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Review Article

Oils and Fats-Largely Unexplored Source of Nutraceuticals

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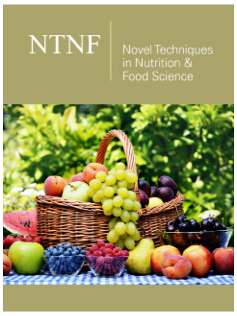

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Abstract

Nutraceutical is a term derived from two words, “nutrition” and “pharmaceutical”. This particular group of food derived products shows various health benefits. These products are being used in the treatment of cancer, arthritis, osteoporosis, cardiovascular diseases, retinopathy, age-related problems and many more physiological and neurological disorders. In the post-COVID-19 scenario the whole world is looking for natural product-based treatment methods and immunity boosting products to improve the general wellness of people. Oils and fats are known as the category of food that supply more than double the energy compared to proteins and carbohydrates. It also gives texture and palatability of foods and enhances the taste of foods by providing characteristic flavour. It also supplies essential fatty acids that human body cannot generate on its own. The polyunsaturated fatty acids (PUFA) present in oils and fats regulate metabolic functions. Another well-known benefit of consumption of oils and fats in food servings is that it supplies the oil-soluble vitamins A, D, E, and K. Deficiencies of these vitamins can have a tremendous effect on the general health of a person. Triglycerides or triacylglycerols are the primary components of oils and fats. However, there are some minor components of oils and fats that show health benefits and can be used for the treatment of various diseases. A good processor tries to keep all these nutraceuticals and nutritionally important components intact in the refined oils and fats products to improve the quality of the oils. However, many of these important components get lost during the refining of oils and fats. Nutraceuticals like lecithin, carotenoids, isoflavones, phytosterol, steryl esters, tocopherols, etc. get concentrated in various by-products of oils and fats processing. Apart from few exceptions, most of these nutraceuticals are not recovered or utilized. There exists a huge scope to isolate these nutraceuticals and explore the health benefits for treatment of various diseases. In this article, the importance of these nutraceuticals that are derived from oils and fats will be discussed.

Keywords: Nutraceuticals; Oils and fats; Essential fatty acids; Tocols; Lecithin; Phytosterols

Introduction

Fats and oils are an integral part of our human diet. Apart from giving double the energy per unit weight compared to proteins and carbohydrates, this particular component of food serves many other functionalities. It provides pleasure to taste buds; and also serves the essential fatty acids which cannot be synthesized in human bodies. These fatty acids take an active role in metabolism and have a huge impact on general health and more importantly in controlling cardiovascular diseases. Oils and fats also supply oil-soluble vitamins like vitamins A, D, E and K. However, it is often forgotten that oils and fats are sources of many minor constituents that show health benefits and in many cases; they are used for the treatment of specific diseases. These compounds are known as nutraceuticals. Stephen L. DeFelice, the then chairman of Foundation for innovation in medicine framed the word “nutraceuticals” by combining the words “nutrition” and “pharmaceuticals”. He had proposed a definition for the term nutraceuticals. As per De Felie, nutraceutical is “….a nutritional product- a single entity or combination which includes special diets- that reasonable clinical evidences have shown to have medical benefit”….[1]. Pharmaceutical formulations are required to cure the patient of specific ailments on the other hand nutrition is required for good general health to be maintained.

The Canadian health ministry later broadened the definition of nutraceuticals. According to that definition, nutraceuticals are products isolated or purified from different food items that show specific physiological benefits and can exhibit protection against known diseases

[2]. These are not exactly taken as food products and are generally available as medicinal products. There are certain advantages of these products. For any specific disease, the pharmaceuticals are the primary medicines and those are mostly synthetically prepared drugs. They are governed by very strict regulatory restrictions [3]. It becomes highly expensive affair to bring a new drug for a specific disease by meeting all these regulations. Some of the drugs show inherent toxicities and have severe side effects. Scientists all over the world were looking forward to finding out some alternatives to these synthetic drugs. Nutraceuticals can have a very important role as they have the proven track record for showing health benefits. Moreover, since they are derived from food items, they are exempted from usual stringent regulations implied for pharmaceutical products [4].

