



Himanthalia elongata: An overview of its chemical composition and health-related benefits

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ABSTRACT

Himanthalia elongata, commonly known as sea spaghetti, is a brown seaweed found along the Atlantic coasts of Europe, particularly in regions such as Ireland, France, and the United Kingdom, where it is considered a delicacy and is commonly used in salads, soups, and as a pasta substitute. It is renowned for its impressive nutritional profile and potential health benefits, offering a significant amount of dietary fiber, vitamins and protein, including all essential amino acids, thus making it an excellent supplement for vegetarian and vegan diets. It is also a rich source of minerals such as iodine, calcium, magnesium, and iron, and valuable phytochemicals such as phlorotannins and fucoxanthin. The high diversity of bioactive compounds found in *H. elongata* makes it remarkably versatile in terms of bioactivities, including the capacity to regulate oxidative stress, inflammation, gut microbiota and several other cellular and physiological functions, thus contributing to healthy aging, risk reduction of cardiovascular disease, cancer, metabolic syndrome and other chronic diseases. This review provides a comprehensive overview of the nutritional and chemical composition of *H. elongata*, highlighting its reported biological activities and potential applications in the food and health industries.

1. Introduction

Global food systems are at a critical point where we must navigate through the intricate and interconnected challenges of ensuring food security while simultaneously ensuring environmental sustainability and economic prosperity. According to the recent UN reports, it is expected that the global population will reach approximately 10 billion by 2050, placing significant strain on finite planetary resources and exacerbating pressure on already fragile ecosystems (Commission et al., 2023). In light of these concerns, macroalgae appear as a viable and sustainable source of nutrition, particularly rich in minerals, vitamins, and proteins, as well as several phytochemicals that can add further functional properties to food products. In fact, over recent years, their use for direct human consumption has become more significant outside of the eastern countries, causing an increasing demand for these marine resources. As a result, global seaweed production has increased more than threefold between 2000 and 2020, with brown seaweeds accounting for approximately 44 % of total seaweed production in 2020 (FAO, 2022).

Among the multiple brown seaweed families, Himanthaliaceae (order Fucales), is of great relevance in Europe due to its edible character and wide distribution on the European Atlantic shores. Comprising a single genus, *Himanthalia*, with only one species, *Himanthalia elongata* (L.), occur in gently sloping rocky areas, with a distribution ranging from the Arctic Ocean south to the Iberian Peninsula: from Scandinavia to northern Spain and Portugal. They are also commonly found along the coasts of Britain, Ireland, and the Faroe Islands (Fig. 1) (Casado-Amezúa et al., 2019). Commonly, it is known as thong weed, sea thong or sea spaghetti, due to its long, strap-like reproductive fronds that can reach a length up to 3 m. Notably, this species is the only member of the Fucales to exhibit a two-stage morphology and a biennial life cycle. It begins with the formation of small vesicles in juvenile seaweeds, which later develop into a club-shaped structure before maturing into a button-like form, considered equivalent to the vegetative thalli in other Fucales species. Once fully developed, long, strap-like reproductive fronds emerge from the center of each button, branching dichotomously numerous times and forming the elongated thongs. After gametes are released, the life cycle of this species ends, and the seaweed dies

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(Pereira, 2015).

Himanthalia elongata is typically harvested and consumed in France, the United Kingdom and Spain (Cofrades et al., 2011), where it is typically eaten fresh when in season or, most commonly, sold in dried or pickled forms, and as alternatives to green beans or semolina spaghetti (Pereira, 2015). Nutritionally, this seaweed is claimed to be a good source of key nutrients, providing high levels of vitamins A, C, B₁ and B₂, important minerals including K, Mg, Ca and I, and dietary fiber (Pereira, 2011). Additionally, this species has a set of mechanical characteristics, including solubility, emulsifying and foaming properties, that make it a suitable option for the formulation of meat systems, sausages, bread, cakes, soups and salad dressings (Afonso et al., 2019; Garcia-Vaquero et al., 2017). Indeed, *H. elongata* has been studied as a functional ingredient in meat products: as gel/emulsion meat systems (Cofrades et al., 2008; Jiménez-Colmenero et al., 2010); beef patty formulations (40 % inclusion) (Cox et al., 2014; Cox and Abu-Ghannam, 2013); restructured poultry steaks (Cofrades et al., 2011); frankfurters (Jiménez-Colmenero et al., 2010). Other than meat products, *H. elongata* was used in cereal products as a source of dietary fiber in breadsticks to enhance their phytochemical content (Cox & Abu-Ghannam, 2013) or to develop functional bread (Rico et al., 2018a). Apart from human nutrition, this seaweed can also be found as part of the formulation of multiple commercialized skincare products and shampoos (Pereira, 2015), and its potential to be exploited for pharmaceutical applications is undeniable. In fact, over the last years, there has been a growing body of research focused on the exploration and utilization of novel compounds and potential applications from this species.

The present manuscript reviews relevant studies on the nutritional and phytochemical composition of *H. elongata*, highlighting the health benefits of its consumption, the main claimed beneficial effects of its major bioactive metabolites and the technological advances using this species.

2. Chemical composition of *H. elongata*

2.1. Polysaccharides

Most of the seaweed polysaccharides have high commercial value, mainly due to their important applications in the pharmaceutical and food industries (Holdt & Kraan, 2011; Tanna & Mishra, 2018;

Venkatesan et al., 2015) and are unparalleled among polysaccharides in land plants. As a species belonging to the Phaeophyta, *H. elongata* polysaccharides comprise all three types usually found in brown algae, i. e., fucoidans, alginates and laminarans. Nevertheless, polysaccharide isolation and characterization in *H. elongata* have not caught much of the scientific community's attention.

2.1.1. Fucoidans

Fucoidans are a family of L-fucose polysaccharides with varying percentages of sulfate groups and different glycosidic linkages. Fucoidan content depends not only on the species but also on factors such as geographical location, the season of harvest, and environmental conditions like salinity and nutrient availability (Bruhn et al., 2017; Holdt and Kraan, 2011; Tanna and Mishra, 2018). Due to differences in the repeating units, fucoidans are classified as type I ([4-sulphate- α -L-fucose-(1 \rightarrow 3)-] repeating units) and type II ([2-sulphate- α -L-fucose-(1 \rightarrow 3)-2-sulphate- α -L-fucose-(1 \rightarrow 4)-] repeating units), although (1 \rightarrow 2) or (1 \rightarrow 4) linked fucopyranose can also be found in fucoidans of some specific brown seaweeds. The backbone of the sulphated-fucose chain can have a distinct branching degree and a minor content of other monosaccharides like galactose, xylose, and/or uronic acids and substituents like acetate groups (Li et al., 2008; van Weelden et al., 2019). Concerning *H. elongata* fucoidan, this is characteristically composed of (1 \rightarrow 2)- and (1 \rightarrow 3)-linked fucose residues with sulfation at C-4. The glucuronic acid and xylose residues are 1 \rightarrow 4 linked, non-sulfated and can be found on the periphery of highly branched molecules (Li et al., 2008; Mian & Percival, 1973a).

The extraction of fucoidans from *H. elongata* was first reported in 1973, with a yield of 18 % based on the dry weight of the seaweed, using ethanol to extract the ground biomass, followed by sequential treatment with diluted acid, alkali solution, and water (Mian and Percival, 1973b, a). The most recent study on the isolation of fucoidans from *Himanthalia* was performed using a greener extraction method consisting of pressurized water extraction. As per the authors, after a fractionation step, it was possible to retrieve a polysaccharide-rich fraction consisting of the fucoidans, which were obtained in a 54.8 % yield (Santoyo et al., 2011).

2.1.2. Alginates

Alginates are polysaccharides composed of (1,4)-linked β -D-mannuronic acid and α -L-guluronic acid, both in pyranose conformation,

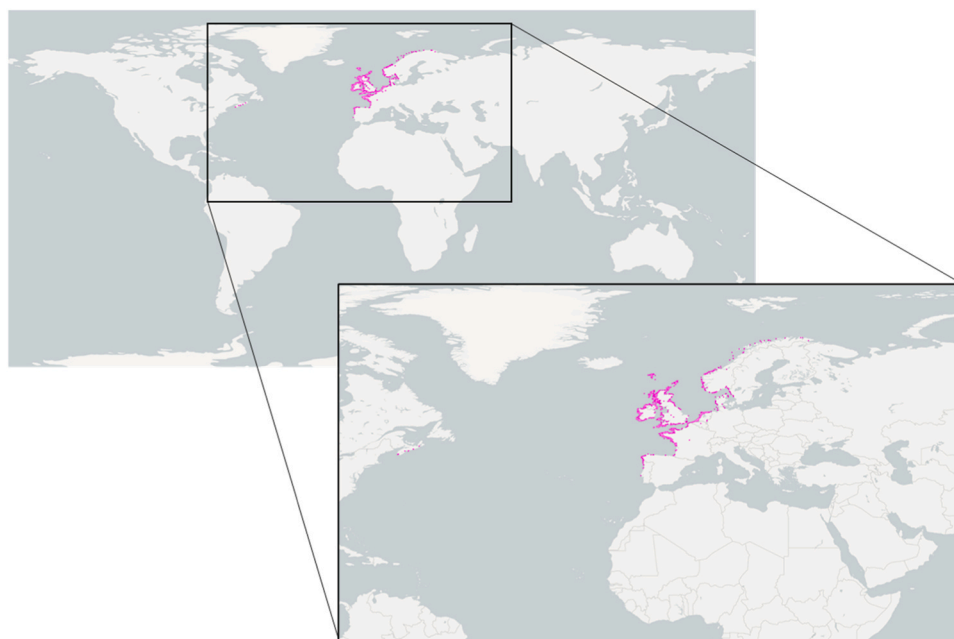


Fig. 1. Geographical distribution of *H. elongata*. <https://www.gbif.org/species/3197836>.

arranged in homopolymeric blocks (MM or GG) and heteropolymeric blocks (MG or GM), being responsible for the seaweed's flexibility. The GG portions form spiral structures that create "egg-box" junctions with divalent ions like Ca^{2+} (Ching et al., 2017), stabilizing the structure and conferring alginates the gelling properties for which they are known commercially. The ratio and length of the polymeric blocks determine the alginate's properties, with higher M/G ratios producing more elastic gels and lower M/G ratios resulting in stiffer gels, influencing their applications. These proportions are, however, significantly different from species to species (Catarino et al., 2018; Ching et al., 2017), and can vary greatly according to seasonality, growth conditions and multiple other biotic and abiotic factors (Catarino et al., 2018; Kelly and Brown, 2000; McHugh, 2023).

The isolation and characterization of alginates from *H. elongata* coincide with the study of fucoidans (Mian and Percival, 1973b,a). Its content may range from 6 % to 41 %, also varying greatly with multiple biotic and abiotic factors, as well as the extraction conditions (Flórez-Fernández et al., 2021; Silva et al., 2023). Due to their potential applications, some authors have focused on establishing a straightforward methodology to quantify the M/G ratio rather than the extraction yields or isolation of alginates from this species (Gómez-Ordóñez and Rupérez, 2011; Sánchez-Machado et al., 2004). In this regard, alginate from *H. elongata* is characterized by the prevalence of β -D-mannuronic acid over α -L-guluronic acid and a high content of MM blocks, consequently showing the potential to form elastic gels (Flórez-Fernández et al., 2021; Pereira et al., 2013; Silva et al., 2023).

2.1.3. Laminarans

Laminarans are homopolymers of β -D-glucose linked by a 1→3 glycosidic linkage, with very occasional 1→6 linkages forming branches and simultaneously interchain linkages. They may have mannitol units in their reducing ends or a few uronic acid residues (Graiff et al., 2016; Rioux et al., 2007). In general, they form relatively small molecules, with polymerization degrees between 20 and 50 units, and can occur in soluble or insoluble forms depending on their branching degree, i.e., higher branching degree correlates to better solubility (Catarino et al., 2018). The first isolation of laminarans from *H. elongata* was achieved by treating the ethanolic extract with an aqueous solution of calcium chloride (Mian and Percival, 1973b). The yield is residual (0.02 %), although it is within the normal range found in other brown macroalgae. In fact, in the literature there is a wide range of laminaran content values, varying from 0.03 % (DW), in *Fucus spiralis* (Graiff et al., 2016) to 32 % (DW) in *Laminaria digitata* (Holdt and Kraan, 2011).

2.2. Proteins and peptides

Due to their nutritional, functional, and environmental benefits, algal protein holds great promise for the food, cosmetic, pharmaceutical, animal feed, and agricultural industries. In fact, algae are gaining much attention as sustainable and health-promoting protein sources (Chen et al., 2024).

Himanthalia elongata contains 5–14.1 % protein (DW) (Cofrades et al., 2010; Gómez-Ordóñez et al., 2010), making it a less substantial protein source compared with animal-, some vegetable- or even other seaweed-based foods. Nevertheless, it still holds considerable value in plant-based diets, providing all the essential amino acids at levels consistent with FAO/WHO recommendations (Cofrades et al., 2010; Gómez-Ordóñez et al., 2010; Mohammed et al., 2021; Oliveira et al., 2023).

As presented in Table 1, the amino acid profile of *H. elongata* is dominated by glutamic acid (5.05–22 g/kg DW), followed by aspartic acid (4.50–11 g/kg DW). This is a pattern consistent with other algal species such as *Fucus vesiculosus*, *L. digitata*, or *Alaria esculenta*, and characteristic of brown seaweed in general (Catarino et al., 2018; Gaillard et al., 2018). In fact, the high content of glutamic acid, known as the main compound responsible for the umami taste sensation, is a

Table 1

Amino acid composition of *H. elongata*.

Amino acid ^a	Content (g/kg DW)
<i>Essential amino acids</i>	
Threonine	2.6–5.5
Valine	0.58–4.7
Methionine	1.05–2.3
Isoleucine	1.85–4.4
Leucine	2.05–6.6
Phenylalanine	1.82–3.4
Lysine	2.9–4.5
Histidine	0.70–10.4
<i>Non-essential amino acids</i>	
Aspartic acid	4.50–11
Serine	1.83–5.1
Glutamic acid	5.05–22
Proline	1.8–3.9
Glycine	2.22–4.4
Alanine	2.20–7.1
Cysteine	0.31–3.14
Tyrosine	0.77–2.7
Arginine	1.75–5.4

^a Tryptophan (Trp) and cysteine (Cys) are absent from the table, as the methods used by the authors do not permit the analysis of these two amino acids.

Adapted from (Cofrades et al., 2010; Martínez-Hernández et al., 2018; Oliveira et al., 2023; Rouxel and Crouan, 1995).

major contributor for the development of the seaweeds' flavor (Ninomiya, 2015). Among the essential amino acids, histidine is clearly the most abundant, with concentrations reaching up to 10.4 g/kg DW, although it varies significantly. Contrastingly, methionine is the most limiting amino acid but remains the most stable. All the remaining essential amino acids have average values around 3 g/kg DW (Cofrades et al., 2010; Oliveira et al., 2023; Rouxel & Crouan, 1995).

