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Bioactive Derivatives from Algae: Properties and Applications in Pharmaceuticals

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***Abstract* – Using algae metabolites is considered a current and innovative topic of interest. Among the various applying sectors such as food, manufacturing, and environment, these organisms are also characterized by a high therapeutic potential. The influence of biotic and abiotic factors allows the production of different bioactive compounds, such as carbohydrates, polyphenols, proteins, vitamins, sterols, fatty acids and many others. The algal biomass is investigated to discover and develop new possible therapies and nowadays different properties have been determined, like antioxidant, antiviral, antimicrobial, anti-inflammatory, antidiabetic. Typical examples include the application of algae in diabetes mellitus, which is a disease that is continually spreading throughout Europe and the world. Numerous trials are currently underway to develop innovative and effective treatments, as well as several algae are being investigated in order to gain a deeper understanding of this pathology. In recent studies it has been demonstrated that metabolites such as polyphenols, polysaccharides and pigments, by their inhibitory activity, are capable of reducing blood glucose levels and increasing the amount of insulin.**

***Keywords* – Algae; algal growth; bioactive; biotic and abiotic factors; biomass; bioproducts; metabolites; pharmacology; therapeutic potential.**

Nomenclature	
ACE	Angiotensin converting enzyme
AGE	Advanced Glycation End-products
APC	Antigen presenting cell
ECHO-1	Enterovirus
HIV-1	Human immunodeficiency virus
HSV-1	Herpes simplex virus type 1
HSV-2	Herpes simplex virus type 2
MUFA	Monounsaturated fatty acid
PUFA	Polyunsaturated fatty acid
ROS	Reactive oxygen species

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1. INTRODUCTION

Marine algae are photoautotrophic eukaryotic organisms, which are mainly found in marine waters, freshwater streams, but also in rocks and surfaces of wetlands. According to the presence of certain pigments, algae can be classified into three main classes [1]:

- *Chlorophyceae*: green algae that contain a high amount of chlorophyll a and chlorophyll b;
- *Phaeophyceae*: brown algae containing chlorophyll a, chlorophyll c, carotenoids and xanthophyll pigments;
- Rhodophyceae: red algae characterized by the presence of chlorophyll a, chlorophyll c, chlorophyll d and R-phycoerythrin pigments.

Algae are considered an excellent resource to obtain micro and macronutrients. Indeed, these organisms are capable of converting sunlight and carbon dioxide into chemical energy and algal biomass, i.e. bioactive compounds even under stress conditions, like osmotic, thermal and nutritional stress. The condition of stress occurs when the environment is excessively saline, which prevents the plant from absorbing water (osmotic stress), as well as when the temperature is excessive (thermal stress) and the nutrients in the environment are lacking (nutritional stress), both of which impair the plant's ability to grow properly [2].

The term algal biomass defines the set of nutritional organic compounds useful for human health and well-being. These compounds, also referred to as metabolites, can be used in food, medical, environmental, pharmaceutical and other manufacturing sectors [2]–[4]. Concerning the pharmaceutical interest, main compounds of the algal biomass are polyphenols, proteins, carbohydrates, fatty acids, pigments, vitamins, sterols and minerals, which are schematically reported in Fig. 1 [5]. Scopes of this research were to evaluate the therapeutic properties of algae bioactive compounds and to assess their importance for the pharmaceutical treatments.

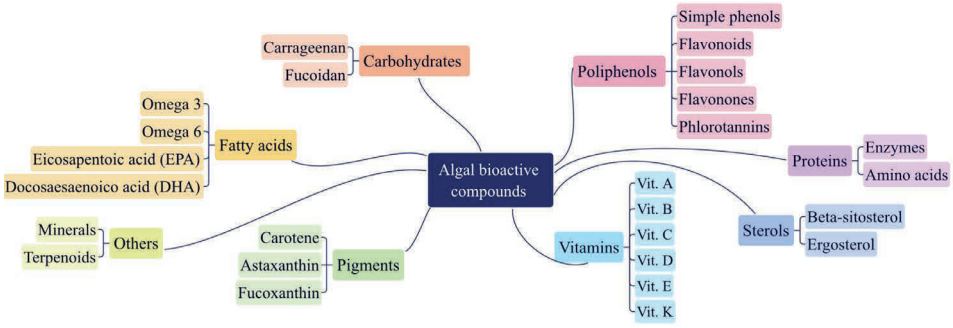

Fig. 1. Main bioactive compounds produced by algae [5].

