of the zinc (II) ion choice, UV synthetic consolidated methodologies, XRD like simple approaches to evaluate the nanosized fleck. It is commonly used to validate morphologies and surfaces [23].

2.1.2. Copper nanoparticle

Copper nanoparticles are also a type of nanomaterial which is biosynthesized by marine algae with lots of medicinal values [41]. Because of that reason, lots of research were carried out by both local and foreign scientists in order to investigate novel medicinal characteristics of marine algae in advance [41], [42]. Despite being used as antimicrobial agents, copper oxide (CuO) nanoparticles perform less well than Ag and ZnO. As a consequence, greater concentration is needed to achieve the intended outcomes. However, some microorganisms are more vulnerable to CuO than Ag. In contrast to B. subtilis and B. anthracis, which were more susceptible to copper, E. coli and S. aureus were more sensitive to silver [43]. Due to the high concentration of amine and carboxyl groups in B. subtilis and B. anthracis cell walls, CuO has a significant affinity for these microbes [39]. CuO NPs produce ROS and damage membranes to show antibacterial action as well [44], [45].

2.1.3. Silver nanoparticles

Silver nanoparticles can be considered as the most engineered type of nanomaterial when talking about consumer products like detergents, textiles, disinfectants and medical devices as they owned intrinsic anti-inflammatory and antibacterial characteristics with them [27], [46], [14]. In this era, utilization of wide varieties of marine algae for the synthesis of nanoparticles have motivated young scientists to come up with novel greener approaches [22]. Research studies conducted up to date has been founded that the physical appearance of silver nanoparticles is circular in shape and reaches the size approximately about 48.59 nm and they are enriched with anti-microbial activities as well [47]. Furthermore, methyl orange photocatalytic degradation is also evaluated spectrophotometrically under obvious light enlightenment by using silver nanoparticles as a nano catalyst [39]. With the aid of novel research findings, scientists have proven the importance of silver nanoparticles in medicine and hence for the natural biosynthesis of them, algal varieties are used in large scale for clinical applications [6].

2.1.4. Gold nanoparticles

Among all the nanoparticles that can be isolated from marine algae, gold nanoparticles play a vital role in clinical applications [14]. They are widely orchestrated from them, where they represent numerous restoratively specific activities including anti-coagulant, antifouling and anti-bacterial characteristics [39]. On behalf of all existing marine algal species, Turbinaria conoides is considered to be the most noticeable source for producing gold nanoparticles [40]. These significant nanoparticles exhibit different morphologies like rectangular, round, poly-dispersed and triangular shapes. In many cases, algal derived gold nanoparticles are combined by consuming chloroauric acid as a forerunner of gold nanoparticles alongside of Turbinaria conoides [6]. Another specific alga called Laminaria japonica also explored as a unique organism in the green generation of gold nanoparticles [39]. It is also founded as a rich wellspring of different phytochemicals including peptides, polyphenols, proteins, carotenoids, nutrients and fibers. Different types of marine algae, for instance, Sargassum myriocystum, Sargassum wightii, Gelidium pusillum and Dictyota bartayresianna are also possess to have green synthesis ability of gold nanoparticles while red alga Lemanea fluviatilis is considered as the only one which is researched for the synthesis of gold nanoparticles by consuming forerunner salt named chloroauric acid [4]. Moreover, Kappaphycus alvarezii and Galaxaura elongate red algae have also been accounted for the synthesis of gold nanoparticles by using its biochemical pathways. In addition to monometallic nanoparticles, Gracilaria edulis a red alga efficiently synthesized bimetallic silver and gold nanoparticles by utilizing a variety of molar proportions of $AgNO_3$ and $HAuCl_4$ [48]. These orchestrated algal bimetallic nanoparticles have represented strong anti-cancer characteristics against MCF-7/breast cancer cells [49], [50]. These algal-mediated biosynthesis of gold nanoparticles also can be utilized for anti-cancer, antioxidant, biocompatibility, and antibacterial studies [51]. These algal derived gold nanoparticles are representing ideal results that encompass solid evidences which are required for the upcoming experiments in the discovery of novel therapeutic drugs [52], [53].

3. Potential health benefits of algal-derived nanoparticles in medicine (Figure 2)

When considering secondary metabolites like minerals, lipids, proteins, fatty acids, fiber, vitamins, polysaccharides and several essential amino acids, they all can be found within various algae found in marine water bodies [54], [55]. Many bioactive compounds found in marine algae have been discovered to have a variety of pharmacological effects, including anticancer, anti-diabetic, anti-inflammatory, anti-microbial and anti-oxidant activities with them [56], [57], [58]. Cyanobacteria like marine blue-green algae are one of the species that have the potential to be one of the richest sources of recognized and novel bioactive constituents including toxins with medicinal applications [59], [60].

3.1. Antimicrobial effects

Almost all of the discovered marine algae are founded to be with the ability of anti-fungal, antibacterial and anti-viral effects [29], [61]. As some evidences revealed, algal-derived silver nanoparticles were tested against some pathogenic microbes including Bacillus subtilis, Vibrio cholera, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, and Micrococcus luteus by taking streptomycin antibiotic as the standard [24] and it is founded that those silver nanoparticles are enriched with ideal to antibacterial effects against all tested bacterial strains compared to the standard. The biological production of algal silver nanoparticles is a quick and easy way to make nanoparticles with tunable optical characteristics controlled by particle size [57], [62], [63]. Apart from that, copper oxide nanoparticles also identified as an ideal nanomaterial composed with anti-microbial activity [24]. Those nanoparticles are also having the ability to inhibit pathogenic bacterial growth as well [44]. The antibacterial impact of the solution made up of nanosized silver colloidal against pathogenic microorganisms was investigated and at the same time, it was discovered that the silver nanoparticles have a high efficacy as a strong antimicrobial agent, which could be used in the food, cosmetics, and pharmaceutical industries [36], [64], [65].

