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Review article

Valorisation strategies for brown seaweed biomass production in a European context

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ABSTRACT

Phaeophyta (brown algae) represent a significant proportion of macroalgal production worldwide. While there are around 1500 species of brown algae, biomass production originates from only a small number of species. Production is far greater in Asia where seaweed farming is part of the cultural background, where the primary use is for human consumption, and where growing conditions are significantly different from the European contexts. With all of this in mind, the cost of European seaweed aquaculture production is not currently economically viable if brown algae biomass were to be produced purely as bulk feedstock for agricultural fertilizers or animal feeds. This review focuses on three target brown algae species (*Laminaria digitata*, *Saccharina latissima* and *Alaria esculenta*), investigating the potential uses for these seaweeds as both bulk feedstock and also for the production of higher value extracted components in the following areas: hydrocolloids, animal feed, chemical production through fermentation, human foodstuffs, agricultural applications, cosmetics and pharmaceutical applications.

1. Introduction

Seaweed farming has grown in interest as a carbon negative activity to produce sustainable feedstocks for food, pharma, and materials [1]. According to the Food and Agriculture Organization of the United Nations (FAO) the global aquaculture production of seaweed in 2016 was about 30 million tonnes, with China (47.9 %) and Indonesia (38.7 %) dominating production with a gross value of US$11.6bn (http://www.fao.org/in-action/globefish/publications/details-publication/en/c/1154074/). The emergence of a global seaweed market driven by the demand for biobased products, particularly in Western countries, has promoted increased interest in seaweed biorefining reflected in the publication of recent reviews focussing on biorefining processes [2–7]. The present review brings a European perspective to the farming of seaweed, facing global competition for feedstocks and markets, and exploring the viability of seaweed farming in a biorefining context. We put particular emphasis on seaweed-derived products that can facilitate the development of aquaculture in the context of environmental impact, regulation, and market demand. Although the present review focuses on brown algae, we will refer to some valuable products derived from both red and green algae in the context of seaweed valorisation.

There has been growing interest in developing a mature industrial scenario for seaweed farming in Western countries, particularly in Europe. In spite of the environmental and social benefits for coastal communities, the relatively large investment required represents a barrier for seaweed farming [8]. These high costs can be offset by developing products with higher market values that compensate the investment required for offshore seaweed farming. Biorefining has been defined as the sustainable processing of biomass into a spectrum of marketable products and energy [9] and can add value to biomass by producing multiple products from the same feedstock, combining low volume/high value with high volume/low value commodities [10]. The chemical diversity of seaweed biomass allows the targeting of diverse markets. Worldwide, the largest use of seaweed is for direct human consumption (80 %), followed by the extraction and production of hydrocolloids for different industrial applications, fertilizer and feed [11].

Macroalgae are multicellular organisms that comprise thousands of taxonomically diverse species and are grouped depending on the colour of their photosynthetic pigment and cell-wall chemistry. The three main groups of red (Rhodophyta), green (Chlorophyta) and brown (Phaeophyta) macroalgae are taxonomically distant as well as chemically diverse. The structure of the cell wall, as in most living organisms,

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represents a network of polymers that comprise a fibrous fraction with structural function and an amorphous matrix that allows the interaction between the cell and the environment. These fractions can have different chemical compositions, but the structural and matrix fractions are an architectural feature present from bacteria to plants. In the particular case of macroalgae, the cell wall also accumulates storage polysaccharides.

The interest in developing European macroalgae farming was initially driven by the possibility of producing biofuels from seaweed biomass. However the unfavourable economic balance of this process coupled with the technological hurdles of producing biofuels from seaweed derived sugars discouraged these applications [12]. The biochemical composition of seaweed-derived fractions does offers the possibility of applications in higher-end markets such as personal care, nutraceuticals and pharmaceuticals [13–16].

While worldwide algae biomass production in 2016 was 32.67 Mt, only 0.57 % of this volume was produced in Europe [17]. In addition to these low production volumes, only a very small proportion of European algae production is generated in aquaculture (defined as 'farming on water') - 98 % comes from wild stocks. By comparison globally over 90 % of algal biomass is produced in aquaculture. As a results aquaculture, and in particular seaweed farming are receiving political attention as part of the transition to a circular and sustainable bioeconomy within the European Union [18]. Within this political context, the EU Blue Growth strategy [19] and more recently the Blue Economy Report in 2022, put seaweed farming at the centre of the sustainable growth of the maritime economy with job creation in coastal areas. This context is reflected in the creation of regional hubs in synergy with other aquaculture activities, as well as in research activities to fill the knowledge gaps at various levels of seaweed production [20]. European seaweed production costs are higher than in Asian geographical locations for a number of reasons: more restrictive regulations, higher cost of labour, and higher sea state (more turbulent oceanic conditions characterized by large, powerful waves and strong winds). As a result, production in Europe will require the targeting of specific medium-high value products from biomass (Fig. 1), as well as coordinated actions to develop an industrial ecosystem that matches both needs and scale.

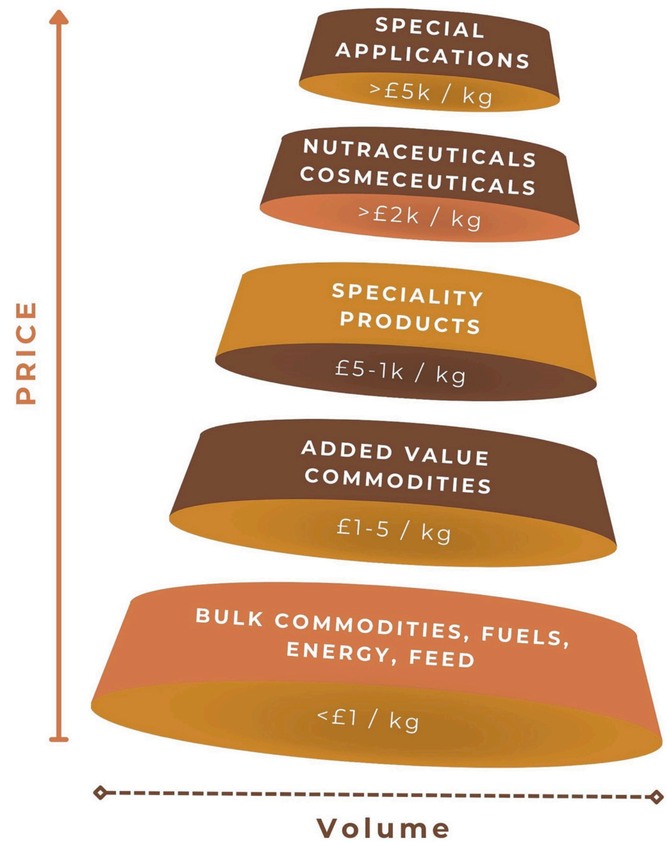

Fig. 1. Value pyramid for products from algal biomass from high volume-low value, to low volume-high value products.

2. Biomass composition of brown algae

Brown macroalgae - which include species belonging to the *Fucus*, *Laminaria*, *Himanthalia*, *Saccharina*, *Undaria*, *Alaria* and *Ascophyllum* genera - make up a total of around 1500 different species, and grow mostly in cold and shallow waters [21]. This makes brown algae suitable for growth in the cooler seas of Europe – as an example, in the UK the following species are already produced commercially: *Saccharina latissima*, *Laminaria digitata*, *Laminaria hyperborean*, *Himanthalia elongate*, *Fucus vesiculosus*, *Fucus serratus*, *Fucus spiralis*, *Ascophyllum nodosum*, *Alaria esculenta* and *Pelvetia canaliculate*.