2. BIOTIC AND ABIOTIC FACTORS

The presence of metabolites in algae depends on biotic and abiotic factors. The biotic factors that influence its formation are algal species-dependent; for instance, the amount of minerals and polysaccharides in the cell wall is variable, depending on the algal species. Other biotic factors are the organisms that affect algae and their metabolism, for example the presence of bacteria in the environment or the presence of plants that can hide the algae from the sunlight. Indeed, in water environment, microalgae interact with microorganisms in symbiotic and asymbiotic relationship, which affects the biomass production [6].

Abiotic conditions such as variations in temperature, pH, concentration of salts in the environment, presence of light and elements such as sulphur, phosphorus, potassium, carbon and oxygen, can have both positive and negative effects on the growth of algae and consequently also on the production of metabolites [7]. Fig. 2 summarizes the key abiotic parameters affecting the algae growth and the main bioactive compounds which are produced by algal activity [2].

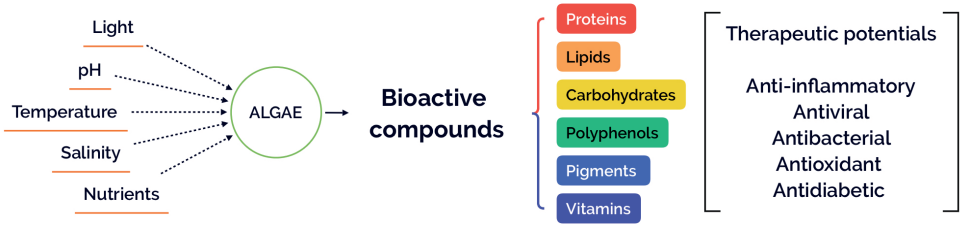

Fig. 2. Abiotic parameters affecting algae growth and bioactive compounds produced by algae.

Temperature is one of the most important environmental factors on which the growth rate of algae and their biochemical composition depend. When the temperature rises above the ideal temperature, photosynthesis and cellular respiration decrease, thus altering the energy in the cells. Conversely, a decrease in temperature reduces the assimilation of carbon, an essential element for the growth of the organisms. The ideal temperature for algae varies from species to species, but on average it is between 35 °C and 37 °C [2], [7], [8].

Another important factor influencing the production of metabolites is the pH of the environment; certain proton concentration ranges, specific for each species, allow for optimal absorption of nutrients; even small variations in acidity or basicity can cause numerous adverse effects on the metabolic processes of the alga [7].

The duration and intensity of light influence the biochemical yield and growth of algae; generally, when the intensity of light increases, the photosynthetic rate also increases and for this reason the presence of a greater number of lipids is required, which are the main components of the chloroplasts responsible for photosynthesis. Light directly effects the algal biomass production together with the carbohydrate synthesis and accumulation [9].

The salts present in the environment influence the biochemistry and structure of the algae. In fact, to counteract the high salinity, algae increase the number of lipids, making the membrane more resistant to their passage [2].

The availability of nutrients is given by the chemical and physical conditions of the substrate, while the variety of algae species determines the absorption of different nutrients. The presence of nitrogen, phosphorus and carbon is essential for the structure and metabolic function of the alga. In particular, carbon is essential for photosynthesis and all other metabolic processes, while phosphorus and nitrogen, which are absorbed by active transport, determine the function of proteins and nucleic acids. CO_2, O_2 and NO_2, on the other hand, are taken in passively and according to a concentration gradient. Other mineral micronutrients important for the body are iron, manganese, cobalt, zinc, copper and nickel [7], [10].