3.2. Antioxidant effects

Seaweeds contain a variety of secondary metabolites with strong radical scavenging activity and could thus be used as an antioxidant source [10], [66], [67]. Syringodium isoetifolium has been founded to be composed with a variety of phytochemical ingredients, including glycosides, resin, saponins, reducing sugars, acidic chemicals, alkaloids and cardiac glycosides, one of which may have antioxidant properties [68], [55]. Syringodium isoetifolium, discovered that this alga owned unique biochemicals with antioxidant properties including sucrose, decane, phytol, hexadecenoic acid, 9,12,15 octadecatrienoic acid, Triethylene glycol monododecyl ether, and 2- hydroxy-1 ethyl ester after conducting GC-MS experiments [68]. In addition to that, a smaller amount of algal derived silver nanoparticles can generate huge level of hydrogen peroxide(H2O2) and they are capable of inducing the formation of the inflammasome in high content. In addition to that, DPPH agitator lurk assay was used to assess the antioxidant activity of bio derived silver nanoparticles [69]. Then the absorption quality of DPPH at 517 nm was degraded by the idle agitator stirring action of silver nanosized particles [30].

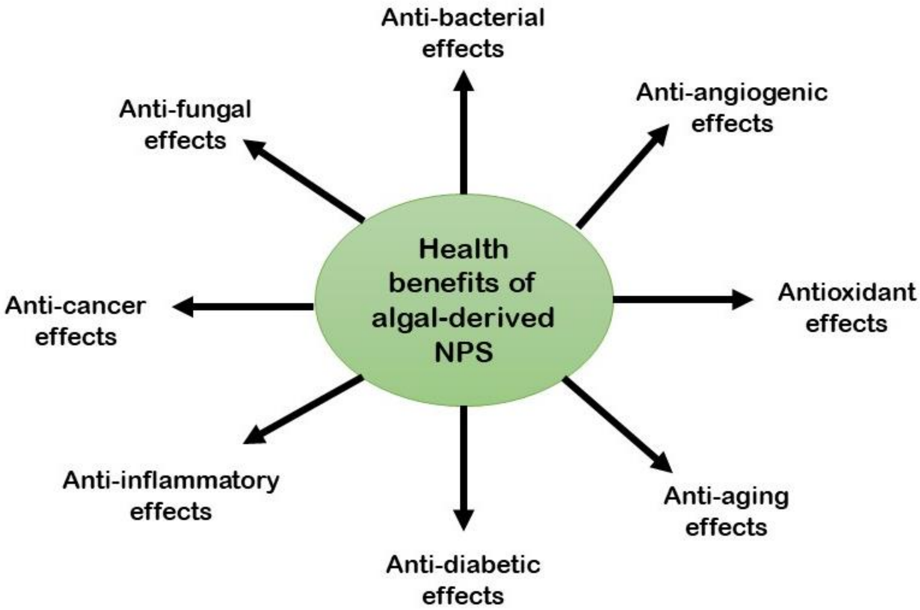

Figure 2: Applications of algal-derived NPs

3.3. Anti-diabetic effects

Because of the presence of bioactive substances such as those indicated above, the antidiabetic activity of oceanic macro and microalgae has been extensively researched in recent years [4], [64]. In vitro antidiabetic action and the in vivo antidiabetic potential of marine brown algae was assessed using animal models to confirm the hypoglycemic effect via various routes [33]. Because of the presence of different nanoparticles, brown seaweeds have been reported to have antidiabetic activities primarily through the inhibitory action of alpha-amylase [70]. Furthermore, when compared to the reference medication acarbose, phlorofucofuroeckol-A and dieckol were found to be the most effective inhibitors of the alpha-glucosidase enzyme among the isolated phlorotannins [64]. When compared to the phloroglucinol, the phlorotannin eckol isolated from Ecklonia maximum had the most potent alpha-glucosidase inhibitory action [71]. Fucofuroeckol-A and dioxinodehydroeckol, both isolated from Ecklonia bicyclis, were found to inhibit the enzymes alpha-amylase and beta glucosidase. Furthermore, isolated phlorotannins and dieckol significantly reduced postprandial blood glucose levels in both normal and diabetes-induced mice [64].

3.4. Anti-cancer effects

Through its cytotoxicity or apoptosis-inducing capabilities, an ideal anticancer drug should be able to inhibit, postpone, or reverse cancer progression [6]. More than half of marine cyanobacteria can be used to extract bioactive compounds that can kill cancer cells by triggering apoptosis or influence cell signaling by activating members of the protein kinase-c family of signaling enzymes [51], [28]. Scytonemin is a yellow-green UV sunscreen pigment derived from the cyanobacterium Stigonema sp. It is found in the extracellular sheaths of many genera of aquatic and terrestrial blue-green algae [37]. Scytonemin suppresses the proliferation of human fibroblasts and endothelial cells through regulating mitotic spindle formation and enzyme kinases involved in cell cycle control [13]. In addition to that, several studies have previously described the use of gold nanoparticles in the effective delivery of chemotherapeutic anticancer medications such as paclitaxel, capecitabine and tamoxifen with the findings indicating that conjugating paclitaxel with gold nanoparticles increased its lethal effects [40]. Some previous studies show G. edulis and G. gracilis algae synthesize zinc oxide nanoparticles with ideal anti-cancer effects [32], [55], [65], [72]. Gallan gum cytotoxicity was reduced sophorolipid-attached gold nanoparticles in glioma cell line LN-229 and glioma stem cell line HNGC-2 when further conjugated with doxorubicin, according to another study [40]. A series of preclinical studies were conducted to understand the role of diosgenin as a therapeutic agent against various types of malignancies. Diosgenin has been shown to cause alterations in lipoxygenase activity in human erythroleukemia cells, supporting the idea that diosgenin can be used to efficiently target cancer cells [40]. Furthermore, research into the route of action of diosgenin in the DU145 human prostate cancer cell line revealed that cells treated with diosgenin had much higher expression of the Capase 9 protein. By limiting the signaling pathways, diosgenin was resulting in autophagy and apoptosis in tumor cell lines [73], [74].