The biochemical composition of brown species of macroalgae is complex and include a unique and heterogeneous carbohydrate composition present in high concentrations (34–76 % DM). Differences between red/green algae and the brown algal cell walls are clear on a biochemical level, with brown algae polysaccharides sharing more similarities with plants (cellulose), animals (sulfated fucans), and also with some bacteria (alginates). Sulfated fucans and alginates represent the main portion of the cell wall in brown algae (~45 %), while cellulose only accounts for a small fraction (1–8 %). Proteins, phlorotannins and halide compounds such as iodide are also components in brown algal cell walls [22]. Fig. 2 shows a model of the organization in brown algae cell walls [22].

2.1. Alginates

Alginate is one of the main structural polysaccharides found in Phaeophyta, an unbranched polymer consisting of 1,4-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G). Composed of homopolymorphic M and G regions alternating with heteropolymorphic M and G regions, alginate does not exhibit a regular repeating pattern in its structure [23]. The pattern of M and G units is the main factor responsible for their physicochemical properties (viscosity, sol/gel transition, and water-uptake). These properties are determined by the spatial conformation of M and G-blocks. While M-block rich alginate does not gel in the presence of divalent cations, G-block rich alginate has a spatial conformation in "zig-zag" able to form 'egg-box' junctions with calcium, bridging two antiparallel chains and therefore increasing the mechanical strength of the resulting gels in aqueous solutions [24]. These physicochemical properties will determine the range of applications for each type of alginate.

2.2. Fucoidans

Fucoidans, another cell wall polysaccharide suggested to have a protective role against drying, is composed of sulfated esters of L-fucose [25]. They can be found in the form of homopolymers (fucans) or heteropolymers (fucoidans). Sulfated fucans occur not only in brown algae, but also in sea cucumbers and in the egg jelly coat of sea urchins. While echinoderm fucans have regular structures composed of linear and repetitive sequences of one, two or four residues, the brown algal sulfated fucans are highly branched polysaccharides, ranging from high uronic acid, low sulfate-containing polymers with significant proportions of xylose, galactose and mannose, to highly sulfated homofucan molecules [26]. Species-dependent structural variations have also been observed in most of the sulfated fucans, with structural features that are characteristic for each group within the Phaeophyta. Interest in fucoidans has significantly increased due to the range of biological activities the polysaccharide has been shown to exhibit (see Section 3).

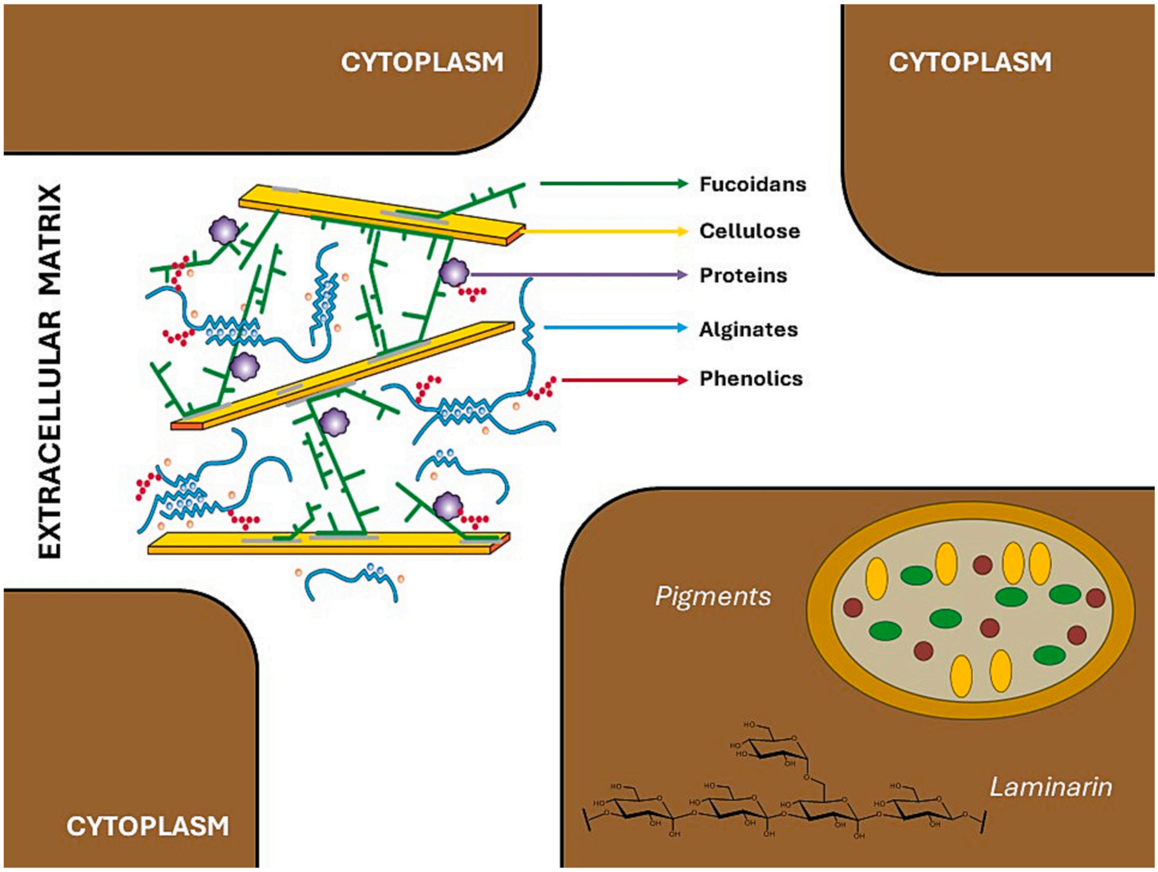

Fig. 2. Model of biomass composition in brown algae. Schematic representation of polymers present in the extracellular matrix and intracellular compounds. The figure is adapted from [22], © Oxford University Press, with authorization. [22].

2.3. Laminarin

Laminarin is a storage glucan typically used as a food reserve in Phaeophyta and represents between 1 and 20 % of the biomass (DM). It is found in cell vacuoles and consists of a linear polysaccharide of β-(1–3)-D-glucose with terminating chains of D-mannitol and occasional β-(1–6)-glycosidic linkages [27]. The structural features of laminarin vary according to species.

2.4. Proteins

Although lower than both red and green algae, the presence of appreciable quantities of proteins in brown algal cell walls has been known for some time [28]. Interestingly, purified sulfated fucan fractions are associated with significant amounts of proteins that are likely to be of structural importance. Association profiles also suggest that the proteins found in the fucan fractions are covalently attached to phenol compounds, although the latter are more frequently associated with alginate blocks [22].

2.5. Other small molecules of note

In addition to these components, the biomass of brown algae has a diversity of small molecules that have markets and applications that make them important targets for valorisation. For example fucoxanthin – a carotenoid that is part of the light harvesting complex of the photosynthetic apparatus in brown algae [29] – has attracted substantial interest due to its therapeutic potential. Besides being proposed as a general antioxidant compound [30], fucoxanthin has shown potential as an inhibitor of cell proliferation in glioblastoma, an aggressive form of cancer occurring in brain or spinal cord tissue [31]. The mechanistic action of fucoxanthin on glioblastoma cells has shown synergy with synthetic pharmaceuticals suggesting potential for combined treatments [32]. While only representing <1 % of the total dry matter content of brown algal biomass, fucoxanthin is a classic example of a potential low volume – high value product.