It was estimated that in 2019, the nutraceutical ingredient market was around 152 billion USD whereas it was predicted to grow at 7% per annum to reach 225 billion USD by 2025 [5]. The demand in developed nations has already reached a high. The forecast predicts the demand in US Market alone will be around 134billion USD by 2025 [6]. In Europe, the nutraceutical market will see a CAGR of around 7.5% because of the increased occurrence of lifestyle-related diseases. People became more aware and are regularly taking nutraceuticals for the prevention or delaying of diseases [7]. Developing nations are also catching up and the Asia Pacific is going to be the largest growing region as far as nutraceutical business is concerned [5].

In the post-COVID-19 scenario, the nutraceutical market is expected to see further growth as many of these ingredients are known for their antioxidant activities, immunity-boosting properties, controlling serum cholesterol levels and maintaining overall wellness. These nutraceuticals are also known for their efficacies in either treating or delaying many diseases like cancer, metabolic disorders, osteoarthritis, eye problem, cardiovascular diseases, brain-related problems, Alzheimer's disease, etc. [4,6]. The whole world is looking for newer sources of nutraceuticals as the demand is growing very fast.

There was a negative vibe about oils and fats as these are linked to obesity and many other diseases. However, as mentioned earlier only oils and fats supply essential fatty acids and fat-soluble vitamins apart from making the food tastier and healthier. Omega-3 fatty acids like eicosapentaenoic acid (EPA), docosahexaenoic acids (DHA) and other polyunsaturated fatty acids (PUFA) are known for their beneficial effects on heart diseases, mental health, brain diseases, eye problems and many degenerative disorders [8]. The major sources of these fatty acids are fish oil, seal blubber oil, borage oil, evening primrose oil, blackcurrant oil, etc. Coconut oil is again the source of medium-chain triglycerides (MCT) and these are approved as GRAS for oral or external use [9]. MCT was used for the treatment of malabsorption [10]. Apart from dietary fatty acids, oils and fats contain many other minor constituents that exhibit health benefits. One of the most important nutraceuticals is tocopherol and tocotrienols. Tocopherols commonly known as vitamin E and act as antioxidants has many applications [11]. Most of the vegetable oils contain tocopherols whereas oils like palm and rice bran contain tocotrienols [12-14]. Oils like soybean, rice bran, sunflower, rapeseed, etc. are major sources of phospholipids. They are widely used in pharmaceutical formulations as excipients [15]. Phosphatidylcholine (PC) and phosphatidylserine (PS) are essential for the proper functioning of cell membranes and some derivatives are known for their use even in cancer treatment [16,17].

Oils and fats are the sources of another very important group of nutraceuticals known as phytosterols and stanols. These show antioxidant properties and they are known to lower serum cholesterol levels [18,19]. Rice bran oil contains γ-oryzanol. This is a group of compounds that have properties to lower serum cholesterol levels [20] and have many other health benefits. Oils like rice bran oil, olive oil, wheat germ oil, palm oil contain hydrocarbon squalene that exhibits various health benefits and have wide use in many pharmaceutical formulations. Shark liver oil is also an important source of squalene. It was projected to have anti-cancer properties [21]. Isoflavones are another group of nutraceuticals present primarily in soybean oil. These are projected to have health benefits against heart diseases, age-related problems, hormone-induced cancer, osteoporosis, etc. [22]. Carotenoids, more specifically β-carotene act as precursor of vitamin A, which is an important factor for treatment of eyes particularly against night blindness [23]. Various lignans present in oils like sesame are found to reduce oxidative stress in rats [24] and also found to act as metabolic regulators and having anti-mutagenic properties [25]. There are some other oils and fat derived nutraceuticals like glycolipids, gallic acid, ellaigic acid, policosanols, etc. which show numerous health benefits and can be used for the treatment of specific diseases. In this review, primarily, the occurrence of these nutraceuticals in various types of oils and fats and their health implications will be discussed.

