Fish - Based Pharmaceuticals and Nutraceuticals and their Applications

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Traditionally fish is considered as the "protein for the poor". It is hailed as the ultimate answer to the problem of protein malnutrition facing the starving millions of the developing nations of the third world. But fisheries development in these countries unfortunately lost focus. Fishing concentration was directed more towards catching exportable species like shrimp for augmenting foreign exchange earnings by export of marine products like shrimp. Low value fishes landed with the shrimp became unacceptable and treated as items that wasted storage space onboard and was even thrown back to the sea. This regrettable wastage of valuable protein has to be prevented, for which technologies have now been developed for making them also lucrative.

With the increased stress and strain in modern life, incidence of cardiovascular problems and carcinogenesis are posing problems to sizeable sections of susceptible urban population. There is an increased awareness\among informed people about the nutritional superiority of fish compared to other protein foods and its beneficial pharmaceutical effects. As a result, low value fishes are fast becoming raw material for making high value nutritional supplements of beneficial pharamaceutical properties. These 'nutraceuticals' from fishery sources are attracting world-wide attention. In the nutrition conscious west, slogans like 'seafood is heart food' and 'you are what you eat' are becoming popular and there is a shift in the protein consumption pattern from egg and meat to fish. Technologies for the production of a variety of nutraceutical products of widely divergent properties and applications, from different low value fishes have been developed. This is fast becoming a thrust area of research in fisheries all over the world. The Central Institute of Fisheries Technology, Cochin has done some pioneering work in this area which is briefly summarised here.

Polyunsaturated fatty acids from fish oil

Fish oils are known to contain large proportions of long chain polyunsaturated fatty acids (PUFA) which give special properties to fish oils. They get easily oxidized which may cause problems of storage. But nutritionally, they are highly beneficial to the consumer.

Generally it is believed that dietary animal protein and fatty food give problems to patients suffering from cardio vascular disorders and they are advised to avoid these foods. But fish is an exception. Dietary fish is beneficial to these patients. The polyunsaturated fatty acids in fish oils are the main ingredients which are responsible for this beneficial effect of dietary fish. Cardio-vascular problems are mostly of two types: (1) Due to deposition of cholesterol on the inner walls of coronary arteries, and (2) Thrombotic problems leading to blood clots because of increased platelet aggregation. The polyunsaturated fatty acids of fish oils are

good remedies for solving both these problems. They are known to reduce serum cholesterol levels and also to prevent excessive platelet aggregation. The capacity of polyunsatuarated fatty acids (especially of the Omega-3 group in which fish oils are rich) to reduce serum cholesterol levels is well known though the exact mechanisms is still a subject of discussions. Preferential esterification and removal of cholesterols by these acids, more effective redistribution of cholesterol between serum and tissues, increased bile flow, are all suggested mechanisms. Their antithrombotic properties were noticed by studies on Greenland Eskimos who take mostly fish based diets and are known to have unusually long bleeding time. Populations in different parts of the world who take more of dietary fish are known to have less of cardio-vascular problems. The Omega-3 polyunsatuarated fatty acids are the precursors of prostaglandins, prostacyclins and thromboxanes which play a vital role in determining the rate of platelet aggregation. While prostacyclines prevent platelet aggregation, thromboxanes increase aggregation. Prostacyline from Omega-3 acids prevent platelet aggregation, but thromboxanes formed from these do not increase platelet aggregation. Thus more Omega-3 acids in diet tilt the balance in favour of preventing platelet aggregation and thrombosis. Omega-3 fatty acids are known to play vital roles in the development of brain cells in children also. In the pure unoxidised state they are known to have anti-carcinogenic properties. However in highly oxidized form peroxides formed can be harmful also.

Attempts have been made in different parts of the world to concentrate these Omega-3 polyunsaturated fatty acids in fish oil, so that they can be encapsulated and marketed as nutritional supplements conferring beneficial effects on patients suffering from cardio-vascular problems. But the technologies involved were costly and complicated involving molecular distillation and super critical fluid carbon dioxide.

