Functional food ingredients in seaweeds; Claims and legislation

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Seaweeds for Human Consumption, Bioactive Compounds, and Combating of Diseases
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Seaweed Bioactive Molecules

Many interesting bioactive molecules
- Protein, peptides and amino acids
- Polysaccharides
- Antioxidants
- Fatty acids

To exploit need access to resource or waste from seaweed processing industry (Agars, carrageenan and alginates)
Key facts Seaweed resource

Total value US$ 6.1 billion
- Food products: US$ 5 billion
- Hydrocolloids: US$ 600 million
- Others: US$ 500 million

Waste based on hydrocolloid extraction figures of 50,000 ton is approx. 150,000 ton globally
Total production (wild harvest and aquaculture) around the 13.5 million ton

<table>
<thead>
<tr>
<th>Product</th>
<th>Global Production</th>
<th>Retail Price</th>
<th>Gross Market Value</th>
<th>Amount Used</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>tonnes/year</td>
<td>US$/kg</td>
<td>US$million/year</td>
<td>Food %</td>
</tr>
<tr>
<td>Agar</td>
<td>10,000</td>
<td>15-40</td>
<td>137</td>
<td>80</td>
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<tr>
<td>Alginate</td>
<td>30,000</td>
<td>5-15</td>
<td>230</td>
<td>67</td>
</tr>
<tr>
<td>Carrageeans</td>
<td>15,500</td>
<td>5-10</td>
<td>100</td>
<td>80</td>
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Functional Natural Foods from seaweed

These products would be new and novel for the European food market but would be logical extensions or enhancements of the health and natural foods in the Current Generation of Food Products

Seaweed possesses many functional benefits associated with:
- Dietary fibre
- Cholesterol
- Diabetes
- Vitamins, antioxidants and minerals
Seaweed protein

Algal protein 10-40% (w/w) per dry weight represent a major untapped resource

- Lectins (haemagglutinins) carbohydrate binding proteins
  - host–pathogen interactions,
  - cell–cell communication,
  - induction of apoptosis,
  - cancer metastasis and differentiation,
  - recognizing and binding carbohydrates

- Commercially produced from Codium fragile, subspecies tomentosoides and from three Eucheuma species and Soleria robusta

- Other bioactive properties: antibiotic, mitogenic, cytotoxic, anti-inflammatory, antiadhesion, anti-human immunodeficiency virus (anti-HIV) activity and human platelet aggregation inhibition

|Phycobiliproteins|

- Patents on the therapeutic applications of Phycobiliproteins (Sekar and Chandramohan, 2008)

<table>
<thead>
<tr>
<th>Application</th>
<th>Patent number</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-inflammatory</td>
<td>US 7,825,965</td>
<td>(Pieloch, 2006)</td>
</tr>
<tr>
<td></td>
<td>JP 256678</td>
<td>(Hirahata et al., 2004)</td>
</tr>
<tr>
<td>Liver protecting</td>
<td>CN 1633889</td>
<td>(Ko and Sun, 2005)</td>
</tr>
<tr>
<td>Anti-viral</td>
<td>CN 1526471</td>
<td>(Que, 2004)</td>
</tr>
<tr>
<td></td>
<td>US 6,346,458</td>
<td>(Chueh, 2002)</td>
</tr>
<tr>
<td>Anti-tumour</td>
<td>CN 1478552</td>
<td>(Ji and Liu, 2004)</td>
</tr>
<tr>
<td></td>
<td>CN 1325729</td>
<td>(Wang and Li, 2003)</td>
</tr>
<tr>
<td></td>
<td>CN 1091976</td>
<td>(Shi and Xia, 1994)</td>
</tr>
<tr>
<td></td>
<td>US 5,163,898</td>
<td>(Morcos and Henry, 1992)</td>
</tr>
<tr>
<td>Treatment of atherosclerosis</td>
<td>JP 065216</td>
<td>(Okuda et al., 1983)</td>
</tr>
<tr>
<td>Lipase activity inhibitor</td>
<td>JP 359638</td>
<td>(Koda and Okuda, 2004)</td>
</tr>
<tr>
<td>Serum lipid reducing agent</td>
<td>JP 137805</td>
<td>(Nagasaki et al., 2003)</td>
</tr>
<tr>
<td>Skin function activation factor</td>
<td>JP 026544</td>
<td>(Kajikawa and Maeshima, 2006)</td>
</tr>
<tr>
<td>Anti-oxidant</td>
<td>JP 330733</td>
<td>(Ohto, 2002)</td>
</tr>
<tr>
<td>As an agent that obstructs absorption of environmental pollutant deposition in the body</td>
<td>JP 157959</td>
<td>(Yonezaki, 2001)</td>
</tr>
</tbody>
</table>
Bioactive peptides