Polyunsaturated fatty acids (PUFA) and Essential Fatty Acids (EFA)

Oils and fats are having a triglyceride structure where three molecules of fatty acids (FA) are esterified to a glycerol backbone. Presence of different types of fatty acids gives rise to various kinds of oils. The fatty acid composition is of utmost importance when evaluating the importance of the oil for nutraceutical applications. Fatty acids can be of basically three types:

1) Saturated fatty acids (SAFA) with no unsaturation,

2) Monounsaturated fatty acids with single unsaturation (MUFA) and

3) Fatty acids with more than one unsaturation or poly unsaturated fatty acids (PUFA) [4]. It is this PUFA that is of prime interest when it comes to an application as a nutraceutical.

Several research communications reported that PUFA is effective against coronary artery disease as well as nerve diseases like Alzheimer's, schizophrenia and metabolic syndrome [26-29]. PUFA is further sub-divided based on the location of the first double bond with respect to the methyl end. n-3 and n-6 fatty acids are the two most important PUFA when it comes to the biological application [30]. Amongst the several PUFA available only two are known to be essential fatty acid (EFA). ω-6 fatty acid Linoleic acid (LA) and ω-3 fatty acid α-linolenic acid (ALA), are considered essential fatty acids because they cannot be synthesized by the human body. Some other fatty acids like Gamma Linolenic Acid (GLA) or EPA/DHA are also considered to be essential in various developmental or disease conditions.

Linoleic acid is a popular fatty acid found in many plant oils like safflower (60-75%), sesame (40-50%) sunflower (60-68%), cottonseed (42-52%), soybean (43-56%), poppy (70-72%), hemp (54-56%), walnut (50-53%) and corn (34-62%) oils. Alpha-linolenic acid on the other hand is abundantly available in oils like flaxseed oil (35-55%), hemp (15-25%), canola (9-11%), soybean (6-8%) etc. [16].

Linoleic acid is labeled as an essential fatty acid as it cannot be synthesized by our body but is necessary for the normal functioning of biological and physiological activities. Linoleic acid plays an important role in various body functions such as cell physiology, immunity and reproduction. In spite of being able to reduce serum cholesterol, one clinical trial reported that a high linoleic acid rich diet has been reported to have some effect as a promoter of cancer tumors in the human cell [31] especially breast, colon, and prostate. To date, no upper limit has been set for the intake of linoleic acid [32], however, intake that supplies 1-2% of energy is recommended [33].

Dietary alpha- linolenic acid (ω-3) has been reported to have a significant positive role in areas of high blood cholesterol, high blood pressure, etc. It helps strengthen the immune system function, reduces male infertility and also gives protection against cancer. Consumption of alpha- linolenic acid (2 to 3g per day) [34] helps maintain good heart and metabolism. It is also helpful in reduction of plaque calcification, reducing lipid content, proper maintenance of endothelial function and has effective antithrombotic functions. It also exhibits anti-arrhythmic and antiinflammatory effects. Alpha-linolenic acid thus protects the human body against cardiovascular risks [35].

Though both linoleic acid and alpha- linolenic acid exhibit excellent health effects, a balanced intake of the same is very important. A ratio of 0.3:1: linoleic acid: alpha- linolenic acid is important for proper physiological functioning [16]. Both linoleic acid and alpha-linolenic acid are been bio-converted to other important fatty acids required by our body including arachidonic acid (AA), gamma-linolenic acid (GLA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Gamma-linolenic acid

GLA is the first bio-converted product formed from linoleic acid by the delta-6 desaturase (D6D) enzyme. Naturally, gamma-linolenic acid is found in oils like evening primrose (8-12%) and hempseed (6-8%), Borage oil (25%), black current seed oil, etc. [36]. Upon consumption, gamma-linolenic acid is converted into dihomo-ϒ-linoleic acid (DGLA; 20:3, n-6) in the human body. This DGLA is particularly important as it is a precursor to prostaglandin PGE1 and 15-OH-DGLA- two important anti-inflammatory metabolites [16]. A dosage of 1.4g/day of GLA has been reported to provide statistically significant improvements in pains like rheumatoid arthritis [37]. Gamma-linolenic acid when metabolized to DGLA reduces inflammation via competitive inhibition of leukotrienes and 2-series prostaglandins. It is also reported to work against atopic eczema, psoriasis, and premenstrual syndrome [38].

