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Perspective

Nutrients and Bioactive Compounds in Seafood: Quantitative Literature Research Analysis

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Abstract: This perspective presents current and updated advances in research on nutrients and bioactive compounds in seafood. It is based on a literature quantitative research analysis approach. The main features of seafood components are introduced. This perspective aims at providing a current framework that relates nutrients, bioactive compounds, and seafood in a novel integrated and multidisciplinary manner, highlighting the current knowledge, the main research lines, and emerging strategies. The literature search was carried out by means of the Scopus database, and 22,542 documents were retrieved in the period from 1932 to 2024. Particularly, from the perspective of nutrition and health outputs, the main terms correlated with research on the relationship between seafood and nutritional and bioactive components, and the main existing research lines focused on this topic, were identified. The top recurring keywords were human/s, female, diet, nutrition, fish, male, adult, food intake.

Keywords: seafood; fish; nutritional value; biological compounds

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1. Introduction

Having a wide variety of species and unique biodiversity, freshwater and marine environments may be considered a rich reserve of nutrients and biologically active substances for human nutrition. Seafood, including fish, mollusks, and crustaceans, are a precious source of high-quality proteins, healthy lipids, vitamins, and minerals in the human diet. In particular, they represent the main source in the human diet of precious long-chain omega–3 polyunsaturated fatty acids (LC-omega–3-PUFA), which play several physiological roles that are important for human health [1].

Over the past decades, a large volume of studies has shown the importance of regular consumption of seafood for good health state at any age. In particular, the inverse relationships between fish consumption and incidence of cardiovascular and cerebrovascular diseases, diabetes, metabolic syndrome, obesity, and neurological disorders have been reported [2–6]. For these reasons, dietary guidelines all over the world recommend the inclusion of seafood at least twice a week within a balanced diet [7,8].

This perspective aims at providing a current framework that relates nutrients, bioactive compounds, and seafood in an integrated and multidisciplinary manner. By means of a literature quantitative research analysis approach, the current knowledge, main research lines, and emerging strategies are highlighted

2. Nutrients and Bioactive Compounds

The interactions between nutrients and bioactive component provide a measure of quality and the potential beneficial properties of a food matrix [9]. The term "bioactive compounds" is taken to mean natural compounds that have the ability to interact with one or more compounds of a living tissue and exert positive effects on human health [10].

An overview of the main components of seafood/fish is here highlighted and contextualized as follows: (i) proteins, bioactive peptides, amino acids, taurine, and anserine; (ii) lipids and LC-omega–3 PUFA; (iii) vitamins, pro-vitamins, and carotenoids; (iv) phytosterols and squalene; (v) minerals and trace elements; (vi) chitin, chitosan, and chito-oligosaccharides. A graphical representation is given in Figure 1.

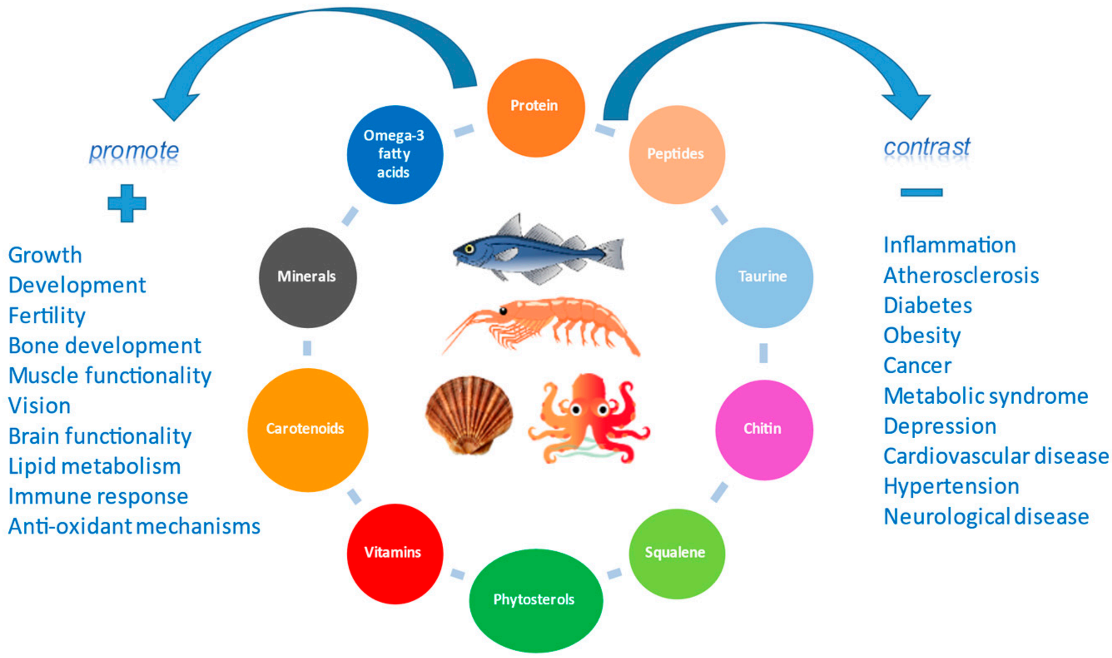

Figure 1. A graphical representation of the seafood/fish/nutrient/bioactive compound search with related health effects.

