
MARINE BIOMOLECULES FOR NUTRACEUTICAL AND COSMECEUTICAL INDUSTRIES

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Marine biomolecules have the potential to provide significant therapeutic and preventive benefits against a wide range of common lifestyle disorders. As the public becomes more aware of the health benefits associated with fish and seafood in general, the groundwork has been laid for the development of traditional nutraceutical products. There are currently only a few well-known marine-derived nutraceutical products on the market. Some of the most well-known nutraceutical products include fish oil (mainly omega-3 PUA), algal oils, shark liver oils, squalens, chondroitin salts, and collagen, gelatine, collagen peptides, chitins, and related compounds. In recent years, marine-derived cosmetics have become increasingly popular in the cosmetics industry due to the numerous benefits they offer to human skin health and beauty. These cosmetics are known for their nourishing and rejuvenating properties, and their ability to provide a variety of health benefits

Chitins

In India, the shrimp processing industry produces over 2 lakh tones per year of head and shells waste that can be economically transformed into chitins and their derivatives. Chitins are the second most abundant polymer after cellulose. Chitins are linear polymers of N-acetyl-D glucose. Chitins can be hydrolysis converted into glucose hydrochloride from chitins. Currently, glucose hydrochloride is marketed as food supplements and glucosamine sulfate as food supplements. Chitins and its derivatives have various applications such as: Germination of seeds; Enhanced protection against pathogens in plants; Inhibition of chitinases and protenases in soil; Antimicrobial action; Antiviral activity; Interactions with living tissues; Skin and bone replacement; Oral delivery as wound healing etc.

Chitin is mainly used in cosmetic formulations as abrasive and as a bulking agent. However, it could also be used as a cosmetic excipient, as it has good surface-active and film-forming properties. Another promising derivative is oligosaccharide, which is soluble in an aqueous medium at physiological pH, and has many bioactive properties that can be used in cosmetic and Cosmeceutical products. Chitosan, and its derivatives, can also be used as UV filters for various cosmetic and skincare products. UV radiation damages the skin by producing reactive oxygen species and causing inflammation. However, antioxidants and anti-inflammation have

been found in chitosans, which may help to reduce the damage caused by UV radiations to the skin. In addition, it can absorb UV rays below 400nm in range.

Fish collagen/gelatin/collagen peptides

Collagen is the main structural protein in connective tissue. The collagen extracted from fish can be used in cosmetic products, foodstuffs, biomedical applications, etc. CIFT developed the method to prepare absorbable surgical suture from fish gut. The hydrolysis form of collagen is called gelatin. Gelatin is used in the development of bio-degradable packaging, foodstuffs and pharmaceuticals. Since both collagen and gelatin are very high molecular weight proteins (about 300 kDa), a large portion of them is not available to the human body for biological function. In recent years, there has been a lot of focus on small molecular weight peptide development from the native collagen. This can be done by hydrolysis where the native collagen / gelatin molecules are broken down to small fragments (less than 5 kDa). Collagen peptides can be incorporated in a variety of food products such as protein bars, cereal bar, protein drink, smoothie, yogurt, cold desserts, soup, cured meats, etc. Collagen / gelatin peptides are gaining more and more attention as they exhibit various biological activities like anti-oxidants, antioxidants, anti-hypersensitivity, proliferative, anti-diabetes, anti-anti-proliferative, anticoagulant, calcium-binding, anti-obesity, anti-diabetic activities and postponement of age-related diseases.