Mannitol is a sugar alcohol that constitutes a significant proportion of seaweed biomass (typically 10–15 %) and has various applications in confectionery, oral care, pharmaceuticals, food, surfactants, and cosmetics [33]. While mannitol is typically commercially produced by the catalytic hydrogenation of fructose [34], in Asia mannitol is extracted from seaweed [35].

3. Target species of brown algae for European cultivation

Around 221 seaweed species are utilised around the world for different applications [36]. *Laminaria digitata*, *Alaria esculenta* and *Saccharina latissima* have been identified in the context of European aquaculture for their potential for cultivation (Fig. 3).

Saccharina latissima, commonly known as sugar kelp, has received particular attention due to the promising performance in aquaculture systems. It is a candidate species for sea farming that has proven its ability to grow under conditions of the cooler regions of western Europe. With regard to cultivation opportunities, a marked difference with *Laminaria digitata* is that it is a short living species and has to be grown every year from fresh seedlings. Primary growth starts from the base of the thallus whereas secondary growing zones (meristoderms) are responsible for its latitudinal growth [37]. In the North Sea, the growing season runs from September until March–May, growing from 4 mm at the end of August to 2.5 m tall, one-bladed thalli. It is more susceptible to herbivores as the thalli are less leathery than those of *L. digitata*. It is currently being investigated whether repeated harvesting will increase

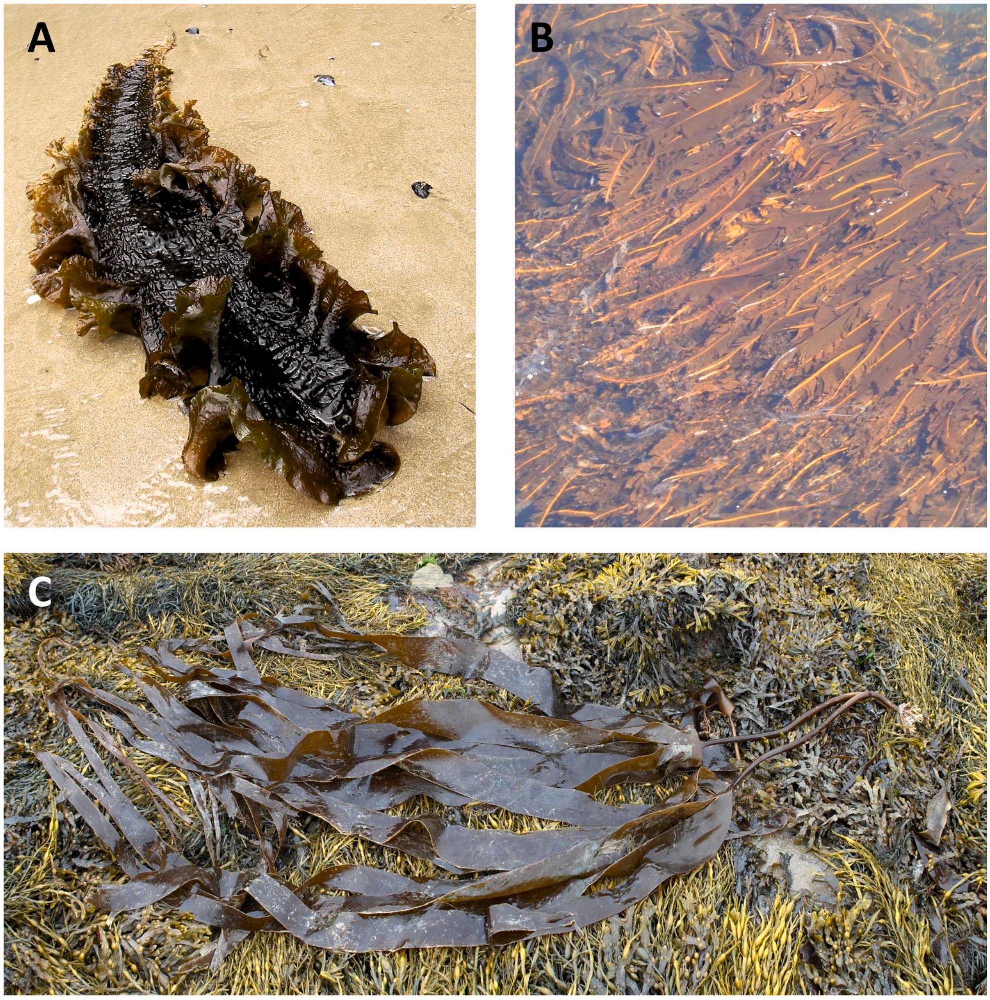

Fig. 3. Target species for aquaculture in the European Atlantic region. A. *Saccharina latissima*, B. *Alaria esculenta*, C. *Laminaria digitata*. (A, Author: Baralloco, License: Creative Commons Attribution-Share Alike 3.0 Unported license; B, Author: Ryan Hodnett, License: Creative Commons Attribution-Share Alike 4.0 International license; C, Author: Stemonitis, License: Creative Commons Attribution 2.5 Generic license).

production volumes, balancing the finances of *Saccharina* farming [8].

Alaria esculenta is mainly cultivated for human consumption as it is rich in sugars, vitamins and contains moderate levels of protein [151]. Also known as 'Atlantic Wakame', it has been cultivated in Ireland for the last 25 years [38] and is an economically attractive species due to its high growth rate of up to 10 cm per day, as well as being native to North Sea coastal waters [38]. Other uses of *A. esculenta* include animal fodder, biochemical extracts used in cosmetic products and the production of alginates, as it contains up to 42 % alginic acid [38]. Since worldwide demand for cultivated kelp is expected to continue to expand, *A. esculenta* farming will continue to grow. The expansion of *A. esculenta* cultivation requires an understanding of the ecological conditions and associated fouling organisms to inform seaweed farmers regarding the best time to harvest their crop to reduce loss of biomass.

Laminaria digitata is well adapted for cultivation under North Sea conditions [39]. The growing period is from September to March/May depending on the location and starts from seedling lines that are twisted around the production lines, growing from 4 mm seedlings up to approximately 2 m long kelps [40]. Primary growth starts from the base of the thallus whereas secondary growing zones (meristoderms) are responsible for its typical fingered shape. It grows at low temperature conditions, tolerating temperatures as high as 18 °C. During winter, the majority of nitrogen in *L. digitata* is stored until early spring, when it starts to increase its protein content and secondary metabolites [41]. Similar to *Saccharina*, repeated harvesting would increase production volumes and prevent unwanted growth of organisms on the thallus. However, the precise effects of these practices remain a subject of research.

4. Potential seaweed uses

Asian countries in which seaweeds have been consumed for centuries have a well-established supply chain as well as volumes and production costs. In European and other Western countries, seaweed consumption is not common practice. At present, seaweed is not farmed at a large scale in the North Sea. Seaweed production in tropical climates is not comparable to seaweed farming in temperate marine waters such as those found in Europe. In Asia, most farming takes place near the shore and relies on manual labour. Offshore seaweed cultivation, on the contrary, requires mechanisation and investment that is not required in tropical marine regions.