In general, protein from seaweed is extracted by means of aqueous, acid and alkaline extraction or enzymatic hydrolysis from dried seaweed powders. The supernatant rich in proteins is collected after centrifugation and the proteins are recovered by ultrafiltration, precipitation using ammonium sulfate or chromatographic techniques

Recently, Garcia-Vaquero and coworkers were able to produce a food grade protein extract from *H. elongata* using ultrasound-assisted extraction that showed excellent emulsifying, foaming and other physical and chemical properties that could serve multiple applications in the food industry (Garcia-Vaquero et al., 2017).

2.3. Liposoluble fraction

2.3.1. Fatty acids

Lipids in seaweed are much less abundant (0.4–5 % DW) than in several terrestrial plants and animals, which means that they are considered low-energy food sources. In *H. elongata*, the lipid content is reported to vary between 0.94 % and 2.0 % DW, depending on various factors as mentioned before (Cassani et al., 2022; Gómez-Ordóñez et al., 2010; Herbreteau et al., 1997; Lopez-Santamarina et al., 2022; Mohammed et al., 2021; Santos et al., 2019). The most common protocol for extracting lipids from biological materials, including seaweeds, is an extraction with a mixture of chloroform and methanol (1:2) (Bligh & Dyer, 1959). However, polyunsaturated fatty acids (e.g., ω -3 fatty acids) are prone to thermal degradation under the conditions typically employed in conventional solvent extraction methods, such as Soxhlet extraction. Studies have shown that pressurized liquid extraction (PLE) of *H. elongata* using different solvents can produce extracts with notable antimicrobial activities against *Staphylococcus aureus* and *Escherichia coli* (Otero et al., 2018). However, alternative extraction techniques, such as supercritical carbon dioxide (SC-CO₂) extraction, have demonstrated promising results for extracting seaweed lipids. This approach offers a more sustainable and eco-friendly process, as it eliminates the need for

high temperatures and organic solvents, thereby preserving thermolabile bioactive compounds and reducing environmental impact (Cheung, Leung, & Ang, 1998). Despite their low lipid levels, seaweeds are recognized for their fatty acid profile, particularly rich in essential ω -3 and ω -6 polyunsaturated fatty acids (PUFAs) (Cardoso et al., 2015; Ganesan et al., 2019; Ilyas et al., 2023; Makkar et al., 2016). Accordingly, PUFAs make up to 55 % of the total fatty acids in *H. elongata*, while saturated fatty acids (SFAs) and monounsaturated fatty acids (MUFAs) account for up to 47 % and 23 %, respectively (Table 2). This results in a PUFA/SFA ratio of around 1, which aligns with WHO recommendations (Chen et al., 2023).

As with other algae species, *H. elongata* primarily contains C16:0 (palmitic acid), which accounts for 5.85–34.6 % of its total fatty acids. This is followed by the MUFA C18:1, ω -9 (oleic acid), ranging from 0.49–19.96 %. Additionally, the PUFAs C20:4, ω -6 (arachidonic acid) and C18:4, ω -3 (stearidonic acid) are present in significant amounts, both reaching up to approximately 17 % of total fatty acids. Notably, C18:4, ω -3 is unique to seaweed, 8:4, ω -3 can only be found in seaweed, with *H. elongata* being one of the richest sources compared to other brown, green, or red seaweed (Holdt and Kraan, 2011). Other important PUFAs found in this species include C20:5, ω -3 (eicosapentaenoic acid), C18:3, ω -6 (γ -linolenic acid), C18:3, ω -3 (linolenic acid), and C18:2, ω -6 (linoleic acid), each contributing about 10 % to the total fatty acid content, enhancing the seaweed's overall PUFA profile (Cassani et al., 2022; Cofrades et al., 2010; Plaza et al., 2010; Sánchez-Machado et al., 2004; Schmid & Stengel, 2015).

The balance between ω -6 and ω -3 fatty acids is also another aspect to be considered for maximizing their health benefits. In Western diets,

Table 2
Fatty acid profile of *H. elongata*. Schmid et al., 2015).

Fatty acid	Content (g/100 g of total FA)
<i>Saturated fatty acids</i>	
C12:0 (Lauric acid)	0.08
C13:0 (Tridecanoic acid)	0.48
C14:0 (Myristic acid)	1.72–9.55
C15:0 (Pentadecanoic acid)	0.17–0.66
C16:0 (Palmitic acid)	5.85–34.6
C17:0 (Heptadecanoic acid)	0.50–0.32
C18:0 (Stearic acid)	0.78–13.2
C20:0 (Arachidic acid)	0.72–1.15
C22:0 (Behenic acid)	0.88
C24:0 (Lignoceric acid)	0.63
<i>Monounsaturated fatty acids</i>	
C14:1, ω -5 (Myristoleic acid)	0.27
C15:1 (cis-10-Pentadecenoic acid)	5.53
C16:1, ω -7 (Palmitoleic acid)	0.9–2.79
C18:1, ω -7 (Vaccenic acid)	0.03
C18:1, ω -9 (Oleic acid)	0.49–19.96
<i>Polyunsaturated fatty acids</i>	
C18:2 trans (Linolelaidic acid)	0.12
C18:2, ω -6 (Linoleic acid)	4.39 – 14.27
C16:3, ω -4 (cis-6, 9, 12 hexadecatrienoic acid)	4.38
C18:3, ω -3 (Linolenic acid)	8.79–11.46
C18:3, ω -6 (γ -Linolenic)	1.45–11.5
C18:4, ω -3 (Stearidonic acid)	4.7–16.90
C20:2, ω -6 (cis-11,14-Eicosadienoic acid)	0.22
C20:3, ω -6 (Dihomo- γ -Linolenic)	0.49–2.30
C20:4, ω -6 (Arachidonic acid)	10.69–17.3
C20:4, ω -3 (Juniperonic acid)	0.39–0.88
C20:5, ω -3 (Eicosapentaenoic acid)	5.50–10.2
ω -3	18.70–34.68
ω -6	8.12–15.08
ω -6/ ω 3	0.24–1.58
SFA	29.3–47.01
MUFA	12.6–22.99
PUFA	29.61–55.0

FA – fatty acid, SFA – saturated fatty acids, MUFA – monounsaturated fatty acids, PUFA – polyunsaturated fatty acids

Adapted from (Cassani et al., 2022; Cofrades et al., 2010; Plaza et al., 2010; Sánchez-Machado et al., 2004; Schmid and Stengel, 2015)

high consumption of refined oils often leads to ω -6/ ω -3 ratios exceeding 25:1, far from the ideal range of 1:1–6:1. Maintaining this optimal ratio is important for supporting normal brain development and decrease the risk for coronary heart disease, hypertension, cancer, diabetes, arthritis, and other autoimmune and possibly neurodegenerative diseases (Simopoulos, 2010). Marine macroalgae are particularly abundant in ω -3 fatty acids, which may represent up to 50 % of their total fatty acid content (Bocanegra et al., 2009). In *H. elongata*, ω -3 levels are typically double those of ω -6, ranging from 19–35 % for ω -3 and 8–15 % for ω -6 (Table 2). Consequently, the ω -6/ ω -3 ratios reported for this species fall between 0.2 and 1.6, which fit within or are even lower than the recommended values. This suggests that consuming *H. elongata* could contribute to mitigate the imbalanced ω -6/ ω -3 rations of the Western diets, contributing to improved health outcomes.

2.3.2. Fucoxanthin

Fucoxanthin, a xanthophyll carotenoid from the tetraterpenoid family, is the primary carotenoid in Phaeophyceae, giving them a brownish tone (Catarino et al., 2018). It features an unusual allenic bond and a 5,6-monoepoxide in its structure, and like other carotenoids, it is quite susceptible to degradation caused by heat, light, oxygen, enzymes, unsaturated lipids, and other prooxidant molecules (Zhang et al., 2015). Fucoxanthin is notable for its antioxidant, anti-inflammatory, antidiabetic, anti-obesity and antitumor properties, among other beneficial effects (Rajauria & Abu-Ghannam, 2013).

Extraction of fucoxanthin from *H. elongata* has been carried out with semi/non-polar solvents including *n*-hexane, diethyl ether, chloroform, acetone or methanol, and mixtures thereof (Rajauria & Abu-Ghannam, 2013; Rajauria et al., 2017; Shannon & Abu-Ghannam, 2017). Recently, Osório et al. reported that using DMSO:water (4:1, v/v) as extracting solvent resulted in an *H. elongata* extract composed almost exclusively of fucoxanthin, demonstrating a high selectivity for this compound (Osório et al., 2020).

Fucoxanthin content in *H. elongata* is generally in the range of μ g/g, though it can vary significantly (2.8 – 51 μ g/g dried sample). This variability may be due, in part, to fucoxanthin's high sensitivity to oxidation (Ferraces-Casais et al., 2011; Osório et al., 2020; Rodríguez-Bernaldo de Quirós et al., 2010).

Interestingly, it has been shown that different cooking/processing methods prior to extraction can have a great impact on the fucoxanthin extraction yields. While rehydration and boiling seem to help produce extracts with higher fucoxanthin content (both retrieving approximately 100 mg/kg DW), drying and steaming resulted in a reduction of 50 % of fucoxanthin. This study lacks, however, the values for the unprocessed seaweed to understand whether these improve or hinder the fucoxanthin recovery from the seaweed (Amorim-Carrilho et al., 2014).

2.4. Minerals

Seaweed, particularly brown seaweed, has a remarkable ability to retain inorganic marine substances due to their cell surface polysaccharides, resulting in generally high mineral content (Catarino et al., 2018). Factors such as harvesting season, geographic location, and wave exposure can influence the mineral levels in seaweed, including *H. elongata*. As a result, the total mineral content in this species is reported to vary from 2 % to 25 % DW (Table 3) (Cassani et al., 2022; Cernadas et al., 2019; Cofrades et al., 2010; Fernandez-Segovia et al., 2018; Lopez-Santamarina et al., 2022; Martínez-Hernández et al., 2018; Mohammed et al., 2021; Rouxel and Crouan, 1995; Sánchez-Moya et al., 2018). Although these levels are not as high as those in other brown seaweeds like *Fucus* sp., *Laminaria* sp. or *Undaria* sp. (Holdt and Kraan, 2011; Rupérez, 2002), they are still notably higher compared to common vegetables, such as potatoes (10.4 % DW), carrots and tomatoes (both 7.1 % DW) or sweet corn (2.6 % DW) (Cardoso et al., 2014). Notably, studies focusing on mineral extraction from algae are uncommon. Therefore, the methods used in the extraction of these inorganic

Table 3
Macrominerals and trace elements in *H. elongata*.

Component	Content mg/100 g DW
<i>Macrominerals</i>	
Ca	600–1512.10
P	77.7–139.3
Mg	121.3–985
Na	605.8–5419
K	1152–13250
<i>Trace minerals</i>	
Br	36.4
Si	25.7
Cu	1.6
Fe	0.5–7.4
Cu	0.015–0.21
Zn	0.35–4.4
Mn	0.94–4.1
I	4.5–18.9
Total	1526–23610

Adapted from (Cassani et al., 2022; Cernadas et al., 2019; Cofrades et al., 2010; Fernandez-Segovia et al., 2018; Lopez-Santamarina et al., 2022; Martínez-Hernández et al., 2018; Mohammed et al., 2021; Rouxel and Crouan, 1995; Sánchez-Moya et al., 2018).

substances from *H. elongata* are mainly for characterization purposes, using acid digestion and incineration in a muffle furnace (Ilyas et al., 2023; Makkar et al., 2016). The use of acid digestion with HNO₃ in a microwave was also reported (Cernadas et al., 2019).

Table 3 details the mineral content of *H. elongata* as reported by distinct authors. Regardless of the high variability found between studies, there is clear evidence that potassium and sodium are the most predominant elements found in this species, as seen in many other species of brown seaweeds (Circuncisao et al., 2018). Values for these two elements can reach up to 13250 and 5419 mg/100 g of DW, respectively, which corresponds to 33 times more K than bananas and 8 times more Na than cheddar cheese (MacArtain et al., 2007). Despite these high levels, the Na/K ratio in *H. elongata* is typically less than 1, often around 0.5, except for one study that reported a ratio of 1.9. This lower Na/K ratio is notable because high Na/K ratios are associated with increased blood pressure and cardiovascular diseases. Indeed, according to the WHO, a Na/K ratio < 1 is believed to be optimal for preserving cardiovascular health (Vulin et al., 2022). Therefore, consumption of *H. elongata* can bring interesting health benefits as it can not only be used as a salt replacer in processed foods, but also help regulate the dietary Na/K imbalance.

Himanthalia elongata can also be seen as a good source of Ca and Mg, with values that range between 600 – 1512 and 121 – 985 mg/100 g of DW, respectively. These values represent between 5 and 13 times more Ca than that found in 100 g of whole milk and 2–18 times more Mg than in whole spinach (MacArtain et al., 2007). Once again, it is important to consider not only the absolute amount but also the Ca/Mg ratio, which is considered optimal at 2:1 (DeLuccia et al., 2019). High Ca/Mg intake ratios have been linked to multiple chronic conditions, including cardiovascular disease, metabolic syndrome and some cancers (colorectal, prostate, oesophageal). Over the years, these intake ratios have risen alarmingly, reaching levels above 3 in the average U.S. adult aged 20 and older (Costello et al., 2021). In turn, the Ca/Mg ratios reported for *H. elongata* range between 0.7 and 1.3 (Cassani et al., 2022; Cernadas et al., 2019; Cofrades et al., 2010; Martínez-Hernández et al., 2018; Mohammed et al., 2021; Rouxel and Crouan, 1995; Sánchez-Moya et al., 2018), which are considerably lower than the recommended values. This suggests that incorporating this seaweed into the Western diet could help counteract the increasing Ca/Mg ratio trend.

In addition to macrominerals, *H. elongata* can be considered a good source of some trace elements. Indeed, as a brown seaweed, it can

accumulate significant levels of iodine (4.5 – 18.9 mg/100 g DW). However, it contains relatively lower iodine levels compared to other brown seaweeds, such as *Fucus* sp. (13 – 73 mg/100 g DW) or *Laminaria* sp. (310 – 901 mg/100 g DW) (Catarino et al., 2018; Circuncisao et al., 2018). Nevertheless, the levels of iodine in *H. elongata* cannot be found anywhere else in land plants, making it an ideal food-safe natural source of this mineral. Likewise, iron or copper are not as high in *H. elongata* (up to 7.4 and 0.2 mg/100 g DW, respectively) as they normally are in other brown seaweeds, which can accumulate up to 150 and 8 mg/100 g DW, respectively (e.g. *Fucus vesiculosus*) (Circuncisao et al., 2018). Still, 100 g of dried *H. elongata* contains higher levels of these two elements than 100 g of a sirloin steak (contains 1.6 and 0.1 mg/100 g of Fe and Cu, respectively) (MacArtain et al., 2007).

