5 Application of Food By-Products in Medical and Pharmaceutical Industries

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5.1 Introduction

The food processing sector, like other natural resource-based processing industries, gives rise to organic waste, leading to environmental, economic and legal concerns regarding the disposal of food waste and by-products. This concern has led to the innovation of value-added bioactive compounds from food waste and by-products. These value-added compounds from food waste exhibit various physiological functions, such as antihypertensive, anti-oxidative, anti-thrombotic, mineral-binding and anti-amnesiac activities (Wilson, 2011).

Food by-products and waste are produced during the entire life cycle of food processing, starting from farm to fork. The distribution of food waste in developed countries is categorized as 42% by household, 39% in the food manufacturing industry, 14% by the food service sector and 5% in distribution and retail (Mirrabella *et al.*, 2014). In the current era, industrial ecology concepts such as cradle-to-cradle and circulatory economy are gaining considerable attention, aiming at a zero waste economy, in which waste materials are used as starting materials for development of new useful products and their applications.

In addition to loss of valuable bioactive materials, the food waste produced by the processing industries raises economic and environmental hazards. The agriculture and food processing sectors of food industry are considered as a sector for bio-refineries (Ghatak, 2011; Kamm and Kamm, 2004), with a special emphasis on potential use of food waste and by-products (Mahro and Timm, 2007). The first step in utilization of waste and by-products in the food processing sector is identification, characterization and quantification of residues (Rosentrater, 2005). Later, the food waste sources and recovery stages of biologically active and value-added ingredients should be characterized (Galanakis, 2012).

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The food industry produces huge amounts of fruits and vegetable waste that affects the environment and health sectors, because of high biodegradability and methane emissions (Misi and Forster, 2002). These residues contain large amounts of waste organic matter that includes approximately 75% sugars and hemicellulose, 9% cellulose, 5% lignin, small amounts of proteins and fats (Kosseva, 2011).

Nowadays, people are interested in healthy diets and lifestyles. Schieber *et al.* (2001) focused on functional and bioactive compounds such as polyphenols, tocopherols, carotenoids and others. They highlight the availability of untapped natural sources of bioactive compounds and micronutrients and their potential to be readily used as healthy ingredients. The biologically active ingredients from food processing by-products such as dietary fibers have received much attention, due to their potential as pharma-foods to reduce blood cholesterol, diabetes, coronary heart disease, ease of constipation and technological attributes such as water-binding, gelling, structure building and fat replacers (Telrandhe *et al.*, 2012).

The utilization of meat by-products is important for the profitability of the meat industry. In the past, meat by-products were a favorite food in Asia, but the health hazards associated with these by-products led to non-food uses, such as pharmaceuticals, cosmetics and animal feed (Rivera *et al.*, 2000). Due to potential components present in food by-products and wastes, the aim is to isolate and utilize high value-added components, such as proteins, peptides, polysaccharides, fibers, flavoring agents, phytochemicals and pharmacological ingredients.

5.2 Agroindustry By-Products and Potential Recovery of Bioactive Compounds

5.2.1 Fruits

The food industry produces huge amounts of fruit and vegetable wastes that present serious health and environmental hazards due to high biodegradability. Vegetable and fruit wastes are mainly comprised of hydrocarbons, comparatively small amounts of proteins and fat, with 80 to 90% moisture content. Therefore the concept of utilization of wastes to isolate and identify bioactive compounds is gaining interest worldwide. The examples of bioactive compounds isolated from fruit processing by-products are shown in Table 5.1.

5.2.1.1 Apples The important waste components of the apples processing industry are pomace and its extracts, which have a great potential for pharmaceutical and biotechnological applications. The waste comprises a heterogeneous mixture of pomace, seeds and peels with high water content and hemicellulose, cellulose and lignin. The apple juice industries utilize 75% of apple and the remaining 25% are by-products as pomace, peels and seeds (Shalini and Gupta, 2010). The apple pomace is composed of mainly simple carbohydrates (glucose, fructose and sucrose), pectin, fibers, proteins, vitamins and minerals (Kosseva, 2011). The flow diagram for

Table 5.1 Bioactive components isolated from byproducts of fruit processing

Components	Class	Source	Health benefits
Beta-carotene	Carotenoids	Various fruits pomace	Neutralizes free radicals and prevent cell damage, maintain cellular antioxidant defense
Lutein, Zeaxanthin		Citrus fruits peels and seeds	Contribute to maintain vision
Anthocyanidins		Berries, cherries, red grapes	Bolster cellular antioxidant defense, maintain brain function
Flavanols-catechins, epicatechins, procyanidins		Apples, grapes	Maintain normal cardiovascular functions
Flavanones		Citrus fruits	Bolster cellular antioxidant defense
Flavonols		Apples	Bolster cellular antioxidant defense
Hesperidine		Lemon and other citrus fruits	Treatment of rheumatoid arthritis
Proanthocyanidins	Flavonoids	Cranberries, apples, grapes	Maintain urinary tract and heart health
Pectin	Hetero-Polysaccharide	Apple, grape, citrus fruits	Decrease cholesterol and tryglyceride level, prevent colon and prostate cancer and diabetes

utilization of fruit and vegetable pomace in food and pharmaceutical industries is shown in Figure 5.1.

Several research studies have focused on biological properties of apple peel due to its high content of antioxidants and phenolic compounds. The high phenolic content in apple peels may prevent various chronic disorders such as cardiovascular diseases and cancers. Huber and Rupasinghe (2009) studied properties of apple peel antioxidants, and it was found that these antioxidants were able to prevent the lipid oxidation of polyunsaturated fatty acids that is a significant issue affecting food quality and health of customers. There is a high percentage of soluble fibers in apple by-products that results in the availability of pectin. Pectin is a polymer that can be used in food and pharmaceutical industries due to its unique characteristics of gelling, thickening and stabilizing. Pectin is also thought to lower cholesterol and delay gastric emptying (Hwang *et al*., 1998; Rha *et al*., 2011; Royer *et al.*, 2006).

These researchers also found significant levels of calcium, magnesium, zinc, iron and copper in apple peel. The iron, copper and magnesium work in synergy as an effective catalyst in the prevention of atherosclerosis and certain other diseases. Garcia *et al.* (2009) studied the presence of bioactive compounds in cider processing by-products of apple. Various important phenolic compounds were found, such as chlorogenic, protocatechui and caffeic acid, flavonols and flavanols. Schieber *et al*. (2003) reported similar findings and found a number of quercetin glycosides, with quercetin 3-galactoside

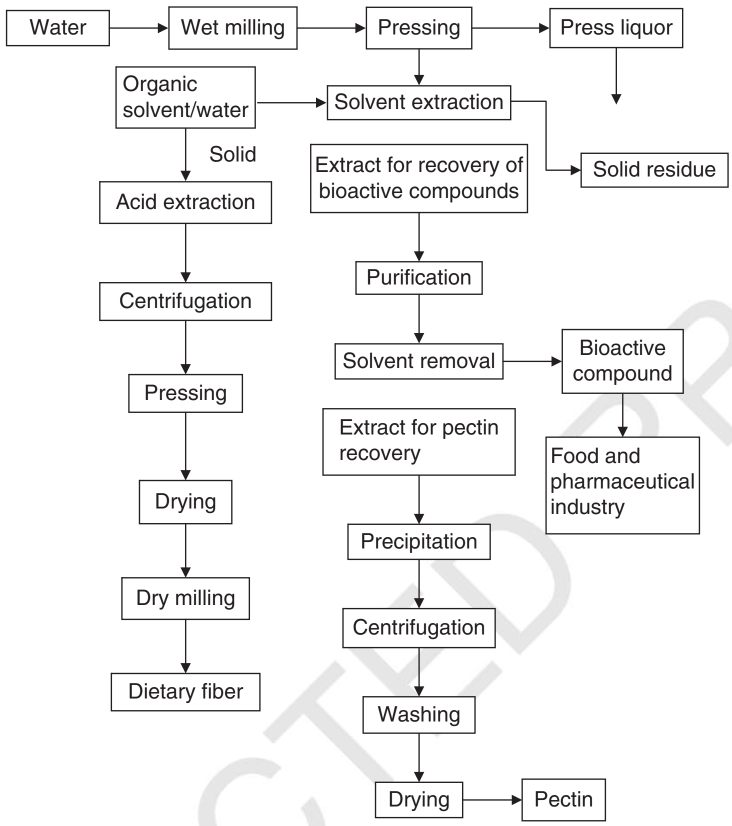

Figure 5.1 Flow chart for utilization of fruit pomace (Dilas *et al.*, 2009).

being the most abundant flavonol. Phloridzin was the most abundant compound in apple seeds.