2.1. Proteins, Bioactive Peptides, Amino Acids, Taurine, and Anserine

Considering its average protein content, which is in the range of 18–20%, seafood provides more than 3.3 billion people globally with about 20% of their average per capita intake of animal proteins [11].

Fish muscle, characterized by short fibers intertwined with thin shields of thermolabile collagen, represents a highly digestible protein source suitable to the needs of consumers of any age, from infants to elders.

Fish proteins are considered complete and highly nutritious because of their balanced amino acid composition, including all the essential and non-essential amino acids [12,13].

Fish proteins, especially those from lean fish, have been shown to act in the prevention of type-2 diabetes by improving insulin sensitivity [14]. Marine collagen, the main protein of the connective tissue present in fish skin, bones, and scales, is of high interest for cosmetic, nutraceutical, and pharmaceutical applications, due to its wound-healing, skin anti-aging, and bone regeneration capabilities [15].

Bioactive peptides originating from the gastrointestinal digestion of fish proteins and protein hydrolysates have been shown to play several health-promoting roles [16], mainly anti-hypertensive [17], anti-diabetic [18], anti-coagulant [19], anti-inflammatory [20], anti-microbial [21], and antioxidant [22] roles.

In addition to accomplishing their specific role of building-blocks for proteins, amino acids play several functional roles in the human organism, including, but not limited to, regulation of gene expression, nutrient transport and metabolism, thermogenesis, appetite, and immune response modulation [23].

Seafood is one of the few dietary sources of taurine, a sulfur-containing free amino acid-derived compound providing antioxidant protection to cells and tissues [24]. Studies on taurine levels in seafood report a high variability, with values ranging from a few milligrams to over 800 mg per 100 g edible portion depending on the species, with the highest levels in mollusks and crustaceans [24–26]. Taurine is involved in many physiological processes, i.e., bile salt formation and fat digestion, membrane stabilization, osmoregulation, and immunomodulation, with beneficial influences on the digestive, endocrine, immune, muscular, neurological, reproduction, and visual functions [27]. The influence of taurine on the modulation of lipid metabolism and protection from cardiovascular disease and type-2 diabetes has also been recently reported [28–30].

Anserine is a functional dipeptide with demonstrated antioxidant activity, abundant in *Perciformes* (i.e., marlin about 15 g/kg wet muscle, croaker about 5 g/kg wet muscle, tuna about 4 g/kg wet muscle) and *Salmonidae* (i.e., salmon about 9 g/kg wet muscle, trout about 3 g/kg wet muscle), as reported by [31]. Multiple health benefits have been associated with anserine, such as protection from infectious disease and inflammation, memory and age-related neurological functions, and cardiovascular functionality [27].

2.2. Lipids and Omega–3 Polyunsaturated Fatty Acids

Among the several beneficial effects of seafood consumption, the most recognized and studied are those ascribed to its peculiar lipid profile, particularly its high content of LC-omega–3-PUFA and low content of saturated fatty acids and cholesterol.

LC-omega–3 PUFA are precursors of prostaglandins and tromboxanes, hormone-like substances with antithrombogenic and antiatherogenic properties crucial for prevention of human chronic inflammatory and cardiovascular diseases, for cancer prevention, and for brain and retina development during the early life stages [32–38]. More recently, some studies have highlighted the importance of a constant supply of seafood with ageing for its role in the prevention of cognitive decline and neurodegenerative diseases [39,40].

The lipid content of seafood products varies considerably depending on the species and on several intra-specific (age and size of individuals, sex, reproductive phase) and exogenous (season of harvest, environment of origin) factors [41,42].

In addition, in the case of aquaculture products, feed formulation, feeding management, and farming techniques have an impact on the lipid profile of final products. However, from low-fat fish, mollusks, and crustaceans (e.g., cod, sole, clams, mussels, crabs) to high-fat species (e.g., herrings, salmon, mackerel), most aquatic animals have a high proportion of LC-omega–3 PUFA as a common fingerprint-like mark of their lipid profile. As reported by Prato and Biandolino [42], the total PUFA percentage is, for example, 32.14% of the total fatty acids in Salema (lipid content 1.67%), with EPA and DHA contributing 7.23% and 17.39% of total fatty acids, respectively, whereas in seabass (lipid content 2.33%), the total PUFA percentage amounted to 32.45% of total fatty acids, with EPA and DHA contributing 6.91% and 13.83% of total fatty acids, respectively.

Current dietary recommendations indicate an intake of 250 mg per day of EPA + DHA in a healthy diet [43].

Taking into consideration these indications, it may be estimated that 1 portion of 150 g of the above-mentioned thin fish may provide the recommended amounts of EPA + DHA.