- Produced by enzymatic hydrolysis of algal proteins
- In addition to their nutritional value exert a physiological effect in the body. About 2-20 amino acids in length and are inactive within the sequence of the parent protein and only become active when released
  - Hydrolysis by digestive enzymes (pepsin or trypsin)
  - Hydrolysis by microbial/bacterial proteinases and peptidases during fermentation
  - Proteolysis by enzymes derived from micro-organisms or plants or a combination of the above

- Bioactivities include: ACE inhibitory, Antioxidant, Antimicrobial, Antithrombotic, Immuno or cytomodulatory and Mineral binding activity

Bioactive amino acids

- In addition to taurine, other bioactive amino acids, such as laminine, kainoids and mycosporine-like amino acids, have been found in marine macroalgae
- Laminine (Laminaria angustata and Chondria amata) depress the contraction of excited smooth muscles, and exert a transitory hypotensive effect
- The kainoid amino acids, kainic and domoic acids have also been found in numerous algal species. High insecticidal, anthelmintic and neuroexcitatory properties
- Compounds currently used in research associated with neurophysiological disorders such as Alzheimer’s and Parkinson’s disease and epilepsy
Some Bioactive polysaccharides

- **Laminarin** (kelp and fucoids)
  - Substratum for prebiotic bacteria, tumour-inhibiting agent, anti-coagulant, anti-bacterial, immuno stimulant.
  - Potential cancer therapeutic
  - Wound repair and reduce serum cholesterol levels and total serum lipid

- **Fucoidan** (brown algae) sulphated polysaccharides (fucans)
  - Antiangiogenesis, antiproliferation for tumor cells inhibition of tumor growth and reduction in tumor size
  - Anti-inflammatory, anticoagulant
  - Some anti-viral properties of sulphated fucans have also been characterized (Herpes Simplex Virus)

- **Mannitol** replace sucrose to make sugar free compound coatings - diabetes, a growing problem in modern society

- **Alginates** act like fibers and help besides clearing the digestive system in protecting surface membranes of the stomach and intestine from potential carcinogens. Prevent proliferation of implanted cancer cells (Doi and Tsuji, 1998)

- **Ulvan** - Rhamnose, a major component of ulvans, precursor for the synthesis of aroma compounds. The production of rhamnose from Monostroma, a Japanese species of Codiales has been patented as well as the treatment of gastric ulcers with ulvans
  - Modify the adhesion and proliferation of normal and tumoral human colonic cells
  - Earlier work demonstrated strain specific anti-influenza activities

- **Agars** and **carrageenans** have similar functionalities attributed to them
Polyphenols and antioxidants

- **Phlorotanins** (Brown algae up to 15%) Strong Antioxidant activity
  - Other flavonoids and their glycosides present in green, brown and red algae.
  - Bactericidal activity
  - Help protect tissues against oxidative stress; certain polyphenols work as preventative medicines for problems such as cardiovascular diseases, cancers, arthritis, and autoimmune disorders.