Many health-enhancing effects are associated with the bioactive compounds found in apple by-products and waste. The predominant effects are cancer cell proliferation, lipid oxidation decrease and reduction in blood cholesterol levels. In turn, these health-enhancing effects present a preventive measure against chronic disorders, for example obesity, cancer and cardiovascular disorders. Procyanidins were found to have high antioxidant potential and inhibition oxidation of low-density lipoproteins. Quercetin is a major flavonoid compound present in apple peals, with a potential to reduce incidence of breast cancer and leukemia (Boyer and Liu, 2004).

5.2.1.2 Berries Berries are used in the food industry for juices, jams and jellies preparations, especially raspberries and blackberries due to their high phenolic content, flavonoids, polyphenols and antioxidant effects. A large amount of waste and by-products are released from industrial manufacturing. These by-products can be successfully recovered for food and pharmaceutical industries. Bakowska-Barczak *et al.* (2009) found that Canadian blackcurrant seed residue proved to be a good source of antioxidants and value-added compounds.

5.2.1.3 Citrus Fruits In the case of citrus fruits, large amounts of waste materials such as peels and seeds are discarded during food and juice processing, because citrus fruits have a comparatively small edible portion. The by-products of citrus fruit juice processing comprises of various compounds, principally soluble sugars, organic acids, fibers, proteins, amino acids, minerals, oils, lipids, vitamins and also flavonoids (Fernandez-Lopez *et al*., 2004). Viuda-Martos *et al*. (2011) determined physicochemical and antimicrobial characteristics of orange by-products after extraction of juice by determining pH, color, soluble solids, antioxidant capacity, phenolic compounds and sugars. Chau and Huang (2003) determined the dietary fiber content in orange peel and found that it contained mostly an insoluble dietary fiber fraction composed of pectic polysaccharides and cellulose. The dominant insoluble fraction provides health benefits, such as intestinal regulation and increased stool volume.

The by-products of lemon after juice extraction constitute almost 50% of the fruit and mainly consist of seeds, peels and fruit pulp. Normally this is left for animal feed or used for pectin extraction (Lario *et al*., 2004). The lemon peel was found to be a good source of iron (Gorinstein *et al.*, 2001). The carotenoid and hesperidine were found in lemon by-products. The flavonoid hesperidine has a great potential in the treatment of rheumatoid arthritis (Gonzalez-Molina *et al*., 2010).

5.2.1.4 Grape Grape pomace consists of stems, seeds and skin, and sometimes this by-product is used for extraction of grape seed oil. The grape pomace is also used for production of citric acid, ethanol, methanol and xanthan gum (Deng *et al.*, 2011). The components of dietary fiber in grape pomace are hemicellulose, cellulose and small portions of pectin (Kammerer *et al*., 2005). The anthocyanins, flavonols and gallic acid are the major polyphenolic compounds found in grape pomace (Ruberto *et al*., 2007).

The pharmacological benefits associated with polyphenols such as anthocyanins and flavonoids have been linked in the reduction of chronic disorders such as cardiovascular disease and some types of cancers. The mechanism behind this pharmacological activity is an increase in antioxidant activity of plasma that in turn results in inhibition of low-density lipoproteins oxidation. The bioactive compounds isolated from grape pomace have been found to reduce systolic blood pressure. The polyphenols such as gallic acid and flavonoids prevent lipid oxidation by reacting with superoxide anions, hydroxyl radicals and lipid peroxyl radicals. Ruberto *et al*. (2007) and Maier *et al*. (2009) demonstrated the availability of flavonoids and phenolic acids in grape pomace. These phenolic compounds have been linked with reducing heart disease.

Spatafora and Tringali (2012) studied anti-proliferative compounds present in grape stem. The active constituents, betulinic acid, stilbenoid trans-resveratrol, trans-viniferin and a mixture of sitosterol 6'-O-acyl-glucosides, were obtained by Gas Chromatography-Mass Spectrometer (GC-MS) analysis. Some of these compounds showed a stronger anti-proliferative effect than 5-fluorouracil in human breast cancer cells.

5.2.1.5 Mango Mango peel has been reported as a rich source of dietary fiber (Ajila *et al.*, 2008). The peel (ripe and unripe) is a good source of polyphenols. Beta carotene was found to be the prominent carotene available in mango peel (Pott *et al.*, 2003). The ripened mango peel is also a good source of antioxidants such as vitamin C and vitamin E (Ajila *et al.*, 2007). The polyphenolic compounds present in mango peel present a wide range of applications in the food and pharmaceutical industries. These phytochemicals prevent DNA oxidative damage, inhibition of cell communication and free radical scavenging. Free radicals have been seen to drain immune system antioxidants, and catalyse unusual proteins, which are known to start progressive disease and ageing and change gene expression (Masibo and He, 2008).

Abdalla *et al*. (2007) studied the composition of mango seed kernels and found amino acids, phenolic compounds, the characteristics of the extracted oil including unsaponifable matter constituents, lipid classes and fatty acids. Results showed that mango seed kernels contained a substantial content of total phenolic compounds, total lipid, unsaponifiable matter, and a low amount of crude protein, but the quality of protein was good because it was rich in all the essential amino acids. The combination of both mango seed kernel extract and oil had optimum antioxidant potency higher than each one alone, and could be used as a natural antibacterial and antioxidant in food and pharmaceutical products.

5.2.1.6 Miscellaneous Fruits Canteri *et al*. (2010) found passion fruit waste (peel) rich in pectin used as a stabilizer and gelling agent, generated in high amounts in the Brazilian food industry. In pineapple processing, the fruit stem is a major waste material and found to be the main source of the enzyme bromelain. Upadhyyay *et al*. (2012) studied biological activities of pineapple stem waste and found antioxidant, antimicrobial, inhibitions against 15-lipoxygenase and advanced glycation end-product formation by pineapple stem waste.

5.2.2 Vegetables

5.2.2.1 Carrots Carrots (*Daucus carota L.*) are normally used, after peeling, in the industrial and household sector, and the peels are generally considered as a waste. Carrot peels contain high amounts of dietary fibers and phenolic acids, especially anthocyanin and carotenoids (Goncalves *et al*., 2010). Chau *et al.* (2004) reported that by-products (carrot pomace) of the carrot juice industry contained a high content of dietary fibers. Carrots pomace is rich in anthocyanins and carotenoids that are responsible for the aroma bitterness and color of carrots (Goncalves *et al.*, 2010). As carrots are a good source of carotenoids, they are recommended for eyesight and due to a high phenolic content, they have strong antioxidant potential. Carrot anthocyanins reduce inflammation and exhibit strong lipid oxidation, thus leading to prevention of heart disease (Arscott and Tanumihardjo, 2010).

5.2.2.2 Cauliflower Many food dishes, such as soups and stews, contain cauliflower (*Brassica oleracea* L. var. *botrytis*) as an important component, but only 40% of the vegetable is used, while the rest is discarded as waste (Femenia *et al.*, 1998). The by-products of cauliflower, such as the floret and stem, were analyzed for non-starch polysaccharides. The stem contained non-starch polysaccharides as 3.11% of fresh weight compared to the floret that was 2.31% of fresh weight (Femenia *et al.*, 1997). The insoluble fraction was dominant, and the soluble fraction in both by-products and major components identified was pectin in a non-starch polysaccharide fraction. Llorach *et al.* (2003) studied the antioxidant activities of cauliflower by-products and found that hydroxycinnamic acid and flavonoids were the main antioxidant compounds present in by-products. They further evaluated that the edible part of the cauliflower was much lower in these phenolic compounds compared to the by-products.

5.2.2.3 Onions Onions (*Allium cepa L.*) are commonly used in fast foods, restaurant food and salads, due to their strong flavor (Griffiths *et al.*, 2002). Currently in Europe, 500 000 tonnes of onion by-products are produced annually (Benitez *et al.*, 2011). Onion by-products mainly consist of skins, roots, fleshy scales, undersized, diseased or damaged onions. Different layers of onions contain dietary fibers in different proportions. The highest levels of total dietary fibers were found in the skin of onions, which is normally considered as waste (Jaime *et al.*, 2002). The phytochemical analysis of onions revealed that phenolic and flavonoid were the main components (Ng *et al.*, 2000). Protocatechuric acid and ferulic acid were in abundance in the papery scales of onions compared to the fleshy scale. The onions by-products were found to be rich in flavonoids that indicated their potential in reducing inflammation, heart disease and cancers. Onions are also rich in organo-sulphur compounds that are associated with various pharmacological activities, which indicates under-utilization of onion by-products (Lanzotti, 2006).

