

Turning fish waste into a resource: the BYTHOS project contribution to the Mediterranean circular economy



Credit artist: Giulia Crimaldi

 **Interreg**
Italia-Malta
BYTHOS

Fondo Europeo di Sviluppo Regionale
European Regional Development Fund



Introduction

BYTHOS is an EU Interreg V-A Italia-Malta project operating in Sicily and Malta to provide blue biotechnologies and expert skills, and to increase synergic action between researchers and enterprise.

BYTHOS, in co-creation with industry, has developed a range of extraction protocols for bioactive molecules (including marine collagen, chitosan and astaxanthin) and omega 3 & 6 oils. The extraction manuals, with step-by-step photographic support, give precise instructions to lab operators on how to extract key bioactive compounds from various different Mediterranean fish and crustacean residues (available in large quantities from the fisheries sector), from handling of the raw materials through to purification stage.

Blue Economy & Blue Biotechnology

The European Commission defines blue economy as turning aquatic biomass into foods, feed, energy, packaging, and other applications, as reflected in the EU Bioeconomy Strategy. In the European Union, blue economy reached a €750,000,000,000 turnover, employing almost 5,000,000 people (in 2018). Blue biotechnology is recognised as a globally significant economic growth sector, being mostly concentrated in the European Union, North America, China, Japan, and Australia. Marine biotechnology in Europe is still in its early stages, evidenced by a high number of publications (globally, around a third of marine biotechnology publications are European), a low number of patents (globally, 13% patents filed in connection with new marine molecules are European) and a high knowledge fragmentation (most of the 12,500 blue biotechnology enterprises employ ten people or less).

Fish Waste Problem in the Central Mediterranean

A pressing issue in the Central Mediterranean is the disposal of fish waste from the fishing and fish processing industries and the food services sector. On the Island of Lipari, a typical fishery enterprise with a small size processing plant produces an average of 40-50 kg of organic raw fish waste every day, which then has to be shipped to mainland Sicily for disposal at huge expense.

Due to inadequate infrastructure and/or service, 20–80% of marketed fish biomass is discarded or wasted between landing and consumption. Large quantities of fish waste are generated as a result of fish processing by industrial-scale fisheries and aquaculture. The by-product is often treated as waste, despite containing valuable compounds. The leftovers from fish typically include trimmings, skins, heads, frames (bone with attached flesh) and viscera. A portion of the by-product can be processed into fish meal and fish oil, and to extract BAMS that can be used in the pharmaceutical and nutraceutical products.



*Tuna fish head waste from Malta.
Credit: Department of Fisheries & Aquaculture*



Biologically Active Molecules (BAMs)

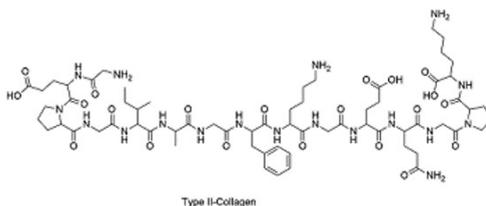
Biotechnologies in Europe have become central to the European Union's strategic priorities. The European Strategy for Life Sciences and Biotechnology has stated that biotechnology "is widely regarded as one of the most promising frontier technologies for the coming decades". Promoting good health is thus an integral part the EU's strategy for smart, inclusive growth within Europe. The European Commission for Public Health promotes innovation, as this can make the healthcare sector more sustainable and find new cures for health conditions. One of its major pilot innovation partnerships aims to "boost and improve the competitiveness of the markets for innovative products and services that respond to the ageing challenge... thus creating new opportunities for businesses". Estimates suggest that the European biotechnology market is worth over €818,000,000,000.

Biologically active molecules (BAMs) can be extracted from several different kinds of chemicals produced naturally by marine species, such as neurotoxins, cardiotoxic peptides, antiviral and antitumor peptides, cardiotoxins and antimicrobial peptides. This broad bioactivity spectrum of marine peptides is of considerable interest to the pharmaceutical, cosmetic and nutraceutical industries for the treatment and/or prevention of various diseases. Despite progress in medicine, infections caused by bacteria, fungi and viruses are still a major threat to public health. Rising numbers of microbial pathogens that have acquired antibiotic-resistance have increased the need for novel and effective antimicrobial compounds. Several bioactive marine peptides have been shown to display a variety of bioactivities such as anti-tumour, antibacterial, anticoagulant, antioxidant, immunoinflammatory effects, and other properties besides. In fact, several marine peptide-derived compounds are currently being assessed in different phases of clinical trials in Europe and the Americas. These include plitidepsin and glembatumumab vedotin, which are used for the treatment of a number of cancers.