Although in Europe direct consumption of seaweed is currently low, globally 75–80 % of all seaweed produced is consumed in Asian diets. The second most important application is the production of thickeners for food and non-food applications. The third and fourth important applications in terms of market value are as fertilizer and seaweed meal [42]. It is worth noting that the potential of seaweed to accumulate minerals represents a potential risk for contamination with heavy metals which may affect the end use of the biomass. However, levels of these contaminants are highly dependent on the ecological location of seaweed production. While in open waters the level of heavy metals will be low, this may not be the case in more confined growth environments. Arsenic levels are of particular concern, as well as very high levels of iodine. The feed industry is heavily regulated and the risk of contaminants with heavy metals may make the introduction of these ingredients challenging. Regulation (EU) No 68/2013 lays down rules for the placing on the European market and use of feed materials and compound feed, and includes provisions for feed derived from seaweed. Under this regulation, seaweed-based feed products must meet certain requirements in terms of composition, labelling, and packaging. The regulation also sets maximum levels for certain contaminants such as heavy metals.

Besides the larger markets of food and feed, several different new markets are of potential interest. Bioactive compounds in seaweed may find application in a processed or isolated form in food additives and/or pharmaceuticals. Brown algal species also contain other chemicals or chemical precursors and macro chemicals (laminarin and proteins) that could be used in chemical production or specialised animal feed, for example for the reduction of enteric fermentation in ruminants [43]. Seaweed-based products for these markets are presently available at small scale.

Based on this global context, we consider that seaweeds grown in European waters can potentially be used for a number of purposes. Due to environmental conditions brown algae would seem to be the seaweed of choice for production in European and particularly North Sea waters, if the biomass can be biorefined into a range of products for markets beyond just food and feed. Some of the most relevant applications are summarised in Table 1 and graphically represented in Fig. 4.

4.1. Human consumption

The predominant use of seaweed in the world is for direct human consumption. This is true particularly in Asia where seaweed has been consumed for centuries and makes up part of the daily diet. Despite old traditions of seaweed consumption in coastal communities in Western countries, the market penetration of seaweed in the food sector is limited and in many places is considered a new food category. There is a positive public opinion of seaweed based food, which is perceived as healthy and nutritious [44]. In particular, consumers give higher scores to seaweed than to land based products, due to their environmental credentials [45]. Moving seaweed-based food products away from niche markets will require an emphasis on personal benefits to the consumer and also on the characteristics of the production process and origin of the seaweed [46].

Despite the small size of the seaweed market in Europe, the use of algae biomass in food applications is still a growing market. The regulatory status of algae and its application as a potential food stuff or ingredient is a particular consideration with respect to European markets. In the EU, novel foods require pre-market authorisation governed by the novel food regulation (EU) 2015/2283 before they can be sold. A food item listed in the Novel Food Catalogue (NFC), which is a non-binding database that reflects the views of Member States of the EU, may have one of the following statuses: novel, not novel, not novel in food supplements or subject to an ongoing novel food status consultation. If a seaweed is listed as not novel, it can be commercialised [47]. The three species on which this report focuses are included in the NFC, making them a simple product to be marketed as food in the EU: *Alaria esculenta*, also listed in France as food, and *Laminaria digitata* and *Saccharina latissima*, both also listed as food in France, Belgium, and Italy. This is not the case for all species of these genera and precise taxonomic determination is required to fall in the food category. Indeed, a number of new farms are harvesting these three species in the UK and marketing the products in the food market as seaweed for direct human consumption.

Table 1
Summary of potential uses for seaweed and seaweed extracts.

Component	Uses		Comments
Bulk biomass	Human consumption	Human food	This represents 75–80 % of the use of seaweed biomass worldwide, though predominantly in Asia. Viewed as 'healthy, nutritious, natural, fresh, a good source of protein, low in calories' with positive environmental credentials. Although currently a small market in European foods, the use of algae biomass in food applications is still a growing market.
	Animal feed	Bulk feed	Although a huge market, compared to the large amounts of imports for animal feed, the small amounts of seaweed produced annually represent a mismatch in scale. Additionally, brown algae has a low protein content (below 10 %) compared with red and green algae species so is an unattractive feedstock.
		Feed additive	There is potential in using algal extracts for the production of feed supplements.
Hydrocolloids	Emulsifiers – used to increase viscosity	Alginates	Unique to brown algae, alginates have gelling properties which have found uses in foods, medicinal science and cosmetics.
Sugars	Chemicals production through fermentation	Biofuels	Several seaweed species and by-products from the seaweed industry have been studied as feedstock for the production of ethanol and butanol. The low price of fuels produced from seaweed biomass fermentation make this valorisation route a low priority.
		Platform chemicals	The production of platform chemicals by fermentation (*e.g.* lactic or citric acid) is a possibility, but the current cost of seaweed feedstock is unlikely to compete favourably with sugar streams normally used for these processes (*e.g.* corn syrup, sugarcane molasses or sugar beet).
Seaweed extract	Agrochemicals	Fertilizer	A traditional use for seaweeds dating back thousands of years. In Europe, farmers incorporated seaweed into the soil or used it as compost.
		Biostimulant	Applied to plants with the aim of enhancing

(*continued on next page*)

Table 1 (*continued*)

Component	Uses		Comments
			nutrition efficiency, abiotic stress tolerance and/or crop quality traits.
	Cosmetics	Polysaccharides	Polysaccharides are the most significant compounds present in macroalgae due to their dermatological activity. Fucoidans and alginates from brown algae have cosmetic applications as photoprotectants, moisturizers and wound-healing agents.
		Phenolics	Phlorotannins from brown seaweed have a wide range of functional bioactivities including antioxidant, antimicrobial, anti-inflammatory and anticancer.
	Cosmetics	Pigments	Brown algae contain the pigments chlorophylls a and c, fucoxanthin, and carotenoids and have cosmetics application as antioxidants and antimutagenics. They are also natural colouring agents, and also have deodorizing and antibacterial properties.
		Proteins & peptides	Brown algae species are generally low in protein compared to other macroalgae and do not have the diversity of bioactive proteins of red and green algae. However protein fractions have shown lipolytic, antioxidant, chelating and radical scavenger activity.
		Topical applications	Topical applications are well-tolerated and can provide localised action for the various benefits of seaweed extracts.
Seaweed extract	Medicinal uses	Pigments	Fucoxanthin is an orange-coloured xanthophyll pigment that exhibit biological activities such as anti-inflammatory, antiobesity, antiangiogenic and anticancer properties.
		Polysaccharides - fucoidans	Fucoidans exhibit numerous pharmacological properties in different mammalian systems: antithrombic, anticoagulant, antitumor, antiviral, contraceptive and antioxidant. Several fucoidans express antiproliferative activity against cancer cells. Antibacterial and antiviral properties of fucoidans have also been demonstrated. Seaweed polysaccharides have been shown to reduce blood glucose levels and total cholesterol levels in diabetic rats.
		Phenolics	Phlorotannins inhibit microbial growth. They can also be used for the treatment of various allergic diseases. Antioxidant activity of phlorotannins has been detected in brown seaweeds and shown to treat neurodegenerative diseases such as Alzheimer's. The properties of phlorotannins are diverse and reports suggest that some possess potent antiproliferative activity against human breast cancer cells are one of many anticancer activities found.

4.2. Animal feed (ingredients and supplements)

The feed market is a large industry and processes significant amounts of raw materials. However, compared to the large amounts of non-seaweed imports for animal feed, the small amounts of seaweed produced annually represent a mismatch in scale. When considering brown algae for animal feed its low protein content makes it less desirable when compared to other seaweed biomass. Red algae presents the highest protein content of all the macro algae (up to 45 % DM), while some green algae are comparable to other common animal feeds like soybean (38 % DM), brown algae protein contents are generally lower (4–24 % DM) [48]. Based on a study in *Polysiphonia* [49], Van den Burg et al. [50] calculated the economic value of kelp species as animal feed. The values expressed as the price (€/100 kg dry product, 94 % DM) for a 5 % inclusion of seaweed into a grower pig diet was negligible for *Laminaria digitata*, €4.40 for *Saccharina latissima* and €11.50 for *Palmaria palmata*. These values/100 kg of product will be insufficient to cover the cost of producing the biomass.