5.2.2.4 Potato Potatoes (*Solanum tuberosum L.*) contain nutrients such as fiber, carbohydrates, minerals and phenolic compounds (Abu-Ghannam and Crowley, 2006). The processing and preparation of potatoes generate tonnes of potato peel and pulp as by-products. Liu *et al.* (2007) studied the composition of three species of potatoes and their peels and found no significant difference in fiber content and other nutrients. Potatoes are rich in chlorogenic acid (soluble fraction) and caffeic acid (insoluble fraction). Mattila and Hellstrom (2007) found that the chlorogenic acid and its derivative compounds were the main soluble phenolic compounds present in potato peels. The phenolic compounds present in potatoes contribute to various health benefits, for example chlorogenic acid exhibits antioxidant activities, tumor suppression and lowering of hyperglycemia. Due to the nutraceutical benefits of potatoes by-products, the concept between phyto-constituents present in potato peel and health benefits is gaining more attention.

5.2.2.5 Tomato Tomato (*Solanum lycopersicum L.*) is used in the preparation of many food products, such as ketchup, sauces, pasta, various food dishes and juices. The processing of tomatoes generates many by-products that still contain numerous phytochemicals, for example lycopene that belongs to the family of carotenoids and helps to reduce the risk of cancers (Chang *et al.*, 2006). Tomato pomace contains fiber as a main ingredient that contributes 50% of the by-product on a dry weight basis (Del Valle *et al.*, 2006). Lycopene is present in abundance in tomato by-products and lowers the risk of prostate, pancreas and stomach cancers (Chang *et al.*, 2006). Lycopene is a cancer-reducing phytochemical and is present in abundance in tomato peel, and it can be included as a nutraceutical in food and pharmaceutical preparations.

5.2.2.6 Olives Olives (*Olea europaea*) are used for the production of olive oil that generates large quantities of waste (Lozano-Sanchez *et al.*, 2011). The by-products of the olive oil industry contain various bioactive and pharmaceutical ingredients with strong antioxidant potential. The waste products generated during the preparation of extra virgin olive oil were analyzed for the presence of phenolic compounds and flavones, and lignans and secoiridoids were found in abundance

(Lozano-Sanchez *et al.*, 2011). The quantitative and qualitative analysis of these phenolic compounds suggested that olive by-products could be considered as a vital source of phenolic compounds and after purification could be used as antioxidants in food and nutraceutical products due to their biological and technological properties. Ramos *et al.* (2013) studied the antioxidant and anti-cancer activities of olive pomace extracts from Portuguese industries. The extracts were found to be potent for antioxidant and breast cancer anti-proliferative activities, proving olive by-products as a potential source of antioxidants in food supplements and nutraceuticals.

5.3 By-Products from Animal Origin

Regulation (EC) No. 1096/2009 has defined animal by-products as the whole body of an animal or parts from the animal body or other products derived from animals which can be but are not meant for consumption by humans. The culture, tradition and religion of country influence the type and generation of by-products. Under-utilization of by-products presents a problem to the environment and economic losses to the producers (Lafarga and Hayes, 2014). Here, the by-products from meat processing, poultry, fish and seafood and their possible applications in the pharmaceutical industry are included.

5.3.1 By-Products from Meat Processing

Both slaughterhouses and meat-processing industries, along with the wholesalers, retailers and renderers, produce tons of solid and liquid by-products annually. The disposal of these by-products has created a huge problem for the producers. They mainly comprise of blood, trimming, skin, bones etc., which contain many bioactive components that can be extracted by using suitable techniques and utilized in food, feed or pharmaceutical industries. There have been several studies on the conversion of by-products into the more value-added components or products (Mora *et al.*, 2014; Toldra *et al.*, 2012). The potential pharmaceutical and medical application of meat by-products are discussed further below (Figure 5.2).

5.3.1.1 Animal Blood Animal blood from slaughterhouses is one of the major by-products of the meat production food chain and constitutes about 4% of the weight of the live animal or around 6–7% of the lean meat of the carcass (Wismer-Pedersen, 1988). Mainly of these blood products are either processed as blood meal, which is a low-value product, or discarded as effluent. However, they can be converted into other products which have high value (Anderson and Yu, 2003). From animal blood, different valuable components have been recovered and used in medical and pharmaceutical applications. Some of these are listed in Table 5.2

Several studies have been done on the isolation of bioactive components from animal blood. It has been revealed that these bioactive compounds, mainly from the bovine and porcine blood fraction, possess antioxidant and antimicrobial properties along with angiotensin I-converting enzyme (ACE)-inhibitory activity, ability to bind mineral and opioid activity. The bioactive peptides that have been generated from bovine and porcine blood have shown ACE inhibitory activity (Bah *et al.*, 2013). Yu *et al.* (2006) mentioned that the peptides obtained from food sources like meat, sea

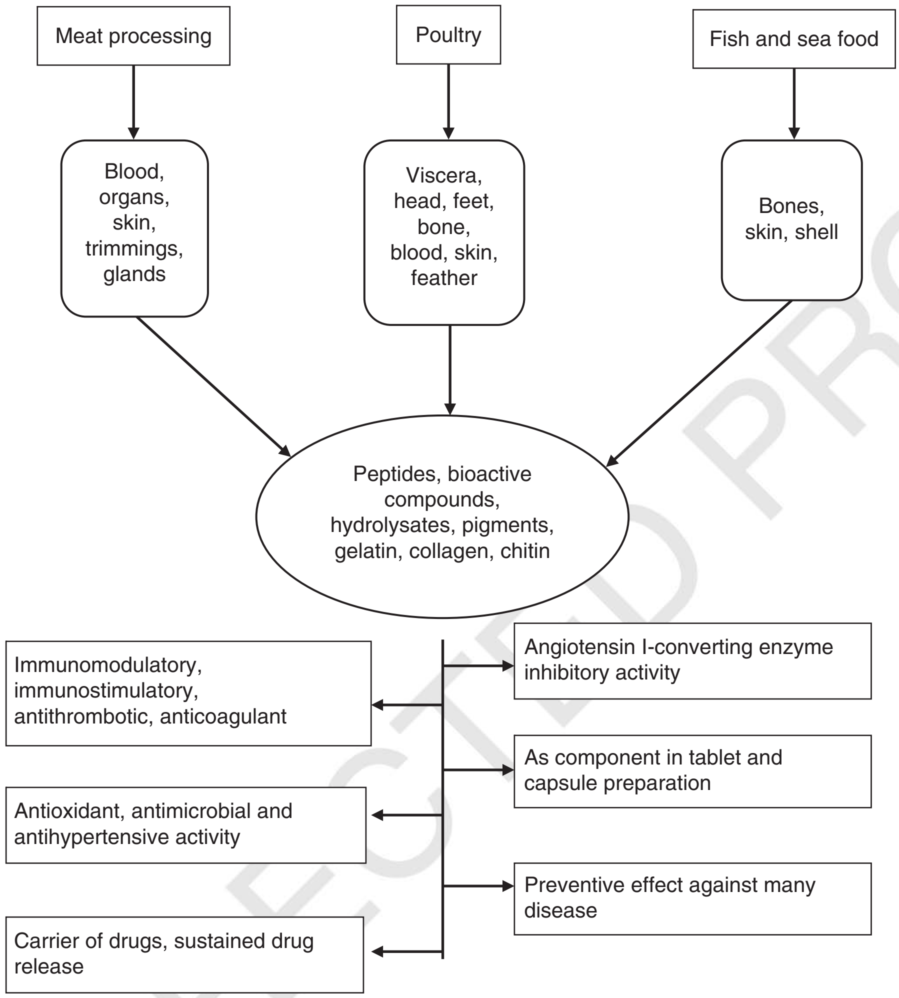

Figure 5.2 By-products from food of animal origin and their possible pharmaceutical and medical applications.

Table 5.2 Application of blood components in medical and pharmaceutical field (adapted from Bah *et al.*, 2013)

S.N	Components from blood	Applications
1	Bovine hemoglobin powder	Production of porphyrin derivative
2	Bovine fibrinogen	As blood clotting reagent in serology laboratories
3	Bovine prothrombin	For production of thrombin as a precursor and its purification
4	Bovine thrombin	Wound treatment, helps in coagulating blood, for holding skin grafts
5	Porcine plasmin enzyme	In heart attack patients, for digesting the fibrin in blood clots

food, milk etc. have ACE inhibitory activity and as compared to synthetic drugs, they are milder and safer for use.