Bromine and silicon can also be found in good amounts in *H. elongata*, and although there is some controversy about their essential status, evidence has shown that these can have beneficial effects on human health. Indeed, bromine has been found to play an important role in the biosynthesis of collagen IV, essential to basement membrane architecture and tissue development, and the immune defense (Kohlmeier, 2015; McCall et al., 2014). Moreover, deprivation of this element has been linked to sleep disturbance and insomnia, although the significance of such effects is still uncertain (Kohlmeier, 2015). In turn, although no clear deprivation symptoms have been attributed to silicon, evidence shows that it significantly improves bone mineralization and strength, and can improve bone volume and density in patients with osteoporosis (Price et al., 2013). Therefore, incorporation of *H. elongata* in a regular diet may bring positive outcomes in the maintenance of good skin and bone health.

2.5. Phenolic compounds

As a species belonging to the Phaeophyceae, the main representative phenolic compounds of *H. elongata* are the phlorotannins. These consist of several units of phloroglucinol linked together via C-C linkages (fucols), C-O-C linkages (phlorethols), a combination of both (fucophlorethols), and other complex structures such as dibenzodioxin linkages (eckols). Additional hydroxyl groups may also occur and, in these cases, two additional phlorotannin groups appear, the fuhalols (phlorethol-like structures with extra *para* and/or *ortho* OH) and carmalols (eckol-like structures containing additional OH groups) (Catarino et al., 2022a).

Like other tannins, phlorotannins are primarily extracted using solid-liquid extraction with hydroacetic solvents and usually quantified via 2,4-dimethoxybenzaldehyde (DMBA) method (expressed in phloroglucinol equivalents, PGE). The Folin-Ciocalteu method (expressed in gallic acid equivalents, GAE) can also be used if looking to a wider spectrum of phenolic compounds. In *H. elongata*, mixtures of 40 and 60 % acetone (> 1.0 mg GAE/100 g seaweed) were shown to extract more than double the amount of polyphenols when compared to other solvents like water or aqueous mixtures with ethanol or methanol (< 0.5 mg GAE/100 g seaweed) (Belda et al., 2016). Nevertheless, many studies reported in literature can be found using methanol (Fernandez-Segovia et al., 2018; Rajauria, 2018; Rajauria et al., 2016), ethanol (Gager et al., 2020; Heffernan et al., 2015; Martelli et al., 2020a, b) and water (Garcimartín et al., 2015; Martínez-Hernández et al., 2018) for extracting phenolics from *H. elongata*. Many of these focus on food applications, which restricts solvent choices (Garcimartín et al., 2015; Martelli et al., 2020a,b), while others do not prioritize phlorotannins as their main concern (Fernandez-Segovia et al., 2018; Rajauria, 2018; Rajauria et al., 2016). Naturally, different extraction approaches will generate variable phlorotannin and overall phenolic content. Nonetheless, the phlorotannin content of *H. elongata* tends to be low (0.05 – 10 % PGE in dry seaweed). Consequently, additional purification steps, such as solvent partitioning, dialysis, or preparative chromatography, are often required to obtain extracts with adequate concentrations (Catarino et al., 2022b; Gager et al., 2020; Heffernan et al., 2015; Kirke et al.,

2019). Novel extraction techniques, such as subcritical water extraction and ultrasound-assisted extraction, have shown promising results in improving both the yield and efficiency, i.e., reducing extraction time, quantity of solvent, or the need of organic solvents (Gomes et al., 2022; Martelli et al., 2020a; Ummat et al., 2020).

Despite the characterization and identification of phlorotannins representing a challenging task, some studies have attempted to elucidate the phlorotannin profile of *H. elongata*. Due to their huge chemical variability and complexity, most studies focus primarily on the degree of polymerization rather than detailed profiling (Heffernan et al., 2015; Kirke et al., 2019; Martelli et al., 2020b). Nevertheless, Kirke et al. investigated seasonal fluctuations in phlorotannin polymerization across several brown seaweeds, revealing that *H. elongata* consistently showed a higher prevalence of phlorotannins with polymerization degrees between 8 and 13 (Kirke et al., 2019). Additionally, the authors concluded that fundamental phlorotannin oligomeric composition is species-specific and not influenced by extrinsic factors such as environmental conditions. In a more recent study, carmalols—a group of compounds typically found in *Ishige okamurae*—were unexpectedly identified in significant quantities in a purified extract from *H. elongata*, highlighting the potential for unique bioactive compounds in this species (Catarino et al., 2022b).

In addition to phlorotannins, several other phenolic compounds, such as hydroxybenzoic and hydroxycinnamic acids, and flavonoids, have been identified in *H. elongata*, particularly in hydroalcoholic extracts. A detailed HPLC-DAD-MS/MS analysis of a solid-phase extraction (SPE) fraction from a crude 60 % methanol extract revealed notable quantities of phenolic compounds: gallic acid (96.3 µg/g ext), chlorogenic acid (38.8 µg/g ext), caffeic acid (44.4 µg/g ext), ferulic acid (17.6 µg/g ext), myricetin (8.6 µg/g ext), and quercetin (4.2 µg/g ext). Naturally, phloroglucinol, the monomeric unit of phlorotannins, was found in significantly higher concentrations (394.1 µg/g ext) compared to other phenolic compounds (394.1 µg/g ext) (Rajauria, 2018).

Similar findings were reported in a study using 60 % ethanol as the extraction solvent: phloroglucinol was found in large predominance (1029.8 µg/g ext), while other phenolics including the acids gallic, caffeic, chlorogenic, coumaric, ferulic, and protocatechuic, and several flavonoids—catechin, rutin, myricetin and quercetin—were detected as minor components (Belda et al., 2016). Interestingly, Rajauria et al. identified carnosic acid and gallic acid as the primary compounds in an ethyl acetate sub-fraction of *H. elongata*, which was purified through liquid–liquid partitioning and column chromatography of a 60 % methanol extract. Additionally, the sub-fraction contained notable amounts of hydroxybenzaldehyde (meta-/para-), phloroglucinol, and kaempferol. Other identified compounds included cirsimaritin and gallic acid 4-*O*-glucoside (Rajauria et al., 2016). Moreover, epigallocatechin (715.6 ± 8.3 µg/g DW) and gallic acid (55.6 ± 9.1 µg/g DW) were found in a 30 % methanol extract (Rodríguez-Bernaldo de Quirós et al., 2010), while cyanidin-3-*O*-glucoside was reported in a lipophilic extract from a mixture of chloroform, diethyl ether and *n*-hexane (1:1:1) (Rajauria, 2019).

3. Bioaccessibility and bioavailability of *H. elongata* phytochemicals

Bioaccessibility and bioavailability are key steps in ensuring the bioefficacy of any food compounds or oral drugs. Bioaccessibility refers to the proportion of a bioactive compound that is released from the food matrix within the gastrointestinal tract, making it available for absorption. Bioaccessibility is defined as the fraction of an ingested bioactive compound that is released from the food matrix in the gastrointestinal tract and becomes available for absorption. It is influenced by several factors, including the chemical structure of the compound, the food matrix and the processing methods. Understanding the bioaccessibility of seaweed bioactive compounds is crucial because it directly impacts their bioavailability. In turn, bioavailability is defined as the fraction of

a bioactive compound that is effectively absorbed from the gastrointestinal tract, enters the bloodstream and is able to reach the target tissue in a biologically active form (Dima et al., 2020).

Several factors can have an impact on the bioaccessibility and bioavailability of seaweed compounds. These include processing techniques (e.g., drying, cooking, fermentation), complexity of the seaweed matrix, possible interaction with other compounds, chemical structure, effects of the digestive process among several others. In the particular case of brown seaweed, because of their unique composition, bioaccessibility and bioavailability present additional challenges. For example, all the three main brown algae polysaccharides (alginate, fucoidan and laminaran) cannot be broken down by the human organism, thus working as dietary fiber (Villanueva et al., 2014). Moreover, because they differ so much from the typical land plant polysaccharides, they are not so readily fermented by human gut microbiota. Nevertheless, several authors have demonstrated that, to some extent, gut microbiota can ferment these kinds of polysaccharides, particularly when they are supplied in lower molecular weight forms (Habibi et al., 2024; Huang et al., 2024; Kuda et al., 2005; Wang et al., 2006). In the particular case of *H. elongata*, low fermentability was observed when testing fucoidan fractions extracted from this seaweed with rat ceacal inoculum. However, fractions rich in laminarans, xylofucoglycuronans and xylomannans showed good fermentability (Mateos-Aparicio et al., 2018).

In terms of protein, while *H. elongata* contains all essential amino acids, this alone does not necessarily classify it as a high-quality protein. According to the FAO, protein quality is related to amino acid composition and bioavailability, which is directly proportional to the digestibility of the ingested proteins (FAO/WHO, 1991). However, due to the limited widespread consumption of macroalgae, there remains a significant gap in understanding the bioaccessibility and bioavailability of algal proteins.

Studies on different brown algae species reported in vitro protein digestibility values between 78 % and 82 % which is comparable to those reported for vegetables (68–80 %), tubers (71–88 %), grains (69–84 %), legumes (72–99 %), oilseeds (75–99 %) and fruits (72–92 %) (Tibbetts, Milley, & Lall, 2016). However, despite the identical digestibility values, this does not necessarily mean identical bioavailability. For instance, according to De Bhowmick and Hayes, despite *F. vesiculosus* showing higher protein digestibility than *F. serratus* (82 % vs 77 %), it demonstrated a k-Protein Digestibility-Corrected Amino Acid Score (k-PDCAAS) of only 0.08 while *F. serratus* exhibited a k-PDCAAS of 0.63, which is indicative of a much higher protein bioavailability (De Bhowmick & Hayes, 2022). Lower protein digestibility in seaweeds has been associated with the complexity of their composition and high content of polysaccharides which can entrap the protein and render it less bioavailable (Marrion et al., 2005). In brown algae, an inverse correlation was observed between protein digestibility and total phenolic content. Therefore, brown macroalgae with higher phenolic content can have lower digestible protein amounts (Tibbetts et al., 2016). Studies on *H. elongata*'s protein digestibility, however, have not been conducted yet. Still, based on its phenolic content, it is possible to have a picture of how high or low digestible its protein can be comparing with other brown algae.

The food matrix particularly influences the bioaccessibility and bioavailability of seaweed minerals, as many of them are prone to interact with dietary fiber, which can render them inaccessible and consequently poorly bioavailable (Circuncisao et al., 2018). It has been demonstrated that interactions with various anionic polysaccharides, such as alginates, agar, or carrageenan, can result in the formation of insoluble complexes with minerals, thereby reducing their bioavailability (Debon & Tester, 2001). In the specific case of brown algae, although they can contain substantial levels of calcium, their absorption has been shown to be quite low, primarily due to their interaction with alginates (Bocanegra et al., 2003). Likewise, despite the fact that brown algae are usually claimed to be excellent sources of iodine, that does not

necessarily mean that all their iodine content is bioaccessible and bioavailable. In fact, in an *in vitro* study on iodine bioavailability on different seaweeds, it has been shown that the percentage of iodine dialysability in the majority of the tested samples was below 5 %, including for *H. elongata* (Romarís-Hortas et al., 2011). In this regard, Domínguez-González et al. reported that di-iodotyrosine, one of the main organic forms of iodine in brown algae, has very low permeability in Caco-2 cells, which could partially explain the poor absorbability of this mineral (Domínguez-González et al., 2017).

Finally, concerning fucoxanthin and phenolic compounds, several studies agree that these algal secondary metabolites tend to be poorly bioavailable. In fact, orally administered fucoxanthin is well known to be completely metabolized into fucoxanthinol at the intestinal level, and amarouciaxanthin A in the liver (Pereira et al., 2021). These metabolites can, however, be the active forms of fucoxanthin that are responsible for the bioactive properties that have been described *in vivo*. In fact, anti-cancer and anti-inflammatory properties of fucoxanthinol are well described (Meresse et al., 2020). Nevertheless, further research needs to be done to confirm that. In turn, although the exact metabolism of phlorotannins, i.e., the main phenolic compounds present in brown algae, is not fully understood, several studies have already demonstrated that total phlorotannin content of algal extracts tend to decrease along the different steps of the upper gastrointestinal digestion, indicating these are sensitive to the extreme conditions of the gut (Catarino et al., 2022b; Catarino et al., 2024; Catarino et al., 2021). Indeed, a study carried out with *H. elongata* phlorotannin extracts revealed that, at the end of the upper intestinal digestion, about 50 % of the total phlorotannin content was lost (Catarino et al., 2022b).

4. Biological activities of *H. elongata*

The diverse range of compounds in *H. elongata* gives it potential nutraceutical and bioactive properties, including antioxidant, antimicrobial, anti-inflammatory, and anti-tumoral effects. Additionally, it has shown promise in preventing hypercholesterolemia and vascular thrombosis, acting as a prebiotic, and providing skin protection, as demonstrated in various *in vitro* and *in vivo* studies (Fig. 2). This section highlights the well-known biological activities of these phytochemicals, their mechanisms of action, and the common assays used for their evaluation.

4.1. Antioxidant activity

While oxidative reactions play a crucial role in cellular function and immune responses, an imbalance between free radical production and antioxidant defenses can result in oxidative stress, leading to damage to proteins, lipids, nucleic acids, and enzymes (Balboa et al., 2013; Chaudhary et al., 2023). Over time, this cumulative damage is linked to the development of many health disorders, such as cancer, diabetes mellitus, and neurodegenerative and inflammatory diseases (Chaudhary et al., 2023).

In food systems, oxidative reactions lead to rancidity, off-flavors, and undesirable texture or color, compromising nutritional quality and safety in food systems (Barden & Decker, 2016). In this regard, natural antioxidants, particularly those from marine sources, have gained much interest in the food, therapeutic and cosmetic industries as cost-effective, safe alternatives to synthetic antioxidants. These compounds have demonstrated the ability to protect cells from oxidative stress and free radical damage, delaying the onset and progression of diseases, and shielding food from oxidative deterioration.

The assessment of antioxidant capacity typically involves a primary screening using different *in vitro* chemical methods, including radical scavenging activity, reducing power, metal-ion chelating ability, and protection against lipid peroxidation. While these assays do not fully replicate physiological conditions, they offer a preliminary understanding of the biological potential of extracts and compounds, shedding light on their mechanisms of action, effective concentrations, and potential synergistic effects. Table 4 provides a summary of the most relevant *in vitro* studies on the total bioactive compound content and antioxidant capacity of crude extracts and purified fractions from *H. elongata*.

Different free radicals have been tested, namely 2,2-diphenyl-1-picrylhydrazyl radical (DPPH[•]), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical (ABTS^{•+}), and reactive species including hydrogen peroxide (H₂O₂) and peroxy radicals. DPPH[•] and ABTS^{•+} are useful for preliminary antioxidant screening due to their stability and reproducibility, although their synthetic nature makes them less biologically relevant. Other radicals such as nitric oxide (NO[•]), superoxide anion (O₂^{•-}) and hydroxyl (HO[•]) are more suitable, as they are generated during normal cellular and metabolic activities (Chaudhary et al., 2023). Non-radical reactive species (e.g., H₂O₂) were also investigated as they


	Biological activity	<i>In vitro</i> study	<i>In vivo</i> study
 <p><i>Himanthalia elongata</i></p>	Antioxidant	✓	✓
	Antimicrobial	✓	✗
	Anti-inflammatory	✓	✗
	Anti-tumoral	✓	✗
	Hypocholesterolemic	✓	✓
	Prebiotic effect	✓	✓
	Skin protective effect	✓	✓

Fig. 2. Schematic representation of different biological properties described for *H. elongata* and current state of research in the field.