CIFT has been trying to develop a simpler and cheaper method for concentrating these biologically active Omega-3 polyunsaturated fatty acids. As a result, it has now become possible to develop a very simple and inexpensive technology for this purpose which ;.. concentrates the active fatty acids to an "extent of 70-80%. Dietary fish protein is also known to exert a cholesterol lowering influence. The amino acids composition of a protein holds the key to "its properties in this regard. The lysine: arginine ratio and alanine: proline ratio in the protein have both been suggested as the ciritical factors. Fish proteins are any way found to be beneficial in this regard.

Fish liver oils

Liver oils of fish, particularly of shark and cod are good sources of natural vitamins A and D though their commercial importance dwindled with the advent of cheaper synthetic vitamin A. They, however, still command poteintial use in many fields. Of the several species of sharks available in Indian waters, only a few are commercially important. On the west coast shark fishery is constituted by Scoliodon, Carcharhinus, Sphyrna and Galeocerdo and on east coast, Galeocerdo, Carcharhinus and Sphyrna (Jhingran, 1982). They yield liver oil of high vitamin content with potency varying from 1000 to 3,53,000

International Units per gram of oil. However, liver oil of some deep-sea sharks is now valued for their high squalene content. Squalene is a hydrocarbon with diverse applications in different fields (Rudolf & Ahmed, 1978). Gopakumar and Thankappan (1986) have enumerated the source, uses and industrial applications of squalene. The recently announced ban on shark fishery is adversely affecting the variety of useful products that are prepared from shark.

Clinical significance of squalene

The triterpene squalene is a highly unsaturated alphatic hydrocarbon (035 HSO) which is widely distributed in nature. It is found in small quantities in many vegetable oils and in larger amounts in certain fish oils. Interest in its medical and cosmeto-dermatological significance increased when squalene was found in human sebaceous secretions, as a precursor of cholesterol and when its possible anti-carcinogenic effect was described. It is the principal hydrocarbon of human surface lipids amounting to 11 percent of total surface fat. It is also seen that squalene plays an important role in embryological development. Besides, certain carcinogenic chemicals are inactivated when exposed to squalene over a period of time. Squalene is not very susceptible to peroxidation and appear to function as a quencher of singlet oxygen, protecting human skin surface from lipid peroxidation due to exposure to UV and other sources of ionizing radiation. It also acts as an immuno protector and exhibits curative effect on colon cancer. Squalene has been found useful in the treatment of dietary hypercholesterolemia also.

Insulin from fish

Possibility of preparing insulin from pancreas of fishes like tuna, cod etc., and of whales was reported a few decade ago. According to Tanikawa (1971) there are a few factories in Japan producing insulin from fish and whales. The percentage of insulin in pancreas of tuna is more than that in cattle. Tuna fishing in India is set for a major expansion and when this happens large quantities of them are expected to be landed. Attempts are being made in India also to obtain good quality insulin from fish and some encouraging results have been obtained. The technology for the production of insulin will help to utilize the waste from fish. But biotechnology has brought in humilins using *E.coli*, which has reduced the interest in fish insulin.

Bile salts from fish

It is known that bile extracted from fish galls contains cholic acid and deoxycholic acid combined with taurine and sodium. Collection of galls from fish is possible although there are some difficulties. Galls can be removed intact only from very fresh fish as there are chances of postmortem shrinkage as well as breaking of the galls during removal. Galls of freshwater fishes like catla, rohu and mrigal are bigger in size compared to those of marine fishes like sardine, mackerel etc. Attempts have been made by Mathew et al., (1986) for isolation of galls and identification of bile salts from freshwater fish. They have reported that the major constituent of bile of rohu and mrigal is taurine derivative of lithocholic acid.

Fish galls have good export market particularly to Japan. The method of isolation and drying of the galls from fish is also available.