3. Pharmaceutical Algae Properties

3.1. Antioxidant

The use of algal metabolites is considered very promising especially for two reasons: their compositions are unique, and applications are possible in many sectors. Each algal species

contains different metabolites and in different quantities, so that it is strategic to select which algae to extract the metabolites from, to obtain a better therapeutic result [11]. Furthermore, thanks to new extraction techniques such as supercritical fluid extraction, enzyme-assisted extraction and pressurized liquid extraction, it is possible to extract the metabolites without damaging their integrity or losing their activity. Compared to traditional extraction methods, these new techniques allow higher extraction yields, have shorter times of process and are also more environmentally friendly.

In 2018, the global market for algae products was valued at $ 33.9 billion. It is estimated that it will reach $ 56.5 billion by 2027, with a compound annual growth rate of 6.0 % [12]. Algae market growth is primarily driven by the health and wellness trend, growing dietary supplement industry, vegetarianism, and rising preferences for algae-derived foods.

Inside the human body, the presence of free radicals such as ROS (Reacting Oxygen Species) and transition metals allows the formation of the hydroxyl radical (·OH), a toxic agent that causes lipid peroxidation. The effect of ROS on DNA can cause different and important damages, like tissue damage and lung dysfunction, but also pathological conditions such as Alzheimer's disease, atherosclerosis, arthritis, cataracts [13].

The ability to exploit the antioxidants from algae is considered an important resource in the medical sector to reduce the toxicity caused by free radicals. Proteins (ferritin), enzymes (reduced glutathione, catalase) and antioxidant metals (selenium, zinc) prevent the generation of radicals, while flavonoids, carotenoids (astaxanthin, beta-carotene) and vitamins, seek out and eliminate those already present in the body. Moreover, some enzymes (proteases, transferases) repair the molecules that have been damaged [5]. It is to mention that it has been demonstrated that it is possible to use beta carotene, which has antioxidant properties, to reduce the toxicity of a drug during a treatment [14]. Example of metabolites from algae with antioxidant properties are phlorotannins from *Alaria esculenta* [15], fatty acids from *Caulerpa lentillifera* [16] and Fucoidan from *Hizikia fusiforme* [17].

3.2. Antiviral

A recent study of Besednova *et al*. has found that the highest antiviral activity is in polyphenols and sulphated polysaccharides [18]. Phenolic acids, bromophenols and flavonoids are the main phenolic compounds contained in red and green algae, while brown algae possess particular compounds called phlorotannins, which are composed of monomeric units of fluoroglucinol and differ according to the different nature of the bonds between the hydroxyl group and fluoroglucinol.

The possible use of phlorotannins as coronavirus protease inhibitors has been studied. In 2017, Park *et al*. obtained 9 phlorotannins from the brown alga *Ecklonia cava* and 8 of these were dose-dependent competitive inhibitors of the SARS-COV 3CL (3-chymotrypsin-like) protease [19].

Recently, Lomartire et al. has published an overview of the antiviral activity of polysaccharides against herpes virus [20]. In particular, fucoidans from *Fucus evanescens* have been analyzed *in vitro* and *in vivo* against Herpes Simplex Virus type 1 (HSV-1), Herpes Simplex Virus type 2 (HSV-2), enterovirus (ECHO-1) and human immunodeficiency virus (HIV-1). The results of the studies show how these polysaccharides can improve resistance against the virus, inhibiting its first phase of replication [20]. The use of antivirals from algae is still at the beginning and it is expected that many applications will be developed in the next future.

3.3. Antimicrobial

The main metabolites in which good antimicrobial activity has been detected are phlorotannins and terpenes, which inhibit the formation of bacterial biofilms. Another family is constituted by

fatty acids, which can inhibit the oxidative phosphorylation of the cell membranes of bacteria. In a study published by El Shafay *et al.* in 2016 [21] the morphological changes of the cell membranes of the bacteria *Staphylococcus aureus* and *Klebsiella pneumoniae* were evaluated thanks to two fatty acids (cyclopentaneacetic acid and 10,13-octadeadedienoic acid) extracted from brown algae (*Sargassum vulgare* and *Sargassum fusiforme*). The obtained results demonstrated that the membranes have been perforated with numerous consequences such as the dispersion of the chromatin, the distortion of the external cell shape, the reduced size of the cells and many other anomalies [22].