Collagen is a type of connective tissue protein that is distributed throughout the body. It plays an essential role in the structure of the skin, skeletal system and blood vessels. As we get older, our body's production of collagen diminishes. This can lead to various health problems such as osteoporosis, osteoarthritis, etc. In addition, the appearance of the body can be seriously affected. Some of the most common issues related to the appearance of a person's body are the appearance of wrinkles and loss of elasticity; hyperpigmentation; skin sagging; loss of gloss; etc. In recent years, researchers have clinically demonstrated that oral ingestion and topical application of collagen hydrolysed helps to reduce the signs of aging and reverse the damage to the skin. Types of Collagen Types of collagen used in cosmetic industry are Type I and III. Type I collagen provides tensile strength, structure and elasticity to the skin and bone whereas Type III collagen provides elasticity and resiliency to the skin, muscle and blood vessels. Types of collagen used in cosmetics are derived directly from bovine, chickens, fish and molluscs. Alternatively, collagen synthesis in the body can be increased by including more collagen-boosting nutrients in the diet such as proline, lysine, L-arginine, vitamin C, vitamin A, anthocyanin, manganese, copper, zinc etc.

Fish calcium

Calcium is abundant in marine ecosystems, mainly in calcium carbonate, calcium phosphate, and other skeletal elements of the teleost, exoskeleton, or coral deposits. A large proportion of total fish catches are discarded as processing residues each year, including

trimmings/fins/frames/heads/skin/viscera. The bone fraction (15-20% body weight) of fish contains high levels of calcium and calcium phosphate (2% dry weight). Fatty fish generally have lower ash content compared to lean fish species. Filleting wastes from tuna and other larger fish are very rich sources of calcium when it comes to calcium. Bone structure also differs between species, as a large proportion of the teleosts (teleoskeletal bones) are acellular, meaning they have no enclosed osteocytes. Cellular bones are limited to a few groups of fish, such as Salmonidae. Acellular fish bones have a higher surface-to-volume ratio, so they are likely to have higher calcium availability than cellular fish bones. Ash content is highest for lean fish species that have a cell-like structure. Apart from that exoskeleton of mollusks and coral deposits are excellent source of calcium. However, the calcium form these deposits are mainly in the form of calcium carbonate.

Hydroxyapatite (HAp)

Hap is the main mineral of bone and teeth. It has the chemical formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. The composition of Hap derived from biological sources is different from synthetic Hap. The lattice has several ion substitutions, including CO_3 (CO_3), F (F^-), Mg (Mg^{2+}) and Na (Na^+). It is a calcium phosphate group member with a 1.67 (Ca/P ratio) stoichiometric value. Hap is one of very few materials that are bioactive and support bone growth and osteointegration in mammalian bone and mammalian hard tissues when used for orthopedic and dental applications. Fish bones and scales are rich sources of Hap. The content of Hap in fish skeleton can range from 40% to 60%. Hap extraction from bone is usually done at very high heat and the higher the temperature, the stronger the HAp structure is. The high heat also burns away organic molecules like collagen protein. About 65% to 70% of fish bone consists of inorganic Hap. Most of these inorganic Hap is composed of calcium and phosphorous.

Squalene:

Squalene is an unsaturated hydrocarbon. It is found in liver oil of deep sea sharks such as Centrophorus, Squalidae, and other species. The liver oil from these species contains 90% of squalene which can be isolated, purified, and used as dietary supplements. Squalene belongs to a group of antioxidant molecules called Isoprenoids. It has been found to be a good chemo preventive agent in mice bearing lung cancer. Squalene helps in reviving damaged body cells and helps in the revival of cell generation. Its main function is to protect cells from oxidative reactions. It helps in cleaning, purifying, and detoxifying the blood from toxins. It helps in the purification of gastrointestinal tract and kidneys. It also helps in the improvement of bowel movements and urination. Squalene also helps in the regulation of the female menstrual cycle. It can also improve irregular and abnormal cycles.