DGLA is further converted to arachidonic acid enzymatically. Once converted arachidonic acid is mostly incorporated in the phospholipid moiety of the cell membrane and brain membrane [39]. Along with being effective for inflammation, arachidonic acid is also recommended for pregnant ladies, babies and adults in limited dosage as it showed promising results against intestinal and blood flukes, maintains cell membrane fluidity and helps control ion channels [40].

EPA and DHA

EPA and DHA are formed from the precursor molecule of alpha-linolenic acid. These two fatty acids are extremely important fatty acids for the normal functioning of the human body. However, they are not synthesized in the human body (or even if then in a small amount) and needs to be supplemented [41]. They are mostly found in marine oil such as salmon, fresh tuna, mackerel, and herring as well as certain microbial oils like algal oil.

These fatty acids are present in various body parts including the cell membranes [42] and have been reported to play important role anti-inflammatory agents, as well as help maintain the viscosity of cell membranes [43,44]. Foetal development, health, and growth is highly influenced by EPA and DHA [45]. Proper brain functioning and retina health are dependent largely on DHA [46]. Several potent lipid mediators important for treatment of memory diseases like Alzheimer's, Parkinson's have been reported to develop from EPA, DHA, making them an inevitable food for the body [47].

Conjugated linoleic acid

Comprising of a family of 28 isomers of linoleic acid [48] Conjugated linoleic acid has two isomers which are found most abundantly as found- cis-9, trans-11 and trans-10, cis-12 isomers [48]. CLA is particularly an important nutraceutical as it has a significant role to play in lipid metabolism in association with inhibition of the entry of glucose in adipose tissues leading to changes in insulin metabolism [49]. In spite of being a trans-fatty acid, CLA has been given a generally recognized as safe (GRAS) status as it is a naturally occurring trans-fatty acid. Also, owing to its effectiveness in preventing cancer and heart diseases, improving immune function and above-mentioned lipid metabolism [50] intake of CLA is recommended highly.

Medium chain triglycerides

Medium-chain triglyceride (MCT) has a glycerol backbone where the -OH groups are esterified with at least two fatty acids having 6-12 carbon atoms. MCT is present in large quantities in coconut oil and palm kernel oil. It is expected that MCT will be broken easily into glycerol and MCFAs and will be directly absorbed into the blood stream [51]. Because of enhanced energy utilization, MCT is reported to cause weight loss [52,53]. Medium-chain fatty acids have more solubility in water than long-chain fatty acids. It is believed that they easily get solubilized in aqueous intestinal fluid and hence get adsorbed faster [54]. Bray et al. [55] suggested that rats given diets containing MCT have more control over food consumption compared to those fed with food having (LCT) [55]. Similar effects were observed even in human beings [56]. It was also observed that MCT has a significant effect on muscle building and muscle strength [57]. It is also claimed that MCT enriched diets have a significant role in controlling diabetes [58]. Researchers have claimed to have beneficial effects for lowering total cholesterol and for regulating age-related problems. However, these claims are to be validated with more significant statistical data.

Vitamin E- tocopherol and tocotrienol

Vitamin E consists of primarily eight isomers of tocopherol and tocotrienol. These are combinedly known as tocols. Most of the vegetable oils contain tocopherols and oils like palm and rice bran contain tocotrienols. These are known as potential antioxidants (Figure 1).