4.3. Hydrocolloids

Seaweed hydrocolloids or industrial gums comprise three categories: alginates (derivatives of alginic acid), agars and carrageenans. These are used in products to increase viscosity and as emulsifiers. They can be found in various materials including ice cream, pet food, bakery goods, and personal care products.

Carrageenans are derived from various red algal species and this market is dominated by producers from the Philippines and Indonesia, using the species *K. alvarezzi* and *Eucheuma denticulatum*. Carrageenans can also be produced from *Chondrus chrispus*, a red seaweed species which grows along the coasts of the northern part of the Atlantic Ocean; the main harvesting areas in Europe are Brittany in France and the Iberian Peninsula.

Agar is extracted from various *Gelidium* and *Gracilaria* species (both red algae) and are found in the coastal waters of Japan, Mexico, southern California, North Africa, and Chile [150]. These species are not native to Europe.

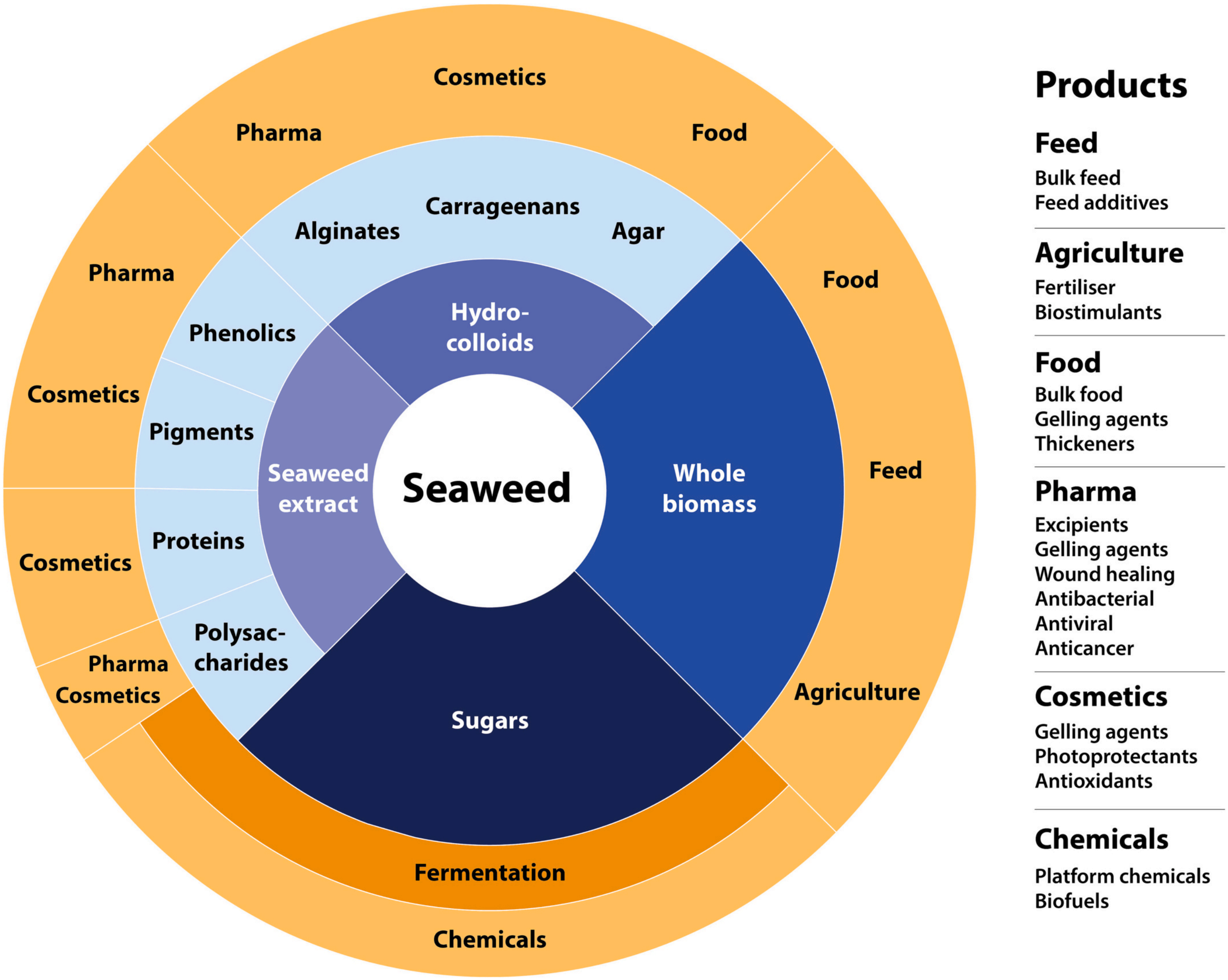

Fig. 4. Potential products and uses of brown seaweed biomass.

A total of 500,000 t of brown algae is used annually for the production of alginate. The world market for alginates is approximately 30,000 t at an average of USD6,000–10,000 per tonne. It takes 16 t wet/fresh seaweed to produce 1 t of alginate. In the last century, the giant kelp *Macrocystis pyrifera* (native to the US Pacific coast) was the principal source of the world's alginate supply. At present, *Laminaria* spp. is the largest source for alginate production [51]. In the last decade, market volume for alginate has increased slightly. Suitable seaweeds for alginate production have become more difficult and costly to obtain. A large body of research is being developed to improve the farming conditions and extraction processes including *Saccharina latissima* as a source of alginate [47,52,53]. Since the quality for different applications of alginate depends on the species and seasonality of the seaweed, *Saccharina* will require further research to become a major source of alginate. In particular there are important knowledge gaps in the link between physiochemical conditions and chemical composition of seaweed biomass (nutrient availability, pH *etc.*), how cultivation density will impact biomass yield, and more general information susceptibility to disease [39].

In the last decade, the hydrocolloids industry has gone through significant changes. The average company size has increased and much of the production capacity is in Asia. Production costs have risen due to increasing chemical and energy prices. The presence of low-cost producers in China also makes it difficult for European producers to compete. Global demand is growing at a few per cent annually, with danger of market saturation. More recently a study has been published showing successful alginate production from brown algal species grown in Norwegian waters [53] but there are currently few examples in the literature of significant hydrocolloid production from algae grown in Europe.

4.4. Production of chemicals by fermentation

The high sugar content for some seaweed species (~75 %) and the potential to cultivate seaweeds at a large scale with high yields has brought interest for their use as feedstock for fermentation processes for the production of a range of chemicals. The main driver for this use is that seaweed-derived sugars represent an alternative to first generation feedstocks (grains, starchy substrates) which are generally used as a source of sugars for the production of chemicals [54]. As with other biomass feedstocks, most seaweed sugars are a part of polymers, requiring some sort of pre-treatment and hydrolysis to make them available for fermentation. Studies have shown that the pre-treatment and hydrolysis conditions needed for the production of seaweed sugars are less severe than those needed for pre-treatment of lignocellulose [55]. Several seaweed species and by-products from the seaweed industry have been studied as feedstock for the production of ethanol (to be used as biofuel) or acetone, butanol and ethanol (ABE), as a platform chemical. Brown algae *Laminaria* and *Saccharina* have been studied for the production of ethanol [27,55,56]. *Saccharina* has also been studied for ABE fermentation [57]. Even though the production of fuels from seaweed is technically possible [58], the relatively low price of fuels and the complication of an unfavourable sugar profile for fermentation make this valorisation route a low priority but also a possible route to valorise the waste streams produced after the extractions of higher value products. The production of higher value platform chemicals by fermentation, such as lactic or citric acid is a possible alternative [59], but the current cost of the seaweed feedstock is unlikely to compete favourably with sugar streams normally used for these processes such as corn syrup, sugarcane molasses or sugar beet.