Polysaccharides also have an excellent antibacterial activity, due to receptors present on the polysaccharides which bind to the bacterial cell wall and the plasma membrane: this results in an increase in the permeability of the plasma membrane.

A study demonstrates that the kappa-carrageenans extracted from the red alga *Hypnea musciformis* have an antimicrobial activity capable of reducing the presence of the microorganisms examined (*Staphylococcus aureus, Escherichia coli, Pseudonomas aeruginosa, Salmonella enteritidis*) by 50 % [23].

3.4. Anti-inflammatory

The term inflammation refers to a sequence of metabolic events which often follows a pathogenesis (cardiovascular diseases, osteoarthritis, cancer and many other pathologies). Inflammations can be counteracted by various metabolites contained in algae [13].

Fucoxanthins have been studied for the anti-inflammatory properties due to their ability to inhibit the production of nitric oxide, which is a major determinant and trigger for cell inflammation.

Other examples are the polyphenols of the seaweed *Laurencia undulate*, which produce an inflammatory response in asthma, the methanolic extract of *Neorhodomela aculeata*, which inhibits reactive oxygen species (ROS) and (inhibits) inflammation in neurological pathologies.

In a study by Ayyad *et al*. published in 2011 [24], the anti-inflammatory action of the two compounds (12Z)-cis-maneonene-D and (12E)-cis-maneonene-E, isolated from the red seaweed *Laurencia obtuse* was highlighted; these two compounds regulate neutrophil apoptosis [13].

Sterols also have anti-inflammatory properties. An example is found in the case of Spirulina algae, in which these particular lipids act as plasminogen activators, useful for preventing the formation of blockages in the blood vessels [25].

3.5. Antidiabetic

Marine phenols, in particular phlorotannins, thanks to their ability to regulate the metabolic pathways, allow the inhibition of the inhibitory enzymes of tyrosine protein-phosphatase and of α-amylase and α-glucosidase, that are enzymes responsible for digestion. Phlorotannins are also able to control the lipid peroxidation, to modulate the oxidative stress induced by glucose, to increase the glucose uptake and to reduce the postprandial hyperglycemia [26]. Moreover, fatty acids such as PUFA (polyunsaturated fatty acid) and MUFA (monounsaturated fatty acid) reduce the inflammation caused by hyperglycemia and adiposity [27].

According to recent studies, fucoidan polysaccharides regulate blood sugar metabolism. For example, Fucoidans extracted from the seaweed *Ecklonia maxima* act as α-glucosidase inhibitors, thus regulating type 2 diabetes [25]. Fucoxanthin pigments, in addition to their antioxidant and anti-inflammatory properties, also have antidiabetic properties, thanks to their structure and in particular to the allenic group (two double bonds joined by the same carbon atom of the C=C=C type).

The polysaccharides of Fucoidan show also good potential against tumors. In particular, in a recent study where they were isolated from the red alga *Gracilaria edulis*, their antiproliferative activity was demonstrated on cells (normal and malignant) of the adenocarcinoma of the sigmoid colon [13].

4. DIABETES

Diabetes (mellitus) is a metabolic dysfunction/pathology characterized by hyperglycemia due to insulin deficiency. High blood glucose concentration can lead to kidney dysfunction (nephropathy), cardiovascular disease, retinopathy or neuropathy [25].

4.1. Types of diabetes

Diabetes is classified into two types:

- Type 1 diabetes, also called 'insulin-dependent'. It consists of the destruction of pancreatic β-cells, which no longer produce insulin. The damage to these pancreatic cells is due to genetic factors (immune response) and/or environmental factors (viruses, xenobiotics...), which generate a 'cascade' of autoimmune responses resulting in the lack of secretion of the hormone insulin [2].