- **Carotenoids** fucoxanthin, B-carotene, violaxanthin are powerful antioxidants.
  - Fucoxanthin demonstrated strong anticancer effects
  - fucoxanthin is an effective natural food constituent to help prevent obesity

Fatty acids

- Eicosapentaenoic and docosahexanoic acids, called oxylipins resemble eicosanoid hormones in higher plants and humans which fulfill a range of physiologically important functions
- Related to prevent inflammation diseases (new classes of anti-inflammatory drugs)

Iodine

- Brown algae up to 0.7% of the dry weight
- Kelp supplement for Iodine deficiency goitre or for under-active thyroids (myxoedema)
- An antitumorogenic role of *Undaria pinnatifida*, or its equivalent iodine content in inhibiting tumorogenesis
- Suggested that the high dietary seaweed content may account for the relatively low prevalence of breast cancer in Japanese women
Health Claims and Europe

- **EU regulation 1925/2006** on the addition of vitamins and minerals and certain other substances to food
- Provides clear rules for the addition of vitamins and minerals to food while herbal ingredients and other substances are not explicitly mentioned in the regulation
- There is currently no additional legislation on food fortification or functional foods
- In respect of functional foods, *amino acids, fish oil* and *lactic bacteria* can generally be used in foods as long as the resulting product is safe

- Food manufacturer must be able to substantiate every health claim on any functional food that is marketed.
- The question “what remains sufficient scientific evidence?” remains as a problem (Korver et al. 2006)
- Although the safety aspects of new functional foods are covered in the EU Novel Foods legislation (258/97/EC) and amended by **EC 1829/2003** and **EC 1882/2003** no European legislation exists for the health benefits itself (efficacy and health claims).
• Therefore Regulation (EC) No 1924/2006 adopted by the European Parliament and of the Council on nutrition and health claims made on foods. This Regulation lays down harmonized rules for the use of nutrition and health claims and contributes to a high level of consumer protection.

• It ensures that any claim made on a food label in the EU is clear, accurate and substantiated, enabling consumers to make informed and meaningful choices.

• The Regulation also aims to ensure fair competition and promote and protect innovation in the area of food.

• Regulation EC No 1924/2006 on nutrition and health claims made on foods came into force on 19th January 2007 and has been applied from 1st July 2007.

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**Functional food vs. medicine**

*FDA blasts General Mills Over Cheerios Claim*

• Cereal maker penalised due to Claim Of Lowering Cholesterol 10 Percent In Month Makes It A "Drug"

• No drug in the USA can be legally marketed without an approved new drug application

• The FDA sent a letter of warning to General Mills accusing them of making unauthorized health claims

• Kellogg agreed to stop a national advertising campaign that misleadingly claimed its Frosted Mini Wheats boost kids' attention spans.
Functional Food Claims Must Not Refer to Diseases or Mislead Consumers

- Many companies investing considerable resources in developing functional food products
- Largely unaware of the significant regulatory hurdles that must be overcome before a new food product can be placed on the market
- All products that bear a health or nutrition claim must be supported by appropriate scientific/clinical evidence

There is now a proliferation of foods making claims in relation to nutrition or health benefits, with many more in the pipeline, with misleading or inappropriate labeling
- Often the legal parameters currently governing such products and any claims made are not clear
- Food labels cannot refer to the prevention or potential cure of a disease, as this would in effect place them in the category of medicines (see Cherios)
Some legal parameters

- It is necessary to ensure that the substances for which a claim is made have been shown to have a beneficial nutritional or physiological effect.
- The substance that is the subject of the claim must be present (or if a reduced claim present in suitably reduced quantities) in the final product in quantities that are sufficient to produce the nutritional or physiological effect claimed.
- The substance must also be available to be used by the body.
- A significant amount of the substance producing the claimed nutritional or physiological effect should be provided by a quantity of the food that can reasonably be expected to be consumed.
- A nutrition or health claim may not be made if it is inconsistent with generally accepted nutrition and health principles or if it encourages excessive consumption or disparages good dietary practice.

Mayonnaise with Omega 3

What kind of claims?