Table 4

Selected *in vitro* studies of antioxidant activity of crude extracts and/or purified fractions from *H. elongata*.

Extraction Conditions	Active compounds	Active compounds content	<i>In chemico</i> Antioxidant Properties	Ref.
Solid-liquid H ₂ O, 20 % - 100 % MeOH 1:10 (w/v), 40°C, 2 h	Polyphenols	TPC (mg GAE/g _{extract} DW) = 116.5 (H ₂ O); 193.6 (20 % MeOH); 259.1 (40 % MeOH); 286.0 (60 % MeOH); 193.9 (80 % MeOH); 59.8 (100 % MeOH) TFC (mg QE/g _{extract} DW) = 46.7 (H ₂ O); 70.2 (20 % MeOH); 96.5 (40 % MeOH); 109.8 (60 % MeOH); 66.0 (80 % MeOH); 44.0 (100 % MeOH) TTC (mg ChE/g _{extract} DW) = 14.6 (H ₂ O); 21.7 (20 % MeOH); 27.2 (40 % MeOH); 35.6 (60 % MeOH); 22.4 (80 % MeOH); 9.8 (100 % MeOH)	DPPH* (EC ₅₀ , µg/mL) = 105.4 (H ₂ O); 92.0 (20 % MeOH); 78.7 (40 % MeOH); 57.2 (60 % MeOH); 87.0 (80 % MeOH); 297.7 (100 % MeOH); FRAP (mg TE/g _{extract} DW) = 6.8 (H ₂ O); 8.7 (20 % MeOH); 10.3 (40 % MeOH); 11.7 (60 % MeOH); 8.3 (80 % MeOH); 4.7 (100 % MeOH) FIC (EC ₅₀ , µg/mL) = 1982 (60 % MeOH) H ₂ O ₂ (EC ₅₀ , µg/mL) = 361.7 (60 % MeOH) LPO (EC ₅₀ , µg/mL) = 546.3 (60 % MeOH)	(Rajauria et al., 2013)
Solid-liquid H ₂ O, 40 % and 60 % Ace; 40 % and 60 % MeOH, 40 % and 60 % EtOH 1:5 (w/v), 60°C, 2 h	Polyphenols	TPC (mg GAE/g _{algae} DW) ~ 1.5 (H ₂ O); ~1.9 (40 % MeOH); ~2.3 (60 % MeOH); ~2.6 (40 % EtOH); ~5.5 (60 % EtOH); ~10.2 (40 % Ace); ~10.9 (60 % Ace)	DPPH* (RSA %) = ~ 13.0 (H ₂ O); ~47.5 (40 % MeOH); ~62.5 (60 % MeOH); ~65.2 (40 % EtOH); ~77.5 (60 % EtOH); ~71.0 (40 % Ace); ~64.9 (60 % Ace)	(Belda et al., 2016)
S-L H ₂ O S-L 40 % Ace S-L 60 % Ace S-L 40 % MeOH S-L 60 % MeOH S-L 40 % EtOH S-L 60 % EtOH	Polyphenols	TPC (mg GAE/g _{algae} DW) ~ 1.5 TPC (mg GAE/g _{algae} DW) ~ 1.9 TPC (mg GAE/g _{algae} DW) ~ 2.3 TPC (mg GAE/g _{algae} DW) ~ 2.6 TPC (mg GAE/g _{algae} DW) ~ 5.5 TPC (mg GAE/g _{algae} DW) ~ 10.2 TPC (mg GAE/g _{algae} DW) ~ 10.9	DPPH* (RSA %) = ~ 13.0 DPPH* (RSA %) = ~ 47.5 DPPH* (RSA %) = ~ 62.5 DPPH* (RSA %) = ~ 65.2 DPPH* (RSA %) = ~ 77.5 DPPH* (RSA %) = ~ 71.0 DPPH* (RSA %) = ~ 64.9	(Belda et al., 2016)
Solid-liquid 50 % Acidified MeOH 1:40 (w/v), RT, 1 h	Polyphenols	TPC (mg GAE/g _{algae} DW) = 18.0	FRAP (µmol Trolox/g _{algae} DW) = 41.1 ABTS* ^{•+} (µmol Trolox/g _{algae} DW) = 65.0	(Fernandez-Segovia et al., 2018)
Solid-liquid 50 % Acidified MeOH → 70 % Ace 1:40 (w/v) RT, 1 h	Polyphenols	TPC (mg GAE/g _{algae} DW) = 13.0	DPPH* (mg TE/g _{algae} DW) = 3.8 FRAP (mg TE/g _{algae} DW) = 4.5	(Mohammed et al., 2021)
Solid-liquid Hex, Et ₂ O, TCM, Mix 1: Hex:Et ₂ O, Mix 2: Hex:TCM, Mix 3: Et ₂ O:TCM, Mix 4: Hex:Et ₂ O: TCM 1:10 (w/v), 40°C, 2 h	Lipophilic compounds (β-carotene, violaxanthin, fucoxanthin, chlorophyll derivatives)	TPC (mg GAE/g _{extract} DW) = 14.1 (Hex); 165.2 (Et ₂ O); 71.2 (TCM); 121.5 (Mix 1); 152.3 (Mix 2); 88.9 (Mix 3); 180.2 (Mix 4) TFC (mg QE/g _{extract} DW) = 11.3 (Hex); 92.1 (Et ₂ O); 37.5 (TCM); 60.4 (Mix 1); 55.8 (Mix 2); 85.8 (Mix 3); 131.3 (Mix 4) TCC (µg/g _{extract} DW) = 1.55 (Hex); 2.18 (Et ₂ O); 2.81 (TCM); 1.79 (Mix 1); 1.93 (Mix 2); 2.66 (Mix 3); 3.15 (Mix 4) TChC (µg/g _{extract} DW) = 1.55 (Hex); 2.18 (Et ₂ O); 2.81 (TCM); 1.79 (Mix 1); 1.93 (Mix 2); 2.66 (Mix 3); 3.15 (Mix 4)	DPPH* (EC ₅₀ , µg/mL) ~710 (Hex); ~190 (Et ₂ O); ~530 (TCM); ~480 (Mix 1); ~300 (Mix 2); ~200 (Mix 3); ~100 (Mix 4) FRAP (mg TE/g _{extract} DW) ~5.5 (Hex); ~23.0 (Et ₂ O); ~9.0 (TCM); ~12.5 (Mix 1); ~15.0 (Mix 2); ~18.0 (Mix 3); ~26.0 (Mix 4) FIC (RSA % at 1000 µg/mL): 22.7 % (Hex); 57.8 % (Mix 4); 100 % (EDTA)	(Rajauria, 2019)

MeOH – methanol; Ace – acetone; EtOH – ethanol; Hex – n-hexane; Et₂O – diethyl ether; TCM – dichloromethane; EA – ethyl acetate; RT – room temperature; Fract – fractionation; SLE – solid-liquid extraction; UAE – ultrasound-assisted extraction; AH – autohydrolysis; AC – autoclave; HPP – high pressure processing; RP – reverse-phase; SPE – solid-phase extraction; TPC – total phenolics content; TFC – total flavonoids content; TTC – total tannins condensed; TCC – total carotenoids content; TChC – total chlorophylls content; TPhC – total phlorotannins content; DW – dry weight; LMW – low molecular weight; LOD – limit of detection; GAE – gallic acid equivalents; QE – quercetin equivalents; ChE – catechin equivalents; PGE – equivalents; TE – trolox equivalents; FRAP – ferric reducing antioxidant power; FIC – ferric ion chelating ability; LPO – lipid peroxidation; RSA – radical scavenging activity; EDTA – ethylenediaminetetraacetic acid; TEAC – trolox equivalent antioxidant capacity; ORAC – oxygen radical absorbance capacity

can generate singlet oxygen and/or hydroxyl radicals, which are powerful oxidizing agents (Balboa et al., 2013; Rajauria et al., 2013; Rajauria et al., 2010). In addition, oxygen radical absorbance capacity (ORAC) assay was occasionally applied to assess the ability for scavenging specific peroxyl radicals, being particularly useful when multiple constituents and complex reaction mechanisms are involved (Balboa

et al., 2013; Rico et al., 2018b). Reducing power assays, which assess a compound's ability to donate electrons and reduce oxidized intermediates, such as transition metals like iron (ferric ion antioxidant power, FRAP), were also widely applied in *H. elongata* (del Olmo et al., 2020; Heffernan et al., 2015; Kirke et al., 2019; Rajauria, 2019; Rajauria et al., 2013). Additionally, some studies evaluated its extracts' ability to

chelate transition metal ions, forming insoluble complexes that reduce metal reactivity and slow oxidative reactions (Balboa et al., 2013; Rajauria, 2019; Rajauria et al., 2013; Rajauria et al., 2010). Finally, β -carotene bleaching assay has also been frequently used to measure *H. elongata*'s compounds protective effects against lipid peroxidation (Cassani et al., 2022; Rajauria et al., 2013, 2016).

Overall, the antioxidant potential of *H. elongata* has been primarily assessed in crude extracts and/or purified fractions, with polyphenols, especially phlorotannins, identified as the major antioxidant compounds. These polyphenols, synthesized by marine plants in response to stress, help protect brown macroalgae from oxidative damage. Crude extracts of *H. elongata* enriched in polyphenols have been obtained using binary aqueous mixtures with organic solvents such as ethanol, methanol, and acetone (Belda et al., 2016; Cassani et al., 2022; Fernandez-Segovia et al., 2018; Mohammed et al., 2021; Rajauria et al., 2013).

Rajauria et al. found that the antioxidant activity of *H. elongata* extracts is influenced by solvent polarity or dielectric constant. Among various solvent mixtures, 60 % methanol was most effective at extracting polyphenols, flavonoids, and tannins, showing superior DPPH[•] radical scavenging activity (EC₅₀, 57.2 μ g/mL) and FRAP values (11.7 mg Trolox equivalents/g extract) compared to water or pure methanol (EC₅₀, 105.4 and 291.7 μ g/mL; 6.8 and 4.7 mg Trolox equivalents/g_{extract}, respectively). The authors also observed that higher extract concentrations increased the scavenging capacity for lipid peroxidation (LPO[•]) and H₂O₂ (Rajauria et al., 2013). Another study highlighted that methanolic crude extracts of *H. elongata*, rich in polyphenols and carotenoids, could delay β -carotene oxidation and prevent crocin oxidation, underscoring its potential as a natural antioxidant in lipid-food systems (Cassani et al., 2022). Although to lesser extent, other constituents of *H. elongata* were described to exert antioxidant properties, including monomeric sugars and lipophilic-based compounds, such as oxygenated fatty acids, carotenoids (fucoxanthin), chlorophyll derivatives, among others (Rajauria, 2019; Rico et al., 2018b).

In addition to conventional solid-liquid extraction, alternative techniques have been explored for their impact on the antioxidant capacity of *H. elongata* extracts. Ummat et al. (2020) observed that ultrasound-assisted extraction improved the polyphenols recovery, leading to stronger DPPH[•] scavenging activity and ferric reducing antioxidant power, comparatively to conventional solvent extraction. In another study, the antiradical activity of *H. elongata* extracts assessed by TEAC and ORAC tests were found increased with autohydrolysis temperature, which could be due to the higher recovery of polyphenols (Cernadas et al., 2019).

Moreover, purification techniques have been applied to crude extracts as a strategy to enhance total phenolic content and antioxidant activity, as well as to identify and characterize the specific molecules responsible for this bioactivity (Heffernan et al., 2015; Kirke et al., 2019; Rajauria, 2018; Rajauria et al., 2016). For instance, improved DPPH[•] scavenging (IC₅₀, 2.4–16.9 mg ascorbate equivalents/g sample) and LPO scavenging capacity (77.3–97.7 %) was achieved when liquid-liquid partition followed by column chromatography was applied to a crude methanolic extract of *H. elongata* (IC₅₀, 36.8 mg ascorbate equivalent/g sample; and 56.4 % for DPPH[•] and LPO, respectively) (Rajauria et al., 2016). This study identified eight polyphenol compounds deriving from the phenolic acid, flavonoid and tannin subclasses as the main contributors to the radical scavenging activity: *m*- and *p*-hydroxybenzaldehyde, gallic acid, gallic acid 4-*O*-glucoside, kaempferol, cirsimaritin, camosic acid, and phloroglucinol. In another study, SPE applied to a crude methanolic extract from *H. elongata* enhanced its antioxidant activity by 3-fold, even surpassing that of ascorbic acid, which was used as standard (Rajauria, 2018). Characterization of the purified SPE fraction revealed that phloroglucinol, a monomeric unit of phlorotannins, exhibited the strongest antiradical activity in *H. elongata*, as it represented more than 65 % of total quantified phenols. However, other compounds from phenolic acid and flavonoid subclasses may also

influence the overall antioxidant activity through synergistic or antagonistic effects. Note that the challenging structural elucidation of phlorotannins hinders the understanding of the relationship between their structure and antioxidant activity. For instance, the antiradical activity of low-molecular weight phlorotannins from *H. elongata*, fractionated by dialysis followed by reverse-phase flash chromatography, was found not only to be dependent on their concentration, but also on their geometric structure arrangement and position of free hydroxyl groups. In fact, Heffernan et al. (2015) demonstrated the structural complexity of low-molecular weight phlorotannins obtained under similar conditions. These compounds exhibited a degree of polymerization ranging from 6 to 12 phloroglucinol units and included more than 96 isomers.

Pharmacokinetics is another aspect that should be considered before establishing the antioxidant properties of these compounds. Considering the digestive system as the main point of entrance of phlorotannins into our system, the impact of gastrointestinal digestion on their structural integrity and bioavailability should be established to properly understand their antioxidant benefits to human health. In this line, a recent *in vitro* study (Catarino et al., 2022b) found reduced NO[•] and O₂^{-•} radicals scavenging capacity along gastrointestinal (GI) tract, which was consistent with the lower phlorotannins concentration.

As mentioned earlier, researchers and the food industry are collaborating on using seaweed extracts as natural antioxidants in food products. However, to ensure microbiological safety and, in most cases, palatability, these products often require heat processing. Therefore, it is crucial to understand how natural antioxidants maintain their stability under such treatments. For instance, the autoclaved hydrothermal processing of *H. elongata* was shown to enhance its antioxidant activity (Rajauria et al., 2010). At the best thermal condition (95 °C), the polyphenols content increased by 64 % compared to untreated seaweed, a fact that the authors correlated with the observed stronger DPPH[•] and H₂O₂ radicals scavenging capacity. Another study showed that high-pressure processing did not affect the antioxidant capacity of *H. elongata* over storage time, despite a loss of up to 50 % of the initial polyphenol content (del Olmo et al., 2020). This suggests that other compounds in the algae may contribute to its bioactivity.