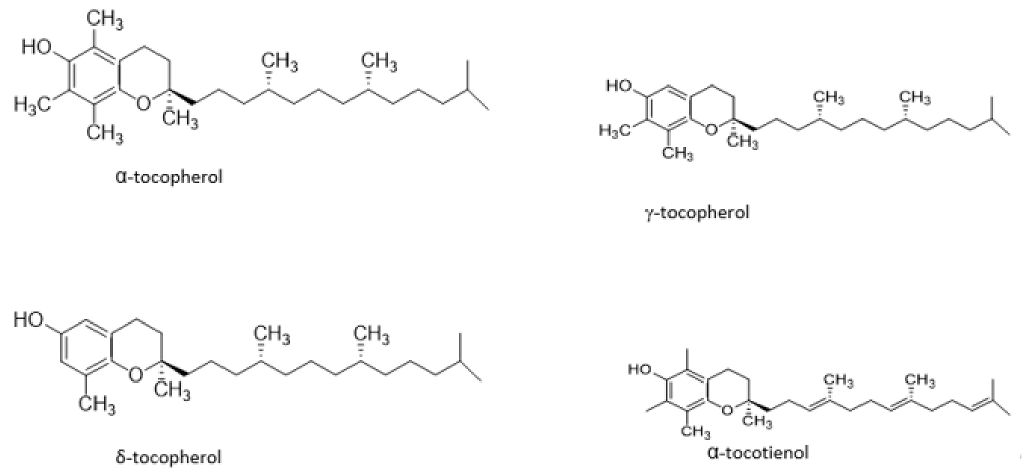

Figure 1: Major types of tocopherols and tocotrienols.

Alpha-tocopherol is the predominant variety of tocol in oil like sunflower, olive, groundnut, etc. [59-61]. On the other hand, oils like soybean, canola, corn, linseed, etc. contain more amount of gamma-tocopherol [62,63]. The major sources of tocotrienols are palm, rice bran, and annatto oil [64-66]. Palm oil was found to contain α, δ tocotrienols wherein α- tocotrienol is the predominant homologue [67]. The most important tocol rich oils are wheat germ oil, barley, and oat germ oil [68-70]. The health impact of vitamin E in the general wellness of the people is tremendous. Due to the deficiencies of Vitamin E, many health problems like anemia, neurological disorders, immunity-related problems, problems in retina, etc. occur [71]. However, these compounds have larger applications, and these are yet to be explored completely. Many studies revealed that the addition of tocopherols and tocotrienols have increased the oxidative stability and shelf life of many oils and fats [72,73]. These showed a synergistic effect with different types of phospholipids as far as antioxidant properties are concerned for oils containing higher amounts of polyunsaturated fatty acids [74]. The antioxidant properties were explored by food, pharmaceutical, and cosmetic industries [75,76]. Tocotrienol rich fractions also showed similar antioxidant properties and improved oxidative stabilities of various oils and food formulations [12].

Vitamin E helps in delaying or treating many age-related ailments [77]. Tocopherols break the free radical chain and protect the cell membranes [16]. Tocopherols and tocotrienols were found to have an important role in the treatment of Alzheimer's disease [78]. Tocotrienols showed a significant role in lowering the risk of cardiovascular diseases [79]. In recent times tocotrienols were utilized as anti-cancer agents. It has shown anti-angiogenic and anti-inflammatory effects and was projected as anti-tumor agents. It may have an important role in the treatment of breast cancer [79,80]. The combined effect of tocotrienol with statin in the treatment of cancer via chemotherapy is also reported. There are many more recent reports showing the potential of vitamin E in the treatment of various diseases, especially in cancer treatment. Different types of tocopherol and specifically tocotrienols are reported to have significant effects on colorectal, prostate, lung cancer. Wong-Weng-Yew and Brown discussed the possibility of use of tocopherol in an anti-obesity formulation [81]. The research is still at its infancy and there exists tremendous scope to improve the understanding of tocotrienol as an anti-cancer agent as well as anti-obesity agent. Tocols are commonly obtained from the deodorizer in a typical oil refining unit [82,83]. The bioavailability and stability of tocols are also important.