In particular, these two factors (genetic and environmental) activate the immune system by favoring the interaction between APCs (antigen presenting cells) and CD4 lymphocytes, which mediate multiple pathways. The link between APC and CD4 T cells media three main processes:

i. The activation of CD8 T cells that lyse β-cells in the pancreatic islets;
ii. The release of proinflammatory cytokines (Interleukin 1β, interferon γ, tumor necrosis factor TNF-α) and ROS by macrophages, neutrophils and natural killer (NK) cells;
iii. The production by B lymphocytes of autoantibodies against pancreatic β-cell proteins [28].

- Type 2 diabetes, also called 'non-insulin-dependent'. This type of diabetes, where there is a lack of insulin, is due to dysfunctions in the pancreatic β-cells and insulin resistance in the organs, i.e. a condition in which the latter struggle to respond to the signals of the hormone insulin. Type 2 diabetes is linked to other conditions such as metabolic syndromes, hypertension and obesity [2].

In 2021 WHO (World Health Organization) and IDF (Internal Diabetes Federation) estimated there are about 536.6 million adult diabetic patients in the world and predict that 783 million will be reached by 2045 [29].

Current therapies have undesirable effects that can lead to further pathologies in patients with diabetes; for this reason, the search for new antidiabetic drugs of natural origin has become of considerable interest. As research has progressed, bioactive compounds, especially polysaccharides, pigments and phenols from algae have shown antidiabetic properties. Research carried out on these organisms has mainly led to a regulation of blood glucose through different targets and different signaling pathways [25].

4.2. Targets of antidiabetic metabolites

Besides medicinal plants, algae contain bioactive compounds that have potential therapeutic properties for type 2 diabetes. Phlorotannins, fucosterols, fucoidans, alginic acids, fucoxanthin, and phycocolloids are among the most important secondary bioactive metabolites in algae and have relevant biological functions, including antidiabetic activity [30].

Main targets of the antidiabetic metabolites from algae are schematically reported in Fig. 3 and described in the following paragraphs.

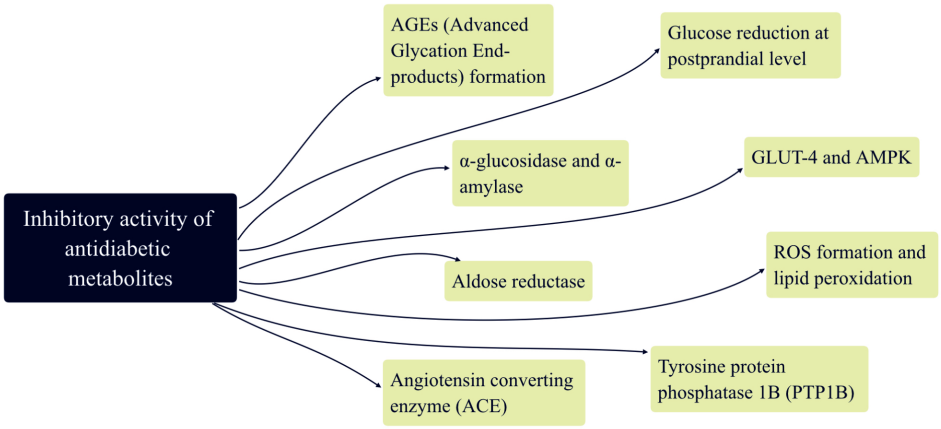

Fig. 3. Summary of the targets of antidiabetic metabolites.

