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e Estratégicos de Tratamento



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(Organizador)

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FISHING INDUSTRY BY-PRODUCTS: FURTHER APPLICATIONS IN FOOD, PHARMACEUTICAL AND COSMETIC INDUSTRIES

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ABSTRACT: The agro-food industries, including the fishing industry, annually produce large quantities of by-products, whose valuation is still minimal or practical null. Currently, it is known that only a small part is reused for direct animals feeding or for composting. Considering that these by-products contain important levels of nutrients and bioactive compounds, some alternative ways of using by-products from the fishing industry are mentioned, namely for pharmaceutical and cosmetic industries. Nevertheless, the importance of sustainability must be taken in consideration, once it is an overly complex

concept that involves economic and social development, without causing major damage to the environment. Biotechnology advances for marine by-products conversion into products of interest are numerous. Despite this, the fish sector is facing several issues such as wild fish stocks reduction while, at the same time, aquaculture rises, augmentation of the importations on a global market, and consumers behaviors. All those influent parameters affect and complicate the definition of an upgrading strategy for the by-products as they directly depend to the raw material processed. In view of the importance that the fishing industry has at international level, this work has attempted to characterize and enhance the by-products generated by this activity, through a detailed description of the nutritional, chemical and biological properties presented in fisheries waste, which can benefit, in the near future, the food, pharmaceutical and cosmetic industries.

KEYWORDS: Fishing industry; fisheries waste; bioactive compounds, biological properties.

RESUMO: As indústrias agroalimentares, incluindo a pesca, produzem anualmente grandes quantidades de subprodutos, cuja valorização ainda é mínima ou praticamente nula. Atualmente, sabe-se que apenas uma pequena parte é reaproveitada para alimentação direta de animais ou para compostagem. Atendendo a que estes subprodutos contêm teores importantes de nutrientes e compostos bioativos, são mencionadas algumas formas alternativas de utilização de subprodutos da indústria pesqueira, nomeadamente para a indústria farmacêutica e cosmética. No entanto, deve-se levar em

consideração a importância da sustentabilidade, por se tratar de um conceito excessivamente complexo que envolve desenvolvimento econômico e social, sem causar maiores danos ao meio ambiente. Os avanços da biotecnologia para a conversão de subprodutos marinhos em produtos de interesse são numerosos. Apesar disso, o setor pesqueiro enfrenta diversos problemas como a redução dos estoques de peixes silvestres enquanto, ao mesmo tempo, a aquicultura aumenta, o aumento das importações no mercado global e o comportamento dos consumidores. Todos esses parâmetros influentes afetam e complicam a definição de uma estratégia de upgrade para os subprodutos, pois dependem diretamente da matéria-prima processada. Tendo em vista a importância que a indústria pesqueira tem a nível internacional, este trabalho procurou caracterizar e valorizar os subprodutos gerados por esta atividade, através de uma descrição detalhada das propriedades nutricionais, químicas e biológicas apresentadas nos resíduos pesqueiros, que podem beneficiar, em um futuro próximo, as indústrias alimentícia, farmacêutica e cosmética.

PALAVRAS - CHAVE: Indústria da pesca; resíduos pesqueiros; compostos bioativos, propriedades biológicas.

1 | INTRODUCTION

Scientific developments of the last 50 years have led to a much-improved understanding of the functioning of aquatic ecosystems, and to global awareness of the need to manage them in a sustainable manner. Thus, the importance of utilizing fisheries and aquaculture resources responsibly is now widely recognized and prioritized. With global demand slowing and trade tensions contributing to a more challenging market, multiple major seafood exporters are seeing trade contractions in 2019 following positive performances in 2018, particularly in Asia. China's total seafood exports are likely to be down significantly for the year, while the export revenues of Indonesia, India and the Philippines are also set to take a hit.[1] With the increase of the fishing industry also increases a high amount of by-products with significant economic and environmental impact.[2] In fact, the reuse of agro-industrial by-products can represent a renewable source for food, pharmaceutical and cosmetic constituents already in use, or even originate new added value ingredients with functional properties.[3]

In view of the above, the dynamic in the scope of scientific research has increased, focusing on the valorization of by-products and food waste, reporting nutritional and chemical composition and their possible integration in foods, pharmaceutical and cosmetics products.[4]

1.1 Fishing Industry

By 2050, world food production is expected to double due to the increasing population rate and due to changes in eating habits. The fishing industry is a major export sector of fish and other marine products.[5] All over the world, fish can be obtained through capture and/or aquaculture. With approximately 1200 ports, the European Union (EU) possesses

the largest maritime surface in the world and, consequently, the largest merchant fleet. [6] The sea route represents 90% of its foreign trade. In 2018, for instance, ~84.4 million tons of fish were caught in the sea and the total value of production derived from capture and aquaculture was ~178.5 million tons.[7] In fact, last year, approximately 131 (85%) million tons were directly utilized as food and the rest (15%) was underutilized as live bait for fishing, ornamental products (pearls and shells), feed for carnivorous farmed species and marine worm. There has been a sustained growth in the fish supply during the last 50 years with an average growth rate of 3.2% each year which is higher than the growth rate of world's population (1.7%).[7]

Therefore, the per capita fish supply increased by 17.5% over the past 10 years. Moreover, the production of fish in China, Indonesia, India, and Russia has increased while fish production decreased in other countries over the ten years period.