As concluded from Table 4, while antioxidant activity studies on *H. elongata* have predominantly been used *in vitro* assays, there is a lack of data regarding its effect on living cultured cells. In this regard, the direct and protective effect of phlorotannins-rich extract of *H. elongata* on cell viability and cellular oxidative status were investigated on cultured liver cells HepG2 (Quéguineur et al., 2013). The study found that concentrations up to 1 μ g/mL had no impact on cell viability. However, concentrations between 0.5 and 50.0 μ g/mL reduced ROS generation and malondialdehyde (MDA) levels, while increasing glutathione (GSH) reductase levels and glutathione S-transferase (GST) activity. No changes in other enzymatic antioxidant defenses, particularly in glutathione peroxidase (GPx) and GSH reductase activities, were noticed. Nevertheless, when cells were submitted to oxidative stress, those treated with phlorotannin-rich extract showed reduced ROS generation and lactate dehydrogenase activity, while no effect was observed for GSH reductase. In turn, the treatment increased enzymatic activities of GPx, GST and GSH reductase, and a dose-response effect was observed for MDA levels. These beneficial effects highlight the ability of phlorotannin-rich extract from *H. elongata* to protect HepG2 cells against oxidative stress.

Antioxidant ability of *H. elongata* on *in vivo* models was only recently assessed, showing evidence that *H. elongata* extracts were able to protect intestinal tissue against ischemia-reperfusion (I/R) injury (Belda-Antolí et al., 2017). In fact, the administration of *H. elongata* 60 % ethanol extracts (830 mg/kg) to I/R Wistar rats reduced the levels of MDA, as well as the activity of superoxide dismutase, GPx and catalase comparatively to the control group, therefore highlighting their potential application in the prevention of ischemic processes. Overall, more *in vivo* studies should be conducted to assess the antioxidant capacity of crude

extracts and purified fractions from *H. elongata*, as well as to test them in food models and cellular systems. Future research focused on the purification of isolated compounds, their mechanisms of action, and their activity against other reactive oxygen species and free radicals will help clarify their antioxidant contribution.

4.2. Antimicrobial activity

The exponential growth of emerging multidrug-resistant microorganisms, including foodborne pathogens, has been posing a threat to the quality, shelf life, and safety of food products (Cabral et al., 2021). Allied to the consumer's increasing demand for healthier, fresh, and whole food products, these aspects have prompted the food industry to come up with alternatives to synthetic preservatives, leading to research on novel, natural and eco-friendly antimicrobial agents. Several studies have reported marine seaweeds as an excellent source of antimicrobial compounds. In fact, algae have evolved to withstand multiple threats in the marine environment by producing secondary metabolites with antimicrobial properties. These compounds help prevent bacterial fouling by inhibiting the attachment and growth of bacterial colonizers. Table 5 summarizes the most relevant *in vitro* studies on the antimicrobial properties of the brown seaweed *H. elongata*.

In general, the most commonly used *in vitro* assays for evaluating the antimicrobial potential of *H. elongata* are disc diffusion and dilution methods, including broth and agar dilution techniques. These tests were

mostly carried out on crude extracts of *H. elongata*, which were obtained using various organic solvents such as methanol, acetone, and ethyl acetate (Cox et al., 2010; Gupta et al., 2010, 2012; Rajauria et al., 2013; Silva et al., 2021). As expected, it has been demonstrated that the antimicrobial activity of *H. elongata* crude extracts varies depending on the extraction solvent (Silva et al., 2021). Ethyl acetate extracts were shown to have the strongest bacterial inhibition, particularly against gram-negative bacteria such as *Salmonella enteritidis* (10.42 mm) and *Pseudomonas aeruginosa* (7.06 mm), outperforming extracts from hexane, ethanol, and chloroform (5.65–7.44 mm). In a different study, aqueous methanolic mixtures, specifically 60 % methanol, were described as the most effective solvent for producing an extract with strong activity against foodborne and food pathogenic microorganisms (Rajauria et al., 2013). At 60 mg/mL, this extract strongly inhibited both gram-negative bacteria (namely *P. aeruginosa* and *Salmonella abony* by 98.7 and 95.6 %, respectively), and gram-positive bacteria (namely *L. monocytogenes* and *Enterococcus faecalis* by 98.7 and 98.0 %, respectively). Furthermore, other studies have shown that crude extracts from *H. elongata* exhibit dose-dependent antimicrobial activity against foodborne and food spoilage microorganisms (Cox et al., 2010; Gupta et al., 2012). In more detail, it has been shown that among various brown and red seaweed species, the crude methanolic extract of *H. elongata* (6.4 mg/mL) exhibited the highest antimicrobial activity, achieving 100 % bacterial growth inhibition against *L. monocytogenes*, *S. abony* and *E. faecalis*, and up to 98.4 % against *P. aeruginosa* (Cox et al., 2010). This

Table 5

Summary of *in vitro* studies for antimicrobial activity of crude extracts and purified fractions obtained from *H. elongata*.

Extraction conditions	Active compounds	Type of Antimicrobial test	Biological effect	Ref.
MeOH, 1:10 (w/v), 40 °C, 2 h	Polyphenols, namely tannins and flavonoids	<i>In vitro</i> : Tryptic soy broth plate-based dilution method; Tested [Extract]: 0.1–6.4 mg/mL Positive controls: Sodium benzoate (SB) and sodium nitrite (SN)	% Inhibition after 24 h at 6.4 mg/mL extract: <i>L. monocytogenes</i> = 100; 96.5 (SB); 96.2 (SN) <i>S. abony</i> = 100; 97.3 (SB); 98.4 (SN) <i>E. faecalis</i> = 100; 89.4 (SB); 93.7 (SN) <i>P. aeruginosa</i> = 98.4; 99.0 (SB); 97.3 (SN)	(Cox et al., 2010)
Raw <i>H. elongata</i> vs. Autoclave (AC) (85 – 121 °C, 15 min); Then, extracted with: MeOH, 1:10 (w/v), 40 °C, 2 h	Halogenated secondary metabolites, namely bromophenols and phlorotannins	<i>In vitro</i> : Tryptic soy broth plate-based dilution method; Tested [Extract]: 7.5–60.0 mg/mL Positive control: SB and SN	% Inhibition after 24 h at 60 mg/mL extract: <i>L. monocytogenes</i> = 98.7 (Raw); ~80 (AC–85 °C); ~50 (AC–121 °C); 96.5 (SB); 96.2 (SN) <i>S. abony</i> = 95.6 (Raw); ~90 (AC–85 °C); ~35 (AC–121 °C); 97.3 (SB); 98.4 (SN) <i>E. faecalis</i> = 98.1 (Raw); ~85 (AC–85 °C); ~40 (AC–121 °C); 89.4 (SB); 93.7 (SN) <i>P. aeruginosa</i> = 98.7 % (Raw); ~90 (AC–85 °C); ~35 (AC–121 °C); 99.1 (SB); 97.3 (SN)	(Gupta et al., 2010)
MeOH → 60 % MeOH, 1:40 (w/v), 40 °C, 2 h Fract: Liquid-liquid partition with H ₂ O:EA (1:1, v/v)	Purified aqueous extract containing phlorotannins	<i>In vitro</i> : Tryptic soy broth plate-based dilution method Tested [Extract]: 0.125–8.0 mg/mL Extract tested in carbohydrate- and protein- model food systems at ≠ concentrations	% Inhibition after 24 h at 8.0 mg/mL of aqueous extract in: 1) Carbohydrate-food system at 1, 5, and 10 % <i>L. monocytogenes</i> : 78.6 (1); 81.9 (5); 90.8 (10) <i>S. abony</i> : 94.9 (1); 96.5 (5); 100 (10) Extract addition → Bactericidal effect 2) Protein-food system at 1, 5, and 10 % <i>L. monocytogenes</i> : 100 (1); 100 (5); 98.5 (10) <i>S. abony</i> : 100 (1); 100 (5); 77.6 (10) Extract addition → Bacteriostatic effect	(Cox et al., 2014)
EtOH, Ace, EA, Hex, and TCM 1:33 (w/v), 50 °C, 24 h; Residue re-extraction with 10 mL each solvent, RT, 1 h	Polyphenols	<i>In vitro</i> : Agar disc diffusion method Negative control: DMSO Positive control: Lactic acid (LA)	Average diameter of inhibition zone (mm) after 24 h: Gram-positive: <i>S. epidermidis</i> → EtOH (8.94); 17.2 (LA); <i>B. cereus</i> → 6.20 (EtOH); 6.36 (Ace); 6.71 (EA); 16.7 (LA) Gram-negative: <i>E. coli</i> → 6.3 (EA); 7.5 (TCM); 18.5 (LA) <i>S. enteritidis</i> → 5.6 (EtOH); 11.7 (Ace); 10.4 (EA); 7.4 (TCM); 19.2 (LA) <i>P. aeruginosa</i> → 6.4 (EtOH); 7.1 (EA); 18.7 (LA)	(Silva et al., 2021)

MeOH – methanol; SB – sodium benzoate; SN – sodium nitrite; AC – autoclave; EA – ethyl acetate; EtOH – ethanol; Ace – acetone; Hex – hexane; TCM – trichloromethane; DMSO – dimethyl sulfoxide; Et2O – diethyl ether; TLC – thin-layer chromatography

level of inhibition was comparable to that of commercial antimicrobials, such as sodium benzoate and sodium nitrite, which were used as positive controls in the study. Identical observations were later reported in a follow-up study, where complete growth inhibition of the same pathogens was observed at the highest concentration (60 mg/mL) of *H. elongata* crude methanolic extract (Gupta et al., 2012). The authors further demonstrated a dose-response relationship, where lower extract concentrations (<60 mg/mL) extended the lag phase duration and reduced the exponential growth rate of the microorganisms. Additionally, the study highlighted the potential of *H. elongata* extract to exhibit not only a bacteriostatic effect but also a bacteriolytic mode of action. The latter was supported by a decrease in the cell density, possibly associated with the complete disappearance of bacterial DNA upon incubation with the seaweed extract at 60 mg/mL (Gupta et al., 2012).

It is important to note that all these studies were conducted using crude extracts, which contain complex mixtures of compounds that, in most cases, have not been chemically identified or characterized. Nonetheless, some of them have indicated polyphenols, in particular phlorotannins and flavonoids, as the primary antimicrobial agents in *H. elongata*. To date, the exact antimicrobial mechanism of action of phlorotannins remains unclear. Some researchers suggest that their antibacterial activity may be influenced by their degree of polymerization, while others propose that it could be linked to their ability to inhibit the oxidative phosphorylation pathway in microbes or interact with microbial proteins, leading to bacterial disintegration (Silva et al., 2020).

Beyond crude extracts, a few studies have explored alternative extraction techniques and purification processes to concentrate bioactive compounds and gain deeper insights into the specific molecules responsible for the antimicrobial activity of *H. elongata*. For example, pressurized-liquid extraction proved to be effective for the obtaining of *H. elongata* extracts enriched in polyphenols and long-chain fatty acids, particularly palmitic acid, which exhibited significant antimicrobial activity, especially against gram-positive bacteria *S. aureus* (Otero et al., 2018). The antibacterial mechanism of fatty acids has been recently elucidated, and it relies on the ability of their amphipathic properties to modulate membrane-lytic behavior, inducing both membrane instability and pore formation, which in turn can result in cell growth inhibition or even cell death (Yoon et al., 2018). Fatty acids are also capable of disrupting the electron transport chain, modifying the oxidative phosphorylation process, inhibiting membrane enzymes, and interfering with the cells' nutrient uptake (Cabral et al., 2021). Furthermore, food-grade extracts of *H. elongata* obtained through a combination of solid-liquid extraction and ultrasound-assisted extraction, were reported to be effective against gram-positive bacteria *L. monocytogenes* (Martelli et al., 2020a). Another study found that fucoxanthin, purified through preparative thin-layer chromatography, had strong antimicrobial activity against *L. monocytogenes* in comparison to the crude extract, showing similar inhibition zones of 10.7 and 9.9 mm, but at very different concentrations of 1.0 and 10.0 mg/mL, respectively (Rajauria & Abu-Ghannam, 2013).

Another important aspect underlying antimicrobial potential is to understand the effectiveness of whole seaweed and its extracts against both pathogenic and spoilage microorganisms when incorporated as ingredients in food products. For instance, a study by Cox et al. (2014) evaluated the antimicrobial activity of a purified aqueous extract of *H. elongata* (0.125–8.0 mg/mL) when added to protein- and carbohydrate-based food model systems. In protein models, antimicrobial activity was shown to be concentration-independent, since 2 mg/mL of extract was enough to inhibit the growth of *L. monocytogenes* and *S. abony* up to 100 %. Conversely, in carbohydrate models, stronger antimicrobial activity was observed along with higher concentrations of glucose and seaweed extract, which may be explained by a synergistic effect, leading to reduced water activity levels. Also, *H. elongata* exhibited a bactericidal effect in the carbohydrate models, while a bacteriostatic effect was described in the protein counterparts, an effect

that the authors attributed to the presence of phlorotannins in the extract. In the same line, heat processing was shown to have an impact on the stability of antimicrobial properties of *H. elongata*, with increasing temperatures resulting in lower antimicrobial activities, especially against gram-negative bacteria, when compared to the non-processed samples (Gupta et al., 2010). Similarly, negative impacts on antimicrobial potential were described when fermentation, sterilization or high-pressure treatments were applied to *H. elongata* (Martelli et al., 2020b). Once again, halogenated secondary metabolites, including phlorotannins, possibly with distinct molecular weights and degrees of polymerization, are highlighted as the main contributors to the described antimicrobial effect (Cabral et al., 2021; Gupta et al., 2010; Martelli et al., 2020b). Overall, further studies using alternative extraction and purification methods are needed to better elucidate the antimicrobial mechanisms of action and explore structure-function relationships of the most promising antimicrobial seaweed compounds. In addition, no studies have been addressed so far regarding the evaluation of antimicrobial efficacy from *H. elongata* compounds using *in vivo* models. Further in-depth research should be focused on investigating microbiological safety and prevention of oxidative spoilage when *H. elongata* compounds are used as natural preservatives in food products. The impact of alternative cooking methods and preservation techniques on their antimicrobial properties should also be explored.

4.3. Anti-inflammatory activity

Inflammation is the immune system's response to various factors, including pathogens, toxins, oxidative stress, cell damage, and allergens (Libby, 2007). These factors can induce acute or chronic inflammatory responses in different organs, potentially leading to several diseases such as atherosclerosis, rheumatoid arthritis, inflammatory bowel disease, neurodegenerative conditions, and cancer (Furman et al., 2019; Libby, 2007). Briefly, immune response comprises a regulated signaling cascade orchestrated by different pro-inflammatory mediators, namely cytokines (e.g. tumor necrosis factor- α , TNF- α), chemokines, adhesion molecules, enzymes, and many others. These mediators trigger important intracellular signaling pathways such as nuclear factor kappa-B (NF- κ B), mitogen-activated protein kinase (MAPK), and Janus kinase (JAK)-signal transducer and activator of transcription (STAT) (Chen et al., 2018). Among them, the NF- κ B pathway drives the inflammatory responses to upregulate pro-inflammatory genes expression such as TNF- α itself, interleukins (ILs), chemokines, adhesion molecules and key inflammatory enzymes, namely cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). The latter is responsible for NO $^{\bullet}$ production, and its expression can also be triggered by bacteria and lipopolysaccharides (LPS) in addition to cytokines (Kleinert et al., 2004). Therefore, as macrophages are the primary defense line against harmful agents, LPS-induced inflammation of RAW 264.7 cells has been widely used as a model to determine the anti-inflammatory capacity of several molecules and natural extracts. In contrast to other bioactivities, the capacity of *H. elongata* to prevent inflammatory processes has been, to date, poorly investigated. Nevertheless, the available studies have focused on its ability to target one or multiple of the previous mediators (Table 6) (Catarino et al., 2022b; Rico et al., 2018b).