The antimicrobial peptides such as cathelicidins and defensins have been derived from the blood of both animals (pigs, goat, sheep, deer and cattle) and poultry (ostrich, chicken and turkey) (Yu *et al*., 2010). The hydrolyzed peptides from bovine hemoglobin have exhibited opioid activity (Zhao *et al*., 1997). These peptides containing short-chain amino acids are capable of binding with the opioid receptors in the brain and have an influence on the nervous system (Pihlanto and Korhonen, 2003). The peptides from animal blood have also been linked with antigenotoxicity potential, which is the ability to prevent DNA damage. The Comet assay of hydrolyzed peptides from bovine albumin, globulin and plasma demonstrated the antigenotoxic effect (Park and Hyun, 2002).

5.3.1.2 Hides and Skins Hides and skins of animals are one of the important by-products generated by animal meat processing. They contain considerable amounts of collagen and from this collagen, gelatin can be extracted. The collagen-based compound can be used for stimulating blood clotting, mainly during surgery. Gelatin can be used in the pharmaceutical industries as a binding agent and a compounding agent in the preparation of tablets and also for manufacturing the outer coatings of capsules. Because of the similarity between the skins of pigs and humans, it can be used for dressing and skin grafting in the treatment of skin burns and ulcers. The skin has to be detached within 24 hours of the pig's death to use as a skin graft (Jayathilakan *et al*., 2012).

5.3.1.3 Trimmings and Cuttings Generally, trimmings and cuttings comprise of gristle, fat and meat and are obtained as the leftovers while removing the muscle meat from bones after the preparation of prime cuts. Trimmings do not include internal organs, ligaments, tendons and the parts of the head. These trimmings are used to prepare hot dogs, a secondary meat product. However, bioactive peptides can be extracted from them, which is a more valuable and cost-effective method. There has been many studies on the antioxidant, antimicrobial and antihypertensive activity of the bioactive peptides from muscle proteins. The peptides obtained after enzymatic hydrolysis of porcine skeletal muscle proteins indicated the ACE-inhibitory activity and this effect was proved *in vivo* by experimenting on hypertensive rats (Mora *et al*., 2014).

5.3.1.4 Glands and Organs Different glands and organs from the healthy animal have been traditionally used for medicinal purposes in many countries like India, Japan and China etc. A rapid freezing technique is used to preserve the glands, as it can inhibit the breakdown of tissue by microbial contamination. Prior to freezing, the glands should be properly cleaned, and fat and connective tissues should be removed and wrapped in waxed paper. Finally, they will be stored at less than or equal to −18 °C. For pharmaceutical applications, these glands are either vacuum dried or extracted with suitable solvents. The excess fat content of the gland is removed by using solvents like ethylene, acetone, gasoline or light petroleum. The dried and defatted extract is then powdered and used for capsule preparation or in the liquid form (Jayathilakan *et al.*, 2012).

Liver extract is considered as a good source of vitamin B_{12}. Therefore, it can be used as a nutrient supplementation for the treatment of different forms of anemia.

Liver extract is also used as a raw material for various pharmaceutical applications. Bile juice obtained from the gall bladder of the animal can be used to treat indigestion, constipation, problems related to the bile tract and to improve liver functioning. Insulin from the pancreas can be used for diabetic patients to regulate blood glucose levels. Similarly, glucagon hormone from the pancreas can maintain blood glucose levels and overdose of insulin. Heparine, an anticoagulant agent, can be extracted from the liver, lungs and small intestine linings. It has been utilized in the thinning of blood and delaying of blood coagulation during organ transplant surgery. The threads for surgical sutures can be prepared from the sheep and calves intestine (Rahman *et al*., 2014).

5.3.1.5 Poultry By-Products Only one-third portion of the total weight of poultry birds is converted into meat during slaughtering and processing, whereas the remainder is by-products and waste. Therefore, these wastes and by-products should be efficiently processed and utilized to produce high-value products. Many by-products can be obtained from the poultry industry, including egg shell, shell membranes, feathers, heads, blood, feet, intestine, glands, gizzards and proventriculus. They can be a good source of calcium, gelatin, collagen, protein hydrolysates, enzymes etc., which can be utilized in many applications as in the food, feed, fertilizer, cosmetics, biochemical and pharmaceutical industries (Lasekan *et al*., 2013; Mishra *et al*., 2015).

Egg shell is a natural and rich source of calcium and almost 90% of it is absorbable. Calcium supplementation using egg shell powder along with vitamin D and magnesium have shown positive results on bone mineral density in osteoporosis conditions. Egg shell membrane consists of collagen which has higher biosafety and is lower in allergic reactions. Collagen from egg shell membranes can be used as a treatment aid in orthopedics and dentistry and for cancer patients for improving the skin and thickening of hair (Kingóri, 2011).

Chicken by-products vary in their compositions, such as the viscera, which is rich in lipids, whereas the head, skin and feet have high protein content (collagenous and keratinous). Thus hydrolysates with high bioactive properties can be obtained from these by-products. These hydrolysates have shown antioxidant and antihypertensive property. The keratinous hydrolysates have shown better antioxidant properties, but the collagenous fraction exhibited strong antihypertensive potential. The hydrolysates from chicken leg bone, viscera, acid hydrolyzed feather and blood have indicated good ACE inhibitory activity. The ACE inhibitory activity of hydrolysates is mostly affected by the type of enzyme, degree of hydrolysis (DH) and the peptide's molecular weight (Lasekan *et al*., 2013). Collagen extracted from chicken neck, feet and other by-products can have various medical applications in the fields of surgery, cardiology, dermatology, orthopaedic, ophthalmology, urology and vascular departments (Silvipriya *et al*., 2015).

5.3.2 Fish and Seafood Processing

In recent years, aquaculture has been considered the fastest growing food-production sector in the world (Kandra *et al*., 2012). The by-products from fish and shellfish processing may contribute to as much as 70% of the initial weight of the catch (Olsen *et al.*, 2014). Most of the by-products from fish processing are used for producing fish meal, fish oil, fish silage, animal food and fertilizer, which holds low economic profitability. Many researches have revealed that fish and shellfish by-products, such as muscle protein, collagen, gelatin, oil, bone, shells of shellfish and crustaceans, comprise of numerous valuable bioactive compounds. They can be extracted and purified as desired using suitable technologies and finally employed in nutraceutical, biotechnological and pharmaceutical applications (Kim and Mendis, 2006).

The important and valuable constituents from fish by-products can belong to proteins, lipids and other compounds. The protein by-product includes collagen, gelatin, fish protein isolates, fish protein hydrolysates, enzymes, bioactive peptides etc., whereas lipid components consist of omega-3 fatty acids, marine oils, cholesterol, vitamins etc. Calcium, astaxanthin, taurine and bioactive compounds comes under other compounds (Rustad *et al.*, 2011). Similarly, Kandra *et al.* (2012) have mentioned that shrimp waste is also a rich source of chitin, minerals, protein and astaxanthin.

5.3.2.1 Bioactive Peptides from Fish Protein Hydrolysates The bioactive peptides extracted from fish protein have been proved to be associated with several bioactive properties such as antioxidative, antithrombotic, antihypertensive and immunomodulatory activities. They have shown strong antioxidant activities in many oxidative systems (Kim and Mendis, 2006). Rajapakse *et al.* (2005) have reported that enzymatic hydrolysis of marine fish can yield proteins with anticoagulant and antiplatelet properties. With the formation of the inactive complex, these proteins were capable of inhibiting coagulation factor XII (FXIIa). A few fish peptides have also been associated with antihypertensive activity that inhibited the ACE (Kim *et al.*, 2000). It has been reported that some fish protein have growth factors and hormone-like peptides, which are capable of accelerating calcium absorption and can be used for treating calcium deficiency disorders such as osteoporosis and Paget's disease (Fouchereau-Peron *et al.*, 1999). The acidic peptides from Atlantic cod hydrolysates have shown strong immunostimulatory effects, which is related with the bactericidal power of phagocytes (Gildberg *et al.*, 1996).

5.3.2.2 Fish Oil Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the important bioactive components that can be isolated from the fish oil by the process called transesterification (Olsen *et al.*, 2014). Intake of omega-3 fatty acids has been associated with numerous health benefits for combating many diseases. Consumption of fish oil raises EPA and DHA levels in the blood. As a result, there is a reduction in the rate of coronary heart diseases through various modes of action. It also helps in the prevention of atherosclerosis by hindering the formation of atherosclerotic plaques (Schacky, 2000). Omega-3 fatty acids have shown the ability to lower blood pressure (Appel *et al.*, 1993), benefits for diabetic patients (Sheehan *et al.*, 1997), effective against asthma (Broughton *et al.*, 1997), preventive against arrhythmias (Christensen *et al.*, 1997) and also protect against chronic obstructive pulmonary diseases (Shahar *et al.*, 1994). Gogos *et al.* (1998) concluded that intake of omega-3 fatty acids along with supplementation of antioxidant may prolong the life of cancer patients with general malignancy through the immunomodulating effect. EPA and DHA can be transformed into prostaglandins and leukotrienes that have natural anti-inflammatory action (Belch and Muir, 1998). Therefore, EPA and DHA can be used for treating kidney diseases (Donadio *et al.*, 1994) and Crohn's disease (Belluzzi *et al.*, 1996).