In Portugal, the fishery sector is a relevant economic activity that promotes a significant importance in the gross domestic product (GDP) and in the national gross added value (GVA). As a matter of fact, Portugal stands out, among the EU countries, for its peripheral location and for its vast exclusive economic zone, resulting from an extensive continental coastline and, also, from the archipelagos of Madeira and Azores. Moreover, fishing is an important source of livelihood for riverine populations.[8] According to the National Portuguese Statistics Institute, the national production of aquaculture in 2019, the most recent information available, was 11.259 tones and generated revenue of 75.2 million euros, which reflected increases of 17.8% in quantity and 38.9% in value, compared to 2018.[9] Portugal is the largest consumer of fishery at EU level (~55.6 Kg/per capita/year) and the 3rd largest consumer worldwide, after Iceland (~90.9 Kg) and Japan (~61.2 Kg). This high consumption is explained by the fact that the Portuguese consumed high amounts of dry salted cod. National and international fishing is also responsible for the creation, valorization, and internationalization of processing industries. This trend must, however, take hold and deepen do more processing of fishery products, to create more value and reduce dependence on imported raw materials. Thus, and as priority objective, the verticalization of production can be identified by national and international industries, driving the increase in exportation, and opening new markets for healthy competition.

1.2 Industry *versus* Environmental Impact

The global population is predicted to reach 9.3 billion by 2050, with a projected increased food demand between 50-70%. In this context of growing demand, ~868 million people are chronically under-nourished, equating to one in eight people worldwide. At the same time, it is foreseen that over one third of all food produced globally for human consumption goes to waste.[10] Therefore, reducing the scale of losses and waste throughout the entire food system is a determinative step towards improving global food security. Europe, like other parts of the world, is currently facing major climate changes that include

habitat loss and degradation, extreme weather events, environmental contamination due to urbanization, agricultural intensification and increased consumption of natural resources. These environmental changes are a consequence of human activity and are leading to loss of biodiversity, increase in natural disasters, threat to access to food, water and energy, impact on human health and degradation of environmental quality. [11,12] Biodiversity is essential to human well-being and offers several benefits. Since ecosystems are adapted to meet human needs (such as water supply, food production, sourcing raw materials, etc.), there must be a balance between protecting the integrity of the environment, ecosystem, and the guarantee of human health. The social and political challenge is to decide which ecosystems are desired in certain habitats in a certain period.[12] Thus, sustainable development involves an integrated approach of social, economic, and environmental dimensions, and depends on considerable efforts in terms of innovation.[13] Moreover, food waste is an extremely important issue for today's society, since it causes a high negative impact on social, economic, and environmental levels. Therefore, the reduction of food loss and waste is one of the greatest objectives to be achieved worldwide. According to Bond et al. [10], food waste refers to edible food products, which are intended for human consumption, but usually are rejected, lost, degraded, or consumed by pests, not including inedible or undesirable parts of food products. Food loss occurs in production, storage, transportation, and processing, which are the chain's phases with the lowest return. On the other hand, food waste occurs at the end of the food supply chain, which includes sales and final consumption, synonymous with greater potential in the value chain, which represents higher costs. Thus, the reduction in these losses over the food system will improve the availability of food in the future and is thus an important step towards achieving global food security. Therefore, the food processing sector, like other natural resource-based processing industries, produces high amounts of food waste and by-products. Due to the presence of different values compounds in by-products and food residues, the main objective is to isolate and use these high biological components (e.g., proteins, peptides, polysaccharides, fibers, flavorings, phytochemicals, and pharmacological ingredients).[14,15]

The world marine capture fisheries contribute more than 50% of the total world fish production. About 70% of fish is processed before final sale, resulting in 20-80% of fish waste depending on the level of processing and type of fish. The majority of fish wastes are disposed of in the ocean. At the industrial level, fish residues and by-products promote high costs for industries, including storage in cold stores and their transport, before being sent to landfills.[16] This significant amount of organic waste, produced during the various stages of the fishing production chain, consists of cheap and high quality raw material, which can be used in the future.[17]

2 I ENHANCEMENT OF FISH BY-PRODUCTS

In general, fish by-products are not usually easily marketed due to their low acceptance by consumers or due to strict health regulations imposed and relative to the obtaining, transportation, storage, handling, processing and use of by-products. In the past, fish by-products were considered low commercial value; however, in recent years they have gained more attention due to the possible use for several purposes.