- The enzymes α-glucosidase and α-amylase. The enzymes amylase and glucosidase have a fundamental role in the digestion of carbohydrates. In fact, enzymes split polysaccharides into monosaccharides and these, once absorbed by the bloodstream, will increase blood glucose levels. In the case of diabetic patients, it is important to inhibit the action of these two enzymes, in order to delay and reduce the absorption of blood glucose. However, continued use of inhibitors can cause several side effects, including kidney tumors and liver damage [26].
- Aldose reductase is an enzyme responsible for the conversion, through various steps, of glucose into fructose using NADH and NAD+. However, in conditions of hyperglycemia, this enzyme causes metabolic deficits that cause tissue damage, therefore its inhibition in diabetic patients prevents the progression of these complications.
- The enzyme tyrosine protein phosphatase 1B (PTP1B) which, located in the endoplasmic reticulum of muscle, liver and adipose tissues, negatively regulates insulin signaling. The inhibitory activity of PTP1B by algal metabolites allows to activate insulin signaling and enhance its sensitivity, thus preventing insulin resistance [26].
- Angiotensin converting enzyme (ACE) is another target of algal bioactive compounds, especially phlorotannins; these inhibit the ACE enzyme, thus lowering blood pressure and reducing diabetic complications. High molecular weight phlorotannins exhibit greater ACE inhibitory activity.
- GLUT-4 and AMPK; generally, the glucose transporter GLUT4 in conditions of low insulin is stored in the cytosol, while when insulin is present in high quantities, there is a translocation of this transporter from the cytosol to the plasma membrane and consequently a rapid increase in glucose absorption. Some algal compounds, such as Dieckol from *Ecklonia cava* and octaphlorethol A from *Ishige foliacea,* promote the increase of GLUT-4 translocation on the plasma membrane, which is molecularly dependent on the protein kinase AMPK [31].
- Advanced glycation is a phenomenon in which the irreversible combination of reducing sugars with proteins (primary amino acids) forms compounds derived from the sugar called AGEs (Advanced Glycation End-products). The formation and

accumulation of these compounds in blood vessels causes various diseases, including insulin resistance, atherosclerosis, nephropathy, retinopathy, and various neurodegenerative diseases. Some algae, such as *Padina pavonica, Sargassum polycystum* and *Turbinaria ornata*, contain metabolites (particularly phlorotannins) capable of inhibiting the formation of AGEs [26].

- Pancreatic β-cells deteriorate due to the oxidative stress and insulin resistance. To solve this problem, some polyphenols allow the reduction of ROS and lipid peroxidation induced by glucose [26].
- It is also possible to act at the postprandial level in those cases in which blood sugar is particularly high to prevent the manifestation of type 2 diabetes. Some polyphenol algae extracts in fact allow a reduction of glucose in the postprandial blood while the phlorotannins inhibit α-amylase and α-glucosidase [30].

Numerous studies show that the *Phaeophyceae* are the algae with the greatest antidiabetic capacity [2], [25], [26]. As summarised in Table 1, the main compounds with antidiabetic activity are polyphenols (in particular phlorotannins), polysaccharides and pigments. The brown seaweed *Eisania bicyclis* contains fucoxanthines and various phlorotannins capable of inhibiting α-glucosidase enzymes, PTP1B and the development of AGE; *Ecklonia cava* also possesses methanolic extracts that reduce plasma glucose and promote the AMPK/ACC pathway. The metabolites of red algae reduce plasma glucose levels (ethanolic extracts of *Gelidim amansii*) and inhibit α-glucosidase (polysaccharides of *Gracilaria lemaneiformis*), while those of green algae repair pancreatic β-cells (ethanolic extracts of *Ulva rigida*). Nowadays the experiments to evaluate the antidiabetic properties of algal bioactive compounds are very competitive [32].

TABLE 1. SPECIES OF ALGAE AND METABOLITES DESIGNED TO PERFORM ANTIDIABETIC FUNCTIONS [2], [25]

Algal type	**Algal specie**	**Metabolites**	**Functions**
Brown alga	*Eisenia bicyclis*	Dioxinodehydroeckol	α-glucosidase inhibition
Brown alga	*Eisenia bicyclis*	7-phloroeckol	α-glucosidase and PTP1B inhibition
Brown alga	*Eisenia bicyclis*	Fucoxanthin	PTP1B inhibition and AGE formation
Brown alga	*Ecklonia cava*	2-phloroeckol	Inhibition of α-glucosidase, PTP1B, aldose reductase and ACE
Brown alga	*Ecklonia cava*	Methanolic extract	Reduction of plasma glucose and increase of insulin level; activation of AMPK/ACC and Pl3/Akt signalling pathways in studies with diabetic rats
Brown alga	*Ecklonia kurome*	Phlorotannins	Inhibition of α-amylase and improvement of hyperinsulinemia
Brown alga	*Sargassum wightii*	Fucoidan	Inhibition of α-D-glucosidase and ACE
Red alga	*Gelidim amansii*	Ethanolic extract	Decreased plasma glucose
Red alga	*Gracilaria lemaneiformis*	Polysaccharides	α-glucosidase inhibition
Green alga	*Ulva rigida*	Ethanolic extract	Regeneration of pancreatic β-cells
Green alga	*Ulva fasciata*	Sulphated polysaccharides	Reduction of blood glucose concentration, restoration of liver glycogen content