Apart from the absolute amounts of Omega–3 PUFA in seafood, the Omega–6/Omega–3 PUFA ratio is an index of nutritional relevance that well describes the quality and functionality of its lipids. The changes in human dietary patterns that occurred in Western industrialized countries during the past century have been associated with an increment in fat consumption together with a qualitative change in dietary fat, consisting of a shift towards saturated fats and Omega–6 PUFA at the expense of Omega–3 PUFA [44].

This means that the Omega–6/Omega–3 PUFA ratio, estimated to be about 1 in the diet of our ancestors, has increased drastically in Western diets, reaching values as high as 15–20 or over, and thus resulting in increased risks of obesity, cardiovascular disease, and diabetes. To correct the unbalanced Omega–6/Omega–3 ratio to healthy values (2-4/1), presentation of correct nutritional information, promotion of seafood consumption, and reducing consumption of meat and processed foods, should be accomplished.

2.3. Vitamins, Pro-Vitamins and Carotenoids

Fatty fish and mollusks are good dietary sources of vitamin D, a vitamin synthesized by sunlight induction from a precursor molecule, namely 7-dehydrocholesterol, present in the skin. A range of cholecalciferol levels, from 0.28 μg/100 g (*Perca fluviatilis*) to 47.7 μg/100 g (*Coregonus* sp.), has been reported in several marine and freshwater fish species (Baltic herring, bream, cod, perch, pike, pikeperch, rainbow trout, vendace, whitefish), with a certain seasonal variability also observed within a species [45].

Since vitamin D deficiency interests many populations, fish consumption also has a protective role towards vitamin D deficiency symptoms, such as osteomalacia and rickets.

Tocopherols, namely the α-, β-, γ-, and δ-homologues, are fat-soluble compounds with vitamin E activity naturally occurring in aquatic organisms. Alpha-tocopherol is the prevalent form in fish, found to have a positive correlation with its dietary levels and with the lipid content, particularly for farmed species. Salmon muscle, for example, may be considered to be a moderate source of tocopherols, since 100 g may provide 1.69 mg/100 g, corresponding to 14% of the recommended dietary allowance for vitamin E [46,47]. Tocopherols act as potent antioxidants in cells and cover multiple functions in biological systems, such as gene expression regulation, signal transduction, and modulation of cell functions through modulation of protein–membrane interactions [48]. Tocotrienols, the unsaturated forms of vitamin E also present in bivalve mollusks, have generated increasing interest because of their hypocholesterolemic, neuroprotective, anti-thrombotic, and anti-tumor effects [49–51].

Seafood, mainly crustaceans, bivalve mollusks, and some fish species such as salmon and trout, are good sources of carotenoids, powerful antioxidant molecules playing an important role in the maintenance of good health and prevention of disease [52]. Different studies have described the wide range of carotenoids naturally occurring in aquatic organisms [53]. Astaxanthin, cantaxanthin, zeaxanthin, mytiloxanthin, carotenoid esters, and related metabolites are only some of the several different forms of carotenoids present in fish, crustaceans, and mollusks at variable levels depending on the species, season, reproductive stage, and other factors. In addition to the provitamin A activity, which is limited only to a few carotenoids, several studies are available on the protective role of carotenoids against chronic degenerative, inflammatory, metabolic, and age-related diseases [54,55]. Therefore, the consumption of carotenoid-rich food and seafood within a balanced diet is highly recommended.

In consideration of their impact on seafood color and consumers' perception of quality, carotenoids such as astaxanthin and canthaxanthin are added to some farmed fish feeds, also incrementing the antioxidant potential and healthiness of final products.

2.4. Phytosterols and Squalene

In seafood, especially marine invertebrates, up to 50% of the sterol pool comprises phytosterols originating from the phytoplankton present in the diet [56]. From a nutritional and functional point of view, sitosterol, brassicasterol, stigmasterol, campesterol, fucosterol, and desmosterol are interesting components because of their capability to compete with cholesterol for intestinal absorption, inhibit growth of cancer cells, stimulate the immune response, and act as anti-inflammatory and anti-oxidant agents [57,58].

Squalene, a polyunsaturated triterpene containing six isoprene units, naturally occurs in animal and plant organisms as an intermediate metabolite in the synthesis of sterols. The liver of deep-sea shark is the best marine source of squalene, but small amounts are also present in fish muscle [41]. Its role in the prevention of cardiovascular heart disease and protection from cancer, and properties as an anti-cancer, skin repairing, UV-filtering, and antibacterial agent, have been the objects of study [59].

2.5. Minerals and Trace Elements

Seafood is a good source of minerals. Sodium, potassium, phosphorus, magnesium, and calcium are the prevalent minerals, but contributions of trace elements such as zinc, iron, copper, selenium, and iodine, depending on the species, may also be significant in seafood consumption.