The viscera, head, spines, fillets (pieces resulting from the “sawdust”), skin, fins, and scales constitute a biomass with several uses, including: fish meal production (only from wild fish); fish oil; fish paste; fish strips; fertilizers; animal feed; ensiled; bioensylates; protein hydrolysates; gelatine; chondroitin sulfate; skins; pharmacological molecules, cosmetic and nutraceutical interest (omega 3 fatty acids such as EPA and DHA), important minerals (calcium), collagen, peptones, hyaluronic acid, among others).[18,19] Considering the mentioned products, some allow a complete waste conversion, namely fish meal and protein hydrolysates. However, all the fish by-products are likely to be used for other purposes and other industrial areas (Figure 1).

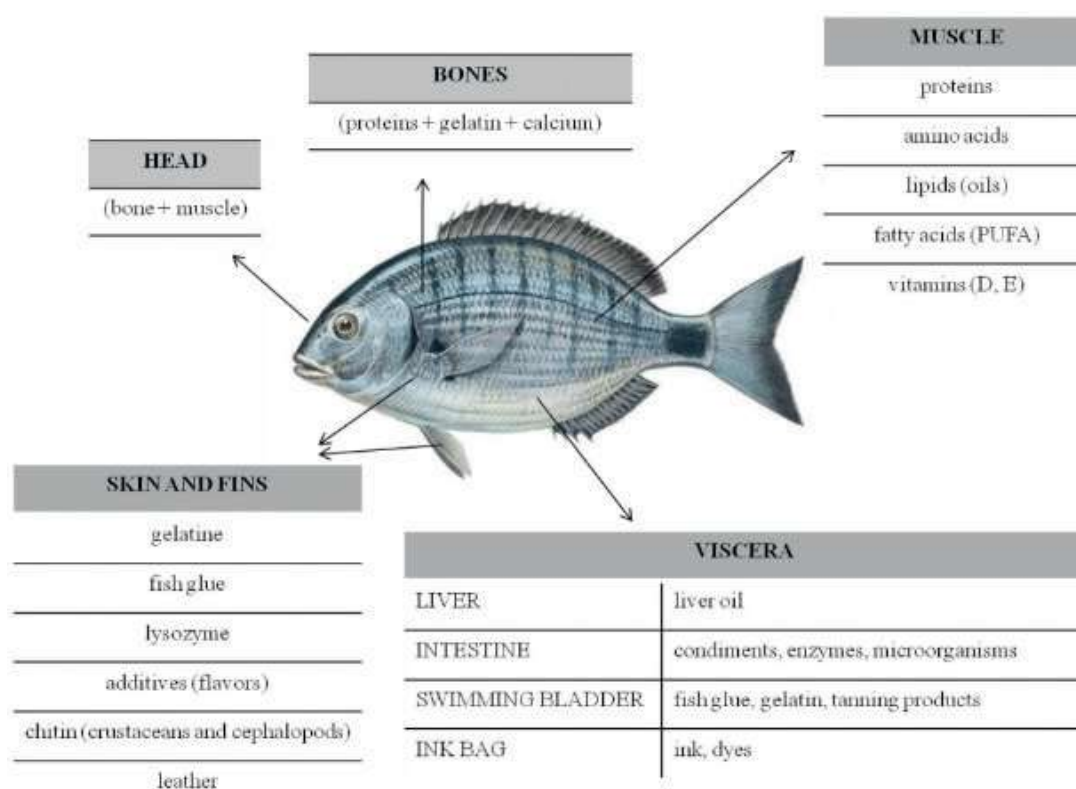


Figure 1. Possible application of fish by-products.

According to Figure 1, all disposable parts by the fish industry can be valued. For example, heads and strips / fillets can be used directly as food for human consumption (sausages, cakes, gelatine and fish sauces),[20] while other by-products may incorporate

feed, fertilizers, biogas, products dietary (chitosan),[16] pharmaceuticals (molecules and oils),[20] natural and cosmetic pigments (collagen).[15, 21] On the other hand, other by-products, such as viscera and other internal organs, need to be processed quickly due to their high perishability, providing protein hydrolysates or specific enzymes (pepsin, trypsin, chymotrypsin, collagenases, and lipases).[22] Cartilage and bones may integrate pharmaceutical products (powders, creams and capsules) due to their high content of collagen, calcium and phosphorus.[23]

According to Khawli et al.[24], activities linked to fisheries sectors produce substantial amounts of by-products which, although they are often rejected or used as low-value ingredients in animal feed, are considered as a potential prominent source of bioactive compounds, with important functional properties. Therefore, they can be isolated or concentrated, giving them added value in high-end markets, such as nutraceuticals or cosmetics.

There are two main aspects for fish by-products production: i) mass exploration, the main sectors which derived from this approach are fertilizers, energy and animal feed; ii) small volume exploitation for higher added-value for sectors as nutrition, health food, nutraceutical, cosmetic or pharmacy. The main difference between these two aspects is the absorption capacity of the market and the income added by the market (Figure 2).