5. EXAMPLE OF *IN VITRO* AND *IN VIVO* STUDY OF ANALYSIS OF ALGAL POLYPHENOLS

In 2019 Yuan *et al*. carried out a study and an experiment in which the polyphenols of the brown seaweed *Lessonia trabeculate* were extracted and purified to analyze its antidiabetic properties in vitro and in vivo [33]. The seaweed was mixed with 70 vol% methanol (schematically called M in Fig. 4). Mixing is a crucial process for the efficiency of algal use. It prevents sedimentation of the biomass, guarantees homogeneity in the culture medium and permits to modulate the penetration of light to lower parts of the reactors [34]–[36]. However, it is necessary to carefully settle the mixing intensity to avoid shear stress on microalgal cells. In Yuan study, the seaweed was placed in a reactor for extraction and purification. Subsequently the sample was filtered, to remove algae and methanol residues, and subsequently a freeze-drying process was provided for further purification.

To analyze the enzymatic inhibitory activities of the algae extracts, operations of fractionation of the solvent and separation by adsorption of the macroporous resin on the column were provided.

Regarding the fractionation of the solvent, the crude extracts were first resuspended with water and then extracted with petroleum ether (PE), ethyl acetate (EA) and n-butanol (BU). Each of these extracts and the remaining aqueous phase were concentrated by means of a rotary evaporator, obtaining, with respect to the total fraction, a fraction of 1.19 % PE, 1.45 % EA, 5.44 % BU and 85.78 % water fraction (W-S in Fig. 4).

For the separation by adsorption, however, the crude extract was dissolved in water and loaded into a glass column, packed with a macroporous adsorption resin. After loading the column with the extract, 3 eluents were added in order: water, 70 % methanol and 100 % methanol. At the end of the separation on the column, each product (eluent + extract) was collected and concentrated by rotary evaporator; in particular, the following three fractions were obtained, thanks to evaporation: 93.51 % of water eluent (indicated with W-C in Fig. 4), 1.74 % of 70 % methanol eluent (indicated with 70 % M in Fig. 4), and 0.51 % of 100 % methanol eluent (indicated with 100 % M in Fig. 4). Subsequently, the total phenolic content and specifically, the quantities of polyphenols bound to each eluent of both techniques used (fractionation and separation by adsorption) were determined. The inhibitory activities of the extracts on some enzymes were then measured, including α-glucosidase, the inhibition of which leads to a reduction in glucose absorption and post-prandial glycemia. From the assay performed during the study and represented in Fig. 4, it was found that the 100 % M and EA fractions had higher α-glucosidase inhibition activities. In particular, the EA fraction at 1 mg/ml was higher than that of the 100 % M fraction. Furthermore, the extract demonstrated to have greater inhibitory properties than the commercial inhibitor ‘Acarbose’. The inhibitory effect is mainly due to the conformational change of the enzymes that bind to the polyphenols through hydrogen bonds and Van der Waals forces [33].

From the results obtained from the mass spectrometry of the different purification fractions, it was possible to demonstrate that the polyphenols of the EA fraction are mainly phlorotannin derivatives. Given the good yield of the latter fraction (EA), it was also used for in vivo studies. Four-week-old male rats (belonging to the C57BL/6J wild type strain) were selected to carry out this experiment; 10 of these constituted the normal group (NC), 8 will constitute the diabetic group (DC), while the other 8 the diabetic group treated with polyphenols (PE). After inducing insulin resistance on DC and PE groups, only to this latter group were administered daily doses of polyphenol extracts. After four weeks, fecal samples were collected, and blood samples were taken from all 3 groups.