**Nutrition claim**
- a normal function of the body
- a risk factor of a disease, without stating, suggesting or implying its reduction

Example: maintains [naming normal vital function of the body]

Classification: Article 13

**Health claim**
- a reduction of a risk factor of a disease, with or without mentioning the disease name

Example: lowers [naming risk factor]

Classification: Article 14
Health Claims

- "Article 13 claims" are health claims describing or referring to:
  - (a) the role of a nutrient or other substance in growth, development and the functions of the body
  - (b) psychological and behavioural functions
  - (c) slimming or weight control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet
- They are referred to as "function claims".
- EU Member States have provided a list with claims, the Commission will consult EFSA and adopt a Community list of permitted claims by 31 January 2010 at the latest (Mayonnaise, beef)
- Claims based on newly developed scientific evidence and/or which include a request for the protection of proprietary data are subject to the authorisation procedure laid down in Article 18 and fall under article 13.5 claims.

- In October 2009, EFSA published the first series of opinions providing scientific advice for more than 500 “general function” health claims on a draft list of 4,185 claims submitted to EFSA by the European Commission between July and December 2008. This list was the result of a consolidation process carried out by the Commission, after examining over 44,000 claims supplied by the Member States.
- Substances and claims are known and products can be brought forward under Article 13.1
Article 13.5

- Claims under article 13.5 are those based on **newly developed scientific evidence**
  - Scientific dossier to EFSA
  - Protection of proprietary data
  - Authorization on a case-by-case basis

Article 13.5 applications submitted to EFSA are included in the Register of Questions, with indication of the food substance and claimed effect.

- The panel has received to date 21 applications, 6 have been withdrawn and so far 13 scientific opinions have been adopted.

For confidentiality reasons, and in accordance with the claim regulation, summaries of these Article 13.5 claims applications are not published.

0232_FR - Art 13.5 Claim, Reg.(EC) No 1924/2006 Actimel®, helps to strengthen the body's natural defences (Withdrawn)

0229_NL - Art 13.5 Claim, Reg.(EC) No 1924/2006 NPU Tabs contain Humulus Lupulus, Female breast enhancement process (Adopted)
Fish farming

- Marine algae as a novel, sustainable organic supplement in feed for fed-fish aquaculture (Salmonids, Bream, Bass, Cod, Pangasius and Talapia).
- Trials with Trout (Soler et al., 2009); Sea Bass (Valente et al, 2006); Red Bream (Nakagawa et al, 1997)
- Salmon (OHT, 2010)
- Replacement of artificial ingredients, antibiotics, colorants and preservatives
- Fish fed on fishmeal, oil and seaweed

Trial results

- Oceanfeed™ is a highly palatable diet.
- Growth rate 14% faster compared to commercial high class organic diet
- Significant sea lice reduction
- 60% less mortality
- Improved FCR (1 point)
- Fish 5-6 kg, harvested, tested and smoked
**Oil and pigments**

- The Oceanfeed™ diet has higher levels of Omega 3 PUFA’s than top Organic fish feed.
- Oil levels in fish flesh did not differ significantly between diets.
- Astaxanthin levels on the other hand were 5 times the levels present in Oceanfeed, while Oceanfeed contained much higher levels of natural pigments notably lutein and other unidentified Esters.
- The SalmoFan values showed that uptake of pigmentation is just as good as in the Oceanfeed diet as in the top Organic diet both with identical values.

**Organoleptic results**

- Results obviously show a preference for the Oceanfeed™ fed fish raw and cooked with an overall score of 2 (Good) compared with the organic diet fed fish with a score of 3.1 (indifferent).
- Effect of the active identified compounds in the Oceanfeed™ having a marked influence on taste.
- Retains better colour after cooking.
Seaweed formula’s as feed supplement in animal nutrition

**Oceanfeed™**

### Conclusion

- Lots of legislation and rules in respect of functional food claims:
  - Marketing as novel or functional food (Article 13.1 and 13.5), health claims and scientific dossiers needed (expensive)
  - High cost of scientific dossier (if new activity or compound discovered)
  - **Functional Food** is a category recognized by the industry only and in legal terms is a virtual category in that there is no specific "Functional Food" legislation only Nutritional and health claims
  - Authorization and labeling of "functional foods" falls under existing legislation that governs all foods.
  - The **Nutrition and Health claims legislation** will only affect the marketing of a product and not its legal status as long as medicinal claims are not made
  - It is a stumbling block and gets more difficult in the future