In a survey study of 96 marine species (fish, mollusks, and crustaceans) from the Northeast Atlantic, potassium, phosphorus, and sodium were indicated as being prevalent macrominerals, while zinc, iron, and copper were the most abundant trace elements [60]. In the same study, fish was the taxonomic group with the highest mean concentration of potassium (3380 ± 990 mg kg^{-1} ww), and crustaceans emerged as the group with the highest mean concentration of calcium (2340 ± 3200 mg kg^{-1} ww) and phosphorus (2180 ± 790 mg kg^{-1} ww). For sodium, the minimum mean concentration was 230 ± 15 mg kg^{-1} ww in *Scomber colias*, whereas the maximum was in *Thunnus albacares* (7410 ± 1100 mg kg^{-1}). In this regard, it is worth mentioning that a dietary low Na/K ratio is important for cardiovascular health [61]. As regards microminerals, bivalves presented the highest zinc (226 ± 560 mg kg^{-1} ww) and copper values (41 ± 110 mg kg^{-1} ww), while gastropods presented the highest values of iron (131 ± 180 mg kg^{-1} ww) and selenium (2.5 ± 3.0 mg kg^{-1} ww); these two minerals are also highly represented in bivalves. Selenium status in the human organism has implications for cardiovascular and neurological diseases, in addition to playing a role in protection against cancer and countering the toxicological effects of mercury, a persistent contaminant present in high predatory fish and seafood [62].

Seafood is among the main iodine sources in nature besides seaweeds; therefore, its consumption has beneficial effects in preventing iodine deficiencies. In a comprehensive study of seafood species consumed in UK, marine species were the richest sources of iodine, with crustaceans (60.3 μg 100 g^{-1} ww), whitefish (Gadiformes 55–427 μg 100 g^{-1} ww), and bivalves (48.3 μg 100 g^{-1} ww) having the highest concentrations, providing from 34% to over 300% of the recommended daily intake of iodine per 140 g serving [63].

2.6. Chitin, Chitosan and Chito-Oligosaccharides

The major structural component of the crustacean exoskeleton, chitin, a polymer of n-acetyl-glucosamine and chitosan, its deacetylation product, has generated wide interest in their multiple applications, from the food to the nutraceutical and pharmaceutical sectors, because of its biodegradability, biocompatibility, chelating, anticoagulant, antioxidant, immunostimulant, cholesterol-lowering, and antimicrobial properties [64,65].

Chito-oligosaccharides, generated by chemical or enzymatic hydrolysis of chitosan, have also found interesting applications in different fields, i.e., agriculture, cosmetics, food, and medicine. Their lack of toxicity, solubility, and positive physiological effects, such as angiotensin-I-converting enzyme (ACE) inhibition, antioxidant, antimicrobial, anticancer, immunostimulant, hypocholesterolemic, hypoglycemic, anti-inflammatory, and anticoagulant properties, have suggested a variety of applications.

3. Literature Quantitative Research Analysis

The paper presents a current and updated literature analysis. As a first step, a wide search was carried out on the relationship between nutrients, bioactive compounds, and seafood to provide an overview under different perspectives. In the second step, a refinement was carried out, moving towards the interface of nutrition and health

On 11 March 2022, the Scopus database was used to carry out a search in order to retrieve publications relating to seafood and nutrients/bioactive compounds. The search string: "seafood*" OR ""fish*" OR "fishery product* AND "nutrient*" OR "bioactive compound*" OR "bioactive molecule*" OR "bioactive component*" was used to extract bibliometric data from the Scopus online database (https://www.scopus.com/home.uri, accessed on 11 March 2022) and bibliographic data, i.e., publication year, publication count, document type, countries/territories of origin, institutions, were recorded.

The functions of the Scopus web online platform named "Analyze" and "Create Citation Report" were utilized for carrying out basic analyses. A single database was selected to extract the data. Therefore, possible publications not indexed in this database were missing from this analysis.

A total of 22,542 documents, published from 1932 to 2024, were found in the literature search. The major subject areas are: *Agricultural and Biological Science*, *Environment Science* and *Medicine*.

The publication trend is reported in Figure 2. The oldest paper was published by Aikawa, H. [66] in 1932 and was entitled "On the Summer Plankton in the Waters of the Western Aleutian Islands in 1928".