It has been reported that a crude methanolic extract from *H. elongata* was non-cytotoxic to macrophages at concentrations of 1.0–500 μ g/mL and effectively inhibited the production of pro-inflammatory mediators NO $^{\bullet}$ and prostaglandin D2 (PGD2) at 500 μ g/mL (Rico et al., 2018b). These abilities were, in part, attributed to the presence of oxygenated fatty acids (e.g. di-hydroxy-oxo-octadecenoic) with α - and β -saturated carbonyl moieties, sulfated sugars and phenolics (e.g. phlorotannins).

The ability of *H. elongata* extract to inhibit key pro-inflammatory enzymes associated with obesity underscores its potential as a functional food ingredient for managing metabolic syndrome. However, a major challenge is understanding how gastrointestinal digestion (GID) affects its bioactivity. In this regard, it was recently found that the

Table 6Summary of *in vitro* studies regarding the anti-inflammatory and anti-tumoral activity of *H. elongata* extracts or purified fractions.

Extraction Conditions	Target Compounds	Model	Test conditions	Observed effects	Ref.
Anti-inflammatory activity					
50 % MeOH, 1:10 (w/v), RT, 1 h	Oxygenated fatty acids, sulfated sugars, phenolic compounds	<i>In vitro</i> : LPS-stimulated RAW 264.7 macrophages cells	Tested [Extract]: 1.0 – 500 µg/mL + 10 µg/mL LPS	No cytotoxic effect; At 500 µg/mL extract: ↓ levels of NO* and PGD ₂ ; no effect on TNF-α	(Rico et al., 2018b)
70 % Ace + 1 % AA, 1:70 (w/v), RT, 3 h (Crude); Fract: liquid-liquid with Hex → EA (Purified)	Phlorotannins (fucophlorethol-type and carmalol-type compounds)	<i>In vitro</i> : LPS-stimulated RAW 264.7 macrophage cells	Tested [Extract]: 12.5 – 200 µg/mL + 0.05 µg/mL LPS	At 200 µg/mL extract: cytotoxic effect At 100 µg/mL extract: ↓ NO* levels in digested and non- digested crude and purified fractions	(Catarino et al., 2022b)
Anti-tumoral activity					
Autohydrolysis (AH), 120 – 220 °C, 1:30 (w/v) Selected extracts: 160 °C and 220 °C	Crude sulphated fucoidan (AH-160) and Phlorotannins (AH-220)	<i>In vitro</i> : Human lung (NCI-H460), breast (MCF-7) and ovarian (A2780) carcinoma cell lines	Tested [Extract]: 10 mg/mL Positive control – Cis Pt: 3.1 µg/mL	Cell inhibition (%): NCI-H460: 27 (160); 69 (220); 74 (Cis Pt) MCF-7: 36 (160); 78 (220); 87 (Cis Pt) A2780: 94 (160); 86 (220); 96 (Cis Pt) IC ₅₀ (mg/mL): NCI-H460: 3.93 (220); 1.76 × 10 ⁻³ (Cis Pt) MCF-7: 4.02 (220); 3.31 × 10 ⁻³ (Cis Pt) A2780: 2.42 (160); 1.31 (220); 0.19 × 10 ⁻³ (Cis Pt)	(Cernadas et al., 2019)
Autohydrolysis, 160 °C, 1:30 (w/v) (AH-160) Fract: Ace (0.5–2.5 v/v): Selected fraction: AH-160-Ace at 0.5 or 1.5 % v/v	Crude sulphated fucoidan and sodium alginates	<i>In vitro</i> : Human epithelial lung adenocarcinoma (A549), colon carcinoma (HCT-116) and Caucasian glioblastoma (T98G) cell lines	Tested [Extract]: < 500 µg/mL Positive control: Staurosporine (Stp)	Cell viability (%) for: 1) AH-160 at 25 µg/mL: A549: 43.71; HCT-116: 50.86; T98G: 48.85 2) AH-160-Ace at 500 µg/ mL: A549: 47.56 (1.5 % Ace); HCT-116: 30.50 (0.5 % Ace); T98G: 56.87 (0.5 % Ace)	(Flórez-Fernández et al., 2021)

MeOH – methanol; Ace – acetone; AA – acetic acid; Hex – *n*-hexane; EA – ethyl acetate; RT – room temperature; AH – autohydrolysis; LPS – lipopolysaccharide; Cis Pt – cisplatinium; Stp – Staurosporine; NO* – nitric oxide radical; PGD₂ – prostaglandin D₂; TNF-α – tumor necrosis factor α

addition of crude and purified (EA) fractions from *H. elongata* in the range of 12.5–200 µg/mL resulted in a dose-dependent inhibition of NO* levels produced by LPS-stimulated macrophages (Catarino et al., 2022). In more detail, while at 200 µg/mL all samples exhibited a cytotoxic effect, at 100 µg/mL both crude and EA fractions submitted to gastrointestinal digestion were more effective in reducing LPS-induced NO* production than their undigested counterparts. The increased activity observed after digestion may be due to degradation products formed from phlorotannins under gastrointestinal conditions. Still, in general, much further research is needed to evaluate both *in vitro* and *in vivo* anti-inflammatory effects of *H. elongata* compounds.

4.4. Anti-tumoral activity

Cancer has a multifactorial etiology, arising from the interaction of genetic factors, unhealthy lifestyle habits, and environmental conditions. It develops when oxidative stress, caused by elevated ROS levels, overwhelms the cell's antioxidant defenses, leading to severe cellular dysfunction (Morry et al., 2017). While chemotherapy is commonly used, some drugs face restrictions due to toxicity concerns. Marine seaweeds are being explored for compounds with potential cancer prevention and treatment benefits. However, research on *H. elongata*'s anti-tumoral activity remains limited, as summarized in Table 6.

To date, the evaluation of anti-tumoral activity of *H. elongata* extracts and/or purified fractions has been assessed only through *in vitro* assays using human carcinoma cell lines. The study of Cernadas et al. (2019) investigated the impact of hydrothermal extraction processes on the anti-tumoral activity of *H. elongata*, demonstrating that the extract obtained at 220 °C was the most effective against the growth of lung

NCI-H460 (69 %) and breast MCF-7 (78 %) carcinoma cell lines, compared to the extract obtained at 160 °C, which achieved lower inhibition rates of 27 and 36 %, respectively. Both extracts demonstrated similar cell inhibition against ovarian A2780 carcinoma cells as the cisplatin standard drug used as a positive control, although their IC₅₀ values were significantly higher. The potential anti-tumoral effect of the extract at 220 °C was attributed to phlorotannins and Maillard-reaction products, while fucoidans were considered the primary contributors of the extract obtained at 160 °C. Moreover, different cell viability percentages were observed, for epithelial lung adenocarcinoma A549, colon carcinoma HCT-116 and Caucasian glioblastoma T98G human cell lines, between subcritical crude water extracts (43.7–48.8 %) and their corresponding purified fractions obtained through acetone fractionation (30.5–56.9 %). However, these effects were achieved at very different concentrations, 25 µg/mL for the crude extract and 500 µg/mL for the purified fraction (Flórez-Fernández et al., 2021). This anti-tumoral effect in subcritical water extracts may be linked to the presence of fucoidans, while sodium alginate occurs in the acetone fractionated extracts. The lower efficiency of alginates can be partially related to the acetone fractionation purification process, which increased their degree of depolymerization and modified their block structure. Considering that *H. elongata* is among the most consumed seaweed in Europe, more *in vitro* studies are needed to effectively validate the antitumoral activity of its compounds. These studies should encompass, for instance, the use of alternative extraction techniques or purification methods, and consider a broader spectrum of tumoral cell lines. For its potential biomedical application, it is important to continue investigating the antitumoral mechanisms of action of these marine compounds and possible synergistic effects. Additionally, validating their bioefficacy through *in vivo*

models is essential.

4.5. Hypocholesterolemic effect

Coronary heart disease, the leading cause of death in developed countries, is primarily driven by excessive dietary cholesterol, which is also linked to cancer, diabetes, and obesity (Cardoso et al., 2015). In fact, cholesterol plays a key role in cell homeostasis, being crucial for cell membrane structure and hormone synthesis, and its balance involves de novo biosynthesis, dietary absorption, and biliary clearance and excretion (Klop et al., 2013). Disruptions in these processes can lead to hypercholesterolemia, marked by high fasting and postprandial levels of total cholesterol, low-density lipoprotein cholesterol (LDL-c), or triglycerides (TGs) along with low plasmatic levels of high-density lipoprotein cholesterol (HDL-c) and apolipoprotein B (apoB) (André et al., 2021; Cardoso et al., 2015). To prevent hypercholesterolemia and complement drug treatments, marine-derived natural extracts, including *H. elongata*, have been studied for their lipid-lowering effects in vivo studies, as detailed in Table 7.

In a study conducted by Villanueva et al. (2014), the authors concluded that diet supplementation of hypercholesterolemic Wistar rats with 21 % *H. elongata* resulted in a 28 % reduction of the TGs serum

Table 7
Summary of *in vivo* studies on hypocholesterolemic effect of *H. elongata*.

Algae dosage and administration mode	Hypocholesterolemic effect	Ref.
Diet supplemented with 21 % seaweed powder (4-week study)	Effect in hypercholesterolemic rats: Serum analysis: ↓ TGs (28 %) and ↑ HDL-c (20 %); Liver analysis: ↓ Free-cholesterol (20 %) and ↓ TGs (12 %) Faeces analysis: ↑ Faecal excretion (34 %); ↑ protein (31 %) and bile acids (46 %) excretion	(Villanueva et al., 2014)
Restructured pork meat with 5 % seaweed powder (5-week study)	Effect in hypercholesterolemic rats: Serum analysis: ↓ Cholesterol (49 %) Liver analysis: ↑ Cholesterol (11 %) ↑ expression CYP7-A1, GR, Cu, Zn-SOD; ↓ expression CAT, Mn-SOD and GPx; ↑ GR activity; No effect on total glutathione, GSSG, GSH and TBARS	(Moreira et al., 2011)
Restructured pork meat with 5 % seaweed powder (5-week study)	Effect in hypercholesterolemic rats: No effect on adipose tissue weight; ↓ Serum cholesterol (49 %); Lipolytic enzymes: ↓ expression HSL and FAS; ↑ expression ACC; no effect on LPL-c	(González-Torres et al., 2012)
Restructured pork meat with 15 % seaweed powder (5-week study)	Effect in hypercholesterolemic rats: ↓ Serum cholesterol (49 %); ↓ expression CYP7-A1; ↑ Liver weight (11 %); ↑ hepatosomatic index (11 %); Liver enzymes: ↑ ALT, AST; no effect in ALP; ↑ Cholestasis; ↑ Hepatocellular damage	(Moreira et al., 2013b)
Restructured pork meat with 15 % seaweed powder; (1-week study)	Effect in hypercholesterolemic rats: ↓ Serum cholesterol (26 %); ↓ expression cytochrome c; ↓ caspase-3 activity; ↓ Sub G1 (% Apoptotic cells); no effect in DNA pattern distribution and DNA indexes	(Moreira et al., 2013a)

TGs – triglycerides; LPL-c – low-density lipoprotein cholesterol; HDL-c – high-density lipoprotein cholesterol; CYP7-A1 – cytochrome P4507 A1; GR – glutathione reductase; SOD – superoxide dismutase; CAT – catalase; GPx – glutathione peroxidase; GSSG – oxidized glutathione; GSH – reduced glutathione; TBARS – thiobarbituric acid reactive species; HSL – hormone sensitive lipase; FAS – fatty acid synthase; ACC – acetyl CoA carboxylase; ALT – alanine aminotransferase; AST – aspartate aminotransferase; ALP – alkaline phosphatase

plasmatic levels, concomitant with a 20 % increase in HDL-c levels. Furthermore, liver analysis of the *H. elongata*-fed rats revealed a 12 % reduction in TGs and a 20 % decrease in free cholesterol. In contrast, fecal analysis revealed an increase of 31 % in protein and 46 % in bile acids, compared to the control group. Based on these results, the inclusion of *H. elongata* in the diet of hypercholesterolemic rats was suggested to promote the excretion of cholesterol as bile salts, likely due to the algae's high dietary fiber content.

Several researchers have focused on developing functional meat-based foods with *H. elongata* to promote cardiovascular health. This strategy responds to the established epidemiological link between high consumption of meat products, especially those rich in cholesterol and saturated fats, and an increased risk of coronary heart disease. In this context, feeding hypercholesterolemic Wistar rats with restructured pork (RP) enriched with 5 % *H. elongata* resulted in reduced plasma cholesterol levels (Moreira et al., 2011). Additionally, an upregulation in the expression of cytochrome P4507 A1 (CYP7 A1), glutathione reductase (GR), and Cu,Zn-superoxide dismutase (SOD) was observed upon ingestion of seaweed-enriched RP, which was concomitant with a decrease in the expression of catalase, Mn-SOD, and glutathione peroxidase (GPx). Finally, the study hypothesized that the high expression of CYP7 A1 activates the cholesterol-7- α -hydroxylase pathway, which improves cholesterol removal. Also, RP enriched with *H. elongata* decreased the negative effect on enzyme expression of high cholesterol levels in the liver, leading to a better antioxidant status of this organ in growing rats.

Similar investigations have described the potential of RP formulations containing 5–15 % *H. elongata* to block the hypercholesterolemic effects of the dietary cholesterol (González-Torres et al., 2012; Moreira et al., 2013a; Moreira et al., 2013b). Indeed, beyond lowering plasma cholesterol plasmatic levels, the inclusion of 5 % *H. elongata* into RP was found to cause a change in the expression of lipogenic and/or lipolytic enzymes in hypercholesterolemic rats, thus reducing damage to their adipose tissues (González-Torres et al., 2012). Consistently, when hypercholesterolemic rats were fed with RP enriched with 5 % *H. elongata*, liver pro-apoptotic short-term effects were suppressed, along with the release of mitochondrial cytochrome c into the cytosol and caspase-3 activity. Contrarily, the study of Moreira and co-workers (2013b) found that RP enriched with 15 % *H. elongata* failed to reduce the incidence of cholestasis and even increased hepatocellular damage in hypercholesterolemic rats, which was consistent with the increased activity of liver enzymes, namely alanine aminotransferase (ALT) and aspartate aminotransferase (AST), observed in those rats. In fact, the authors suggest that the lower cholesterol levels in those rats may be related to the decrease in β -VLDL synthesis. This, in turn, could lead to larger amounts of cholesterol being excreted into the bile, resulting in its accumulation in the bile ducts and thus causing cholestasis. Collectively, these studies have pointed out dietary soluble fibers (e.g. sodium alginate) and polyphenols (e.g. phlorotannins) as the major compounds responsible for the hypocholesterolemic effects of *H. elongata*.