Phytosterols, steryl esters and phytostanols

Oils and fats are sources of another very important group of compounds called phytosterols and phytostanols. Phytosterols are structurally similar to cholesterol-the sterol of the mammalian cell. In phytosterol, the steroidal molecule has unsaturation at Δ-5 position whereas, in the case of stanols, it is saturated [84]. Most of the oils and fats contain phytosterols, steryl esters, and these are primarily isolated from deodorizer distillates along with many other nutritional components. Enzymatic methods were also developed to prepare steryl esters and stanyl esters [85]. The major advantage of these molecules lies in the fact that they are capable of lowering serum cholesterol levels in human beings [19,84]. Westen showed that probable mechanism of lowering of cholesterol level may be due to less absorption of cholesterol in small intestine [86,87]. β- sitosterols, campesterol, stigmasterol, Δ 5-avenasterols are the major phytosterols present in oils like flaxseed, soybean, rice bran olive, peanut, sesame, corn, rapeseed, etc. Rice bran oil has more amount of all these sterols compared to other oils [14,88]. Stanol esters are often derived from tall oil [89] by hydrogenating the phytosterols. Both phytosteryl esters and phytostanyl esters had shown similar cholesterol-lowering properties [90]. Law indicated that intake of 2g/day of phytosterol or phytostanol may reduce the risk of heart disease by around 25% [91]. There are many products available in the markets that are enriched in steryl and stanol esters from plant sources. Some second-generation products are also going to be marketed soon. One of the promising products is corn fiber oil.

Phospholipids (Lecithin)

Many oils and fats have phospholipids as an important component. Soybean oil contains around 2.5-3.5% of gums. Rice bran oil, sunflower oil, rapeseed oil, cottonseed oil and other resources like egg yolk, bovine whole milk, and fish oils contain good number of phospholipids. Lecithin is the general term given to the mixture of phospholipids isolated from oils and fats. Soybean is the predominant source of lecithin for food applications. Lecithin is used in food industries as natural emulsifier and has a market of around 1.5 to 1.7 lakh tons. Apart from getting the emulsifier properties, lecithin may also show antioxidant properties [92]; (Figure 2).

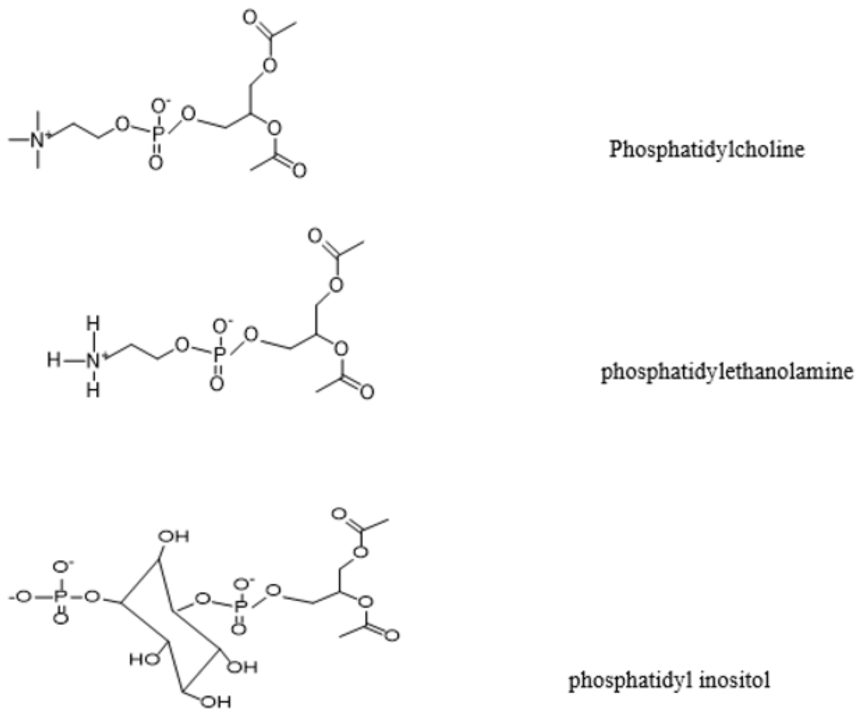

Figure 2: Major types of phospholipids.