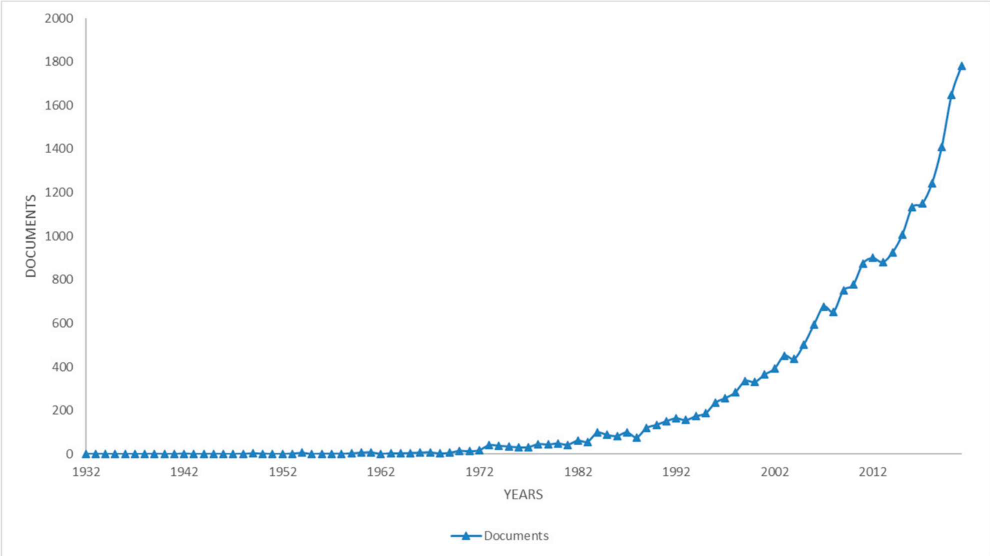

Figure 2. Publication trend (1932–2021) of the seafood/fish/nutrient/bioactive compound search. (Based on data from Scopus).

Figure 3 reports the distribution of documents by type concerning seafood/fish/nutrients/bioactive compounds publications. It includes mainly "Article", representing 80.6%, followed by "Review" 8.2%, and "Conference paper" (5.7%).

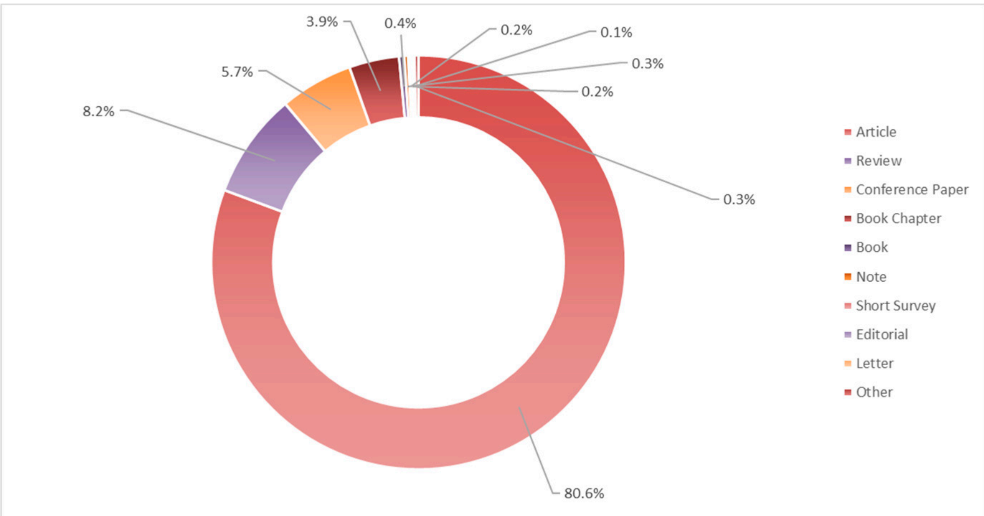

Figure 3. Distribution of documents by type. (Based on data from Scopus).

The most recent article addressed fatty acid profile variations after exposure to textile industry effluents in Indian Major Carps [67], whereas the most recent review focused on promising biologically active compounds from the marine environment and their potential effects on various diseases [68]. The most recent book describes the case study of industrialization of the Humboldt current ecosystem as part of the fishmeal revolution [69].

Figure 4 reports the most productive authors. The most productive author is Jeppesen, E., having 122 documents. His most-cited document showed an analysis of contemporary long-term data from 35 case studies concerning the lake responses to reduced nutrient loading [70], whereas his most recent document focused on consequences for taxonomic and functional diversities, and ecosystem multifunctionality, through a case study on regime shifts in a shallow lake over 12 years [71].

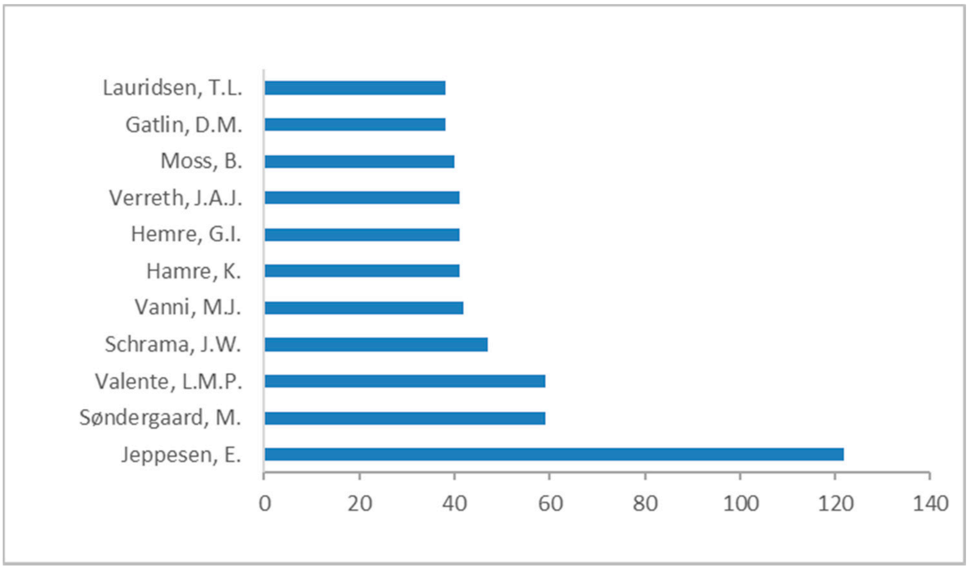

Figure 4. The most productive authors. (Based on data from Scopus).