Products from prawn waste

Chitin (a polymer of N-acetyle glucosamine) is the most important organic constituent of the skeletal material of invertebrates and its only economic source at present is the body peelings of prawn, lobster, squilla, crab etc. The prawn head and shell waste constitutes roughly 60% of weight of whole prawn. Apart from chitin, it also contains a good amount of protein.

The technology for the production of protein extract, chitin, chitosan (Anon, 1980), glucosamine and cholesterol from prawn waste has been worked out and successfully commercialised by Central Institute of Fisheries Technology, Cochin; Central Food Technological Research Institute, Mysore and National Chemical Laboratory, Pune also have done some work in this area (Ingle et al., 1973; Anon, 1981). Studies on diverse applications of chitin and chitosan have been reported (Madhavan, 1992).

CIFT has developed a process for preparation of chitin from prawn shell waste. Chitin can be incorporated in the diet for broiler chicks. The diet with chitin was found to improve the feed efficiency, resulting in about 10-12% weight gain in the birds compared to a chitin free diet. Use of chitin for the production of glucosamine hydrochloride which finds application in antibiotics and baby food formulations is already known. Chitin is also a raw material for the preparation of chitosan. Chitosan is a valuable chemical substance finding use in several fields. Chitosan can be used as sizing material for textiles. It can be used as a water/wine clarifying agent and also in the preparation of cosmetics, pharmaceuticals etc. Recent studies have shown the effectiveness of chitosan in the form of micro-fined powder, impregnated gauze and film for treatment of chronic wounds and external ulcers and to arrest/minimise bleeding in neurosurgery. It is used for slow release of drugs also. Chitosan film can also be used as artificial skin and kidney membrane, and as contact lens. Incorporation of chitosan during mixing and homogenisation of shrimp and fish feeds, for pelletisation and granulation of the feed imparts very good water stability to the feed without the use of sophisticated machinery. Prawn shell wastes which were an environmental problem earlier have now become a valuable industrial raw material.

Collagens

Collagens from skin and airbladder of fish find use in dentistry and as artificial skin. Chitosan impregnated collagen films are effective in preventing blood loss, fluid loss and also infection when used as artificial skin. They are absorbable and do not produce any allergic tissue reactions.

Fish guts

Fish guts have been found to yield fine grade absorbable sutures which can be used for microsurgeries, ophthalmic surgery etc.

Fish hydrolysate and peptone

Fish hydrolysate can be produced from fish protein by a process employing proteolytic enzymes of vegetable or microbial origin. By controlling the conditions of the process, end products of desired properties can be obtained.

Food formulation for human consumption incorporating fish hydrolysate has been described by Prabhu et al., (1975) and Lekshmy et al , (1985). The commercial interest in hydrolysates is centered on its use in milk replacers. By using fish protein to replace the milk protein in animal feeds, it is possible to produce a cheaper feed for young calves, lambs and baby pigs (Windsor & Barlow, 1981). The bitter taste of fish hydrolysate limits its use for human consumption. Methods for the preparation of bitterness free hydrolysates have been reported by Lalasidis & Sjoberg (1978) and Lalasides et al., (1978).

Shark cartilage

The skeleton of shark is made of cartilaginous bones, which is about 10-15% of the body weight. Until recently, only very small quantity of these bones was made use of, that too from the small shark, for making buttons and necklaces. This cartilage is rich in chondroitin sulphate which has got application in medicine for treatment of atherosclerosis, blood vessel thrombosis and also to prevent infections. Now there is very good demand from Europe, USA and Australia for processed shark bones.

The collected head and vertebral column of the shark are to be processed to a presentable and stable form before export. A procedure has been developed for the processing of the cartilage into a clean, dry, white, attractive material without any characteristic smell. The products are well accepted by the overseas buyers. The ban on shark fisheries is going to affect all these products, as mentioned above.

Shark fin rays

Shark fin rays are valuable products of export from India. Formerly, only shark fins were being exported. But now, fin rays are extracted and exported. CIFT has developed a technique for extracting rays from shark fins.