4. Clinical applications of algal derived nanoparticles

Algae have been shown to produce chemicals that protect nerve cells, reducing the progression of neurodegenerative disorders including Parkinson's and Alzheimer's [35], [75]. Among those algal varieties, Spirulina maxima has been shown to lower oxidative stress and protect against neurotoxicity caused by 1-methyl-4-phenyl-1,2,3,6, tetrahydropyridine. When considering nanomaterials, cytotoxicity is a key concern [76]. Conjugates of drug and gold nanoparticles can be made by encapsulating the drug in gold nanoparticles or attaching it to the surface of modified gold nanoparticles [40]. Gold nanoparticles usually have high conductivity and are extremely sensitive to metal surface absorption. As a result, they are frequently linked to a variety of helpful therapeutic applications, such as biosensing, imaging, drug administration, wound healing, cancer, and microbial therapy [61], [77], [78]. In addition to that, gold nanoparticles are employed in a wide range of consumer products, including cosmetics, electronics, textiles, and food products, due to their effective antibacterial qualities [79]. Apart from that, topical ointments or implants impregnated with gold polymers were developed to prevent infections of burned and injured areas since they have been shown to cause bacterial cell membrane lysis [80]. Furthermore, if biosynthesized nanoparticles can evade the immune system by overcoming biological barriers and the complicated tumor microenvironment, they can be exploited as effective regulated and disease-targeted drug delivery vehicles.

Table 1 – Marine algal NPs and their potential benefits in medicine

Nanoparticle	***Name of the alga***	***Algal group***	***Clinical significances***	***References***
Silver NPs	*Ulva fasciata*	Green alga	Anti-bacterial, antioxidant effects	[30]
Silver NPs	*Ulva reticulata*	Green alga	Anti-bacterial, antioxidant effects	[30]
Silver NPs	*Ulva compressa*	Brown alga	Anti-bacterial, antioxidant effects	[30]
Silver NPs	*Sargassum plagiophyllum*	Brown alga	Anti-bacterial, antioxidant effects	[30]
Ferrous ion NPs	*Chlorococcum sp.*	Green alga	Anti-bacterial, antioxidant effects	[31]
Zinc NPs	*S. muticulum*	Brown alga	Antibacterial, antifucgal, anti-angiogenesis effects	[39]
Gold NPs	*Laminaria japonica*	Green alga	Anti-coagulant, anti-bacterial and antifouling effects	[39]
Gold NPs	*Sargassum myriocystum,*	Green alga	Anti-coagulant, anti-bacterial and antifouling effects	[4]
Gold NPs	*Sargassum wightii*	Green alga	Anti-coagulant, anti-bacterial and antifouling effects	[4]
Gold NPs	*Gelidium pusillum*	Green alga	Anti-coagulant, anti-bacterial and antifouling effects	[4]
Gold NPs	*Dictyota bartayresianna*	Green alga	Anti-coagulant, anti-bacterial and antifouling effects	[4]
Gold NPs	*Lemanea fluviatilis*	Red alga	Anti-coagulant, anti-bacterial and antifouling effects	[4]
Gold NPs	*Kappaphycus alvarezii*	Red alga	Anti-coagulant, anti-bacterial and antifouling effects	[48]
Gold NPs	*Galaxaura elongate*	Red alga	Anti-coagulant, anti-bacterial and antifouling effects	[48]
Gold, zinc and silver NPs	*Gracilaria edulis*	Red alga	Anti-coagulant, anti-bacterial and antifouling, anti-diabetic, anti-cancer effects	[48]
Gold, zinc and silver NPs	*Ecklonia maximum*	Brown alga	Anti-diabetic effect	[71]
Gold, zinc and silver NPs	*Ecklonia bicyclis*	Brown alga	Anti-diabetic effect	[62]
Gold, zinc and silver NPs	*Ecklonia cava*	Brown alga	Anti-bacterial effects	[62]
Gold, zinc and silver NPs	*Gracilaria gracilis*	Red alga	Anti-cancer effects	[62]
Gold NPs	*Hypnea musciformis*	Red alga	Anti-fungal effects	[62]

Furthermore, several researchers have founded that spherical nanoparticles are better for biomedical purposes as well. (Chakraborty et al., 2009). Furthermore, some scientists demonstrated that nanoparticles synthesized by extracts from the brown seaweed Ecklonia cava elicit a significant anti-bacterial activity against Escherichia coli and Staphylococcus aureus, as well as an efficient antioxidant activity in vitro and an anti-cancer activity against human cervical (HeLa) cells through an apoptosis mediated mechanism [19], [55]. Given the widespread usage of nanoparticles in medicine, toxicity testing is a significant consideration. The cytotoxicity of these nanoparticles is linked to the easy oxidation of gold nanoparticles to Ag^+ ions, which are extremely poisonous to biological systems and cellular components, regardless of their surface coating [81]. In addition to that, gold nanoparticles are ideal for biomedical instruments for use in radiology as a radiation enhancer, targeted medication delivery, biosensing, cancer diagnostics, and cancer therapy using hyperthermal treatment [21]. The ability to produce particles with controlled form, monodispersity, size, stability, and chemical composition is critical for gold nanoparticles to be used in these applications. Due to their extremely small diameter, they may be easily manufactured using a variety of processes and hence can be quickly transmitted to tissues and cells, exactly like DNA and proteins [4]. For instance, some studies demonstrated that gold nanoparticles produced by the red macroalgae Hypnea musciformis, causes enormous floating blooms, can inhibit Aspergillus niger and Mucor spp [4]. Unlike silver nanoparticles, which have sparked a lot of interest as antimicrobials, gold nanoparticles have mostly contributed to a new field of research and cancer nanomedicine. This is due to the fact that, in comparison to typical anti-cancer medications nanoparticles offer a tailored strategy that avoids side effects [37]. Although the majority of in-vitro studies have shown that nanoparticles are non-toxic to cells, their cytotoxicity is dependent on their absorption and intracellular distribution, which is dependent on the size and shape of them as well as the ligands surrounding them. Furthermore, several researchers have founded that spherical nanoparticles are better for biomedical purposes as well [59].