Figures 5 and 6 report, respectively, the most productive countries/territories and institutions. Among the countries/territories, United States (n = 5877) is the most productive country, followed by China (n = 1857), and United Kingdom (n = 1478).

For United States, examples of the most recent papers are: the research published by Shepon et al. [72] on how sustainable optimization of the global aquatic omega–3 supply chain may substantially narrow the nutrient gap; and the research published by Taylor, and Karagas [73], in 2022, in *Chemosphere*, which addressed the exposure to arsenolipids and inorganic arsenic in marine-sourced dietary supplements. For China, the most recent paper reported the effects of aquaculture on the shallow lake aquatic ecological environment of Lake Datong, China [74]. For United Kingdom, the most recent document was written by Besnard et al. [75], on the diet consistency and large-scale isotopic variations in a deep-sea shark, by studying the case of the velvet belly lantern shark, *Etmopterus spinax*, in the northeastern Atlantic region and Mediterranean Sea.

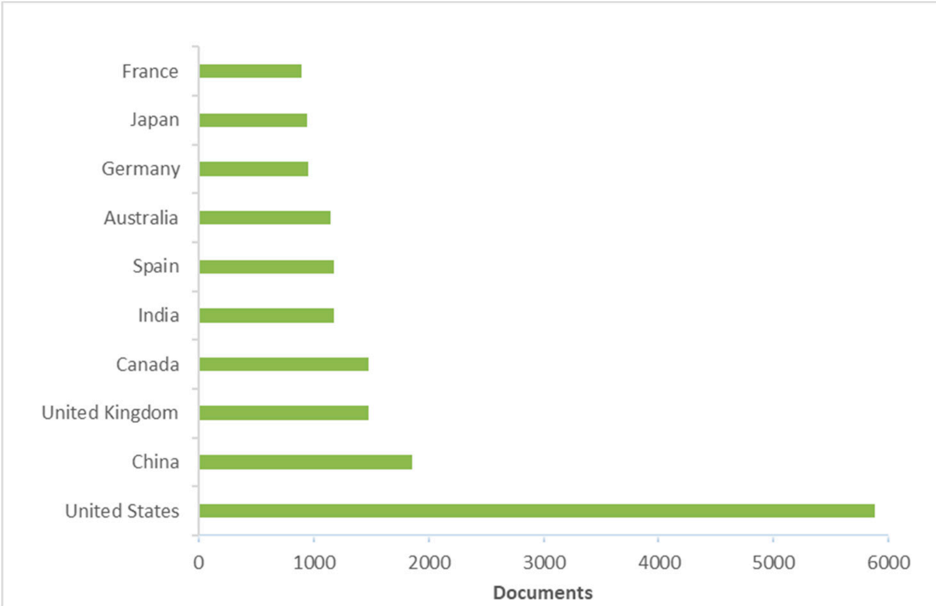

Figure 5. Most productive countries/territories. (Based on data from Scopus).

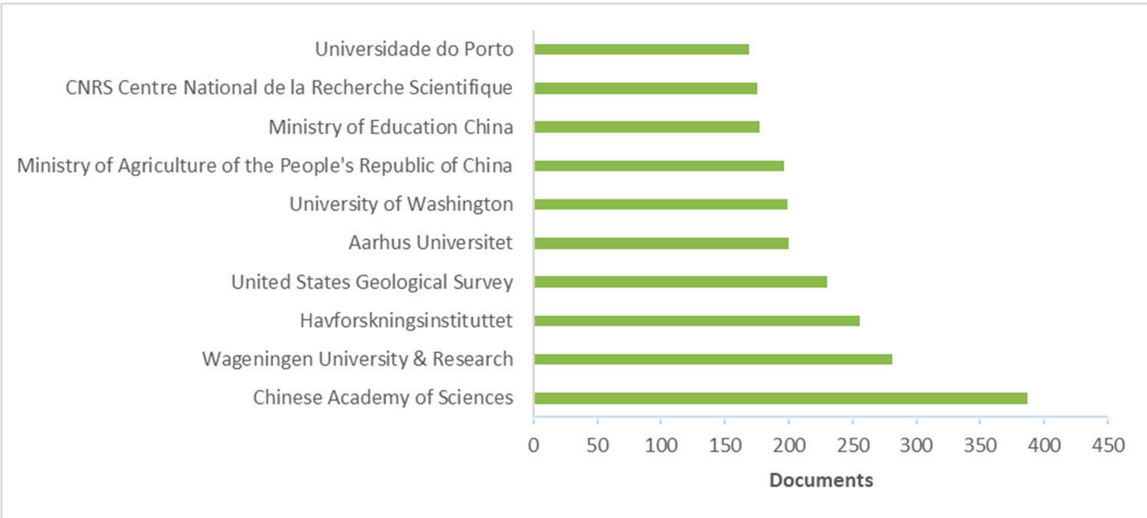

Figure 6. Most productive institutions. (Based on data from Scopus).