Lecithin is prepared from crude gums obtained in the degumming process by using water/phosphoric acid whereas in the case of enzymatic degumming lysolecithin is formed as it hydrolyzes the lecithin and cleaves one fatty acid group from lecithin moiety and converts into a water-soluble product. Lecithin contains primarily four types of phospholipids like PC (Phosphatidylcholine), PE (phosphatidylethanolamine), PI (phosphatidylinositol), and PA (phosphatidic acid). Phosphatidylserine (PS) regulates the function of body cells and is available in the market as a memory enhancer [16]. The surface-active properties of lecithin due to the presence of hydrophilic and hydrophobic groups in single molecule made it useful as emulsifier, wetting agent, anti-spattering agent, etc. [92]. Apart from the industrial uses, phospholipid showed antioxidant properties also [93-95]. PC with some definite fatty acid profile has been projected for potential uses in various pharmaceutical formulations [96]. Phospholipid based vesicles or liposomes could also be used in the drug delivery system [97]. Some formulations showed specificity in delivering the drug [98]. Abnormal phospholipid metabolism is said to be associated with cancer and it has become an important area of research [99-101]. Lyso-PC was found to possess anti-cancer activities [17]. The research on phospholipids and their applications in health-related formulations is going on in full swing and newer uses are expected. This is one of the major by-products that is exploited considerably at least for soybean oil. Technologies are being developed for oils like rice bran.

Isoflavones

Isoflavones are another group of nutraceuticals present in oils and fats more specifically in soybean and legume seeds [102] like lentils, beans, etc. These particular groups of compounds are known as phytoestrogen as these are obtained from plant sources and resemble the chemical structures of 'estrogen' [103]. Soybean oil is the richest source of these group of isoflavones namely Genistein, Daidzein, Genistin, Glycitein, and glycitin, etc. [104]. These isoflavones are found to possess antioxidant properties [105], to improve cardiovascular health [106] and also delay osteoporosis [107,108]. Isoflavones are reported to have anti-inflammatory properties [109]. However, higher dosages may have a risk [110]. Formulations with natural isoflavones are available in the open market particularly for pre and postmenopausal women. However, most of the naturally occurring isoflavones are underutilized because of the non-availability of proper technology.

Lignans

Lignans are a class of polyphenolic compounds founds in various plants as secondary metabolites. Oilseeds like flaxseed, sesame, and pumpkin are the most abundant source of these lignans [111]. Flax is a rich source of a lignan called secoisolariciresinol diglycoside (SDG) (1-4%) [112] which is found mainly in the fat-free portion of flax [113]. SDG is converted to enterodiol (ED) and enterolactone (EL) by bacteria in the colon of humans. Additionally, Whitting [114] and Mazur et al. [115] reported the presence of minor amounts of other lignans like matairesinol (MAT) (11μg/g of full-fat flaxseed), pinoresinol, pinoresinol diglucoside, isolariciresinol, etc. [114,115].

Flaxseed lignans are reported to exhibit antioxidant activity, [116-119] and also act as estrogenic and anti-estrogenic compounds [120,121]. However, its role is dependent on body estradiol levels. Under normal conditions, flaxseed lignans act as estrogen antagonists, but in postmenopausal women (having low estradiol levels) they can act as weak estrogens [122,123]. Flaxseed lignans have reported having an appreciable protective influence against various cancer treatments, especially breast, colon, skin, and prostate cancer. A low-fat diet rich in lignans namely enterodiol, and enterolactone (classified as phytoestrogen) showed growth inhibition in 3 human prostate cancer cell lines [124,125] as well as colon and skin cancers in cell cultures and in animal studies [126,127]. Flaxseed lignans particularly SECO, SDG, END, and ENL have also been reported to show appreciable results in reducing hypercholesterolemia, atherosclerosis, and diabetes [117,118]. Apart from flaxseed, sesame, one of the oldest indigenous oil-seed crops of India, is a rich source for lignans. Sesame oil is rich in (up to 2.5%) furofuran lignans (dimers of phenyl propane units).

According to Shi et al. [128] sesame oil generally contains about 3.38 to 11.53mg/g of total lignan [128]. It is the presence of these lignans which makes sesame oil important in particular, for edible purposes. The major fat-soluble aglycon lignans of sesame include sesamin and sesamolin. Sesamol, sesaminol, sesamolinol, pinoresinol, matairesinol, lariciresinol, and episesamin form minor aglycons of sesame oil [129-135]. Among the various varieties of sesame cultivated, black sesame seeds in comparison to the white variety, contain higher amount of sesamin and sesamolin which is about 1.98-9.41mg/g and 1.06-3.35mg/g respectively [128]. They, singly or in combination, help cure or control various physiological activities and act as anti-hypertensive, anti-cancerous and hypo-cholesterolemic agent, making sesame oil an oil of tremendous research interest in recent years [135].