Future prospectives and challenges

The use of algal nanotechnology to increase the accumulation of secondary metabolites and biomolecules is an appealing alternative for pharmaceutical companies who looking to expand their output [29]. As magnetic nanoparticles can clog, they may be able to minimize the high cost of algae harvesting [20]. Algal harvesting, which comprises sedimentation, centrifugation, and filtering, currently accounts for almost 20–30% of overall algae production costs [24]. This inhibits algae's capacity to be used as raw materials for high-value-added products with low volume requirements but great economic worth. The addition of nanotechnology will allow algae to transition from a niche raw resource to a less expensive pharmaceutical alternative [18]. Because nanoparticles have a beneficial effect on algae, future research should concentrate on commercializing algal nanotechnology. Apart from that, algae's ability to recycle anthropogenic CO2, wastewater, and sunlight into beneficial metabolites, combined with accelerated growth owing to nanoparticles, can be regarded a likely and practical solution to some of the world's most important concerns, such as global warming, climate change, and hunger [22]. Aside from that, because of their potential human applications, nanoparticles made from algae must be closely monitored in terms of sustainability and safety. The mechanism of algal nanoparticle synthesis has to be investigated further using a different algal source that has yet to be investigated. Aside from the synthesis, numerous hurdles must be overcome before nanoparticles generated by algae can be used [68]. Furthermore, biosynthesized nanoparticles have a wide range of forms and size features. As a result, a deeper grasp of the biosynthesis process is required [11]. Moreover, the production of nanoparticles involves a mechanism that is still in its infancy. The biosynthesis of nanoparticles is often slow, necessitating parameter tuning to speed up the process [18]. Aside from these challenges, as algae is a natural source of nanoparticles, there will be multiple variations in the same species as the location and surrounding environment change [17]. With the same species and identical operational conditions, there are variances in various batches. As a result, identifying the biomolecules involved in the production of nanoparticles is critical for commercialization [82]. In addition to that, majority of the research is done in the lab or on a small scale, and further scaling up is critical for algae nanotechnology to succeed. Nanoparticle producing enzymes and routes can only be determined with a lot of investigation and for commercialization, a low-cost and simple synthesis process must be devised [83]. These protocols must be implemented to synthesize other nanoparticles such as sulfides, carbides, metal oxides, and nitrides, as current algal nanoparticle production is confined to metals [4]. Finally, nanotechnology has enormous promise in the fields of human medicine, necessitating substantial research in the fields of pharmaceuticals in order to get public approval.

5. Conclusion

Chlorophyta, Rhodophyta, and Phaoephyta are a few examples of marine algae whose nanoparticles can be used to make dependable medicinal applications in this era. Algal-derived nanoparticles have been used by scientists in the treatment of widespread illnesses, medication transport methods, antibacterial agents, biosensors, and cancer treatments. Since biosynthesis is more affordable, ecologically friendly, and adaptable than traditional techniques, it is thought to be better at creating nanoparticles. The use of nanoparticles in health is not new. Over the past few years, the use of nanoparticles in health has gradually increased. The holes in the existing corpus of research will be filled by studying the toxicity associated with them. Even though there has been extensive study on this topic, there are still discrepancies in the results and no recognized global standards for the toxicity of nanoparticles, which need to be swiftly addressed before they can be applied in practical settings. Despite these challenges, it is expected that researchers will make progress in creating algal-derived nanoparticles for practical uses in future medicine.

Conflict of interest

"The authors declare no conflict of interest".

References

1. Rizki, I. N., Klaypradit, W., & Patmawati. (2023). Utilization of marine organisms for the green synthesis of silver and gold nanoparticles and their applications: A review. Sustainable Chemistry and Pharmacy, 31. https://doi.org/10.1016/j.scp.2022.100888
2. Pikula, K., Kirichenko, K., Chernousov, V., Parshin, S., Masyutin, A., Parshina, Y., Pogodaev, A., Gridasov, A., Tsatsakis, A., & Golokhvast, K. (2023). The Impact of Metal-Based Nanoparticles Produced by Different Types of Underwater Welding on Marine Microalgae. Toxics, 11(2), 105. https://doi.org/10.3390/toxics11020105
3. Asif, A., Kasim, N. H. A., Amir, M. K., Shamsuddin, M. R., & Ismail, M. H. (2021). A review on marine algae's nanoparticle-mediated synthesis and its potential applications. Arabian Journal of Chemistry, 14(12), 103387. https://doi.org/10.1016/j.arabjc.2021.103387
4. Uzair, B., Liaqat, A., Iqbal, H., Shahzadi, T., & Khan, M. A. (2020). Green and cost-effective synthesis of metallic nanoparticles by algae: Safe methods for translational medicine. Bioengineering, 7(4), 129. https://doi.org/10.3390/bioengineering7040129
5. Merin, D. D., Prakash, S., & Bhimba, B. V. (2010). Antibacterial screening of silver nanoparticles synthesized by marine microalgae. Asian Pacific Journal of Tropical Medicine, 3(10), 797-799. https://doi.org/10.1016/S1995-7645(10)60191-5
6. Viswanathan, S., Palaniyandi, T., Chellam, D. C., Ahmed, M. F., Shoban, N., Pushpakumar, M., Abdul Wahab, M. R., Baskar, G., Ravi, M., Sivaji, A., Natarajan, S., & Sankareswaran, S. K. (2023). Anti-cancer activity of Hypnea valentiae seaweed loaded gold nanoparticles through EMT signaling pathway in A549 cells. Biochemical Systematics and Ecology, 107, 104606. https://doi.org/10.1016/j.bse.2023.104606
7. Sithranga Boopathy, N., & Kathiresan, K. (2010). Anticancer drugs from marine flora: An overview. Journal of Oncology, 2010, 214812. https://doi.org/10.1155/2010/214812
8. Ibañez, E., & Cifuentes, A. (2013). Benefits of using algae as natural sources of functional ingredients. Journal of the Science of Food and Agriculture, 93(4), 703-709. https://doi.org/10.1002/jsfa.6023
9. Grey, I., Arora, T., Thomas, J., Saneh, A., Tohme, P., & Abi-habib, R. (2020). Co-transesterification of waste cooking oil, algal oil and dimethyl carbonate over sustainable nanoparticle catalysts. Psychiatry Research, 293, 113354. https://doi.org/10.1016/j.psychres.2020.113354
10. Alekseyenko, T. V., Zhanayeva, S. Y., Venediktova, A. A., & Zvyagintseva, T. N. (2007). Antioxidant activity of sulfated polysaccharides from the seagrass Zostera marina. Chem Nat Compd, 43, 329-331. https://doi.org/10.1007/s10600-007-0112-2
11. Gerwick, W. H., & Fenner, A. M. (2013). Drug Discovery from Marine Microbes. Microbial Ecology, 65(4), 800-806. https://doi.org/10.1007/s00248-012-0181-4
12. Ouyang, Y., Qiu, Y., Liu, Y., Zhang, M., & Chen, J. (2021). Cancer-fighting potentials of algal polysaccharides as nutraceuticals. Food Research International, 147, 110522. https://doi.org/10.1016/j.foodres.2021.110522
13. Dongare, P. N., Motule, A. S., More, M. P., & Kadam, P. V. (2021). World Journal of Pharmaceutical Research. World Journal of Pharmaceutical Research, 10(1), 950-956. https://doi.org/10.20959/wjpr20211-19566