4.5. Fertilizers (agrochemicals)

Seaweeds have been used in agriculture for millennia. During ancient Roman times, plant seedlings were covered with algae to promote their growth, while in European coastal areas farmers would incorporate seaweeds in the soil to improve crop yields. By the 1940s 18 countries had developed their seaweed resources for fertilizers, and in 1947 a product that can be considered as the pioneer in the seaweed extract reached the market [60]. Even though applications of seaweed range from biochar as soil conditioner to fertilizers, the majority of the present applications are as biostimulants [61]. Current commercial extracts are manufactured mainly from the brown seaweeds *Ascophyllum nodosum*, *Laminaria* spp., *Ecklonia maxima*, *Sargassum* spp., and *Durvillaea* spp. Seaweed extracts are widely used as plant biostimulants which are defined as either a substance or microorganism that is applied to plants to enhance various properties including nutrition efficiency, abiotic stress tolerance and other crop quality traits [62]. Seaweed extracts constitute more than a third of the total biostimulant market worldwide and are predicted to reach a market value of around a billion Euro in the next 5 years. The extracts in the market are aqueous preparations made by processes using water, alkalis or acids treatments, or mechanical deconstruction by low temperature milling to give a "micronized" suspension of fine particles. Micronized seaweed suspensions are mildly acidic and the most widely used process for extraction involves heating the seaweed with alkaline sodium or potassium solutions. Reaction temperatures may be elevated by pressurizing the vessel as in the high temperature process developed for the early commercial product Maxicrop [63]. Alternatively, the algal cells can be ruptured using high pressure homogenisation and the soluble cellular components recovered by filtrations and dried for further dilution. Physical disruption avoids the use of organic solvents, acids or alkalis. Where necessary seaweed extracts can be fortified with plant fertilizers and micronutrients. This practice can take advantage of the chelating properties of the seaweed extracts and prevent trace metal ions from precipitating.

The increase in crop productivity promoted by seaweed extracts is obtained through stimulation of diverse physiological processes involved in plant growth and development, as well as improvement of product quality. The effect of the application of *Kappaphycus alvarezii* seaweed extract on maize at the grain filling stage produced an increase of 15 % in yield, enhancing seed number and cob length. Different doses of *K. alvarezii* were investigated and 7.5 % was found to be the best application rate in both studies [64,65]. Similarly, a commercial seaweed extract based on *Duvillaea potatorum* and *A. nodosum* on strawberry at nursery and production stages showed an increase in root length, suggesting that seaweed extracts could be involved in enhancing plant water and nutrients use efficiency by phytohormones [66]. A number of studies with a range of seaweed species as well as crops show that seaweed extracts are either a source of phytohormones or induce their synthesis in plants. The numerous effects reported range from the induction of photosynthesis, to branching and changing the biochemical composition of the plant. The effects observed on maize by the application of *Laminaria* extracts are a typical case of this seaweed application [67]. Even though the most commonly used species for these studies is *Ascophyllum*, stimulant effects on crops have been reported for a number of species such as *Sargassum*, *Jania*, *Macrocystis Eklonia*, *Codium*, and others.

The biostimulant properties of seaweed extract are particularly evident under abiotic stress. Application of seaweed extract moderate the detrimental effects of drought, salinity, extreme temperatures, and nutrients deficiencies. These protective effects might be associated with the alleviation of the oxidative processes that are common factors in abiotic stress conditions. For instance, the potential of polysaccharides extracted from *Lessonia nigrescens* to enhance salt stress adaptability of wheat seedlings has been established [68]. The polysaccharide extract significantly enhanced shoot and root lengths of wheat under stress, attenuating the oxidative damage by decreasing membrane permeability and lipid peroxidation. It also increased the antioxidant activity of superoxide dismutase, peroxidase and catalase enzymes.

Seaweed extracts also reduce the limitation on growth and development of crops under low temperatures. 'Algafect' is a commercial seaweed extract which has been shown to both enhance root length density and reduce leaf necrosis in maize over a two week period when plants were subjected reduced temperature of 12–14 °C to simulate cold spring conditions [69].

One of the most studied effects of seaweed extracts is the increase in nutrient use efficiency and alleviation of soil nutrients deficiencies. Application of *A. nodosum* extracts have been shown to mitigate the effects of N, P, K and Fe deficiencies in a number of crops which is proposed to be through a mechanism of improved uptake of these nutrients [70–73]. The effect of optimising nutrient use efficiency is particularly relevant in the present context of high energy prices and limited fertilizer production due to the war in Ukraine.

4.6. Cosmetics

Cosmeceuticals are products that improve or alter skin functions and appearance by promoting improvements to skin appearance, structure, and physiology [74]. The diversity in the composition of seaweed and the chemical nature of seaweed components make them one of the best potential sources of novel, naturally sourced cosmeceuticals. Marine macroalgae produce both primary metabolites including proteins, amino acids, polysaccharides, fatty acids, *etc.*, and secondary metabolites such as phenolic compounds, pigments, sterols, vitamins, and other bioactive components. The cosmetics industry has an annual gross revenue of approximately US $170 billion, and in the mid-2010s the European cosmetics market was the largest in the world (approx. 77 billion Euro) followed by the US and Brazil [75]. The continuous growth of the cosmetics sector relies on the use of natural ingredients that are environmentally friendly, have fewer side effects than synthetic chemicals and are safe to use. In this space, seaweeds are a major target in the search for bioactive compounds that could be exploited as functional ingredients for cosmetic applications.

Cosmeceutical applications of seaweeds are based on bioactive compounds and display a wide range of bioactivities [76].

Polysaccharides are the most significant and studied compounds present in macroalgae due to their dermatological activity. Brown seaweeds are well known for many different types of polysaccharides – such as fucoidans and alginates - that have a wide variety of applications, such as photoprotection, moisturizer, wound-healing agents, thickening agents, emulsifiers, and preservatives [77–79]. Some examples of the activity targets for seaweed polysaccharides include: regulation tyrosinase inhibition to reduce hyperpigmentation; promotion of skin repair through the inhibition of collagenase and elastase; reduction matrix metalloproteinase activity to reduce stress-induced premature ageing; reduction of reactive oxygen species by induction of antioxidant activity. There are well documented effects of fucoidan anti-inflammatory activity and inhibition of matrix enzymes against hyaluronidase, heparinase, tyrosine kinase, and phospholipase A2 [80,81]. Fucoidans are also topical anti-inflammatories for cosmetic after-sun damage, allergic-conditions, and post-surgical wound healing [81].

Polysaccharides extracts from *Eklonia*, *Sargassum*, *Saccharina japonica*, *Fucus* sp. and *Laminaria* sp. have been shown to inhibit the activity of tyrosinase [82], collagenase and elastase, promote antioxidant activity [83], skin-whitening effects [84], display antiviral and antimicrobial properties [85], as well as moisture retention activities [86].