Squalene is the main component of skin surface Polyunsaturated lipids. It has several advantages for the skin, such as antioxidant, emollient, hydration, and skin condition. Squalene is a strong oxidizing agent. It is stable against attacks from peroxide radicals. It protects

human skin from oxidative damage from UV light and from other sources. It suppresses superoxide anion production, which may reduce skin irritation. Squalenine has a high rate constant for the quenching of singlet oxygen compared to other lipids on human skin surface. It also has a stable rate constant against attacks from peroxide radicals. When adequate levels of Squalenine are present, Lipid Peroxidation Chain Reaction (LPR) is less likely to occur. Supplementation with Squalenine can reduce erythema in the skin. It absorbs a large amount of erythema from the skin. It helps to prevent skin diseases such as acne, comedones, and wrinkles. As an emollient, it is quickly absorbed into the skin, restoring suppleness and flexibility without leaving an oily residue. Squalene has also been found to increase skin hydration by preventing water loss through occlusion. Squalene supplementation was found to be effective in reversing the detergent induced transepidermal water loss and increased riboflavin penetration in both rat and human skin

Taurine

Taurine (2-Amino-Sulfonic Acid) is an amino acid that contains sulfur and is non-protein. Taurine plays a vital role in neurotransmission and cell volume regulation. It also stabilizes cell membranes and facilitates the transport of ions like sodium, potassium, potassium and magnesium ions in and out of cells. Taurine also plays an important role in detoxifying xenobiotics. It is also essential for the efficient absorption of fat and for the solubilisation of fats. Taurine can be synthesised from methionine or cysteine with Vit B6. Taurine has important functions in the visual pathway, brain and nervous system as well as cardiac function and cholesterol metabolism. Taurine deficiency has been linked to cardiomyopathy (heart disease), retinal (retinal) and tapetum (tapetum) degeneration, immune (nervous system) dysfunction, muscle atrophy (muscle weakness), developmental abnormalities, premature aging and impaired reproduction. However, taurine's importance in biological systems has only recently been recognized and is now considered a 'conditionally essential' amino acid.

Taurine protects against the tissue damage caused by oxidative stress caused by mercury induced toxicity. Taurine plays an important role in the development of the fetus and the infant. Studies have shown that increased intake of taurine reduces the risk of hypertension. Deficiencies of taurine do not cause immediate health problems, but long-term lack of taurine can affect a wide range of metabolic pathways. Taurine is a key component of bile and plays a vital role in maintaining normal gastrointestinal development and function. Taurine can be found in higher concentrations in almost all animal products. Meat, breast milk and dairy products, fish, and shell fish contain higher concentrations of taurine than fin fish. According to Zhao et al., (1998) crustaceans and mollusks have the highest taurine content, ranging from 300 to 800 mg per 100 g of meat. Red algae is considered a good edible source for taurine. It is proposed that taurine may play a beneficial role in the prevention of Parkinson's and

Huntington's disease by reducing oxidative stress and promoting apoptosis. Eventhough, the cellular and biochemical mechanisms mediating the actions of taurine are not fully revealed, mounting evidences suggest that taurine might be a key functional ingredient for use as a nutritional supplement to protect against oxidative stress, neurodegenerative diseases, atherosclerosis and hypertension.

Glucosaminoglycans

Glycosaminoglycan (GAG) is a linear polysaccharide with repeating disaccharide sequences. Each GAG contains an amino sugar (usually N-acetyl-glucosamine) and an uronic acid (usually glucuronic acid, iduronic acid, or galactose). The major members of the GAG family are: Hyaluronic Acid (HA), Keratin Sulfate (KS), Chondroitine (CS), Dermatan Sulfate (DS), Heparin and Heparin Sulfate (HS). Hyaluronic acid has a high molecular weight (typically $2 \cdot 10^7$ Da) and a chain length of 2-25 μm . Other GAGs have a short chain length (typically 15-20 kDa). Hyaluronan does not have sulfate groups and does not covalently bind to protein. The other GAGs have sulfates at different positions and are covalently bound to a protein core. Dermatan sulfate differs from chondroitine sulfate in that it contains iduronic acid and keratan sulfates. GAGs are primarily considered as the components of various structural and connective tissues. Apart from the structural role, GAGs have been found to be associated with the regulation of a number of proteins, including chemokines, cytokines, defensins, growth factors, enzymes, proteins of the complement system and adhesion molecules. Apart from that, a few members like heparin possess anticoagulant, and anti-inflammatory properties. Dermatan sulfate (chondroitin sulfate B), also has a range of biological properties, although it has not yet been considered for therapeutic purposes. Marine heparin extracted from shrimp and sea squirt has proven anti-inflammatory properties.