14. Castro, L., Blázquez, M. L., Muñoz, J. A., González, F., & Ballester, A. (2013). Biological synthesis of metallic nanoparticles using algae. IET Nanobiotechnology, 7(3), 109-116. https://doi.org/10.1049/iet-nbt.2012.0041
15. Kushwaha, S. K. S., Rastogi, A., Rai, A. K., & Singh, S. (2012). Novel drug delivery system for anticancer drug: A review. International Journal of PharmTech Research, 4(2), 542-553.
16. Harvey, A. L. (2008). Natural products in drug discovery. Drug Discovery Today, 13(19-20), 894-901. https://doi.org/10.1016/j.drudis.2008.07.004
17. Saeidnia, S. (2015). New Approaches to Natural Anticancer Drugs. In R. Atta-ur (Ed.), Studies in Natural Products Chemistry (pp. 159-180). Elsevier. https://doi.org/10.1016/B978-0-444-63299-9.00006-3
18. Li, Y. X., Himaya, S. W. A., & Kim, S. K. (2013). Triterpenoids of marine origin as anti-cancer agents. Molecules, 18(7), 7886-7909. https://doi.org/10.3390/molecules18077886
19. Moghadamtousi, S. Z., Karimian, H., Khanabdali, R., Razavi, M., Firoozinia, M., Zandi, K., & Abdul Kadir, H. (2014). Anticancer and antitumor potential of fucoidan and fucoxanthin, two main metabolites isolated from brown algae. Scientific World Journal, 2014, 768323. https://doi.org/10.1155/2014/768323
20. Navarro, E., Baun, A., Behra, R., Hartmann, N. B., Filser, J., Miao, A. J., Quigg, A., Santschi, P. H., & Sigg, L. (2008). Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants, and fungi. Ecotoxicology, 17(5), 372-386. https://doi.org/10.1007/s10646-008-0214-0
21. Jacob, J. M., Ravindran, R., Narayanan, M., Ranganathan, B., Samuel, M. S., & Pugazhendhi, A. (2021). Microalgae: A prospective low-cost green alternative for nanoparticle synthesis. Current Opinion in Environmental Science & Health, 20, 100229. https://doi.org/10.1016/j.coesh.2021.100229
22. Zhang, C., Show, P., Ho, S. (2019). Bioresource Technology Progress and perspective on algal plastics– A critical review. Bioresource Technology, 289, 121700. https://doi.org/10.1016/j.biortech.2019.121700
23. Taherzadeh Soureshjani, P., Shadi, A., & Mohammadsaleh, F. (2021). Algae-mediated route to biogenic cuprous oxide nanoparticles and spindle-like CaCO3: a comparative study, facile synthesis, and biological properties. RSC Advances, 11, 10599-10609. https://doi.org/10.1039/d1ra00187
24. Siddiqi, K. S., & Husen, A. (2020). Current status of plant metabolite-based fabrication of copper/copper oxide nanoparticles and their applications: A review. Biomaterials Research, 24(1), 15. https://doi.org/10.1186/s40824-020-00192-4
25. Chen, F., Xiao, Z., Yue, L., & Zhang, X. (2019). Algae response to engineered nanoparticles: Current understanding, mechanisms and implications. Environmental Science: Nano, 6(4), 1026-1042. https://doi.org/10.1039/C9EN00059A
26. Bhakya, S., Muthukrishnan, S., Sukumaran, M., & Muthukumar, M. (2016). Biogenic synthesis of silver nanoparticles and their antioxidant and antibacterial activity. Applied Nanoscience, 6, 755-766. https://doi.org/10.1007/s13204-015-0461-3
27. Yan, N., & Wang, W. X. (2021). Novel Imaging of Silver Nanoparticle Uptake by a Unicellular Alga and Trophic Transfer to Daphnia magna. Environmental Science & Technology, 55(8), 5143-5151. https://doi.org/10.1021/acs.est.0c08588
28. Pratt, C. M. (1988). Asymptomatic ventricular arrhythmias in patients with obstructive lung disease. Should they be treated? Chest, 94(2), 219-225. https://doi.org/10.1378/chest.94.2.219
29. Koyande, A. K., Chew, K. W., Manickam, S., Chang, J. S., Lakshmanan, M., & Show, P. L. (2021). Emerging algal nanotechnology for high-value compounds: A direction to future food production. Trends in Food Science & Technology, 116, 290-302. https://doi.org/10.1016/j.tifs.2021.07.022
30. Venkatesan, J., Kim, S. K., & Shim, M. S. (2016). Antimicrobial, antioxidant, and anticancer activities of biosynthesized silver nanoparticles using marine algae Ecklonia cava. Nanomaterials, 6(12), 235. https://doi.org/10.3390/nano6120235
31. Folmer, F., Jaspars, M., Dicato, M., & Diederich, M. (2010). Photosynthetic marine organisms as a source of anticancer compounds. Phytochemistry Reviews, 9(4), 557-579. https://doi.org/10.1007/s11101-010-9183-5