Phenolic compounds are the water-soluble secondary metabolites that have numerous biological activities. Despite a large chemical diversity, the common structural feature is the presence of phenolic units, and phenolic compounds can be simple phenols or condensed groups forming polyphenols. Among the many phenolic compounds extracted from seaweeds, phlorotannins from brown seaweed are the most important secondary metabolites, with a wide range of functional bioactivities including antioxidant, antimicrobial, anti-inflammatory, and anticancer [87]. Phlorotannins are phloroglucinol units linked to each other in various ways. *Ecklonia*, *Hizikia*, *Eisenia*, *Undaria*, *Sargassum thunbergii*, and *Laminaria japonica* have been studied to determine the biological activity of their phlorotannins [88]. Phlorotannins are well known for their wide-ranging applications which include antimelanogenesis, antiaging, and antioxidant [89–91]. As a result of these bioactivities, phlorotannins have a number of cosmeceutical applications [92].

Macroalgae contain a large variety of pigments which absorb the light for photosynthesis due to the adaptation for light harvesting under water. Brown algae, which are the focus of this report, present chlorophylls a and c, fucoxanthin, and carotenoids. Alongside their roles in photosynthesis, pigments play a protective role under an excess of energy or uncoupling of the physical and biochemical functions in photosynthesis. It is this property which can be exploited in the application of seaweed pigments in the cosmetics industry as antioxidants and antimutagenics [93]. Besides the use of role of chlorophylls as natural colouring agents, they can be used for their deodorizing and antibacterial properties. *Saccharina latissima* chlorophylls have high antioxidant activity and the ability for tissue growth stimulation, making them useful to the cosmetic industry [94].

Carotenoids are widely applicable as natural dyes and antioxidants with antitumor, anti-inflammatory, and radical sequestering benefits [95]. They have been shown to protect the skin against UV light by modulating UVA-induced gene expression [96]. Among the carotenoids present in brown algae, fucoxanthin has received a lot of interest due to its protective effects on skin, making it consequently beneficial in cosmetics [97].

Macroalgae in general contain significant amounts of protein and different types of aliphatic amino acids, hydroxyl-group-containing amino acid, aromatic amino acid and mycosporine amino acids. However, most brown algae species have relatively low amounts of proteins and do not have the diversity of bioactive proteins seen in red and green algae. In spite of this, biological activities have been reported in this group. Protein fractions of *Laminaria digitata* have shown lipolytic activity [98], *Eklonia cava* and *Sargassum* have antioxidant, chelating agent and radical scavenger activities, and *Fucus* sp. has anti skin-ageing properties [99]. Some species of brown algae contain mycosporine-like amino acids that play a role in the absorption of solar energy that can prevent photo-ageing, as well as photo-damaging protection [100].

4.7. Medicinal uses

The beneficial effects of seaweed on health goes beyond the skin, and the addition of seaweed compounds for the formulation of novel natural drugs is one of the aims of marine pharmaceuticals, a new branch of pharmacology. Research on marine drugs has made important progress and many studies assess biological compounds of seaweed in *in vitro* and *in vivo* tests with the aim of evaluating their mechanisms of action and exploiting them for pharmaceutical purposes. Pharmacokinetic studies of marine-derived polysaccharides have led to their potential use in pharmaceutical formulations. There are a growing number of reports about novel marine compounds but few detail any pharmacokinetic pathways [101,102]. Topical applications are based on skin absorption, avoiding the extensive first-pass metabolism and provide direct access and localization at the site of action. Topical applications are usually well-tolerated and there are a number of reports on fucoidans from *Fucus versicolor* pharmacokinetics using topical applications [103,104].

As mentioned in the cosmetics section above (Section 4.6), brown algae are recognised as an important source of bioactive compounds beneficial to human health. Fucoxanthin is an orange-coloured xanthophyll pigment that exhibits biological activities such as anti-inflammatory [105,106], anti-obesity [107,108], antiangiogenic [109] and anticancer properties [10,32]. Assays showed inhibition of tumour growth in lung cancer due to fucoxanthin isolated from *Laminaria japonica* [110], while fucoxanthin isolated from the marine algae *Ishige okamurae* inhibited the growth of melanoma cells implanted in mice [111]. Fucoxanthins from *Laminaria japonica* also showed a significant reduction *in vivo* on lung metastasis [112]. Isolated fucoxanthin from *Colpomenia sinuosa* and *Sargassum prismaticum* showed *in vitro* anticancer activity and *in vivo* antioxidant activity on colon adenocarcinoma, breast adenocarcinoma and liver adenocarcinoma cell lines [113].

Polysaccharides from brown algae are also a subject of intense research with respect to their pharmacological effects. Fucoidans among them are the most interesting group. Fucoidans exhibit a number of pharmacological properties in different mammalian systems, such as antithrombic and anticoagulant [114], antitumor [115], antivirus [116], contraceptive [117] and antioxidant properties [114]. These potent activities probably reside in the ability of the fucoidans to mimic the structure of the carbohydrate moieties of mammalian glycosaminoglycans [118].

Several fucoidans express antiproliferative activity against cancer cells. For example, fucoidans from *Undaria pinnatifida* decrease cell proliferation against human lung adenocarcinoma cells [119].

Antibacterial properties were also investigated with crude and purified fucoidans from *Fucus vesiculosus*. A bacteriostatic effect was observed on *Escherichia coli*, *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Bacillus licheniformis*, with *Escherichia coli* being the most sensitive to each of the fucoidans [120]. The fucoidans extracted from *Cladosiphon okamuranus*, have antibacterial activity against *Helicobacter pylori* infection, inhibiting the urease enzyme and preventing *Helicobacter pylori* adhesion to the gastric mucosa [121]. Interesting, although fucoidans from *Laminaria japonica* exhibited no antibacterial activity, oligofucoidans derived from them possessed good antibacterial activity both against *Escherichia coli* and *Staphylococcus aureus* [122]. Depolymerized fucoidans combine with membrane proteins and cause a membrane-disrupting effect which in turn leads to the collapse of membrane structures and eventual cell death.

Antiviral effects of brown algae polysaccharides have been studied against herpes virus strains. Fucoidan extracted from *Sargassum* were tested against Herpes Simplex Virus, enterovirus and human immunodeficiency virus (HIV-1) [123,124].

Anti-coagulant bioactivities of the high molecular weight fucoidan from *Fucus vesiculosus* have been observed in several *in vitro* models [125]. These anticoagulant activities of fucoidan have been also detected in *in vivo* assays by oral administration of fucoidan from *Undaria pinnatifida* [126].

In vitro fucoidans antioxidant activity was evaluated for their radical scavenging activities, and were found to display increased total antioxidant activities in a dose-dependent manner [127].

Fucoidans are active against diabetes. Polysaccharides from *Sargassum fusiforme* and *Macrocystis pyrifera* in high-fat diet and streptozotocin-induced diabetic rats reduced the levels of blood glucose, triglyceride and total cholesterol in diabetic rats [128], indicating that these polysaccharides from brown seaweeds could be candidates for novel medicines and functional foods for the treatment of diabetes.