The dried fins are soaked in dilute acetic acid for sufficient time to get the muscle and skin softened. The skin is then scraped off and the fins further treated with the dilute acetic acid when separation of the rays in clusters becomes easy. The rays are then dried and packed in polyethylene bags.

The rays are utilised in the preparation of soup in many foreign countries. There is good internal demand also for shark fin rays especially in major star hotels.

Tuna eyes

Tuna eyes are an item of commerce. Its demand is attributed particularly to its content of polyunsaturated fatty acids like decosahexaenoic acid. This fatty acid is valued for its medicinal properties in combating atherosclerotic and thrombotic problems of chronic heart patients and also for its reported anti-carcinogenic and brain developing properties. Extraction and preservation of eyes of tuna and its marketing have good prospects.

Fish calcium

Calcium powder processed from the backbone of tuna can be used to combat calcium deficiency in children, which can lead to bone failure and spine curvature. The method of production of calcium involves mainly removing the gelatin from the crushed bones and pulverising the remaining portion. A process recommended for processing calcium powder from the backbone of skipjac tuna involves the following steps. The bone frame is crushed and washed i clean water a number of times. A 10%, solution of calcium carbonate is added to the residue and is left for an hour. After draining the solution, washing and treatment with calcium carbonate is repeated a number of times. Finally, bone residue is washed dried and pulverised to the required mesh size.

Fish ensilage

Fish ensilage is a liquid product made from whole fish or parts of fish by the acids or enzymes. It is a stable liquid with a malty odour containing all the water present in the original material. The process of preparation of ensilage is simple and requires single capital investment particularly when non-fatty fishes are used. The use of fatty fish needs oil separating equipment.

Ensiling is achieved either by treating the fish directly with a mineral acid (sulphuric) or organic acid (formic or propionic) or lactic acid produced in situ by fermentation. The fish is partially digested and preserved by the acidity (Arul James, 1966). Amino acids and vitamins are not destroyed in the process. The final pH should be around 4.5. As fish ensilage is highly nutritious it can be used to supplement poultry and cattle feeds.

Extensive studies on the production, nutritional evaluation, economics, storage and utilization of fish ensilage have been made in IPFC region (Disney, 1979; Disney & James, 1980). Durairaj et al., (1985) also have reported production of ensilage using fermentation process and its applications. The simplicity of the process and low investment indicate the possibility of adopting the technology for the utilization of scattered landings of fish.

Beche-de-mer

Beche-de-mer is the commercial name for cured Holothurians commonly known as sea cucumbers. This is a high unit value dry fish item almost entirely exported. Beche-de-de-mer is known to have a unique place in Chinese diet probably due to its reputation as an aphrodisiac and for its therapeutic value in the treatment of high blood pressure. An improved technique has been evolved for processing beche-de-mer. The process involves evisceration of fresh sea cucumbers, cooking in boiling water, drying and packing in gunny bags.

Ambergris: Ambergris is a product of marine origin. It is valued fabulously and is being used in pharmaceutical field and in the perfume industry. It is widely used in the orient as an aphrodisiac. Ambergris has a characteristic musk odour which finds application in blending of a large number of exotic perfumes. It is often seen in tropical and sub-tropical seashores of countries like Australia, New Zealand, India and Bahamas, either as large number of fragments or as a whole mass. Ambergris is considered as a morbid secretion from the intestinal tract of male sperm whale (*Pyster catadan*). A large mass as big as 412 kg in weight has been recorded in the past. Eighty percent of the ambergris is composed of cholesterol, and the rest of some other constituents. The current value of ambergris is approximately Rs. 50,000/- kg.

Fish protein concentrate

Fish protein concentrate (FPC) is a shelf-stable product prepared out of lean fish of less commercial value. It is meant for human consumption and is highly protein enriched. Attempts to prepare fish protein concentrates have been carried out since several decades. The work done on these lines during the last thirty years or so has brought about products of desirable characteristics. The Food and Agriculture Organisation (FAO) of the United Nations has classified FPC into three types based on the quality. They are:

Type A - a virtually odourless and tasteless powder having a maximum total fat content of 0.75% and protein content 60 - 88%.