32. Priyadharshini, R. I., Prasannaraj, G., Geetha, N., & Venkatachalam, P. (2014). Microwave-Mediated extracellular Synthesis of Metallic Silver and Zinc Oxide Nanoparticles Using Macro Algae (Gracilaria edulis) Extracts and Its Anticancer Activity Against Human PC3 Cell Lines. Applied Biochemistry and Biotechnology, 174, 2777-2790. https://doi.org/10.1007/s12010-014-1225-3

33. Etman, S. M., Elnaggar, Y. S. R., & Abdallah, O. Y. (2020). Fucoidan, a natural biopolymer in cancer combating: From edible algae to nanocarrier tailoring. International Journal of Biological Macromolecules, 147, 799-808. https://doi.org/10.1016/j.ijbiomac.2019.10.106

34. Yacoob, M., Ali, S., Anuradha, V., Mohanan, S. V., Ameen, F., & Al-Nahdi, N. (2017). Green synthesis of copper oxide nanoparticles and its effective applications in curing fungal and bacterial infections. NanoWorld Journal, 6(2), 61-67. https://doi.org/10.17756/nwj.2017-049

35. Javed, F., Qadir, M. I., Janbaz, K. H., & Ali, M. (2011). Novel drugs from marine microorganisms. Critical Reviews in Microbiology, 37(3), 245-249. https://doi.org/10.3109/1040841X.2011.560328

36. Konishi, Y., Ohno, K., Saitoh, N., Nomura, T., Nagamine, S., Hishinuma, T., & Takahashi, Y. (2007). Bioreductive deposition of platinum nanoparticles on the bacterium Shewanella algae. Journal of Biotechnology, 128(3), 648-653. https://doi.org/10.1016/j.jbiotec.2006.11.014

37. Gupta, A. P., Pandotra, P., Sharma, R., Kushwaha, M., Gupta, S., & Dhar, J. K. (2013). Marine resource: A promising future for anticancer drugs. In R. Atta-ur (Ed.), Studies in Natural Products Chemistry (pp. 229-325). Elsevier. https://doi.org/10.1016/B978-0-444-59574-4.00006-9

38. Fawcett, D., Verduin, J. J., Shah, M., & Banfield, J. F. (2017). A Review of Current Research into the Biogenic Synthesis of Metal and Metal Oxide Nanoparticles via Marine Algae and Seagrasses. Journal of Nanoscience, 2017, 8013850. https://doi.org/10.1155/2017/8013850

39. Alnadhari, S., Alhajji, E., & Alfadly, S. (2021). Biosynthesis and effects of copper nanoparticles on plants. Environmental Chemistry Letters, 19, 165-171. https://doi.org/10.1007/s10311-020-01082-7

40. Jabeen, S., Iqbal, M., Faisal, A., Imran, M., & Sajjad, S. (2021). Synthesis of diosgenin conjugated gold nanoparticles using algal extract of Dictyosphaerium sp. and in-vitro application of their antiproliferative activities. Materials Today Communications, 27, 102360. https://doi.org/10.1016/j.mtcomm.2021.102360

41. Araya-Castro, K., del Pilar Díaz-Contreras, M., & Acuña, E. (2021). Marine algae as a source of novel bioactive compounds with potential therapeutic applications. In M. G. Rasteiro, & F. G. Araújo (Eds.), Marine Algae: Biodiversity, Taxonomy, Environmental Assessment, and Biotechnology (pp. 157-175). Nova Science Publishers.

42. Ramaswamy, S. V. P., Narendhran, S., & Sivaraj, R. (2016). Potentiating effect of ecofriendly synthesis of copper oxide nanoparticles using brown alga: Antimicrobial and anticancer activities. Bulletin of Materials Science, 39, 361-364. https://doi.org/10.1007/s12034-016-1173-3

43. Jayakumarai, G., Gokulpriya, C., Sudhapriya, R., & Venkatachalam, P. (2015). Phytofabrication and characterization of monodisperse copper oxide nanoparticles using Albizia lebbeck leaf extract. Applied Nanoscience, 5, 1017-1021. https://doi.org/10.1007/s13204-015-0402-1

44. Kasana, R. C., Panwar, N. R., Kaul, R. K., & Kumar, P. (2017). Synthesis, characterization and biological activity of copper oxide nanoparticles. Environmental Chemistry Letters, 15(2), 233-240. https://doi.org/10.1007/s10311-017-0612-5

45. Jillani, S., Jelani, M., Hassan, N. U., Ali, S., & Shah, M. (2018). Synthesis, characterization and biological studies of copper oxide nanostructures. Materials Research Express, 5, 034001. https://doi.org/10.1088/2053-1591/aab864

46. Xiong, S., Cao, X., Fang, H., & Liu, Y. (2021). Formation of silver nanoparticles in aquatic environments facilitated by algal extracellular polymeric substances: Importance of chloride ions and light. Science of the Total Environment, 775, 145867. https://doi.org/10.1016/j.scitotenv.2021.145867