Polyphenols are also a group of compounds that exhibit multiple biological activities. Phlorotannins from *Padina australis* inhibit microbial growth by damaging the cytoplasmic membrane and destroying the cell bacteria resulting in retarded growth and bacterial death [129,130]. Phlorotannins have been used for the treatment of various allergic diseases. Phlorotannins from *Sargassum hemiphylum*, *Ecklonia stolonifera* and *Eisenia arborea* have been used for the treatment of atopic allergic reactions, such as atopic dermatitis [131,132]. Antioxidant activity of phlorotannins has been detected in brown seaweeds and shown to treat neurodegenerative diseases such as Alzheimer's. The anticholinesterase activity of seaweed extracts has been tested against acetylcholinesterase (AChE) and butyryl cholinesterase (BChE), which are the main enzymes identified as part of processes associated with Alzheimer's disease [133]. The species *Fucus spiralis*, *Bifurcaria bifurcata*, *Cystoseira stricta*, and *Dictyota humifusa* showed potential anticholinesterase activity [134–137], which could be used in the future as therapeutic agents for treating Alzheimer's disease.

Phlorotannin-rich fractions extracted from *Cystoseira sedoides*, *Cladostephus spongeosis* and *Padina pavonica* displayed *in vivo* antioxidant activity. Phlorotannins have a strong antioxidant activity towards free radicals preventing inflammatory reactions in mice. The anti-inflammatory potential of phlorotannins is shown by decreasing the production of malondialdehyde (MDA) [138]. Properties of phlorotannins are diverse; and reports that the compound eckol isolated from *Ecklonia cava* possess potent antiproliferative activity against human breast cancer cells are one of many anticancer activities found. Phlorotannin extracts from *Fucus vesiculosus*, *Alaria esculenta*, *Ascophyllum nodosum*, *Laminaria japonica*, *Sargassum muticum* and *Bifurcaria bifurcata*, among others, were shown to dose-dependently reduce the cell proliferation of numerous tumour cell lines such as human fibroblast, gastric cancer cells, human colon cancer cells lines, human hepatoma, mouse leukaemia and mouse teratocarcinoma [139–144].

5. Cost and considerations for European seaweed aquaculture

In spite of limited share of global seaweed biomass production, macroalgae production is a relatively well-established sector in Europe. There are presently 225 companies active in the seaweed sector, with concentrations around Spain, France and Ireland. In terms of biomass volume, Norway (57 %), France (18 %), and Ireland (10 %) are the largest European producers [145]. An interesting observation from these authors is that over the last decade the number of companies in the sector has increased by 150 %, reflecting the growing interest and activity within the industry.

While seaweed production moves away from exclusive wild harvesting (currently 99 % of the total production) [146] the largest production volumes are seen in the Atlantic region where farming practices focus on brown seaweed species that have been traditionally exploited at an industrial scale. Norway, France, and Ireland have increasingly employed mechanical harvesting to increase yields. The development of aquaculture farming also has the effect of protecting the seas from the environmental impact of scaling up wild harvesting that inevitably depletes natural stocks.

Most of the seaweed farming operations occur offshore or in coastal waters (76 %), while land-based operations are directed to specific products that require controlled conditions of growth. Norway has licenced 834 ha for offshore aquaculture, while Spain, Portugal and France have both land-based and offshore full scale operations [147]. Iceland, Ireland and the UK have operations predominantly based offshore.

The supply chain of commercial seaweed production comprises three main activities: 1) Propagation and breeding, ensuring that the best genotypes for each environment are bred, 2) Farming and harvesting at custom built seaweed farms, 3) Processing and products, turning the seaweed into standalone products or into ingredients of final products. Along this supply chain there are a number of constraints: variability in biomass composition, the small European market for seaweed commodities, the complex regulations in cultivation licenses, and the limited technological development in the production and processing of seaweed.

The decision towards targeting particular products and processes using seaweed biomass is determined to a large extent by the cost of producing the biomass. As mentioned previously, the costs involved in seaweed farming operations in Asian countries are significantly lower compared to the context of European and particularly North Sea conditions.

When evaluating the potential of European industrial brown seaweed production, there are a number of issues to be taken into account which can have direct and indirect effects on economic feasibility:

1. **Environmental impacts:** Seaweed farming can have a range of environmental impacts (both positive and negative), including changes to water quality and habitat alteration.
2. **Regulation:** Seaweed farming is a new and rapidly developing industry, and there is often a lack of clear regulation and oversight.
3. **Competition with other uses of coastal space:** Seaweed farming requires space in the coastal zone, which is also used for a variety of other activities, such as fishing, tourism, and recreation.
4. **Siting and infrastructure:** In Asia, seaweed is often grown using a "long-line" farming method, in which seaweed is grown on ropes or nets that are suspended from buoys. In Europe as well as long-line farming, a variety of other methods are used including "off-bottom" farming, in which seaweed is grown on structures that are placed on the seafloor, and "floating raft" farming, in which seaweed is grown on rafts that float on the surface of the water. Finding suitable locations for these facilities can be challenging and can have a huge impact on the overall economic feasibility of commercial seaweed production.
5. **Market demand:** While demand for seaweed products is growing, it is still a relatively small market compared to other agricultural commodities.

A number of projects have investigated the feasibility of seaweed farming in the North Sea and Atlantic European waters using various technologies. Many of these involve the use of Integrated Multi Trophic Aquaculture (IMTA), where fish farming is combined with seaweed farming [148]. These projects include work in Spain, Portugal, France and Ireland [50]. From these European studies, the final estimation of the total production costs for farmed seaweed is between €1000 and €1500 per tonne of dry matter (excluding transport and harvesting). A recent study of the economic feasibility of seaweed farming in Scotland shows similar costs [149]. In this context, a positive cost/benefit balance will require the targeting of high value applications of the seaweed biomass to achieve a sustainable system [11].

6. Conclusions

China and Indonesia dominate global seaweed production – in 2016 they produced over 85 % of total global supply. The predominant end route for macroalgae is into the Asian human food market, although interest in seaweed cultivation is gathering pace from Western nations due in no small part to its positive environmental credentials. In addition to use as a food, seaweed extracts are already used widely in the cosmetics and agricultural sectors, and indeed more recently in pharmaceuticals [32].

Seaweed is a highly sustainable and renewable resource, as it can grow many times faster than land-based plants to produce the sample amount of biomass and does not require any fresh water or arable land to cultivate. In addition, seaweed absorbs excess nutrients and carbon dioxide from the water, helping to reduce water pollution and mitigate the effects of climate change. But the benefits of seaweed cultivation go beyond the environmental realm. The global market for seaweed is expected to reach $22 billion by 2024, with Europe being a significant player in this market. Growing brown seaweed in Europe would also create new economic opportunities and support the growth of local communities. Seaweed cultivation can create jobs in the aquaculture industry and provide an additional source of income for coastal communities. Research suggests that the production of seaweed biomass for a low value/high volume market in Europe is not economically feasible or able to compete with already established Asian industries. Given the costs associated with seaweed farming, commercial scale production in a European context needs to target high/medium value products from biomass. As outlined in this review, these compounds most often find applications in the cosmetic, nutraceutical and pharmaceutical sectors.

In conclusion, the commercial case for growing brown seaweed in Europe is clear. Seaweed cultivation offers environmental, economic, and food security benefits, and has the potential to play a significant role in the future of Europe's aquaculture industry. But for this to be realised, the extraction of high value compounds from brown algae biomass needs to be front and centre if European production is to be both economically feasible and competitive in the existing marketplace.

CRediT authorship contribution statement

JPB: Investigation, Methodology, Writing - review & editing. LFR: Investigation, Writing review & editing, LDG: Conceptualization, Writing – original draft, review & editing, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Leonardo Gomez reports financial support was provided by European Commission. Leonardo Gomez reports financial support was provided by Biotechnology and Biological Sciences Research Council.

Data availability

Data will be made available on request.

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