Type B - a powder having no specific limits as to odour and flavour, but definitely having a fishy flavour and a maximum fat content of 3% and protein content of 70-75%.

Type C - normal fish meal produced ender satisfactorily hygienic conditions.

Fish protein concentrate is generally recommended for protein fortification of cereal foods. The FPC process has several inherent disadvantages including high cost of production and possible presence of solvent residues in the product. These have been overcome by recent development of a simple technique of production of spray dried protein concentrate, having better functional properties (Muralidhran, V. Gopakumar, K. (1998). This functional protein is prepared from deodourised, de-fatted (by water leaching) and structured protein gels of low cost fishes such as Atlantic mackerel, Atlantic herring etc. Being low in

cholesterol and high in functional and nutritional characteristics, this protein concentrate is being increasingly used as protein binder and protein extender in several food products.

Fishmeal

Fishmeal is a highly concentrated nutritious feed supplement consisting of high quality protein, minerals, vitamins of B group and other vitamins and unknown growth factors. It is produced by cooking, pressing, drying and grinding the skeletal remains along with the adhering proteinaceous tissues of fish from filleting or canning operations or by processing whole miscellaneous fish mainly caught along with prawns, which include jew fish, sole, silver bellies, ribbon fish and the like.

The composition of fishmeal differs considerably due to the variations in the raw materials used or the processing methods and conditions employed. Fishmeal is rich in all essential amino acids, B group vitamins and minerals particularly phosphorous and calcium and therefore finds an important place as a feed supplement for poultry and cattle and in fish and crustacean feeds.

Fish can be reduced to fishmeal by two general processes namely dry-rendering and wet-rendering. Dry-rendering or dry-reduction process is suitable only for lean or non-oil fish such as silver bellies, jew fish, sciaenids, ribbon fish, sole, anchoviella, carcasses of shark etc., fish offal and filleting waste. Wet-rendering or wet reduction process is normally applied to fatty fish or offal where simultaneous production of fishmeal and fish body oil is envisaged.

Bacteriological peptone

Bacteriological peptone can be prepared from fish by controlled hydrolysis of fish. lyer et al., (1978) used fish peptone in the preparation of media for culturing terrestrial as well as marine bacteria and they have reported the results comparable to those obtained with other standard brand peptone.

Squid based products

Squid meal prepared out of squid offal is reported to have efficient growth promoting effect for farmed fish. An average 30-40% growth improvement in several species of shrimp has been reported with the addition of squid protein fraction (SPF). The ink sac in the mantle cavity contains dark coloured sepiomelanin, which had been used as ink for writing in ancient times. In Japan it has also been used as a preservative and flavour enhancer in the preparation of salted squid. Recent scientific studies have revealed the preservative and antioxidant values of squid ink. A protein extracted from squid in very low concentration has been shown to inhibit the growth of *Staphylococcus aureus*. Oxidised squid oil is reported to be anti-bacterial in action. Application of squid ink in canned squid preparations has been reported world-wide. In recent times the inclusion of squid ink in bread making has gained popularity in Japan. Squid ink is also reported to have anti-cancer properties.

Recent advances in biotechnology have shown greater scope for the production of innovative neutraceutical preparation. Synthesis of newer enzymes with higher activities and selection of highly efficient strains of microorganisms for fermentations and biosynthesis of nutritive supplements are getting greater attention of food technologists (Venugopal, V., Alur, M.D. & Nerkar, D.P. (1989) Immoblised microorganisms and enzymes have various applications in foods and they have been recognized as safe. These organisms include *Sachromyces cerevisiae, Aspergillus oryzae, A. niger, Rhizopus oryzae, Bacillus subtilis, B. coagulans and Streptomyces olivacius* (Reichett, J.R. Baking (1983) Genetic engineering techniques have been found to increase the efficiency of the cells in secreting enzymes. Solid state APRI fermentation using such organisms can influence deodourisation of fish mince, modification of functional properties and improvement of nutritional value.

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