5.3.2.3 Gelatin and Collagen from Fish Skin and Bones Almost 30% of the waste from the fish processing industry includes fish bones, skin and fins. Collagen and gelatin having diverse applications can be isolated from the skin and bones. The contribution of collagen from these sources is in the range of 36% to 54%. Thus, the collagen obtained has potential for use in the food, pharmaceutical and cosmetic industries (Blanco *et al*., 2007). There is an increase in demand for collagen and gelatin for industrial uses (Karim and Bath, 2009). Structurally, collagen has a triple helix arrangement made from three extended protein chains wrapped around one another. When collagen is partially hydrolyzed, gelatin can be obtained. So collagen and gelatin are different forms of the same macromolecule (Gomez-Gillen *et al*., 2002; Kim *et al.*, 1994). In general, acid treatment is used to extract collagen followed by solubilization, so that the triple helix structure is not lost. The heat treatment of collagen breaks the triple helix structure and converts collagen into gelatin. Hence, a simple hot water treatment can be applied for solubilizing collagen from the source to obtain gelatin (Djabourov *et al.*, 1993). Both collagen and gelatin have good biodegradability and biocompatibility in the physiological environments, so are used widely in the pharmaceutical and medical industries (Young *et al.*, 2005).

The gelatin extracted from fish skin by enzymatic hydrolysis has shown antioxidant and antihypertensive properties, which was assumed to be present due to the unique amino acid sequence Gly–Pro–Ala in gelatin peptides. Along with this, further research on animals has suggested that these gelatin peptides can increase the bioavailability of calcium by accelerating the calcium absorption (Kim and Mendis, 2006). Gelatin has been used in the pharmaceutical industries as a stabilizer in live attenuated viral vaccines (mumps, rabies, measles, diphtheria etc.) (Burke *et al.*, 1999), as intravenous infusions (Saddler and Horsey, 1987) and injectable microspheres for drug delivery (Rao, 1995).

Pharmaceutical application of collagen includes its use as carrier molecules for drugs, proteins and genes (Lee *et al.*, 2001). For cancer treatment, microfibrous collagen sheets are utilized as drug carriers (Sato *et al.*, 1996). In addition, collagen is also used in the manufacture of vitreous implants and wound dressings (Takeshi and Suzuki, 2000). Moskowitz (2000) has mentioned that collagen can help in the functional expression of cells and tissue and organ formation. Further research has shown that intake of gelatin or collagen hydrolysates are effective in reducing the pain of osteoarthritis patients and they also take part in cartilage matrix synthesis.

5.3.2.4 Chitin, Chitosan and their Oligomers from the Shell of Crustacean Chitin is the ubiquitous abundant polysaccharide, which can be obtained from many organisms, including cell wall of fungi and algae, exoskeleton of insects, endoskeleton of cephalopods and shells of crustacean. But the major commercial source is contributed by marine organisms. Around 10^{10}–10^{11} tonnes of chitin are produced annually by living organisms (Revathi *et al.*, 2012; Merzendorfer, 2011). Chitin is a polymer of β-(1→4)-linked 2- acetamido-2-deoxy-D-glucopyranose, whose structure is similar to that of cellulose, where the hydroxyl group of cellulose in C-2 is replaced by the acetamido group in chitin (Kurita, 2006). It is white to cream in color, odorless, with varying degrees of acetylation (Meyers *et al.*, 2008). Chitin have three different polymorphic forms: α, β and γ forms. The most abundant and stable form is α-chitin. β-chitin, found in squid pen. is more reactive than the α- form.

Table 5.3 Application of chitin and chitosan biomedical and pharmaceutical field (adapted from Hamed *et al.*, 2016; Kim *et al.*, 2008)

Field	Uses
Biomedical	Manufacturing of surgical stitches Fabrication of scaffolds for tissue regeneration Barrier against microbial infections
Pharmaceuticals	Encapsulation of gene and active constituents Carrier of ingredients and controlled drug release For improvement of arrival of nucleic acids to the therapeutic targets Wound healing properties Non-viral vectors for delivery of genes

γ-chitin is a combination of the α and β form, which is comparatively rare and only found in the squid's stomach and cocoons of two genera of beetles (Hamed *et al.*, 2016).

The exoskeletons of crustacean are demineralized and deproteinized in order to obtain chitin. One of the main drawbacks of chitin is its strong hydrophobicity. Therefore chitosan, a deacetylated derivative of chitin, is produced as it is water soluble and the only known natural cationic polysaccharide (Du *et al.*, 2014). Both chitin and chitosan are biodegradable, renewable, biocompatible and non-toxic compounds that are linked with several biological activities that include anti-cancer (Salah *et al.*, 2013), antimicrobial (Goy *et al.*, 2009) and antioxidant properties**.** The possible pharmaceutical and biomedical application of chitosan and its derivatives are listed in Table 5.3.

5.3.2.5 Astaxanthin from Crustacean Shell The ketocarotenoid astaxanthin, 3,3′-dihydroxy-β, β-carotene-4, 4′-dione, is the oxidized derivative of β-carotenoid. It is the natural substance with properties like highly versatile, non-toxicity and solubility in both water and lipid, which allows it to be used for many applications. It is also considered in food and medical applications due to its attractive pink color, high antioxidant activity and functionality as a precursor of vitamin A. Astaxanthin can be synthesized or extracted from many sources such as plants, bacteria, algal cells, crustacean shells and egg yolk. One of the richest sources is shrimp shell waste. Astaxanthin is one of the major pigments in crustacean shells, constituting 74–98% of the total pigments. Therefore, crustacean shell can be used for extracting astaxanthin along with the recovery of chitin (Ferraro *et al.*, 2010).

The antioxidative effect of astaxanthin is stronger than β-carotene, vitamins E and vitamin C. In addition, it was found to enhance the immune system, and protect against cancers and ultraviolet radiation damage. It has been demonstrated that astaxanthin inhibits prostate cancer and modulating immune responses against tumor cells. It also inhibits bladder carcinogenesis. Astaxanthin can be extracted from the crustacean shell through various methods such as by fermentation, enzymatic process, using hydrochloric acid, edible oils and organic solvents. Many vegetable oils such as sunflower, coconut, palm, ground nut, soybean, ginger and rice bran oils have been used for extracting astaxanthin from fish by-products and crustaceans. The solution of proteolytic enzymes such as pepsin, trypsin and papain dissolved in citrate phosphate has been used for precipitating astaxanthin present in the crustacean shell. Currently, the lactic acid fermentation process is one of the feasible methods to obtain partially concentrated astaxanthin from crustacean shells. This method also preserves the biomass from bacterial decomposition (Ferraro *et al.*, 2010; Kandra *et al.*, 2012).

5.4 Conclusion

Food processing operations generate a huge amount of by-products, which have a large variety of applications but are generally handled with low economic value. Mostly, they are used in the field of food, feed, cosmetics, fertilizers etc. However, valuable components can be recovered from these by-products and exploited as high value-added compounds. Several studies have proven that the bioactive constituents from food by-products, including the agroindustry, meat, poultry and fish processing, have numerous beneficial properties. Therefore, they can be utilized in medical and pharmaceutical applications. Various physiological functions such as antioxidant activity, antihypertensive, anti-thrombotic, mineral-binding and anti-amnesiac activities have been found to be associated with the bioactive compounds from food by-products. Hence, this shows that there is a great potential of these by-products for effective utilization in the field of medical and pharmaceutical applications that will be more cost-effective and efficient.

References

Abdalla, A.E., Darwish, S.M., Ayad, E.H. and El-Hamahmy, R.M. (2007) Egyptian mango by product. 1: Compositional quality of mango seed kernel. *Food Chemistry*, **103**(4): 1134–1140.

Abu-Ghannam, N. and Crowley, H. (2006) The effect of low temperature blanching on the texture of whole processed new potatoes. *Journal of Food Engineering*, **74**(3): 335–344.

Ajila, C.M., Bhat, S.G. and Rao, U.P. (2007) Valuable components of raw and ripe peels from two Indian mango varieties. *Food Chemistry*, **102**(4): 1006–1011.

Ajila, C.M., Leelavathi, K. and Rao, U.P. (2008) Improvement of dietary fiber content and antioxidant properties in soft dough biscuits with the incorporation of mango peel powder. *Journal of Cereal Science*, **48**: 319–326.