Bioactive peptides are also commonly incorporated into nutraceutical products. These products contain marine-derived hydrolysates with opioid-like peptides which act as active ingredients and have a considerable market in the Americas and Europe. For example, a commercially available fermented fish protein concentrate called Seacure[®] was found to modulate the mucosal immune response and induce biological repair-promoting response in the gut. Another two examples are the two products from marine protein hydrolysates, Nutripeptin[®] and Hydro MN Peptide[®], which were found to lower the postprandial blood glucose level and alleviate type II diabetes symptoms. Nutripeptin[®] is extracted from fish muscles. One of the components of Hydro MN Peptide[®] is Peptide N[®], which is a marine protein hydrolysate. Both products are used to prevent body fat deposition and for weight management.

Fish waste is a potential source of BAMs of interest to the pharmaceutical, nutraceutical and cosmetics industries. Pharmaceutical distribution companies are extremely interested in specific types of BAMs (including collagen). The extraction of these BAMs from fish waste is a means to re-use fish waste, leading to a subsequent reduction in the organic waste needing treatment or removal.

Zero waste is subsequently achieved by turning the remaining fish waste into a fish feed product for the local fish-farming sector, stimulating activity in the biomedical technologies sector, the fish farming and fish product industry, the food services industry and the organic waste disposal management industry.



Collagen

Collagen is a protein naturally found in the human body, and is an integral component of connective tissue in skin, bones, muscles, ligaments and tendons. Collagen supports the skin's structure and the strength of bones. Collagen can thus enhance skin strength and elasticity, serving as an anti-wrinkle agent for skin. Collagen is applied in many skin-care products to treat dry/damaged skin by addressing flaking and restoring suppleness. Skin care products have the highest market value amongst all cosmetics in the EU. Collagen is used in face masks, face creams, serums, and several other skin-care products. Collagen is also added to beauty drinks aimed to enhance skin and nail quality. The importance attached to sports and fitness is all the more increasing within Europe, with millions of EU residents participating in sports, and thus so is the demand for fitness supplements. As a result, collagen is increasingly being used in protein supplements that help in muscle, joint and cardiovascular health. Collagen also has an extensive applicative range in the medical and pharmaceutical fields, where it is used in bone reconstruction, plastic surgeries, burn care, orthopaedics, wound care, dentistry and cardiovascular practices. Collagen is also swallowed in pill form, serving as a supplement to aid joint mobility. Collagen is also consumed to help boost the immune system. The European market for collagen is predicted to grow at an annual growth rate of 5.29% until 2024, and this is probably the result of the increase in health awareness, which is encouraging many businesses to market protein supplements. Many companies are manufacturing collagen sourced from fish. In 2018, the collagen market was estimated at €2,933,297,500 and it is projected to grow due to the increasing demand for supplements. The main businesses dealing with collagen are located in Germany, USA, France, Japan, Vietnam, Spain, Italy, Brazil and China.



Lyophilised acid soluble collagen extracted from tuna bone.
Credit: University of Malta

Astaxanthin

Astaxanthin can be extracted from red shrimp shells, which are usually discarded as waste by local red shrimp companies. In Sicily, the red shrimp is commercially the most important crustacean and a considerable amount of waste is produced each year from this industry.

Astaxanthin is a reddish-orange keto-carotenoid and is the source of the vibrant reddish-pink colour seen in shrimps and other organisms. It is the strongest natural antioxidant, and is used to prevent cancer, treat Alzheimer's and Parkinson's diseases, and as a skin protector.

The global astaxanthin market size was estimated at €865,653,150.80 in 2019. More than 95% of the current market deals with synthetically derived astaxanthin, which raises food safety, pollution, and sustainability issues.