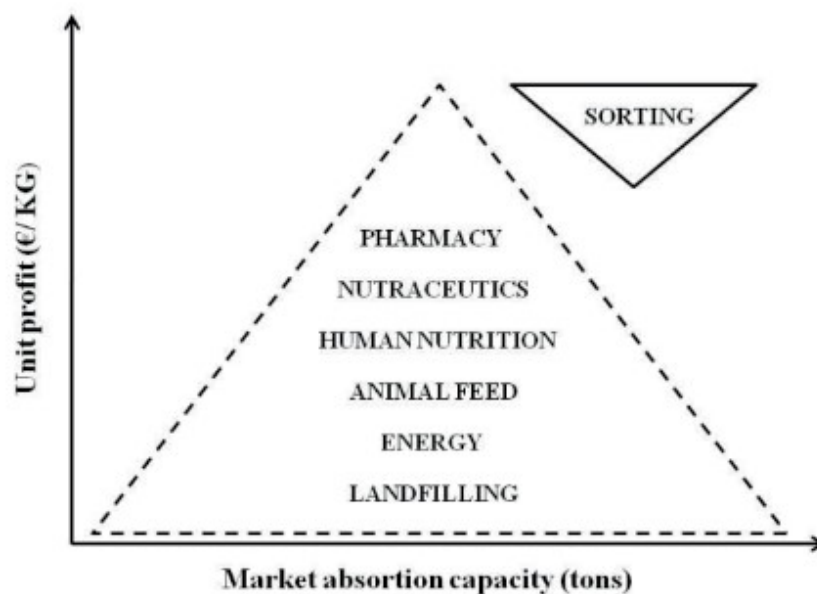


Figure 2. Scale of marine by-products upgrading modes.

The sorting is a key factor of success to upgrade by-products in high value products because the sectors which treat them work on specific compounds contained in specific type of by-products (e.g., collagen in skins), sometimes in specific species (e.g., siki liver oil for aeronautics).

The consumer market has become accustomed to the introduction of new innovative products, which forces production companies to design new product lines and to use updated processing technologies. Thus, in view of the aforementioned, and in accordance with the objective of this work, the following subchapters will focus on compounds and ingredients resulting from the waste / by-products of the fishing industry, in a perspective of valuing and making known the importance of using these in different applications in the food, pharmaceutical and cosmetic areas.

2.1 Fishmeal

Fishmeal is a traditionally used livestock feed supplement. Nutritive value of fish feed depends largely on the quality of protein of the ingredients used in the formulation of feed. Fishmeal has been established as the most reliable source of protein used in fish feed formulation thorough out the globe, due to their high protein content (usually 60-75%), excellent amino acid profile (high levels of lysine, methionine and cysteine, three of the essential amino acids which the animal bodies cannot synthesize), high nutrient digestibility and lack of antinutrients. It is also a good source of B-group vitamins like cyanocobalamine (B12), chlorine, niacin, pantothenic acid and riboflavin, and several minerals, like calcium, phosphorus, copper and iron. In fact, aquaculture production is dominated by Asian countries being China the biggest producer (58795.3 thousand tones (Tt)) followed by Indonesia (14330.3 Tt), India (4884 Tt), Vietnam (3411.Tt), Philippines (2337.6 Tt), Bangladesh (1956.9 Tt), Republic of Korea (1567.4 Tt), Norway (1332.5 Tt), Chile (1227.4 Tt) and Egypt (1137.1 Tt).[1] As aquaculture increases in production numbers, it is natural that the demand for fishmeal will become even higher. This flour can also serve as an ingredient for other food products. There are some published works describing future applications of fish and their by-products as flour in baked foods for human nutrition. For instance, Fasasi et al.[25] studied the functional characteristics of a corn flour with Nile tilapia flour (*Oreochromis niloticus*) proving that this new ingredient provides greater nutritional support and could be effectively incorporated into the food systems in countries with high fish production. Bastos et al.[26] investigated the enhanced mineral content of zinc, iron, potassium and calcium in wheat breads processed by fish fillet meal flours, showing the significant increase of these minerals in bread (4.2%, 8.4%, 12.6% and 16.8%, respectively). Hence, the addition of fish processing residue to breads is a way to provide essential nutrients to the population through a well-accepted, accessible, and low-cost product. Talib and Zailani [27] proved that tuna (*Thunnus albacares*) fishbone flour contains high levels of macro and micro minerals and can be used as an alternative ingredient to supply minerals for people who are allergic to dairy products. Due to high levels of calcium, tuna fishbone flour could be used for therapeutic purposes, as an ingredient in osteoporosis therapy drugs.

2.2 Fish Oils

Approximately 45% of the fish tissue remains after processing, including offals, fins, skin, internal organs, head, bones, which are not used as foods. Some of these fish processing by-products are utilized, but huge amounts are still discarded as wastes. In particular, fish processing by-products contain valuable protein and lipid fractions, as well as vitamins and minerals. Fish oils have well documented beneficial health effects.[28-30] They are readily available sources of polyunsaturated fatty acid (PUFA), especially the n-3 series consisting mainly of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and the n-6 series including arachidonic acid (AA) and γ -linolenic acid (GLA). These PUFAs have many physiological functions, including preventing many diseases such as atherosclerosis, coronary heart disease, lower blood cholesterol levels, cancer, platelet mellitus, diseases of the bone joints, asthma, and preventing the aging process.[31] For example, EPA has been used for the treatment of arteriosclerosis and hyperlipemia since 1990 in Japan. However, the fish oil contents and fatty acid compositions of these fishes are not constant, and great variations are reported, in terms of fat content and fatty acid composition, for various marine.[29,30] Despite, ~50% of the fish body weight comprises fish processing by-products, usually such by-products are used to produce fishmeal (with fish oil as a by-product), or as fertilizers. Fish oil content depends on the fish species and tissue, and also due to feeding habits, environmental temperature, fish age and sexual maturity, and location of the catch. For instance, fish from tropical climate were found to have lower amounts of total lipids compared to fish from the Arctic region. Moreover, the levels of essential fatty acids in marine fish oil are significantly higher than those found in freshwater fish and aquaculture oils.[30]