47. Nallamuthu, T., Venkatalakshmi, R. P., Chinnasamy, A., & Kannaiyan, P. (2012). Synthesis of silver nanoparticles and the antibacterial and anticancer activities of the crude extract of Sargassum polycystum C. Agardh. Nano Biomedicine and Engineering, 4(2), 89-94. https://doi.org/10.5101/nbe.v4i2.p89-94

48. Prasad, T. N. V. K. V., Kambala, V. S. R., & Naidu, R. (2013). Phyconanotechnology: Synthesis of silver nanoparticles using brown marine algae Cystophora moniliformis and their characterization. Journal of Applied Phycology, 25(1), 177-182. https://doi.org/10.1007/s10811-012-9851-z

49. Manikandan, S., & Krishnan, M. (2016). Green synthesis of silver nanoparticles using Piper nigrum concoction and its anticancer activity against MCF-7 and Hep-2 cell lines. Journal of Antimicrobial Agents, 2, 123. https://doi.org/10.4172/2472-1212.1000123

50. Moshfegh, A., Jalali, A., Salehzadeh, A., & Jozani, A. S. (2019). Biological synthesis of silver nanoparticles by cell-free extract of Polysiphonia algae and their anticancer activity against breast cancer MCF-7 cell lines. Micro & Nano Letters, 14(6), 581-584. https://doi.org/10.1049/mnl.2018.5260

51. Kiruba, N. J. M., Pradeep, M. A., & Thatheyus, A. J. (2018). Discovering promising anti-cancer drug candidates from marine algae. Science International, 6(2), 44-50. https://doi.org/10.17311/sciintl.2018.44.50

52. Govindaraj, M., Suresh, M., Palaniyandi, T., Viswanathan, S., Wahab, M. R. A., Baskar, G., Surendran, H., Ravi, M., & Sivaji, A. (2023). Bio-fabrication of gold nanoparticles from brown seaweeds for anticancer activity against glioblastoma through in vitro and molecular docking approaches. Journal of Molecular Structure, 1281, 135178. https://doi.org/10.1016/j.molstruc.2023.135178

53. Naveenkumar, S., Kamaraj, C., Ragavendran, C., Vaithiyalingam, M., Sugumar, V., & Marimuthu, K. (2023). Gracilaria corticata red seaweed mediate biosynthesis of silver nanoparticles: larvicidal, neurotoxicity, molecular docking analysis, and ecofriendly approach. Biomass Conversion and Biorefinery. https://doi.org/10.1007/s13399-023-04026-x

54. Donaldson, M. S. (2004). Nutrition and cancer: A review of the evidence for an anti-cancer diet. Nutrition Journal, 3(1), 19. https://doi.org/10.1186/1475-2891-3-19

55. Gamal, A. A. E. (2010). Biological importance of marine algae. Saudi Pharmaceutical Journal, 18(1), 1-25. https://doi.org/10.1016/j.jsps.2009.12.001

56. Martínez Andrade, K. A., Lauritano, C., Romano, G., & Ianora, A. (2018). Marine microalgae with anticancer properties. Marine Drugs, 16(5), 165. https://doi.org/10.3390/md16050165

57. Abd-Elnaby, H. M., Abo-Elala, G. M., Abdel-Raouf, U. M., & Hamed, M. M. (2016). Antibacterial and anticancer activity of extracellular synthesized silver nanoparticles from marine Streptomyces rochei MHM13. Egyptian Journal of Aquatic Research, 42(3), 301-312. https://doi.org/10.1016/j.ejar.2016.05.004

58. Badr, Y. M., Almeer, R., Alarifi, S., Fawzy, M., & Ibrahim, S. (2023). Algae-mediated synthesis of silver nanoparticles: Assessment of antibacterial, cytotoxic, and wound healing activities. Materials Science and Engineering: C, 124, 112056. https://doi.org/10.1016/j.msec.2021.112056

59. Chakraborty, C., Hsu, C. H., Wen, Z. H., & Lin, C. S. (2009). Anticancer drugs discovery and development from marine organisms. Current Topics in Medicinal Chemistry, 9(16), 1536-1545. https://doi.org/10.2174/156802609789909783

60. Subhashini, G., Ruban, P., & Daniel, T. (2018). Biosynthesis and characterization of Magnetic (Fe3O4) Iron oxide nanoparticles from a red seaweed Gracilaria edulis and its antimicrobial activity. International Journal of Advanced Science Research and Management, 3(4), 184-189. https://doi.org/10.5281/zenodo.1236911

61. Capillo, G., Savoca, S., Costa, R., Branca, C., D'Angelo, V., Vella, A., Pittalà, V., Leone, R., & Ferrante, M. (2018). New insights into the culture method and antibacterial potential of Gracilaria gracilis. Marine Drugs, 16(12), 492. https://doi.org/10.3390/md16120492

62. Gunathilaka, T. L., Samarakoon, K., Ranasinghe, P., & Peiris, L. D. C. (2020). Antidiabetic potential of marine brown algae - A mini-review. Journal of Diabetes Research, 2020, 1230218. https://doi.org/10.1155/2020/1230218

63. Krishnamoorthy, S., Zait, N. N., Nasir, A. M., Ishar, S. M., Hamzah, N. H., Rus Din, R. D., & Osman, K. (2023). Towards development of green nanoparticles in applied health application: A mini review. Materials Today: Proceedings. https://doi.org/10.1016/j.matpr.2023.02.022