Astaxanthin extracted from red shrimps.
Credit: University of Palermo



Chitosan

Chitosan can be extracted from red prawns. Chitosan is a polysaccharide used as a fining agent in the wine-making industry, as a biopesticide in agriculture and, in the medical field, current research is centred around using chitosan in wound dressing to reduce bleeding, in drug delivery and in medical devices. It is also used in water purification and wastewater treatment and in the cosmetics, bioplastics and pharmaceutical industries. It is even being considered as an edible antimicrobial film to improve the shelf-life of perishable foods.



*Chitosan extracted from red prawns.
Credit: University of Palermo*

More Sustainable Aquaculture

A large portion of fish-feed may be sourced from sustainable marine origins. Fish-feed needs to have a high protein content, be easily digestible, and have a balanced composition of essential amino acids, minerals, vitamins and polyunsaturated fatty acids.



*Fishmeal produced by AquaBioTech Group.
Credit: AquaBioTech Group*

The BYTHOS Project

The BYTHOS Project is managed for and by a team of Sicily- and Malta-based researchers, entrepreneurs and experts in biotechnology, business and industry. Through this project and its funds, the BYTHOS team members are investing in and utilising technologies, tools and expert skills, leading to innovation and research in biotechnology for human health and blue growth.

Through the set-up of a joint lab in the two countries, the BYTHOS project has led to the development of BAM-based antibacterial/antimicrobial/antitumor products from fish waste, at zero waste. The biotechnologies used in the BYTHOS project are for the extraction of BAMs and the subsequent production of an eco-innovation fish feed product. The main source of the BAMs for this project is fish waste from the fishery sector and the food services sector. Researchers and business experts are working together to create innovative products tailor-made to meet the needs of enterprise.

This cross-border approach has proven fundamental for a number of reasons. Firstly, Sicily-based experts have transferred the know-how for BAM extraction to Malta. Secondly, Malta has a strong fish farming sector which has the know-how for the development and industrialisation of eco-innovative fish feed, and through BYTHOS this know-how has been transferred to Sicily, whose aquaculture industry requires a supply of fish-feed. The products which BYTHOS is developing are the fruit of collaboration between the two islands. Sicily's strong research experience in the sector of biotechnology for human health and blue growth through the University of Palermo's STEBICEF department has provided Malta with the necessary skills to develop BAM extraction - knowledge transfer for Maltese biotechnologists at the University of Malta ensuring that the skills and competences are transferred to Malta. BYTHOS biotechnology experts have characterised fish waste on a molecular level and have analysed these molecules for potential bioactive properties. The fish waste samples have also been analysed to determine their protein, carbohydrate and fat content (with the fat content being also examined in terms of ω 3-polyunsaturated fatty acids). The protein

components have been separated using chromatography, and the resulting proteins are being analysed to determine possible biological properties, such as antitumor, antibacterial, antimicrobial, and/or antioxidant activity. Based on results of the preliminary screening, the exact amino acid composition of the protein molecules has been determined using mass spectrometry.

The greatest cross-border factor is the complementarity of fish species from the two areas. The researchers working on this project have selected specific BAMS to satisfy the demand by the biomedical technology markets. Experts are also extracting collagen from Maltese fish species. BYTHOS is exploring the creation of a combined product using BAMS from the two areas (for example, a collagen sheet with antibacterial film). Furthermore, there is already a history of trade in the pharmaceuticals sector between the two islands, which BYTHOS is building upon.

An integral part of the BYTHOS Project is stakeholder communication and management strategy, fundamental in order to engage the local community, to provide the basis for valuable R&I cocreation activities, to stimulate innovation in existing products and to promote the design of new products/services, since BYTHOS's primary aim is to increase synergic action between researchers and enterprise. The project results (BAMS, collagen and fish feed, all from fish waste) are all highly-replicable results of interest to any community with a strong fishery sector or coastal food services industry, or communities where aquaculture plays a central role.

One of the major needs identified by the EU is an increased reduction in pollution. BYTHOS is using fish waste from the fishing and food service industries to obtain BAMS and reduce the process to zero waste by turning left-over material into fish-feed product. This process provides greater resource-use efficiency and reduces risks posed to the environment by the waste itself and its subsequent need for disposal.