Selmi and Sadok [32] found extensive lipid deposits in the head and belly cavity of mackerel and capelin. Pink salmon by-products have been reported to contain 10.9% oil in the heads and 2% oil in the viscera.[28] Tuna heads are known to be rich in omega-3 PUFA, mainly docosahexaenoic acid (DHA).[33,34] At pharmaceutical and cosmetic level, fish oil has been broadly reported as a potential supplement to ameliorate the severity of some skin disorders such as photoaging, skin cancer, allergy, dermatitis, cutaneous wounds, and melanogenesis.[31,34] Thus, there has been increasing interest in the relationship of fish oil with skin protection and homeostasis, especially with respect to the omega-3 polyunsaturated fatty acids (PUFAs). The topical and oral use of PUFAs present in fish oil is believed to be advantageous in the prevention and treatment of skin aging.[34,35] The use of these fatty acids in pharmaceutical and cosmetic products is already known, however, the use of fish oil (in a perspective of valuing the by-products of the fishing industry), could also be integrated in pharmaceutical and cosmetic formulation products, because in addition to PUFA, also contains minerals, vitamins A and D.

2.3 Proteins and Aminoacids

Fish is an important source of dietary amino acids for human to sustain an adequate protein nutrition and health. In fact, fish contains high amounts of protein and balanced proportions of all amino acids relative to human requirements. As previously mentioned, the nutritional composition of the fish depends on the species, age, gender, health, nutritional status and time of year.[24] Nevertheless, in general, different studies report that nutritional composition is characterized by considerable levels of proteins (15%-30%), lipids (0%-25%) and high water contents (50%-80%).[36,37] The healthy compounds present in fish composition are also part of its by-products. Therefore, it is necessary to analyze these by-products, especially regarding their nutritional properties.

According to Ghaly et al.[5] About 70-80% of fish muscle is made up of structural proteins and the remaining 20-30% is constituted of sarcoplasmic proteins with 2-3% of insoluble connective tissue proteins. Myofibrillar proteins are the primary dietary proteins that fish produce, representing 66-77% of the total protein content in muscle. These proteins contain about 50-60% of myosin and 15-30% of actin.[5] Regarding aminoacid profile, the proline contents found in by-products is higher than those described in the muscle (edible portion), with percentages above 5% vs. 3.5%. The skin, fishbone, and head display the highest contents of proline, values around 948.6, 932.4, and 883.5 mg/100 g of tissue, respectively.[36] Also, fish proteins contain many bioactive peptides that are easily absorbed and can be used for several metabolic activities.[38] Many peptides have been referred to as angiotensin converting enzyme (ACE) inhibitors, showing an important role in the treatment of arterial hypertension.[39] Several studies have been developed with the objective of reused non-edible fish and by-products of edible fish for the production of commercially enriched products. Several studies have been developed with the objective of reusing non-edible fish and by-products of edible fish for the production of commercially enriched products.[36-39] Thus, hydrolyzed proteins and extracted from industrial waste show to be a good alternative as bioactive compounds and / or natural ingredients, as they become a concentrated and purified product. According to Wangkheirakoam et al.[40], hydrolyzed proteins from fish not used for direct consumption or edible fish by-products can provide stability to food products, noble drugs and nutraceuticals. Peptides isolated from hydrolyzed proteins from several fish also showed other biological activities, such as antioxidant, anti-thrombotic and immunomodulatory.[40] *In vitro* tests have shown that the peptides have anticoagulant, anti-platelet properties and the ability to exert potent antioxidant activities in different oxidative systems.[39] So, enzymatic hydrolysis of protein can yield a by-product which is found to be rich in nutrients and bioactive compounds with pharmaceutical and industrial application as food.

Regarding the enzyme fraction of marine by-products, there has been research over the last 25 years on isolation, purification and characterization of enzymes from fish

intestines made it possible its applications in different industries such as food, natural skin care products, cosmetics and pharmaceuticals.[41] Hydrolytic enzymes, such as cod serine proteases, trypsin, chymotrypsins, elastase and serine collagenases. Because these cold-active or psychrophilic enzymes are more active at low temperatures than the correspondent mammalian or bacterial enzymes and plus have higher catalytic efficiency, higher sensitivity to heat and low pH and higher activity towards native proteins, they can be beneficial in different industrial processes, including medical, pharmaceutical, hygienic and cosmetic processes, because of the smaller concentrations needed due their higher catalytic efficiency.