Pigments

Astaxanthin, fucoxanthin, melanin etc. from different fish resources are found to have a variety of bioactive properties. The filleting discards of salmonids and the shell wastes of crustaceans contain significant amounts of carotenoid pigments such as astaxanthin and canthaxanthin. The protective role of these pigments against the oxidative alteration of LDL cholesterol can be studied by incorporating them into health drinks. Carotenoids are one of the most sought after natural food colours in the market. Cephalopode ink is another underutilized reservoir of a spectrum of bioactive substances with curative and curative properties. It is a complex combination of melanin, black pigment, glycosaminoglycan, protein, lipids and minerals. It has been shown to have anti radiation action, antitumour action, immune modulatory action, anti coagulant action, prothrombotic action, anti-cancer action, anti-hypertensive action, anti IDA etc.

Melanin

Cephalopods (squid, octopus, etc.) are an important resource of the world's oceans and their economic value is increasing day by day. Cephalopods are an important part of the marine products and are considered a major delicacy for export markets in recent years. While a few products are made (fillets, tube, rings etc.) of cuttlefish, octopus, a large number including the ink sac are disposed of as waste. It is interesting to note that cephalopode ink was found to be the most useful source for the commercially relevant pigment melanin. In essence, squid ink is a mixture of melanin and proteins, as well as lipids and carbohydrates, as well as various minerals. Melanin is the predominant component of the ink and is composed of ~1 g melanin and Protein-polysaccharide complex. Melanin accounts for ~15% of total wet weight of the ink with other proteins.

The basic structure of melanin comprises of covalently linked indole structure (Takaya and others 1994). Melanin performs a number of biological functions in the body, the main function being to protect the organism from harmful agents such as ultraviolet (UV) radiation; melanin is capable of dissipating over 99% of absorbed UV light. Besides, in the biological system, melanin plays a vital role in providing mechanical strength and protecting proteins from degradation. Numerous reports published in last thirty years reveal the therapeutic, prophylactic and curative value of cephalopod ink. The anti-ulcerogenic properties and anti-inflammatory activity of squid melanoprotein against paw edema was demonstrated in 80's by Mimura et al. through a series of rat model studies. Later on, several researchers confirmed the effect of squid melanin on both phenylbutazone induced ulceration in gastric mucosa and secretion of gastric juice in rats. Apart from that, melanin has been reported to have radio-protective activity, antitumor activity, immunomodulatory activity, procoagulant function and so on. Natural melanin has been reported to have defense activity, protection function and metal chelating ability. It could participate in physiological and pathological activities in human body and even in the treatment of Acquired Immune Deficiency Syndrome (AIDS). A new generation photo-thermal dopamine-melanin colloidal nanospheres was developed by Liu et al. (2012) which could efficiently damage tumour cells at low power density and short duration, without damaging healthy tissues. Melanin also functions as photoprotective and chemoprotective pigment, protecting the body from damaging radiations, as observed at an effective dose of 50 mg/kg body weight in mice model. Similarly, oral administration of melanin for protection against radiation was reported by Dadachova et al (2016). The protective activity of melanin is primarily attributed to the inhibition of radiation-induced hematopoietic damages. Several other physiological studies conducted on squid ink also revealed significant effects on granulopoiesis of hemopoiesis impaired mice induced by ^{60}Co γ irradiating or cyclophosphamide, but has no effect on erythropoiesis. Melanin has been widely and conventionally used as an antioxidant and natural colorant in food formulation. The most interesting thing is that melanin can be used as food additives to prevent the rancidity caused