The most productive institution is the Chinese Academy of Sciences (n = 387). All of the 10 highest-ranked institutions contributed with at least 169 publications.

Regarding the interface between nutrition and health, a search was carried out using the string: "seafood*" OR ""fish*" OR "fishery product* AND "nutrient*" OR "bioactive compound*" OR "bioactive molecule*" OR "bioactive component*" AND "nutrition" AND "health"

The "full records and cited references" were exported to VOSviewer software (ver-sion 1.6.18, www.vosviewer.com, accessed on 11 March 2022) for further bibliometric analyses and additional processing [76–79].

A total of 1227 publications, from 1973 to 2022, were found in the literature search, and were collectively cited by 41,537 documents. The main subject areas are: *Medicine*, *Nursing*, and *Agricultural and Biological Sciences*.

The most recent document is that of Shalders et al. [80], which reviewed and summarized the nutritional and sensory quality of seafood in a changing climate; changing ocean temperature, pH, and salinity can lead to reductions in seafood macro- and micronutrients, including essential nutrients, i.e., protein and lipids. The authors also noted how the nutritional quality of seafood appears to be more resilient in taxa that inhabit naturally variable environments, such as estuaries and shallow near-coastal habitats. Criteria for assessing confidence in categorizing the nutritional quality of seafood as vulnerable or resilient to climate change was also developed in the above-mentioned research [80] and applied to a subset of seafood nutritional studies. It was found that confidence levels are generally low and may be improved by more realistic experimental designs and research collaboration [80].

Analyzing the most recent documents, it is worth mentioning a critical review on the health benefits of fish consumption and its bioactive constituents published by Chen et al. [81], in 2022, in *Food Chemistry*. Another relevant study is that of Koehn et al. [82], which investigated if the world's national policies for fisheries and aquaculture align with those for nutrition. The study found that 77 of 158 national fisheries policies identify nutrition as a key objective in the sector, and 68 of 165 public health nutrition policies identify the importance of fish and shellfish consumption as key objectives. The same authors reported that countries with higher overweight prevalence had fisheries and public health nutrition policies that were not aligned [80].

Concerning the safety aspects, the work by Meng et al. [83] addressed the contribution to aquatic product nutrition and toxic risk assessment, by studying metals content in ten commercial demersal fish from the East China sea. Spiny red gurnard had the highest concentrations of calcium, copper, and iron, whereas pufferfish and threadfin porgy represented good sources of zinc and magnesium. The same authors reported that the levels of lead, cadmium, and inorganic arsenic in all samples were below the limit values according to the Chinese national standards [83]. In this regard, although some concerns were raised about the concentration of mercury (Hg) in threadfin porgy, silver croaker, and fivespot flounder, molar ratios (selenium, Se:Hg) and the Se health benefit value indicated that they were safe for human consumption [83].

A systematic review of fisheries, aquaculture, and aquatic food literature (2017–2019) was carried out by Simmance et al. [84] to orient fisheries and aquaculture research towards food systems. A diversity of species in diets, system-wide flows of nutrients, trade-offs amongst objectives, and the nutritional needs of vulnerable social groups are approaching the ambitions of the food systems concept, which is necessary to address the global challenges of equity, nutrition, and sustainability [84].

Documents belonging to the "Book" category include those focused on marine functional food [85]; and dietary nutrients and additives, fish health [86], biodiversity, environmental chemistry, and ecological impacts of seaweeds [87].

Among more recent documents belonging to the "Editorial" category, the following documents are reported: the article of Tlusty et al. [88] on reframing the sustainable seafood narrative, and that of Tiwari et al. [89] on nutraceuticals from marine bionetworks.

A total of 1283 terms were identified from the quantitative literature research analysis and are visualized as a term map in Figure 7. Figure 7 allows us to identify the main terms correlated with research on the relationship of seafood/fish/nutrients/bioactive compounds under the perspectives of nutrition and health, and identifies the main existing research lines focused on this topic. The top recurring key-terms were human/s, female, diet, nutrition, fish, male, adult, and food intake.