2.4 Collagen and Gelatin

Collagen is largely available, as it can be extracted from many animal sources, it can be easily absorbed upon topical administration, and hence it is largely used in the cosmetic and pharmaceutical industry for the treatment of premature aging. Bioactive peptides, such as collagen hydrolyzed, are among the most used ingredients for the development of nutraceuticals - food or food ingredients that have defined physiological effects. During fish processing operations, the removal of products with collagen and gelatin can reach 30% of the total by-products obtained after filleting.[19] Fish skin waste is a good source of collagen and gelatin, which are regularly used in the food, pharmaceutical and cosmetic industries. Collagen and gelatin are two different forms of the same macromolecule.[5] Collagen is a structural protein in connective tissue (skin, cartilage, tendons and bones) and is produced in connective tissue by fibroblasts in numerous epithelial cells. As is well known, collagen represents about 30% of the body's protein mass and is essential in the structure of different types of tissues, providing rigidity and integrity to bones and skin. There are many types of collagen, the main ones being type I, II and III. Dermal fibroblasts produce elastin and collagen types I and III, along with other extracellular matrix proteins.[42] Gelatin formation results from the irreversible denaturation of the collagen molecules. To stop this denaturation process, a chemical or thermal treatment can be applied. For instance, heat treatment of collagen denaturation is used both in beauty techniques, in medical techniques such as orthopedics, plastic surgery, dental or ophthalmological treatments, but also in the pharmaceutical or food industry. Gelatin is commonly used in the food industry due to the different bioactivities of collagen peptides, especially high biocompatibility and bioavailability. Collagen can be extracted from both animal and vegetable sources, algae and marine organisms, including fish and their by-products. In pharmaceutical, cosmetic and food industries, the use of collagen of marine origin is preferred.[43] Collagen and other bioactive substances can be extracted from marine organisms. Among the marine organisms from which collagen is extracted are invertebrates such as jellyfish, sponges, sea urchin, octopus, but also vertebrates including cod, salmon and marine mammals. Unlike collagen of animal origin, collagen obtained from marine sources is more easily absorbed,

has low molecular weight and is preferable to industry due to low inflammatory reactions and low number of contaminants. In the cosmetic industry, marine collagen is successfully used for the treatment of wounds, burns and ulcers but also for antimicrobial protection, preventing the loss of moisture and heat from the injured tissue.[5,42] Moreover, physico-chemical and functional properties of fish gelatin have been extensively studied, especially in relation to its rheological, emulsifying, foaming, film-forming and sensory characteristics. Its composition is rich in non-polar amino acids, such as glycine, alanine, valine and proline. Gelatins are produced on a large scale from the skin and bones of terrestrial mammals, mainly of bovine and porcine origin, by alkaline or acid extraction. However, recently, the use of fish skin and bones for gelatin production has gained more interest due to greater safety, since there is no risk of disease transmission. Since it is made from by-products of the fish processing industry, marine gelatin avoids waste and pollution caused by this industry. In addition, gelatins extracted from fish by-products are accepted in some geographic areas due to religious objections related to animal origin.[44]

2.5 Minerals

Fish bones are normally separated after muscle proteins removal and contain ~60 to 70% of several minerals, mostly calcium, phosphorus and zinc.[2] For this reason, fish bones can be used as an important source of inorganic calcium, in which can be applied in the food industry. This mineral can be used to fortify powdered milk and other foods.[5,39] Fish bones are also a good source of hydroxyapatite, which consists in a phosphate calcium mineral form and can be used as bone graft material in medical and dental applications. [46] Hydroxyapatite was very attractive for using as bone implant material for a long period due to the close similarity with natural bone in composition and osteoconductive properties. Hydroxyapatite is also quite attractive as a bone substitute as it is non-toxic and non-immunogenic, has the desired mechanical strength and surface properties for bone regeneration. It is therefore used in orthopedic and dental applications. Currently, it is possible to produce hydroxyapatite in a synthetic way, using chemical methods, however the advantages of hydroxyapatite from fish bone are more similar to human bone, greater biological activity, better physical-chemical properties, namely support and strength and , even lower production costs.

3 | CONCLUSIONS

Fish waste management has been one of the problems having the greatest impact on the environment all over the world. Fish farming detrimental effects on the marine environment in particular have become an issue of public concern. For instance, in European Union, several Directives, Decisions and Regulations were voted in an attempt to minimize the environmental impact of fisheries within the frame of Integrated Coastal Management.

This work showed that treated fish waste has found many applications among which the most important are animal feed, biodiesel/biogas, dietic products (chitosan, gelatin), natural pigments (after extraction), food-packaging applications (chitosan), cosmetics (collagen), enzyme isolation, soil fertiliser and moisture maintenance in foods (hydrolysates). In this context, scientific research can contribute to the sustainable exploitation of such fish resources, suggesting the most suitable methodologies and strategies for the valorization of these high added value products.