Future Prospects

Although Sicily has the highest number of fish processing companies on a regional level in Italy, the enterprises are smaller on average and suffer from a substantial technological gap. In Malta, very little fish processing takes place; the fishery sector on the island is dominated by fish farming (including Bluefin tuna penning), and most of the fish feed (pelleted or whole fish) is imported. There is, unquestionably, a huge market potential for sustainable fish feed production to satisfy demand from the tuna farming industry; this would not only tackle the environmental problem of fish waste but also make the industry more profitable through savings from reduced imports.

The BYTHOS 'BAMS from fish waste' biotechnology lab is highly innovative, above all with regards to the combination of biotechnology for human health and blue growth. The long-lasting positive effects of this project will be both socio-economic and environmental, since the processing of any remaining fish waste resources to create eco-innovation fish feed will not only create new job opportunities throughout the sector and extend the value chain, but will also lead to greater rationalisation of the production process, ensuring a more sustainable use of natural resources.



*Fish waste, from which collagen is extracted.
Credit: University of Malta*



Zero-waste in the fisheries sector also means addressing the strategic area of the programme which addresses ‘safeguarding the environment’. More specifically, this will be achieved by:

- i) optimising the use of natural resources;
- ii) reducing the amount of organic waste that an enterprise in the fish or fish product/food service sector needs to dispose of (such a reduction will reduce waste management costs to the enterprise and increase competitiveness);
- iii) reducing organic waste management costs to the local community (an aspect of particular concern to island economies) and reducing the effects on the environment due to waste disposal and due to pollution caused by transport (both Malta and the smaller Sicilian islands transport their waste to other areas at considerable financial cost to the community and cost to the environment in the form of pollution from transport and pollution from disposal);
- iv) reducing the many knock-on effects caused by the need for the Maltese fish-farming industry to import fish feed from abroad to satisfy demand (the fish feed currently used is often highly pollutant to the waters around Malta).

By using the raw waste from the fishing industry to create a biomedical technology high-added value product, BYTHOS is leading to an increased investment in the biotechnology sector, creating a centre of excellence for biotechnology for human health and the blue growth, extending the value chain of fish and fishery products, creating diversification both for local communities and individual business enterprises, ensuring the sustainable reuse of natural resources from the fishing industry, and creating opportunities to employ tertiary-education graduates. BYTHOS is fuelling science and technology knowledge-intensive business services within the field of biotechnology for human health, ensuring that SMEs in the fishing (and other) sectors have access to research infrastructure and the necessary information and training for the adoption of new technologies and skills, bringing results obtained in biotechnology research directly to local enterprises.

With the added value of the BAMs extraction to render the fish processing industry more profitable, and through the creation of specific business models for local enterprises, the BYTHOS project will provide new opportunities for the entire cooperation area. As islands situated in the Mediterranean Sea, both Sicily and Malta have a strong coastal, fishing sector. Sicily has an active fish-processing sector, producing large amounts of fish waste. The lab hopes to engage entrepreneurs from this area to stimulate interest in extending sector activities to include BAMs extraction. Although, the fish processing industry in Malta is very small, there is a large food services sector due to the highly developed tourism industry on the island, and fish farming also plays a prominent role in the local economy. The food services industry is a vital source of fish waste for the further development of the biomedical technology sector in Malta, with the fish-farming industry being an important buyer of zero-waste fish feed product. Demand for the product in Malta is great enough to ensure interest in initial Sicilian production too. A set of guidelines are being produced which will then be available as open source material and easily adopted by other regions or organisations with similar territorial needs. The concept



*Cultured sea bass being fed with sustainable feed.
Credit: Aquabiotech Group.*



of a synergic lab within the domain of biotechnologies for human health and blue growth is an extremely important innovative development for the cooperation area and Europe.

BYTHOS has developed a model of interaction between science and technology communities and local economies, dominated by dependency on one or two key sectors to close the technology gap and introduce 'smart' diversification. The European Commission has even placed this concept of 'synergic interaction between the main actors of a community' within the Innovation Europe Common Strategic Framework.



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INTERREG V-A Italy-Malta Programme
Project part financed by the European Union
European Regional Development Fund (ERDF)
Co-financing rate: 85% EU Funds; 15% National Funds