Although many studies have explored the hypocholesterolemic effects of brown algae and their crude extracts, purified fractions, or isolated compounds, research specifically on *H. elongata* is still limited. In addition, further investigation is needed to identify the algal compounds responsible for cholesterol-lowering effects and to understand their mechanisms of action on various proteins, transporters, and lipids involved in cholesterol metabolism. Also, it should be noted that consumption of brown macroalgae, in particular *H. elongata*, should be considered as a complementary strategy for preventing hypercholesterolemic conditions, and that possible interactions and side effects when consumed with prescribed drugs should be carefully addressed.

4.6. Prebiotic effect

Gut microbiota is critical for maintaining intestinal health, but factors like diet, age, and disease can disrupt its balance, leading to

conditions such as diabetes, obesity, cancer, and cardiovascular diseases (Conlon & Bird, 2015; Farias et al., 2019). Prebiotics, which resist digestion and are fermented by gut microbes to promote their growth and activity, are used to manage gut health. The potential prebiotic effects of *H. elongata* are summarized in Table 8.

The *in vitro* evaluation of prebiotic potential is commonly carried out using anaerobic batch fermentation inoculated with human fecal slurries. For instance, after submitting the whole seaweed to *in vitro* GI digestion using a model of the human distal colon, Lopez-Santamarina et al. (2022) realized that *H. elongata* was used selectively by the *Bacteroides* genus, particularly by the species *Bacteroides ovatus*, while inulin (applied as positive control) was used by the *Parabacteroides* genus, particularly by *Parabacteroides distasomis*. Also, the digested *H. elongata* increased Firmicutes and Proteobacteria populations after 24 h incubation, whereas changes by inulin were observed only after 48 h. Conversely, no differences were observed in the *Bifidobacterium* population for both substrates, while *Lactobacillus* declined throughout the fermentation assays. The study also demonstrated that *H. elongata* fermentation, like inulin, increased SCFA levels, in particular acetic, formic, propionic, and butyric acids. Compared to inulin, digested *H. elongata*, which is rich in dietary fiber and protein, appears to be more rapidly utilized by gut microbiota. This faster consumption likely explains the significant effects observed within the first 24 h of fermentation (Lopez-Santamarina et al., 2022).

In a different study, polysaccharide-rich fractions from *H. elongata* demonstrated varying fermentability patterns when incubated with rat cecal microbiota (Mateos-Aparicio et al., 2018). Fractions high in fucans and laminarans were more fermentable, producing higher levels of total SCFA (in particular acetic and propionic acids). Fractions rich in alginates led to greater production of branched SCFAs, such as isobutyric, isovaleric, and valeric acids. This suggests that the chemical structure, composition, and molecular weight of algal polysaccharides influence their fermentative behavior, though other components like resistant proteins may also play a role in their prebiotic activity (Mateos-Aparicio et al., 2018).

The prebiotic effects of *H. elongata* were also demonstrated to benefit

hypercholesterolemic Wistar rats. When included at 21 % (w/w) of their diet, rats showed a 10 % increase in gastrointestinal tract length, a 37 % rise in cecum weight, and a 58 % boost in SCFA production, particularly acetic, propionic and butyric acids. Again, these beneficial effects were attributed to *H. elongata* fermentable carbohydrates, found to enhance mucosal cell proliferation either through increased bacterial metabolism or a direct effect of SCFAs. Additionally, rats under *H. elongata* supplementation improved calcium and magnesium absorption and retention, likely due to increased SCFAs, such as calcium acetate, and/or the expansion of the gastrointestinal tract (Villanueva et al., 2014).

Overall, while *H. elongata* has been shown to exhibit high prebiotic potential; further *in vitro* and *in vivo* research is needed to definitively establish the prebiotic effects of its dietary fibers or other components, whether in whole seaweed or extracts. Additionally, the potential production of harmful oligosaccharides by gut microbiota should be evaluated. Given that *H. elongata* is widely consumed in Europe, in-depth investigations should be focused on addressing its potential prebiotic effect when used as an ingredient in food products.

4.7. Skin protective effect

Increasing awareness of the harmful effects of UV radiation has led to a search for natural alternatives in skincare. UV exposure can cause skin damage, including photosensitivity, burns, oxidative stress, and disorders such as hyperpigmentation, premature aging, and even skin cancer (Lopez-Hortas et al., 2021). Marine seaweed, including *H. elongata*, is emerging as a valuable source of bioactive compounds with protective and cosmetic benefits. Table 9 summarizes the research on the skin health benefits of *H. elongata* extracts and purified fractions.

Phlorotannin-enriched fractions from *H. elongata* demonstrated notable photoprotective activity, with sun protection factor (SPF) and UVA protection factor (PF-UVA) values exceeding 1. This activity was found to be seasonal, with autumnal fractions showing the highest photoprotective factors and phenolic content (Gager et al., 2020). In turn, fucoidan-rich extracts obtained by hydrothermal treatment at 160°C did not exhibit anti-aging activity, as they failed to inhibit

Table 8
Summary of different studies on prebiotic evidence of *H. elongata*.

Extraction conditions	Type of study	Seaweed dosage and exposure time	Active compounds	Main biological effect	Ref.
Whole seaweed submitted to GI digestion	<i>In vitro</i> anaerobic batch fermentation using fresh human faecal samples from 3 healthy donors	Inoculation of 1 % (w/v) digested HE or inulin (positive control) with 10 % (v/v) diluted faeces; Incubation time: 0, 10, 24, and 48 h	Major components of digested <i>H. elongata</i> : Dietary fiber (36 %), carbohydrates (15 %), protein (7.5 %)	After 24 h incubation vs. 0 h: Firmicutes (↑ HE; ↓ inulin); Bacteroidetes (↑ HE; ↓ inulin); Proteobacteria (↑ HE; ↑ inulin) After 48 h incubation vs. 24 h: Firmicutes (~ HE; ↑ inulin) Bacteroidetes (↓ HE; ↑ inulin); Proteobacteria (~ HE; ↑ inulin) At all incubation times, no changes in <i>Bifidobacterium</i> and ↓ <i>Lactobacillus</i> HE: ↑ SCFA at 24 h and Inulin: ↑ SCFA at 48 h	(Lopez-Santamarina et al., 2022)
Sequential extraction H ₂ O (20 and 60 °C) → HCl 0.1 M → KOH 2 M → Final Residue	<i>In vitro</i> anaerobic batch fermentation using caecal content of rats	Inoculation of 10 % (w/v) HE fractions or lactulose (positive control) with 25 % (v/v) of rats' caecal content Incubation time: 24 h	F-H ₂ O – fucoidans, laminarans, alginates and fucans; F-HCl – fucans and laminarans; F-KOH – alginates; F-Res – cellulose, fucans, and xylomannans	After 24 h incubation: Total SCFA (%) = 11.8 (F-H ₂ O); 8.2 (F-HCl); 10.4 (F-KOH); 11.6 (F-Res) Main SCFA produced: acetic and propionic acid	(Mateos-Aparicio et al., 2018)
Whole seaweed	<i>In vivo</i> hyper-cholesterolemic Wistar rats	Rats supplemented with 21 % HE powder during 4 weeks	Dietary fiber and proteins	HE-fed group vs. control: ↑ GI tract, large and small intestine length ↑ Caecum weight ↑ Total SCFAs ↑ Ca and Mg absorption	(Villanueva et al., 2014)

GI – gastrointestinal; HE – *Himanthalia elongata*; SCFA – short-chain fatty acids; HCl – hydrochloric acid; KOH – potassium hydroxide

Table 9Summary of different studies on the potential skin protective effect of *H. elongata*.

Extraction Conditions	Active compounds	Biological activity	Main effects	Ref.
Autohydrolysis, 120–220°C, 1:30 (w/v) Selected extract: 160°C	Crude sulphated fucoidans	Anti-aging activity	No anti-elastase activity: IC ₅₀ (g/mL) = 2.56 (160°C),	(Cernadas et al., 2019)
50 % EtOH, 1:10 (w/v), 2 h, 40°C Fract: DCM → Ace → EtOH → EA	Phlorotannins	Photoprotective activity	Sun protective factor: Summer: 1.51; Autumn: 2.24 UVA-protective factor: Summer: 1.27; Autumn: 1.69	(Gager et al., 2020)
H ₂ O, 1:25 (w/v), 65°C → Addition 7.5 % CA → Acid hydrolysis with sulphuric acid, 2 h, 70°C Fract: Resin – crude extract adsorption → washing with EtOH → H ₂ O	Phlorotannins, fatty acids and polyol sugars	Photoprotective activity in hyperpigmentation disorder	<i>Ex vivo</i> skin explants senile lentigo (SeL) and solar lentigo (SoL) models: Stress: ↓ SDF-1 (–34 % SeL; –48 % SoL); Stress + Extract at 3 %: ↑ SDF-1 (+27 % SeL; +38 % SoL); ↓ Melanin (–51 % SeL; –60 % SoL); Specifically, in SoL models: ↓ Oxidized proteins (–40 %); ↓ Lipofuscin (–39 %) <i>In vivo</i> clinical studies on the effect of extract after 28 days in pigmented spots: ↓ Melanin (–103 % in Caucasian's hands, –156 % in African's face; –91 % in Asian's face)	(Meunier et al., 2023)

EtOH – ethanol; DCM – dichloromethane; Ace – acetone; EA – ethyl acetate; H₂O – water; CA – citric acid; SeL – senile lentigo models; SoL – solar lentigo models; SDF-1 – stromal cell-derived factor 1

elastase (Cernadas et al., 2019).

More recently, *H. elongata* has been shown to help alleviate hyperpigmentation disorders, such as senile lentigo, caused by chronological aging and loss of melanogenesis control, and solar lentigo, which results from UV exposure and leads to increased oxidized proteins, melanogenesis, and lipofuscin accumulation. Compared to basal levels, a decreased expression of stromal cell-derived factor 1 (SDF-1), a key protein in pigmentation regulation, was observed in *ex vivo* skin explant models simulating senile or solar lentigo. However, treatment with a 3 % (w/v) purified fraction of *H. elongata* over five days restored SDF-1 expression in both models. This restoration led to reduced melanin production, thereby diminishing skin pigmentation.

In the solar lentigo *ex vivo* model, *H. elongata* extracts reduced oxidized proteins and lipofuscin, which are linked to UV-induced skin aging. A clinical study on Caucasian, Asian, and African volunteers showed that after 28 days of topical application, the extract significantly reduced melanin content and dark spots on the hands (Caucasians) and faces (Asians and Africans) compared to the placebo (Meunier et al., 2023).

Interestingly, most of the technological advances with *H. elongata* in this field have been developed over the past 10 years under private research, as can be confirmed by the high number of patents issued (Section 4). This underscores the significant potential of *H. elongata* in skincare applications and highlights its promising economic value in the cosmeceutical industry. Nevertheless, new extraction strategies are needed to increase the feasibility of the extraction process, isolation, and characterization of *H. elongata* compounds with skin benefits. Other skin-related properties should also be investigated, including anti-aging, anti-acne, and antibacterial whitening ability. At the same time, understanding the photoprotection mechanisms of these seaweed compounds is imperative to ensure both their efficacy and safety in cosmetic formulations.

4.8. Other biological activities

Metabolic syndrome and obesity are major risk factors for cardiovascular diseases, driving interest in the anti-obesity and antidiabetic potential of seaweed compounds. However, research on the antidiabetic and antihypertensive properties of *H. elongata* remains limited. Notably, the water extract of *H. elongata* showed a 70 % inhibition of α -glucosidase activity after 30 min, likely due to its high soluble dietary fiber and polyphenol content. Meanwhile, the ethanolic extract significantly inhibited glucose diffusion (up to 65 %) but had a minimal effect on α -glucosidase (Moreira et al., 2014). The combination of these two

extracts could offer promising potential as functional food ingredients with antidiabetic and hypoglycemic properties.

Rico et al. (2018b) recently demonstrated the potential of aqueous methanolic extracts from *H. elongata*, rich in polyphenols and lipids, to mitigate metabolic syndrome. Among various seaweed species, *H. elongata* uniquely exhibited angiotensin-converting enzyme I (ACE-I) inhibition with an IC₅₀ of 65 μ g/mL. Additionally, at 0.1 mg/mL, the extract reduced triacylglyceride accumulation by 52 % in mature 3T3-L1 adipocytes after 24 h, with no cytotoxicity. These antihypertensive and lipid-lowering effects suggest *H. elongata* could be valuable in functional food development for the metabolic syndrome, though the use of methanol raises safety concerns.

As a brown seaweed rich in sulphated polysaccharides, *H. elongata* may also exhibit notable anticoagulant properties. Indeed, a water extract containing these polysaccharides was reported to have a dose-dependent inhibition of factor IIa, reducing activity by 40 % at 5 μ g/mL (Adrien et al., 2017). However, its inhibitory strength (IC₅₀ = 258 μ g/mL) was weaker compared to *L. digitata* and *Ascophyllum nodosum* (IC₅₀ = 2.6 and 7.5 μ g/mL, respectively). The extract also prolonged clotting time at concentrations above 8.3 μ g/mL, but no propensity to prolong prothrombin time (Adrien et al., 2017). These results indicate that *H. elongata*'s sulphated polysaccharides primarily target the antithrombin-mediated coagulation pathway, affecting the intrinsic and/or common pathways more than the extrinsic one.

5. Patented products

A patent review is a useful way of understanding the progress and innovations made in a certain technological field, offering a good overview of which industrial sectors and/or geographical regions show the most interest and/or invest the most in its development. As perceived by the number of patents that have been filed in recent years (Table 10), there is clear evidence that *Himantalia*'s economic interest is growing steadily. Moreover, Fig. 3 demonstrates that most of the patents filed are distributed between European and Asian countries, although the high number of world patents indicates the interest in expanding these technologies to other regions. It is also interesting to note that patents regarding *H. elongata* applications can be divided into two main technological fields: food and beauty & skin care. Moreover, these patents follow two distinct chronological trends. From the first application in 2001 and over the next decade, most of the patents filed were focused on food applications, and after 2015, cosmetic applications started to appear and gain ground.

Within the food applications, several patents describe the

Table 10
Patents/patent applications for products containing *H. elongata* extracts or compounds.