REFERENCES

1. FAO, Food and Agriculture Organization of the United Nations. Globefish highlights: a quarterly update on world seafood market. 2: 2019 with Jan.–Dec. 2018 Statistics.
2. Abdel-Shafy HI, Mansour MSM. (Solid waste issue: Sources, composition, disposal, recycling, and valorization). Egypt J Pet, 2018; 27(4): 1275-1290.
3. Szabo K, Cătoi AF, Vodnar DC. (Bioactive compounds extracted from tomato processing by-products as a source of valuable nutrients). Plant Foods Hum Nutr, 2018; 73(4): 268–277.
4. Faustino M, Veiga M, Sousa P, Costa EM, Silva S, Pintado M. (Agro-food by-products as a new source of natural food additives). Molecules, 2019; 24(6): 1-23.
5. Ghaly AE, Ramakrishnan VV, Brooks MS, Budge SM, Dave D. (Fish processing wastes as a potential source of proteins, amino acids and oils: A critical review). J Microb Biochem Technol, 2013; 5(4): 107-129.
6. European Commission (EC). Closing the Loop-An EU Action Plan for the Circular Economy. Brussels, Belgium. (2015).
7. FAO. The state of world fisheries and aquaculture. Food and Agriculture Organization of the United Nations, 2020; Rome.
8. Direção-Geral das Pescas e Aquicultura. (Plano Estratégico Nacional para a pesca 2007-2013). Lisboa, 2013.
9. INE. (Estatísticas da Pesca – 2019). Instituto Nacional de Estatística, 2019.
10. Bond M, Meacham T, Bhunnoo R, Benton TG. (Food waste within global food systems). A Global Food Security report, 2013. (www.foodsecurity.ac.uk).
11. Leung KMY, Yeung, KKY, You J, Choi K, Zhang X, Smith R, Zhou GJ, Yung, MMN, Arias-Barreiro C, An YJ, Burket R, Dwyer R, Goodkin N, Hii YS, Hoang T, Humphrey C, Iwai CB, Jeong SW, Juhel G, Kyriazi-Huber K, Lee KC, Lin BL, Lu B, Marin P, Nillos MG, Oginawati K, Rathnayake IVN, Shoeb M, Tan CH, Tsuchiya MC, Ankley GT, Boxall ABA, Rudd, MA, Brooks BW. (Toward sustainable environmental quality: priority research questions for asia). Environ Toxicol Chem, 2020; 39(8): 1485-1505.

12. Hamadache M, Benkortbi O, Amrane A, Hanini S. (QSAR approaches and ecotoxicological risk assessment). *Ecotoxicol*, 2020; 25: 615-638.
13. Seppänen L. (Learning challenges and sustainable development: A methodological perspective). *Work*, 2017; 57(3): 315-324.
14. Sadiq MB, Singh M, Anal AK. (Application of food by-products in medical and pharmaceutical industries). In A. K. Anal (Ed.), *Food Processing By-Products and their Utilization*, 1st ed, 2017. Wiley.
15. Vinha AF, Sousa C, Oliveira MBPP. Food waste and by-products recovery: nutraceutical and health potential of carotenoids as natural pigments. 1st ed. 2020. Lambert Academic Publishing.
16. Madende M, Hayes M. (Fish by-product use as biostimulants: an overview of the current state of the art, including relevant legislation and regulations within the EU and USA). *Molecules*, 2020; 25(1122):1-20.
17. Larsen R, Eilertsen KE, Elvevoll EO. (Health benefits of marine foods and ingredients). *Biotechnol Adv*, 2011; 29(5): 508-518.
18. Cholewski M, Tomczykowa M, Micha, T. (A comprehensive review of chemistry, sources and bioavailability of omega-3 fatty acids). *Nutrients*, 2018; 10(1662): 1-33.
19. Blanco M, Vázquez RIPM, Sotelo CG. (Hydrolysates of fish skin collagen: an opportunity for valorizing fish industry by-products). *Mar Drugs*, 2017; 15(131): 1-15.
20. Välimaa, AL, Mäkinen S, Mattila P, Marnila P, Pihlanto A, Mäki M, Hiidenhovi J. (Fish and fish side streams are valuable sources of high-value components). *Food Qual Safet*, 2019; 3: 209-226.
21. Alves AL, Marques ALP, Martins E, Silva TH, Reis RL. (Cosmetic potential of marine fish skin collagen). *Cosmetics*, 2017; 4(39): 1-16.
22. Pylak M, Oszust K, Frac M. (Review report on the role of bioproducts, biopreparations, biostimulants and microbial inoculants in organic production of fruit). *Ver Environ Sci Biotechnol*, 2019; 5: 597-616.
23. Halim NRA, Yusof HM, Sarbon NM. (Functional and bioactive properties of fish protein hydrolysates and peptides. A comprehensive review). *Trends Food Sci Technol*, 2016; 51: 24-33.
24. Al Khawli F, Pateiro M, Domínguez R, Lorenzo JM, Gullón P, Kousoulaki K, Ferrer E, Berrada H, Barba FJ. (Innovative green technologies of intensification for valorization of seafood and their by-products). *Mar Drugs*, 2019; 17: 689.
25. Fasasi OS, Adeyemi IA, Fagbenro OA. (Functional and pasting characteristics of fermented maize and Nile tilapia (*Oreochromis niloticus*) flour diet). *Pak J Nutr*, 2007; 6(4): 304-309.
26. Bastos SC, Tavares, T, Pimenta MESG, Leal R, Fabrício LF, Pimenta CJ, Nunes CA, Pinheiro ACM. (Fish filleting residues for enrichment of wheat bread: chemical and sensory characteristics). *J Food Sci Technol*, 2014; 51(9): 2240-2245.