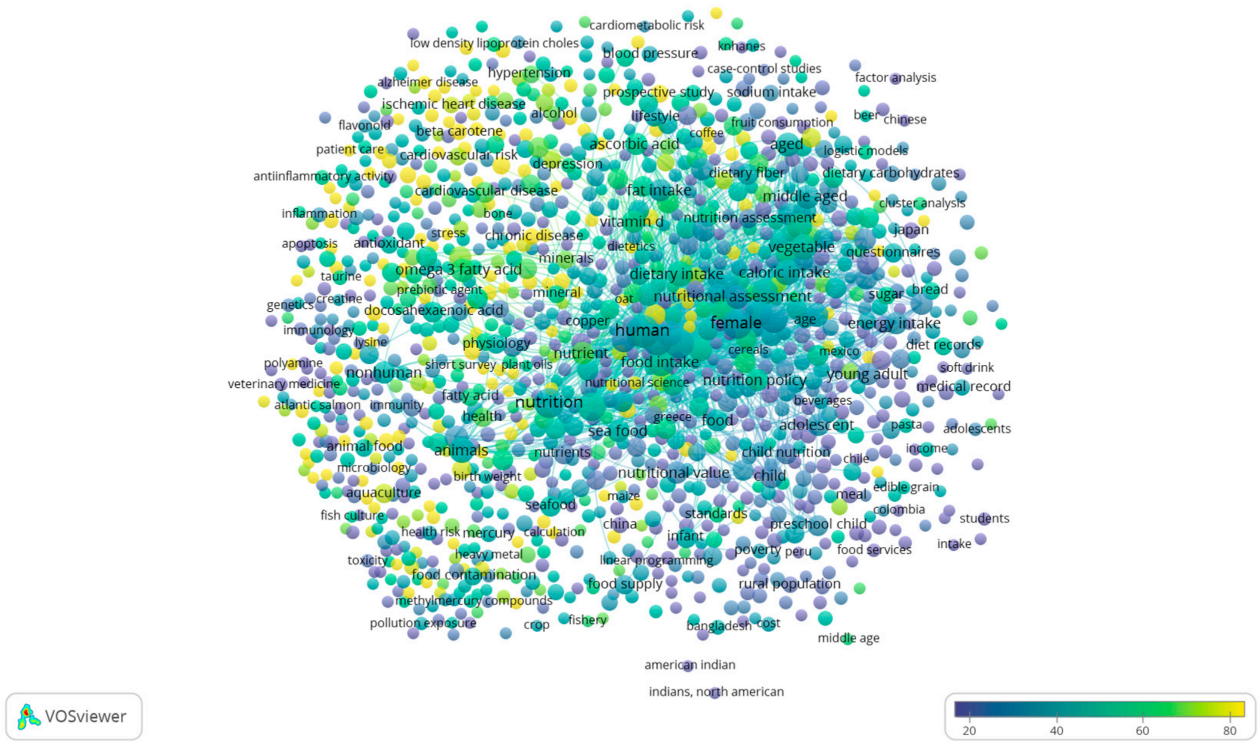

Figure 7. Term map of the seafood/fish/nutrients/bioactive compounds relationship, shown as a bubble map visualizing words from titles, abstracts, and keywords of the 1227 publications. Bubble size indicates the number of publications. Bubble color represents the citations per publication (CPP). Two bubbles are closer to each other if the terms co-appeared more frequently. (Based on data from Scopus and elaborated by VOS viewer software).

4. Conclusions

An emerging and modern image of research on seafood, nutrition, and health status should be based on a multidisciplinary approach that involves chemical science, food science, and nutrition.

The aquatic foods represent a rich source of nutrients, and bioactive components fundamental for human health, and fisheries and aquaculture are recognized globally for their contribution to reducing nutrient deficiencies and health risks related to diet. The health benefits of fish consumption and its bioactive constituents is marked and promoted, in addition to the importance of considering safety aspects along the food chain.

A strict linkage between environments, ecosystems, and food quality is highlighted. Numerous studies, including exposure research, address, for example, nutrients' aquatic environment, artificial feed for aquaculture species, climate change effects, and industrialization effects. The concept of the taxonomic and functional diversities, in addition to ecosystem multifunctionality and sustainable resources management, represents another key research line, by highlighting the importance of evaluating ecological impacts and creating marine bionetworks.

Currently, the new frontier is the exploitation of unconventional foods, i.e., seaweeds, in addition to fish by-products and wastes as sources of value-added compounds following biorefinery and circular economy approaches. Different studies have addressed the recovery of natural compounds, e.g., omega–3 fatty acids and α-tocopherol, from fish processing by-products, and their reutilization in the development of new food products for human nutrition, in addition to nutraceuticals [90,91]. Algal biomass produces a wide range of potentially bioactive compounds. Seaweeds represent an emerging and valuable source of important biologically active compounds, by exhibiting biological activities such as antiviral, antibacterial, antifungal, and anticancer activities [92,93], with great potential in different applications, e.g., in the nutraceutical and pharmaceutical [94–96] or bioenergetic fields [97]. At the same time, the application of emerging technologies such as nanotechnologies should also take into account the relevant regulations and safety aspects. The exploration of new applications and uses is increasing, triggering global interest in this research field.

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