by the presence of bacteria by quenching the bacterial quorum sensing. Squid melanin was reported to have hemopoietic function in Iron Deficiency Anaemic rats, which might be exploited as a safe, efficient new iron tonic. Deficiency of melanin is associated with disorders such as vitiligo and oculocutaneous albinism. Interestingly, melanin is thought to play a protective role against the age-associated and noise-induced hearing loss. Recently, the anti-ageing property of melanin was demonstrated in mice model, suggesting its use in neutracosmetic formulations. Eventhough melanin is a part of normal human diet, research on dietary intake of melanin is not much explored.

Melanin as such or melanin coated pigments can be utilised in various skincare products, such as lotions, soaps, creams, as well as in make-up products such like eye-shadows, eyeliners, foundations and lipsticks. Melanin is naturally present in hair and offers protection against damage caused by UV radiation and other environmental stressors. Incorporating melanin in haircare products, such as rinses, shampoos and hair dyes, can further improve the overall appearance of hair (Honda et al., 1995). When added to shampoo, melanin can help to strengthen and protect the hair, improve its overall appearance, and reduce damage caused by styling tools and environmental factors. In addition, melanin's antioxidant properties can also protect hair from oxidative damage, promoting healthy hair growth and reducing hair breakage. Since melanin is mostly found in the cortical matrix, its natural protection is mainly limited to matrix layer of hair. However, the cuticle, the outer layer of hair that is exposed to various physical and chemical factors including UV radiation, is responsible for the aesthetic appearance of hair. Exposure to UV radiation has the greatest impact on the endocuticle and the cell membrane complex (Richena & Rezende, 2016). This can cause photodamage, causing breakage, cuticle deformation and exfoliation, ultimately leading to tweaker hair shafts (Bloch et al., 2019). Furthermore, prolonged exposure to sunlight can convert eumelanin to oxymelanin (Draelos, 2006), which fades the natural colour and glossiness of hair. (Binsi et al., 2022)conducted a study to evaluate the photoprotective effects of cuttlefish melanin on human hair. The researchers coated the cuticle surface of hair fibers with melanin and found that UV irradiation caused much greater damage to uncoated hair fibers than to melanin-coated ones. Based on these findings, the study suggests that cuttlefish melanin could be an effective photoprotective agent in hair-care products. There are various synthetic hair-care products available commercially that claim to protect hair from photoaging. The UV filters can be organic or inorganic; the organic filters such as Para-Aminobenzoic acid (PABA) absorb UV radiation, while inorganic filters such as titanium dioxide scatter and reflect UV rays. While these synthetic UV filters are effective, they can have serious adverse effects like photo-allergenicity and gene toxicity (Gilbert et al., 2013).

Astaxanthin

Astaxanthins are carotenoids that are naturally found in shrimp, salmon, and algae. These carotenoids are known for their powerful antioxidant properties and are often used as an ingredient in cosmetics. Astaxanthins have different chemical compositions depending on their source. In marine environments, microalgae is the primary source. The most common types of microalgae used to produce astaxanthins include *H. placulatus*, *Chloraplum* ssp, and *Chiplococccum* ssp. *H. placulatus* is considered to be the most promising natural source for the production of acanthin. Acanthin produced from *H. placulatus* is a di-keton composed of 2 hydroxyl group and 2 ketone group, esterified by fatty acids (Palmitic Acid, Oleic Acid, Linoleic Acid, etc). The yield of acanthin from *h. placulatus* ssp. can range between 0.1%-4% dry biomass depending on the cultivars and extraction methods used.