64. Gunathilaka, T. L., Samarakoon, K. W., Ranasinghe, P., & Peiris, L. D. C. (2019). In-vitro antioxidant, hypoglycemic activity, and identification of bioactive compounds in phenol-rich extract from the marine red algae Gracilaria edulis (Gmelin) Silva. Molecules, 24(20), 3708. https://doi.org/10.3390/molecules24203708
65. Mohamed, A., Gowdhami, B., Jabbir, M. S. M., Anbu, S., Arun, M., Gopinath, P., Ganesan, S., Raja, R. B., & Rajarajan, S. (2019). Anticancer potential of zinc oxide nanoparticles against cervical carcinoma cells synthesized via biogenic route using aqueous extract of Gracilaria edulis. Materials Science and Engineering: C, 103, 109840. https://doi.org/10.1016/j.msec.2019.109840
66. Abirami, R. G., & Kowsalya, S. (2017). Quantification and correlation study on derived phenols and antioxidant activity of seaweeds from Gulf of Mannar. Journal of Herbs, Spices & Medicinal Plants, 23(1), 9-17. https://doi.org/10.1080/10496475.2016.1240132
67. Mohamed, A. R., Gowdhami, B., Jabbir, M. S. M., Anbu, S., Arun, M., Gopinath, P., Ganesan, S., Raja, R. B., & Rajarajan, S. (2019a). Anticancer potential of zinc oxide nanoparticles against cervical carcinoma cells synthesized via biogenic route using aqueous extract of Gracilaria edulis. Materials Science and Engineering: C, 103, 109840. https://doi.org/10.1016/j.msec.2019.109840
68. Jayaprakash, J., & Ragunathan, M. (2021). In vitro anti-oxidant and anti-cancer efficacy of silver nanoparticles synthesized from the seaweed Syringodium isoetifolium (D. Uttar Pradesh Journal of Zoology, 42, 54-67.
69. Elgamouz, A., Idriss, H., Nassab, C., & Ali, M. (2020). Green synthesis, characterization, antimicrobial, anti-cancer, and optimization of colorimetric sensing of hydrogen peroxide of algae extract capped silver nanoparticles. Nanomaterials, 10(9), 1861. https://doi.org/10.3390/nano10091861
70. Mawatha, D. S., & Lanka, S. (2018). In vitro antioxidant activity and α-amylase inhibitory activity of methanolic extract of Sri Lankan marine brown algae Chnoospora minima (Hering 1841). In Proceedings of the 11th International Research Conference General Sir John Kotelawala Defence University (pp. 1841-1845)

.

71. Capasso, R., & Di Cesare Mannelli, L. (2020). Marine algae as a promising source of bioactive compounds for neuroprotection and neuroregeneration. Marine Drugs, 18(8), 405. https://doi.org/10.3390/md18080405
72. Torres, P., Santos, J. P., Chow, F., & dos Santos, D. Y. A. C. (2019). A comprehensive review of traditional uses, bioactivity potential, and chemical diversity of the genus Gracilaria (Gracilaria, Rhodophyta). Algal Research, 37, 288-306. https://doi.org/10.1016/j.algal.2018.11.016
73. Roshni, K., Younis, M., D, I., & Abdurrahman, H. (2018). Anticancer activity of biosynthesized silver nanoparticles using Murraya koenigii leaf extract against HT-29 colon cancer cell line. Journal of Cancer Science & Therapy, 10, 521-525. https://doi.org/10.4172/1948-5956.1000521
74. Acharya, D., Satapathy, S., Somu, P., Panda, P. K., & Singha, S. (2021). Apoptotic effect and anticancer activity of biosynthesized silver nanoparticles from marine algae Chaetomorpha linum extract against human colon cancer cell HCT-116. Biological Trace Element Research, 199(5), 1812-1822. https://doi.org/10.1007/s12011-020-02304-7
75. Olasehinde, T. A., Olaniran, A. O., & Okoh, A. I. (2019). Macroalgae as a valuable source of naturally occurring bioactive compounds for the treatment of Alzheimer's disease. Marine Drugs, 17(9), 465. https://doi.org/10.3390/md17090465
76. Hamida, R. S., Ali, M. A., Redhwan, A., & Bin-Meferij, M. M. (2020). Cyanobacteria – a promising platform in green nanotechnology: A review on nanoparticles fabrication and their prospective applications. International Journal of Nanomedicine, 15, 6033-6066. https://doi.org/10.2147/IJN.S261037
77. Pradhan, B., Nayak, R., Patra, S., Behera, C., Bhutia, S. K., & Jena, M. (2020). Bioactive metabolites from marine algae as potent pharmacophores against oxidative stress-associated human diseases: A comprehensive review. Molecules, 26, 37. https://doi.org/10.3390/molecules26010037
78. Rosemary, T., Arulkumar, A., Paramasivam, S., Shanmugam, S., & Aravindhan, R. (2019). Biochemical, micronutrient and physicochemical properties of the dried red seaweeds Gracilaria edulis and Gracilaria corticata. Molecules, 24(12), 2225. https://doi.org/10.3390/molecules24122225

79. Sankar, R., Karthik, A., Prabu, A., Karthikeyan, S., Shivashangari, K. S., & Ravikumar, V. (2013). Origanum vulgare mediated biosynthesis of silver nanoparticles for its antibacterial and anticancer activity. Colloids and Surfaces B: Biointerfaces, 108, 80-84. https://doi.org/10.1016/j.colsurfb.2013.02.033

80. Fass, L. (2008). Imaging and cancer: A review. Molecular Oncology, 2(2), 115-152. https://doi.org/10.1016/j.molonc.2008.04.001

81. Moavi, J., Buazar, F., & Sayahi, M. H. (2021). Algal magnetic nickel oxide nanocatalyst in accelerated synthesis of pyridopyrimidine derivatives. Scientific Reports, 11(1), 85832. https://doi.org/10.1038/s41598-021-85832-z

82. Hund-Rinke, K., & Simon, M. (2006). Ecotoxic effect of photocatalytic active nanoparticles (TiO2) on algae and daphnids. Environmental Science and Pollution Research, 13(4), 225-232. https://doi.org/10.1065/espr2006.06.311

83. Tan, L. T. (2010). Filamentous tropical marine cyanobacteria: A rich source of natural products for anticancer drug discovery. Journal of Applied Phycology, 22, 659-676. https://doi.org/10.1007/s10811-010-9522-z