Anderson, R.C. and Yu, P.L. (2003) Isolation and characterisation of proline/arginine-rich cathelicidin peptides from ovine neutrophils. *Biochemical and Biophysical Research Communications*, **312**: 1139–1146.

Appel, L.J., Miller, E.R., Seidler, A.J. and Whelton, P.K. (1993) Does supplementation of diet with fish oil reduce blood pressure? A meta-analysis of controlled clinical trials. *Archives of Internal Medicine*, **153**: 1429–1438.

Arscott, S.A. and Tanumihardjo, S.A. (2010) Carrots of many colors provide basic nutrition and bioavailable phytochemicals acting as a functional food. *Comprehensive Reviews in Food Science and Food Safety*, **9**(2): 223–239.

Bah, C.S.F., Bekhit, A.E.A., Carne, A. and McConnell, M.A. (2013) Slaughterhouse blood: An emerging source of bioactive compounds. *Comprehensive Reviews in Food Science and Food Safety*, **12**: 314–331.

Bakowska-Barczak, A.M., Schieber, A. and Kolodziejczyk, P. (2009) Characterization of Canadian black currant (*Ribes nigrum L.*) seed oils and residues. *Journal of Agricultural and Food Chemistry*, **57**(24): 11528–11536.

Belch, J.J.F. and Muir, A. (1998) n-6 and n-3 essential fatty acids in rheumatoid arthritis and other rheumatic conditions. *Proceedings of the Nutrition Society*, **57**: 563–569.

Belluzzi, A., Brignola, C., Campieri, M., Pera, A., Boschi, S. and Miglioli, M. (1996) Effect of an enteric-coated fish-oil preparation on relapses in Crohn's disease. *The New England Journal of Medicine*, **334**: 1557–1560.

Benítez, V., Mollá, E., Martín-Cabrejas, M.A., Aguilera, Y., López-Andréu, F.J. *et al*. (2011) Characterization of industrial onion wastes (*Allium cepa L.*): Dietary fiber and bioactive compounds. *Plant Foods for Human Nutrition*, **66**(1): 48–57.

Blanco, M., Sotelo, C G, Chapela, M.J. and Perez-Martin, R.I. (2007) Towards sustainable and efficient use of fishery resources: Present and future trends. *Trends in Food Science Techology*, **18**: 29–36.

Boyer, J. and Liu, R.H. (2004) Apple phytochemicals and their health benefits. *Nutrition Journal*, **3**(5): 12.

Broughton, K.S., Johnson, C.S., Pace, B.K., Liebman, M. and Kleppinger, K.M. (1997) Reduced asthma symptoms with n-3 fatty acid ingestion are related to 5-series leukotriene production. *American Journal of Clinical Nutrition*, **65**: 1011–1017.

Burke, C.J., Hsu, T.A. and Volkin, D.B. (1999) Formulation, stability and delivery of live attenuated vaccines for human use. *Critical Reviews in Therapeutic Drug Carrier Systems*, **16**(1): 1–83.

Canteri, M. H., Scheer, A.P., Wosiacki, G., Ginies, C., Reich, M. and Renard, C.M. (2010) A comparative study of pectin extracted from passion fruit rind flours. *Journal of Polymers and the Environment*, **18**(4): 593–599.

Chang, C.H., Lin, H.Y., Chang, C.Y. and Liu, Y.C. (2006) Comparisons on the antioxidant properties of fresh, freeze-dried and hot-air-dried tomatoes. *Journal of Food Engineering*, **77**(3): 478–485.

Chau, C.F. and Huang, Y.L. (2003) Comparison of the chemical composition and physicochemical properties of different fibers prepared from the peel of *Citrus sinensis L*. Cv. *Liucheng. Journal of Agricultural and Food Chemistry*, **51**(9): 2615–2618.

Chau, C.F., Chen, C.H. and Lee, M.H. (2004) Comparison of the characteristics, functional properties, and *in vitro* hypoglycemic effects of various carrot insoluble fiber-rich fractions. *Lebensmittel-Wissenschaft and Technologie (LWT)*, **37**: 155–160.

Christensen, J. H., Korup, E., Aaroe, J., Toft, E., Moller, J., *et al*. (1997). Fish consumption, n-3 fatty acids in cell membranes, and heart rate variability in survivors of myocardial infraction with left ventricular dysfunction. *American Journal of Cardiology*, **79**: 1670–1673.

Del Valle, M., Cámara, M. and Torija, M.E. (2006) Chemical characterization of tomato pomace. *Journal of the Science of Food and Agriculture*, **86**(8): 1232–1236.

Deng, Q., Penner, M.H. and Zhao, Y. (2011) Chemical composition of dietary fiber and polyphenols of five different varieties of wine grape pomace skins. *Food Research International*, **44**(9): 2712–2720.

Dilas, S., Canadanovic-Brunet, J. and Cetkovic, G. (2009) By-products of fruits processing as a source of phytochemicals. *Chemical Industry and Chemical Engineering Quarterly*, **15**(4): 191–202.

Djabourov, M., Lechaire, J.P. and Gaill, F. (1993) Structure and rheology of gelatin and collagen gels. *Biorheology*, **30**: 191–205.

Donadio, J. V. Jr., Bergstrahl, E.J. and Offord, K.P. (1994) A controlled trial of fish oil in IgA nephropathy. *New England Journal of Medicine*, **331**: 1194–1199.

Du, J., Tan, E., Kim, H.J., Zhang, A., Bhattacharya, R. and Yarema, K.J. (2014) Carbohydrate polymers. Comparative evaluation of chitosan, cellulose acetate, and polyethersulfone nanofiber scaffolds for neural differentiation. *Carbohydrate Polymers*, **99**: 483–490.

Femenia, A., Lefebvre, A.C., Thebaudin, J.Y., Robertson, J.A. and Bourgeois, C.M. (1997) Physical and sensory properties of model foods supplemented with cauliflower fiber. *Journal of Food Science*, **62**(4): 635–639.

Femenia, A., Robertson, J.A., Waldron, K.W. and Selvendran, R.R. (1998) Cauliflower (*Brassica oleracea L*), globe artichoke (*Cynara scolymus*) and chicory witloof (*Cichorium intybus*) processing by-products as sources of dietary fiber. *Journal of the Science of Food and Agriculture*, **77**(4): 511–518.

Fernández-López, J., Fernández-Ginés, J.M., Aleson-Carbonell, L., Sendra, E., Sayas-Barberá, E. and Pérez-Alvarez, J.A. (2004) Application of functional citrus by-products to meat products. *Trends in Food Science and Technology*, **15**(3): 176–185.

Ferraro, V., Cruz, I.B., Jorge, R.F., Malcata, F.X., Pintado, M.E. and Castro, P.M.L. (2010) Valorisation of natural extracts from marine source focused on marine by-products: A review. *Food Research International*, **43**: 2221–2233.

Fouchereau-Peron, M., Duvail, L., Michel, C., Gildberg, A., Batista, I. and Gal, Y.I. (1999) Isolation of an acid fraction from a fish protein hydrolysate with a calcitonin–gene-related-peptide-like biological activity. *Biotechnology and Applied Biochemistry*, **29**: 87–92.

Galanakis, C.M. (2012) Recovery of high added-value components from food wastes: Conventional, emerging technologies and commercialized applications. *Trends in Food Science and Technology*, **26**(2): 68–87.

García, Y.D., Valles, B S. and Lobo, A.P. (2009) Phenolic and antioxidant composition of by-products from the cider industry: Apple pomace. *Food Chemistry*, **117**(4): 731–738.

Ghatak, H.R. (2011) Biorefineries from the perspective of sustainability: Feedstocks, products, and processes. *Renewable and Sustainable Energy Reviews*, **15**(8): 4042–4052.

Gildberg, A., Bogwald, J., Johansen, A. and Stenberg, E. (1996) Isolation of acid peptide fractions from a fish protein hydrolysate with strong stimulatory effect on Atlantic salmon (*Salmo salar*) head kidney leucocytes. *Comparative Biochemistry and Physiology*, **11**: 97–101

Gogos, C.A., Ginopoulos, P., Salsa, B., Apostolidou, E., Zoumbos, N.C. and Kalfarentzos, F. (1998) Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy. *Cancer*, **82**: 395–402.

Gomez-Gillen, M.C., Turnay, J., Fernandez-Diaz, M.D., Ulmo, N., Lizarbe, M.A. and Montero, P. (2002) Structural and physical properties of gelatin extracted from different marine species: A comparative study. *Food Hydrocolloids*, **16**: 25–34.