27. Talib A, Zailani K. (Extraction and purification of yellowfin tuna fishbone flour as an ingredient of future traditional medicine). *J Pharm*, 2017; 7(11): 8-14.
28. Spalvins K, Blumberga D. (Production of fish feed and fish oil from waste biomass using microorganisms: Overview of methods analyzing resource availability). *Environl Climate Technol*, 2018; 22(1): 149-164.
29. Šilovs M. (Fish processing by-products exploitation and innovative fish-based food production). *Res Rural Develop*, 2018; 2: 210-215.
30. Shahidi F, Ambigaipalan P. (Omega-3 polyunsaturated fatty acids and their health benefits). *Ann Rev Food Sci Technol*, 2018; 9: 1-37.
31. Febrianto R, Sudarno D. (Fish oil production process from waste catfish (*Pangasius Pangasius*) in Balai besar pengujian penerapan hasil perikanan (BBP2HP) East Jakarta). *J Mar Coast Sci*, 2020; 9 (2): 65-69.
32. Selmi S, Sadok S. (The influence of season on lipid content and fatty acids profile of *Euthynnus alletteratus* fillets and by-products). *J. Muscle Foods*, 2010; 21: 365-378.
33. Gammone MA, Riccioni G, Parrinello G, D'Orazio N. (Omega-3 polyunsaturated fatty acids: Benefits and endpoints in sport). *Nutrients*, 2019; 11(1): 1-16.
34. Huang T, Wang PW, Yang SC, Chou WL, Fang JY. (Cosmetic and therapeutic applications offish oil's fatty acids on the skin). *Mar Drugs*, 2018; 16(256): 1-20.
35. Dini I, Laneri S. (Nutricosmetics : A brief overview). *Phytother Res*, 2019; 33(12): 3054-3063.
36. Pateiro M, Munekata PES, Domínguez R, Wang M, Barba FJ, Bermúdez R, Lorenzo JM. (Nutritional profiling and the value of processing by-products from gilthead sea bream (*Sparus aurata*)). *Mar Drugs*, 2020; 18: 101.
37. Kundam DN, Acham IO, Girgih AT. (Bioactive compounds in fish and their health benefits). *Asian Food Science Journal*, 2018; 4(4): 1-14.
38. Franco D, Munekata PES, Agregán R, Bermúdez R, López-Pedrouso M, Pateiro M, Lorenzo JM. (Application of pulsed electric fields for obtaining antioxidant extracts from fish residues). *Antioxidants*, 2020; 9(2):90.
39. Senevirathne M, Kim S. Utilization of seafood processing by-products: medicinal applications. In: *Advances in Food and Nutrition Research*, 1st ed., Vol. 65., 2012. Elsevier Inc.
40. Wangkheirakpam MR, Mahanand SS, Majumdar RK, Sharma S, Hidangmayum DD, Netam S. (Fish waste utilization with reference to fish protein hydrolysate - A review). *Fishery Technol*, 2019; 56(8): 169-178.
41. Vannabun A, Ketnawa S, Phongthai S, Benjakul S, Rawdkuen S. (Characterization of acid and alkaline proteases from viscera of farmed giant catfish). *Food Biosci*, 2014; 6: 9-16.

42. Lupu MA, Pircalabioru GG, Chifiriuc MC, Albulescu R, Tanase C. (Beneficial effects of food supplements based on hydrolyzed collagen for skin care). *Experimental and Therapeutic Medicine*, 2020; 20: 12-17.
43. Silva TH, Moreira-Silva J, Marques AL, Domingues A, Bayon Y, Reis RL. (Marine origin collagens and its potential applications). *Mar Drugs*, 2014; 12: 5881-5901.
44. Duan R, Zhang J, Liu L, Cui W, Regenstein JM. (The functional properties and application of gelatin derived from the skin of channel catfish (*Ictalurus punctatus*)). *Food Chem*, 2018; 239: 464-469.
45. Abbey L, Glover-Amengor M, Atikpo MO, Atter A, Toppe J. (Nutrient content of fish powder from low value fish and fish byproducts). *Food Sci Nutr*, 2017; 5(3):374-379.
46. Shi P, Liu M, Fan F, Yu C, Lu W, Du M. (Characterization of natural hydroxyapatite originated from fish bone and its biocompatibility with osteoblasts). *Mater Sci Eng C*, 2018; 90: 706-712.