From the results of the blood samples, it was determined that the polyphenols administered to the PE group lowered the blood glucose level and effectively restored the insulin level by attenuating hyperglycemia, compared to the DC control group, which was not administered the extracts. As regards fecal samples, compared to the NC group, deficiencies of acetic acid, propionic acid and butyric acid were detected in the DC group, which were however recovered in the PE group.

It has also been demonstrated that the administration of polyphenols can positively modulate the intestinal microbiota and can lead to an improvement in the pathology of diabetes [33].

The current interesting example confirms the high therapeutic potential of the metabolites of a single alga against diabetes. Based on the success of the experiments, this strategy could also be used to evaluate the bioactive compounds of other algal species. Finally, through comparisons, it could be assessed which metabolites are more suitable in terms of availability in the environment, ease of use, working times, therapeutical efficiency, disposal processes and economic convenience.

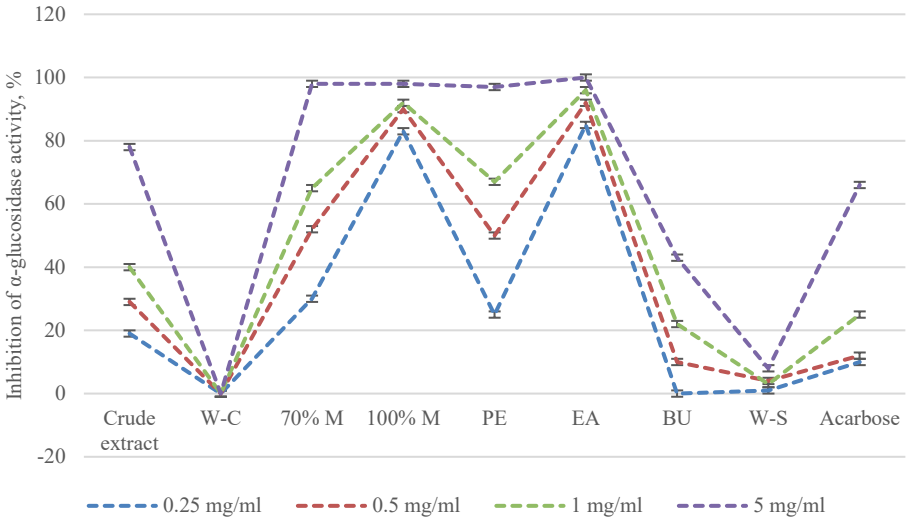

Fig. 4. Graph representing the inhibitory activity of α-glucosidase by the analyzed polyphenolic extracts. Dashed lines are only guide to the eye [33].

6. CONCLUSIONS

Numerous are the advantages of algal metabolites; the tested pharmaceutical properties include antioxidant, anti-inflammatory, antibacterial, antiviral and antidiabetic effects.

Supporting algal research offers several opportunities, including the development of better protocols, expanding or verifying existing trials, discovering new molecules and using them in biotechnology applications in order to introduce novel medical and pharmacological uses into modern medicine. In the case of diabetes, the use of algal polyphenols for the treatment and prevention of this disease has been analyzed in various trials, with positive results demonstrating their effectiveness. These algae compounds reduce blood glucose levels and increase those of insulin, though the inhibition of enzymes and the intervention on metabolic pathways.

Currently, the development of new drugs is increasingly necessary and required, due to the emergence of new pathologies, mutations and the increase in drug resistance. To identify new therapies involving the use of algae-derived products, it is first and foremost necessary to increase the search for new targets present in the human body to use them as new targets for active compounds and, consequently, to experiment with new specific treatment options. Numerous studies have been conducted to demonstrate the benefits of using these organisms and new studies and research are needed to be repeated, refined, enriched and expanded to develop future drugs that are increasingly efficient.

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