Gonçalves, E.M., Pinheiro, J., Abreu, M., Brandão, T.R.S. and Silva, C.L. (2010) Carrot (*Daucus carota L.*) peroxidase inactivation, phenolic content and physical changes kinetics due to blanching. *Journal of Food Engineering*, **97**(4): 574–581.

González-Molina, E., Domínguez-Perles, R., Moreno, D.A. and García-Viguera, C. (2010) Natural bioactive compounds of Citrus limon for food and health. *Journal of Pharmaceutical and Biomedical Analysis*, **51**(2): 327–345.

Gorinstein, S., Martín-Belloso, O., Park, Y.S., Haruenkit, R., Lojek, A., Ĉíž, M. and Trakhtenberg, S. (2001) Comparison of some biochemical characteristics of different citrus fruits. *Food Chemistry*, **74**(3): 309–315.

Goy, R.C., de Britto, D. and Assis, O.B.G. (2009) A review of the antimicrobial activity of chitosan. *Polimeros*, **19**: 241–247

Griffiths, G., Trueman, L., Crowther, T., Thomas, B. and Smith, B. (2002) Onions – A global benefit to health. *Phytotherapy Research*, **16**(7): 603–615.

Hamed, I., Ozogul, F. and Regenstein, J.M. (2016) Industrial applications of crustacean by-products (chitin, chitosan and chitooligosaccharides): A review. *Trends in Food Science and Technology*, **48**: 40–50.

Huber, G.M., and Rupasinghe, H.P.V. (2009) Phenolic profiles and antioxidant properties of apple skin extracts. *Journal of Food Science*, **74**(9): C693–C700.

Hwang, J.K., Kim, C.J. and Kim, C.T. (1998) Extrusion of apple pomace facilitates pectin extraction. *Journal of Food Science*, **63**(5): 841–844.

Jaime, L., Mollá, E., Fernández, A., Martín-Cabrejas, M.A., López-Andréu, F.J. and Esteban, R.M. (2002) Structural carbohydrate differences and potential source of dietary fiber of onion (*Allium cepa L.*) tissues. *Journal of Agricultural and Food Chemistry*, **50**(1): 122–128.

Jayathilakan, K., Sultana, K., Radhakrishna, K. and Bawa, A.S. (2012) Utilization of by-products and waste materials from meat, poultry and fish processing industries: A review. *Journal of Food Science Technology*, **49**(3): 278–293.

Kamm, B. and Kamm, M. (2004) Principles of biorefineries. *Applied Microbiology and Biotechnology*, **64**(2): 137–145.

Kammerer, D. R., Schieber, A. and Carle, R. (2005) Characterization and recovery of phenolic compounds from grape pomace: A review. *Journal of Applied Botany and Food Quality*, **79**(3): 189–196.

Kandra, P., Challa, M.M. and Jyothi, H.K.P. (2012) Efficient use of shrimp waste: Present and future trends. *Applied Microbiology Biotechnology*, **93**: 17–29.

Karim, A.A. and Bath, R. (2009) Fish gelatin: Properties, challenges and prospects as an alternative to mammalian gelatin. *Food Hydrocolloids*, **23**: 563−576.

Kim, I.Y., Seo, S.J., Moon, H.S., Yoo, M.K., Park, I.K. *et al*. (2008) Chitosan and its derivatives for tissue engineering applications. *Biotechnology Advances*, **26**: 1−21.

Kim, S. and Mendis, E. (2006) Bioactive compounds from marine processing byproducts: A review. *Food Research International*, **39**: 383–393

Kim, S.K., Byun, H.G. and Lee, E.H. (1994) Optimum extraction conditions of gelatin from fish skins and its physical properties. *Journal of Korean Industrial and Engineering Chemistry*, **5**: 547–559.

Kim, S.K., Choi, Y.R., Park, P.J., Choi, J.H. and Moon, S.H. (2000) Screening of biofunctional peptides from cod processing wastes. *Journal of the Korean Society of Agricultural Chemistry and Biotechnology*, **43**: 225–227.

Kingóri, A. M. (2011) A review of the uses of poultry eggshells and shell membranes. *International Journal of Poultry Science*, **10**(11): 908–912.

Kosseva, M.R. (2011) Wastes from agriculture, forestry and food processing: Management and processing of food wastes. In: *Comprehensive Biotechnology*, 2nd edition (ed. M. Moo-Young), vol. **6**, Elsevier, Spain, pp. 557–593.

Kurita, K. (2006) Chitin and chitosan: Functional biopolymers from marine crustaceans. *Marine Biotechnology*, **8**: 203–226.

Lafarga, T. and Hayes, M. (2014) Bioactive peptides from meat muscle and by-products: Generation, functionality and application as functional ingredients. *Meat Science*, **9**: 227–239.

Lanzotti, V. (2006) The analysis of onion and garlic. *Journal of Chromatography A*, **1112**(1–2): 3–22.

Lario, Y., Sendra, E., Garcí, J., Fuentes, C., Sayas-Barberá, E. *et al*. (2004) Preparation of high dietary fiber powder from lemon juice by-products. *Innovative Food Science and Emerging Technologies*, **5**(1): 113–117.

Lasekan, A., Bakar, F.A. and Hashim, D. (2013) Potential of chicken by-products as sources of useful biological resources. *Waste Management*, **33**: 552–565.

Lee, H.C., Singla, A. and Lee, Y. (2001) Biomedical applications of collagen. *International Journal of Pharmaceutics*, **221**: 1–22.

Liu, Q., Tarn, R., Lynch, D. and Skjodt, N.M. (2007) Physicochemical properties of dry matter and starch from potatoes grown in Canada. *Food Chemistry*, **105**(3): 897–907.

Llorach, R., Espín, J.C., Tomás-Barberán, F.A. and Ferreres, F. (2003) Valorization of cauliflower (*Brassica oleracea L. var. botrytis*) by-products as a source of antioxidant phenolics. *Journal of Agricultural and Food Chemistry*, **51**(8): 2181–2187.

Lozano-Sánchez, J., Giambanelli, E., Quirantes-Piné, R., Cerretani, L., Bendini, A. *et al*. (2011) Wastes generated during the storage of extra virgin olive oil as a natural source of phenolic compounds. *Journal of Agricultural and Food Chemistry*, **59**(21): 11491–11500.

Mahro, B. and Timm, M. (2007) Potential of biowaste from the food industry as a biomass resource. *Engineering in Life Sciences*, **7**(5): 457–468.

Maier, T., Schieber, A., Kammerer, D.R. and Carle, R. (2009) Residues of grape (*Vitis vinifera L.*) seed oil production as a valuable source of phenolic antioxidants. *Food Chemistry*, **112**(3): 551–559.

Masibo, M. and He, Q. (2008) Major mango polyphenols and their potential significance to human health. *Comprehensive Reviews in Food Science and Food Safety*, **7**(4): 309–319.

Mattila, P. and Hellström, J. (2007) Phenolic acids in potatoes, vegetables, and some of their products. *Journal of Food Composition and Analysis*, **20**(3): 152–160.

Merzendorfer, H. (2011) Chitin. In: *The Sugar Code: Fundamentals of Glycosciences* (ed. H.J. Gabius). John Wiley & Sons, Weinheim, Germany, p. 597.

Meyers, M.A., Chen, Po.-Yu., Yu-Min Lin, A. and Seki, Y. (2008) Biological materials: Structure and mechanical properties. *Progress in Materials Science*, **53**: 1−206.

Mirabella, N., Castellani, V. and Sala, S. (2014) Current options for the valorization of food manufacturing waste: a review. *Journal of Cleaner Production*, **65**: 28–41.

Mishra, J., Biswas, S., Sarangi, N.R., Mishra, R.P., Kumar, N. and Mishra, C. (2015) Efficient utilization of poultry by-products for economic sustainability – The need of the hour. *International Journal of Livestock Research*, **5**(10): 1–9.

Misi, S.N. and Forster, C.F. (2002) Semi-continuous anaerobic co-digestion of agro-wastes. *Environmental Technology*, **23**(4): 445–451.

Mora, L., Reig, M. and Toldra, F. (2014) Bioactive peptides generated from meat industry by-products. *Food Research International*, **65**: 344–349.

Moskowitz, R.W. (2000) Role of collagen hydrolysate in bone and joint disease. *Seminars in Arthritis Rheumatism*, **30**: 87–99.

Ng, A., Parker, M.L., Parr, A.J., Saunders, P.K., Smith, A.C. and Waldron, K.W. (2000) Physicochemical characteristics of onion (*Allium cepa L.*) tissues. *Journal of Agricultural and Food Chemistry*, **48**(11): 5612–5617.