Product (patent nr)	Year	Type of extract	Active ingredients	Claims	REF
Fruit dessert	2001	Concentrated edible extract with 20–40 % of dry matter	Magnesium	Increases the magnesium levels to at least 45 mg/100 mL of dessert (15 % RDA)	(Maxime, 2001)
Algae aperitifs	2001	Whole algae	Not specified	Process for drying <i>H. elongata</i> , followed by cutting it into strips of five centimeters and subsequently fried in very hot olive oil	(Luis, 2001)
Dietary supplement in granular or capsule or tablet form	2004	Grounded powder or extract	Glutamic acid	Increases de umami taste of the product	(Tatsuro, 2004)
Food supplement for menopausal or premenopausal women	2004	Water extract at RT - 60 °C	Iodine	Counteracts the possible hypothyroidal effects from the anti-thyroid thiocyanates present in the soybean flour also used in the supplement formula	(Dominique et al., 2004)
Healthy meat product	2011	Seaweed flour	Dietary fiber, protein, minerals, vitamins, polyphenols, tocopherols, carotenoids, and small amounts of n–3 PUFAs	Allows reduction of NaCl and improves water and fat binding properties	(Cofrades et al., 2011)
Comestible preparation	2012	Two-step hot water extracts	Protein, polyphenols, flavonoids, antimicrobials, polysaccharides, and condensed tannins	Edible substance that can be used for preparation of a dietary supplement, probiotic, food additive, medical preparation, food product or cosmetic product	(Rajauria & Abu-Ghannam, 2012)
Tooth enamel strengthening complex, oral hygiene composition and toothpaste	2012	Glycerol extract	Minerals (Ca, Fe and Mg), salts (KCl, NaCl, K ₂ SO ₄ and Na ₂ SO ₄), vitamins (A and C)	High cleaning capability, anti-caries effect, reduction of gum inflammation, reduction of teeth sensitivity to temperature and tactile stimuli and reduction of pigmented plaque	(Jur'evna et al., 2012)
Skin repair facial mask	2015	Unspecific extract	Not specified	Relieves and repairs weak skin and enhances skin activity	(Kuihua, 2015)
Hair care complex and cosmetic	2017	Non-specified extract	Proteins and amino acids	Increases hair strength through reduction of the porosity and increase of the hair core thickness; increases hair growth density	(Yurevna et al., 2017)
Composition for cosmetic application	2017	65–80 % Ethanol extract at 65–80 °C	High-concentration vitamin A, C and E, minerals and amino acids	Improves dark and yellow complexion; brightens dark skin and increases bright color; reproduces skin neatness and flawlessness	(Ping, 2017)
Gluten-free bread containing <i>H. elongata</i>	2019	Whole seaweed flour	Vitamin C, minerals (K, Ca, Mg, Mn), glutamate, PUFAs	Production of a gluten-free bread suitable for celiac and non-celiac consumers enriched in nutrients, minerals, PUFAs and vitamins from the seaweed	(Rodriguez et al., 2019)
Firming cosmetic composition	2019	Triglycerides extract	Fucosterol and fucosterol derivatives	Induces the synthesis of elastin synthesis, p63 protein, collagenase inhibitor and MMP1; exhibits protective and/or repairing effect of the contractile capacity of fibroblasts	(Fidji, 2019)
Topical skin composition	2019	Aqueous extract or commercial extract under the trade name Slendyl by Biosil Technologies, Inc.	Not specified	UV-A and UV-B absorption properties; reduces the appearance of the hyperpigmented skin	(Gan and Kalahasti, 2020)
Salami	2020	Whole seaweed (powder)	Not specified	Higher protein content and higher energy value	(Rodica et al., 2020)
Whitening, anti-wrinkle and antioxidant cosmetic composition	2020	Water, ethanol, methanol, butylene glycol, propanediol or a mix of said solvents	Dietary fiber, vitamin A and C, laminaran	Reduces ROS, stimulates collagen synthesis and inhibits melanin synthesis	(Kim et al., 2020)
Topical composition	2020	Water extract or commercial extract known as Slendyl by Biosil Technologies, Inc.	Not specified	Increases procollagen–1, lysyl oxidase and elastin expression in the skin; inhibits melanogenesis	(Norman et al., 2020)
Cosmetic agent	2021	Commercial extract under the trade name Marine Bamboo TG by Odycea	Fucosterol and phyco-carotenoids	Protects the keratin fibers from UV, eases combability and washability of pollen and fine dust, enhances moisture supply of the hair, increases fibers' breaking strength, and improves gloss	(Germany, 2021)
Lip sunscreen composition	2021	CO ₂ supercritical extract in an oil solution	Not specified	Provides a milder ultraviolet protection (UV-A and UV-B) with lower health risk and higher durability	(Wenna et al., 2021)
Facial mask composition	2021	Unspecific extract	Not specified	Regulates expression of metallothionein, NQO1, Ki67 and MMP1; strengthens dermis structure through targeting collagen I and hyaluronic acid; strengthens oxidation resistance of skin	(Ziyan et al., 2021)
Extraction process of <i>H. elongata</i> hydrolat	2021	Pure tap water extract	Not specified	Helps scar fading, promotes blood circulation, removes blood stasis, promotes a ruddier and finer skin after long term use and promotes overall beauty and young appearance	(Baishan, 2021)
Whitening essence milk	2021	Unspecific extract	Alginate, vitamins and amino acids	Promotes cell regeneration; strengthens skin metabolism; removes cutin; refreshes the skin; prevents wrinkles formation; controls melanin	(Chunyu et al., 2023)

(continued on next page)

Table 10 (continued)

Product (patent nr)	Year	Type of extract	Active ingredients	Claims	REF
Cosmetic composition	2021	Aqueous extract	Polyphenols, particularly phlorotannins, fatty acids, citric acid, D-mannitol, D-altritol	production and prevents color spots appearance Exerts anti-tyrosinase, anti-hyaluronidase, anti-collagenase and anti-elastase effects	(Humeau et al., 2021)

PUFA – polyunsaturated fatty acid; RDA – Recommended daily dose; RT – Room temperature; ROS – Reactive oxygen species; NQO1 - NAD(P)H quinone dehydrogenase 1; Ki67 - Marker of proliferation; Ki-67; MMP – Matrix metalloproteinase

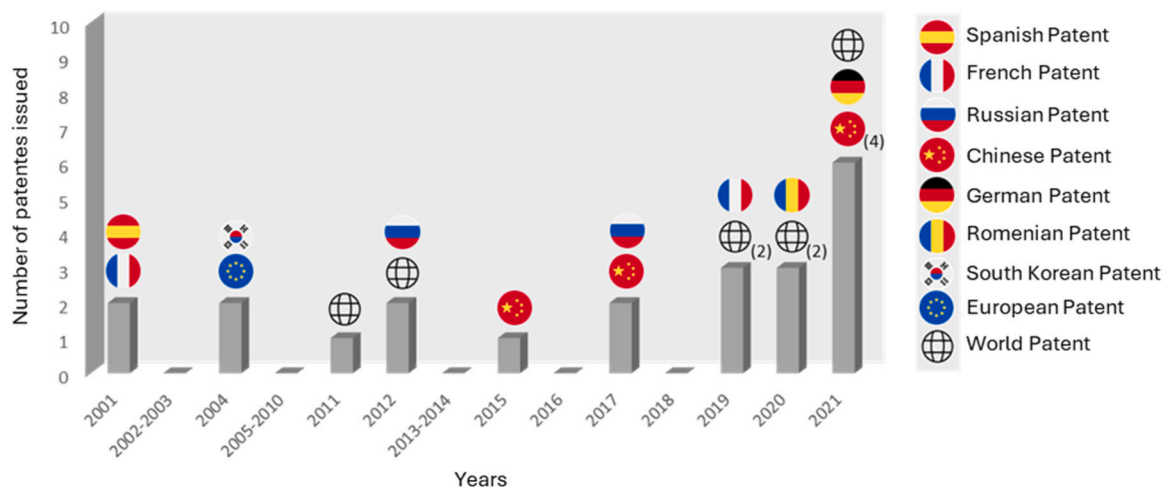


Fig. 3. Distribution of patent applications per year and geographical coverage.

incorporation of seaweed flour or concentrated extracts of *H. elongata* into food products. These patents focus on enhancing nutritional value (Rodríguez et al., 2019) or give a certain sensorial characteristic (Tatsuro, 2004). Additionally, patents have been filed for the development of dietary supplements with health-promoting properties (Dominique et al., 2004) and for specialized seaweed preparation processes (Luis, 2001).

In turn, the patents filed in the cosmetic field usually describe the use of different extracts for the preparation of several compositions (topical skin, hair, lip or facial compositions) capable of providing UV protection (Gan & Kalahasti, 2020; Germany, 2021; Wenna et al., 2021), helping with scar fading (Baishan, 2021), or interfering with the activity of different proteins (e.g., elastin, collagenase, tyrosinase, hyaluronidase, among others), consequently improving hair strength (Yurevna et al., 2017), skin firmness and brightness (Ping, 2017), and cell regeneration (Chunyu et al., 2023), as well as reducing the formation of ROS (Kim et al., 2020), wrinkles and color spots/hyperpigmentation (Gan and Kalahasti, 2020).

In a slightly different field, i.e., oral care, a glycerol extract from *H. elongata* rich in minerals, salts and vitamins A and C was also described as component of a patented tooth enamel strengthening complex, oral hygiene composition and toothpaste that is claimed to have anti-caries effects, reducing teeth sensitivity, gum inflammation, and plaque pigmentation, thus providing a higher cleaning capability (Jur'evna et al., 2012).

Apart from the patents herein listed, in which *H. elongata* constitutes a main ingredient, there are over 400 entries in World Intellectual Property Organization (WIPO) database for patents that vaguely mention or include *H. elongata* seaweed and/or extracts in their claims.

6. Challenges of *H. elongata* processing

Despite the potential health benefits and applications of *H. elongata*, there are significant challenges that should be considered when

considering the widespread utilization in the food, pharmaceutical, and nutraceutical industries. One of the first issues faced right after harvesting is its high moisture content, which can go from 75 % to 85 % (Pereira, 2011), making *H. elongata*, like any other seaweed, extremely perishable in their fresh state. Therefore, dehydration processes or other preservation techniques must be applied to prevent biomass spoilage and deterioration, as soon as possible after harvesting, which usually involves relatively complex logistics. On top of it, the choice of such preservation techniques also needs to be carefully chosen as they can have a significant impact on the seaweed's nutritional properties and/or on the phytochemical stability and bioactivity. Indeed, forced-air oven drying of *H. elongata* at 25 °C was shown by different authors to induce the loss of its phenolic content and concomitant halving of its antioxidant activity (Cox et al., 2012; Gupta et al., 2011).

But whilst this and other economic challenges such as the cost of production, harvesting and downstream processing may play a significant role in limiting the scalability of the use of *H. elongata* as food ingredient, the major challenging factors are usually associated with consumer's sensory acceptance of the seaweed itself and/or foods containing it. Indeed, its aroma and fishy taste are considered to be one of the main problems regarding the application of *H. elongata* in foods. Moreover, upon drying or processing, *H. elongata* may as well develop a tough, fibrous texture, which makes it unappealing to consumers and limits its incorporation into foods. For that reason, the addition of *H. elongata* to foods can only be tolerated in low concentrations, usually below 5 % depending on the food matrix. According to Vilar et al., the addition of 1 % of *H. elongata* flour to reformulated frankfurters caused a reduction in their hardness and chewiness (Vilar et al., 2020). Moreover, *H. elongata*-containing frankfurters were, overall, underscored compared to the control samples, mostly influenced by the seaweed flavor and aroma. Interestingly, in a similar study in which *H. elongata* at 5 % was added to low-fat frankfurters, instead of a reduction in hardness and chewiness, the opposite occurred (Lopez-Lopez et al., 2009). Nevertheless, this did not make much difference upon sensory analysis

as *H. elongata*-added sausages ended up getting much lower scores than the control samples, once again with the off-flavors being pointed out as the major cause.

The use of *H. elongata* as a food ingredient has also been explored in other products such as bread and dairy. Indeed, Cox et al. reported that the addition of 10.33 % *H. elongata* flour in breadsticks resulted in poor acceptance by panelists, with taste receiving the lowest score among all evaluated parameters (aroma, appearance, texture, and taste). However, when the seaweed concentration was reduced to 6.08 %, a significant improvement in sensory evaluation was observed, with all parameters reaching values comparable to those of the control (Cox and Abu-Ghannam, 2013). In contrast, a study on bread loaves incorporating 8 % *H. elongata* flour yielded less favorable results, as all tested sensory parameters (color, texture, and odor) were rated lower compared to the control bread (Rico et al., 2018a). Following the same trend, when adding 1 % of *H. elongata* to yogurt or quark cheese, all the sensory scores decreased compared to the respective controls (Nuñez & Picon, 2017).

Considering these limitations, the application of intermediate processing methods such as blanching or fermentation may be necessary to attenuate the unfavorable sensory attributes of this seaweed. However, because of the nature of its polysaccharides and overall chemical composition, common food processing strategies may not be effective on these marine macroalgae. For example, fermentation of *H. elongata* using lactic acid bacteria was found unsuccessful since neither heat-treated nor raw seaweed were able to support the growth of *Lactobacillus plantarum* (Gupta et al., 2011). It is, therefore, necessary to expand these studies to different organisms or consortiums of organisms to find an effective way of processing *H. elongata* so that a final product with better acceptance by the consumer can be achieved. Ingredient pairing and final formulation will also play a crucial role when it comes to the development of *H. elongata*-containing foods, as combinations with seasonings or incorporation in foods that typically have strong flavors may help mask the seaweed off flavors.

7. Concluding remarks

In summary, *H. elongata* is a nutrient-rich seaweed packed with a wide array of bioactive compounds that support health through multiple pathways. The high fiber content of this species has been seen to aid in digestive health by promoting gut homeostasis and supporting a healthy gut microbiome, while some specific polysaccharides have demonstrated important bioactivities such as anti-inflammatory, antitumor (e.g. fucoidans and alginates) or anticoagulant (e.g. fucoidans) agents. Its iodine content may importantly contribute to proper thyroid function, while the presence of a balanced Na/K ratio, together with omega-3 fatty acids contributes to cardiovascular health, potentially reducing the risk of heart disease. Furthermore, its Fe and Ca content, alongside its valuable protein profile makes *H. elongata* a promising and healthy addition to a vegan or vegetarian diet where these elements tend to be more difficult to get. Antioxidant and anti-inflammatory compounds like phlorotannins, fucoxanthin, fucoidans and alginates have great potential to combat oxidative stress and inflammation, lowering the risk of cancer and chronic diseases in general.

Overall, the diversity and versatility of the compounds found in this species grant potential for its exploration as a natural source of ingredients for the development of multiple industrial and technological applications, particularly in the food, pharmaceutical and cosmetic sectors. This potential is evidenced by the growing number of patents issued in recent years, especially in the food and cosmetic sectors. While this underscores the species' economic value, much remains to be explored. Further research is needed to uncover new compounds and bioactivities, understand their interactions within the body, and determine safe and effective ways to maximize their benefits for future applications.

CRediT authorship contribution statement

Catarino Marcelo D.: Writing – review & editing, Writing – original draft, Conceptualization. **Circuncisão Ana R.:** Writing – original draft. **Silva Sónia:** Writing – original draft. **Pinto Diana C G A:** Writing – original draft. **Pereira Olivia R.:** Writing – original draft. **Cardoso Susana M.:** Writing – review & editing, Supervision, Conceptualization.

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Data availability

No data was used for the research described in the article.

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