Astaxanthin is found in the shells and exoskeleton of crustaceans, including shrimp and krill. Shrimp astaxanthin is free carotenoids and does not esterify with fatty acids. The chemical structure of shrimp astaxanthin has two hydroxyl group and two ketone group. However, the yield of shrimp waste astaxanthin can vary according to the species of shrimp. The yield of krill astaxanthin depends on the extraction method. Astaxanthin produced from krill can be as low as 0.1% by weight and as high as 0.3%. *Phaffia Rhodozyma* is a yeast that produces astaxanthin. It is a di-ketone esterified with hydroxyl groups (2 hydroxyl groups) and ketone groups (2 ketone groups). The yeast can be grown using various carbon sources.

Astaxanthin has become popular in the cosmetics industry because of its many skin-protective properties. It helps protect the skin against oxidative damage. Ascanthin is a compound that has been shown to be effective in accelerating wound healing. In a study in mice with fully-thickened dermal wounds, wounds treated with Ascanthin showed a significant increase in the expression of biological markers related to wound healing, such as collagen type I alpha1 and bFGF. It has also been shown to increase skin hydration and elasticity, improve skin texture, and delay the appearance of wrinkles. In a study of 65 healthy female patients, it was found that a dose of 6 mg (or 12 mg) of Ascanthin dose decreased the secretion of an inflammatory cytokine (IL-1) and an inflammatory protein (MMP-1), both of which are known to reduce the appearance of hyperpigmentation on the skin. Additionally, skin elasticity improvements were observed in the high-dose astaxanthin group compared to the placebo group, especially in participants with high skin moisture content.

Marine algae

Algae, in particular, are virtually fat and calorie-free, making them increasingly sought for commercial purposes. Macroalgae, *generally referred as seaweeds*, have been found to be good sources of dietary fiber and carotenoids with antioxidant activity and play important roles in the prevention of neurodegenerative diseases. Several bioactive compounds have been isolated from brown algae with different pharmacological activities such as cytotoxic, antitumor, nematocidal, antifungal, anti-inflammatory and antioxidant. Algins, carrageenans

and agar are examples of polysaccharides derived from algae that are widely used as thickeners and stabilizers in foods as well as for gels. Sulphated fucans, carrageenans and ulvans, have been known to act as modulators of coagulation as well as reveal antithrombotic, anti-inflammatory, antioxidant, anticancer and antidiabetic activities, among. Soluble polysaccharides from algae have tremendous potential as dietary fiber for human nutrition and are being evaluated as new possible prebiotic compounds. Microalgae are considered important producers of some highly bioactive compounds found in marine resources; they can be used to improve food nutritional profile due to their richness in PUFAs and pigments such as carotenoids and chlorophylls.

Future Dimensions

The key to successful recycling and management of seafood waste lies in the development of appropriate environmentally friendly reprocessing technologies that can convert all the valuable components of the waste into valuable products and reduce the amount of waste requiring disposal. However, there are many challenges that must be overcome to achieve this goal.

- 1) Consumer awareness and education is one of these challenges. Without consumer acceptance of food waste reduction approaches, no sustainable, environmentally friendly food waste recovery and management strategy can succeed. This requires appropriate efforts by research and extension organisations.
- 2) The fisheries sector is a poorly organised sector. The widely dispersed seafood processing plants (in the domestic market and processing plants) pose collection and processing problems.
- 3) Seafood is inherently perishable due to its unique richness in proteins, peptides, enzymes, and microbial flora. This often leads to massive public resistance to starting a business in the area.
- 4) Strict legal and environmental restrictions from regulators, as seafood waste is not classified as “inactive/inert” waste, is a major barrier for entrepreneurs to invest in this resource
- 5) Inadequate cold chain management from source of production to processing, as processors are least interested in investing further in residues
- 6) There is no baseline data on the availability and economics of production collected in recent years, leading to uncertainty about the economics and market demand for secondary products
- 7) The lack of a clear legal classification of secondary products in the international market is another major challenge for investors
- 8) The lack of uniform quality assurance protocols (such as HACCP) for secondary products leads to frequent rejections by buyers.

Suggested readings

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