Olsen, R.L., Toppe, J. and Karunasagar, I. (2014) Challenges and realistic opportunities in the use of by-products from processing of fish and shellfish. *Trends in Food Science and Technology* **36**: 144–151.

Park, K.J. and Hyun, C.K. (2002) Antigenotoxic effects of the peptides derived from bovine blood plasma proteins. *Enzymes and Microbial Technology*, **30**: 633–638.

Pihlanto, A. and Korhonen, H. (2003) Bioactive peptides and proteins. In: *Advanced Food Nutrition Research* (ed. S.L. Taylor). Elsevier Inc, San Diego, US, pp. 175–276.

Pott, I., Breithaupt, D.E. and Carle, R. (2003) Detection of unusual carotenoid esters in fresh mango (*Mangifera indica* L. cv. 'Kent'). *Phytochemistry*, **64**(4): 825–829.

Rahman, U., Sahar, A. and Khan, M.A. (2014) Recovery and utilization of effluents from meat processing industries. *Food Research International*, **65**: 322–328.

Rajapakse, N., Jung, W.K., Mendis, E., Moon, S.H. and Kim, S.K. (2005) A novel anticoagulant purified from fish protein hydrolysates inhibits factor XIIa and platelet aggregation. *Life Sciences*, **76** : 2607–2619.

Ramos, P., Santos, S.A., Guerra, Â.R., Guerreiro, O., Felício, L. *et al*. (2013) Valorization of olive mill residues: Antioxidant and breast cancer antiproliferative activities of hydroxytyrosol-rich extracts derived from olive oil by-products. *Industrial Crops and Products*, **46**: 359–368.

Rao, K.P. (1995) Recent developments of collagen-based materials for medical applications and drug delivery systems. *Journal of Biomaterials Science Polymer Edition*, **7**(7): 623–645.

Regulation (EC) No. 1069/2009 of the European Parliament and of the Council of 21 October 2009. Laying down health rules as regards animal by-products and derived products not intended for human consumption and repealing Regulation (EC) No 1774/2002 (Animal by-product Regulation) [2009] OJEU L300/1.

Revathi, M., Saravanan, R. and Shanmugam, A. (2012) Production and characterization of chitinase from Vibrio species, a head waste of shrimp *Metapenaeus dobsonii* (Miers, 1878) and chitin of *Sepiella inermis* (Orbigny, 1848). *Advances in Bioscience and Biotechnology*, **3**: 392–397.

Rha, H.J., Bae, I.Y., Lee, S., Yoo, S.H., Chang, P.S. and Lee, H.G. (2011) Enhancement of anti-radical activity of pectin from apple pomace by hydroxamation. *Food Hydrocolloids*, **25**(3): 545–548.

Rivera, J.A., Sebranek, J.G., Rust, R.E. and Tabatabai, L.B. (2000) Composition and protein fractions of different meat by-products used for pet food compared with mechanically separated chicken (MSC). *Meat Science*, **55**(1): 53–59.

Rosentrater, K.A. (2005) Strategic methodology for advancing food manufacturing waste management paradigms. *International Journal of Environmentally Conscious Design and Manufacturing*, **13**(1): 1–13.

Royer, G., Madieta, E., Symoneaux, R. and Jourjon, F. (2006) Preliminary study of the production of apple pomace and quince jelly. *LWT – Food Science and Technology*, **39**(9): 1022–1025.

Ruberto, G., Renda, A., Daquino, C., Amico, V., Spatafora, C. *et al*. (2007) Polyphenol constituents and antioxidant activity of grape pomace extracts from five Sicilian red grape cultivars. *Food Chemistry*, **100**(1): 203–210.

Rustad, T., Storro, I. and Slizyte, R. (2011) Possibilities for the utilisation of marine by-products. *International Journal of Food Science and Technology*, **46**: 2001–2014.

Saddler, J.M. and Horsey, P.J. (1987) The new generation gelatins. A review of their history, manufacture and properties. *Anesthesia*, **42**: 998–1004.

Salah, R., Michaud, P., Mati, F., Harrat, Z., Lounici, H., *et al*. (2013) Anticancer activity of chemically prepared shrimp low molecular weight chitin evaluation with the human monocyte leukaemia cell line, THP-1. *International Journal of Biological Macromolecules*, **52**: 333–339.

Sato, H., Kitazawa, H., Adachi, I. and Horikoshi, I. (1996) Microdialysis assessment of microfibrous collagen containing a p-glycoprotein mediated transport inhibitor, cyclosporine A, for local delivery of etopocide. *Pharmacological Research*, **13**: 1565–1569.

Schacky, C.V. (2000) n-3 fatty acids and the prevention of coronary atherosclerosis. *American Journal of Clinical Nutrition*, **71**: 224–227.

Schieber, A., Stintzing, F.C. and Carle, R. (2001) By-products of plant food processing as a source of functional compounds: Recent developments. *Trends in Food Science and Technology*, **12**(11): 401–413.

Schieber, A., Hilt, P., Streker, P., Endress, H. U., Rentschler, C. and Carle, R. (2003) A new process for the combined recovery of pectin and phenolic compounds from apple pomace. *Innovative Food Science and Emerging Technologies*, **4**(1): 99–107.

Shahar, E., Folsom, A.R., Melnick, S.L., Tockman, M.S., Comstock, G.W., *et al*. (1994) Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease. *New England Journal of Medicine*, **331**: 228–233.

Shalini, R. and Gupta, D. K. (2010) Utilization of pomace from apple processing industries: A review. *Journal of Food Science and Technology*, **47**(4): 365–371.

Sheehan, J. P., Wei, I. W., Ulchaker, M. and Tserng, K.Y. (1997) Effect of high fiber intake in fish oil-treated patients with non-insulin-dependent diabetes mellitus. *American Journal of Clinical Nutrition*, **66**: 1183–1187.

Silvipriya, K.S., Kumar, K.K., Bhat, A.R., Kumar, B.D., John, A. and Lakshmanan, P. (2015) Collagen: Animal sources and biomedical application. *Journal of Applied Pharmaceutical Science*, **5**(3)*:* 123–127.

Spatafora, C. and Tringali, C. (2012) Valorization of vegetable waste: Identification of bioactive compounds and their chemo-enzymatic optimization. *The Open Agriculture Journal*, **6**(1): 9–16.

Takeshi, N. and Suzuki, N. (2000) Isolation of collagen from fish waste material – Skin, bone and fins. *Food Chemistry*, **68**: 277–281.

Telrandhe, U.B., Kurmi, R., Uplanchiwar, V., Mansoori, M.H., Jain, V., *et al*. (2012) Nutraceutical – A phenomenal resource in modern medicine. *International Journal of Universal Pharmacy and Life Sciences*, **2**(1): 179–195.

Toldra, F., Aristoy, M.C., Mora, L. and Reig, M. (2012) Innovations in value-addition of edible meat by-products. *Meat Science*, **92**: 290–296.

Upadhyay, A., Chompoo, J., Araki, N. and Tawata, S. (2012) Antioxidant, antimicrobial, 15-LOX, and AGEs inhibitions by pineapple stem waste. *Journal of Food Science*, **77**(1): H9–H15.

Viuda-Martos, M., Fernandez-Lopez, J., Sayas-Barbera, E., Sendra, E. and Perez-Alvarez, J.A. (2011) Physicochemical characterization of the orange juice waste water of a citrus by-product. *Journal of Food Processing and Preservation*, **35**: 264–271.

Wilson, J., Hayes, M. and Carney, B. (2011) Angiotensin-I-converting enzyme and prolyl endopeptidase inhibitory peptides from natural sources with a focus on marine processing by-products. *Food Chemistry*, **129**(2): 235–244.

Wismer-Pedersen, J. (1988) Use of haemoglobin in foods: A review. *Meat Science*, **24**: 31–45.

Young, S., Wong, M., Tabata, Y. and Mikos, A.G. (2005) Gelatin as a delivery vehicle for the controlled release of bioactive molecule. *Journal of Controlled Release*, **109**: 256–274.

Yu, P. L., van der Linden, D.S., Sugiarto, H. and Anderson, R.C. (2010) Antimicrobial peptides isolated from the blood of farm animals. *Animal Production Science*, **50***:* 660–669.

Yu, Y., Hu, J., Miyaguchi, Y., Bai, X., Du, Y. and Lin, B. (2006) Isolation and characterization of angiotensin I-converting enzyme inhibitory peptides derived from porcine hemoglobin. *Peptides*, **27**: 2950–2956.

Zhao, Q., Garreau, I., Sannier, F. and Piot, J.M. (1997) Opioid peptides derived from hemoglobin: Hemorphins. *Biopolymers*, **43**: 75–98.

Queries in Chapter 5

Q1 Please confirm if the shortened running head is correct.