Sesamin is found to assist lipid and glucose metabolism, play an important role in hypertension management, acts as anti-inflammatory by inhibiting delta 5-desaturase and help in free radical scavenging mechanism [136]. Another important role of sesamin is in decreasing the low-density lipoprotein (LDL) and increasing high-density lipoprotein (HDL) levels [137,138] of blood thereby inhibiting blood cholesterol level absorption and biosynthesis which in turn burns fat and reduces risks of obesity, atherosclerosis and related diseases in human [139]. Sesaminol and sesamolin both have shown results in inhibiting membrane lipid peroxidation (140). The free radical activity is however seen to be highest for sesamol compared to that of sesamin, sesamolin, and Pinoresinol [140-143]. It, therefore, exhibits higher efficiency towards preventing cell membrane lipid peroxidation, as well as LDL oxidation [144]. Sesamol when packed into nearly spherical solid lipid nanoparticles of average particle size of nearly 120.30nm showed enhanced hepatoprotective bioactivity than free sesamol against sub-chronic liver injury in rats [129]. Prisna et al. [145] mentioned that sesame lignans are now being explored for hormone therapy and replacement owing to its estrogen agonistic effect which is useful for postmenopausal women [145].

Episesamin has also been reported to show anti-cancer activity when tested against in-vitro leukemia cells. Lesser-known lignans found in sesame have also been reported to exhibit anti-fungal activities. Although found in minor amounts Chlorosesamone, hydroxysesamone and 2, 3- epoxysesamone have been reported to show inhibitory effects on the spore germination of the pathogenic fungus *Cladosporium fulvum* [146]. The episesamin was also reported to possess anticancer activity against human lymphoid leukemia cells in vitro [147]. Lignans are acquiring immense popularity in recent years due to their many fold applications as pharmaceutical and nutraceutical sectors. However, presently flaxseed and sesame oil are the only major sources of the same. Thus, more research in this respect regarding the exploration of other sources as well as increased synthesis of the same needs to be focused upon. Even technologies are to be developed for extraction of these lignans from oils and deoiled cakes for commercial explitation.

Oryzanol

This is an important group of compounds available in rice bran oil in the range of 1 to 1.3%. Chemically speaking these compounds are esters of triterpene alcohols and phytosterols with ferulic acid [148]; (Figure 3). The most important health benefit of this nutraceutical is its ability to reduce serum cholesterol level [149] and hence can be used for treatment of hyperlipidaemia [150].

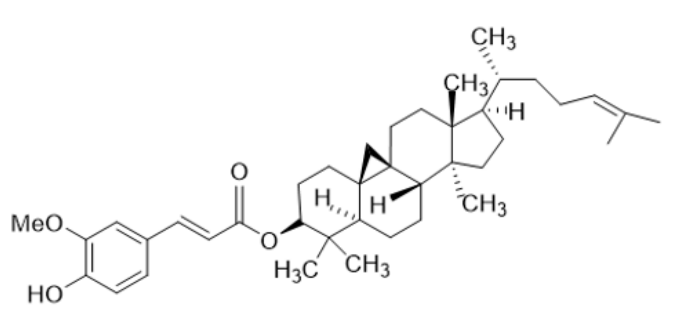

Figure 3: γ- oryzanol.

γ- oryzanol is also believed to have a role in ameliorating insulin resistance [151]. Oryzanol was shown to have some benefits in the treatment of cirrhosis of the liver [16]. γ-oryzanol also possesses anti-atherosclerotic activity and antioxidant properties. Cicero and Goddi [152] reviewed the properties of rice bran oil and oryzanol in particular for use in various diseases. γ- oryzanol was found to modulate the secretion of the pituitary gland, inhibit gastric acid secretion, and also regulate platelet aggregation. γ - oryzanol also exhibits the ability to protect skin from UV radiation. This can also delay the aging of the skin [153]. Oryzanol is also used in various hair care products [154]. Different formulations and soft gels of γ-oryzanol are available in the market. This can be isolated from soap stock produced during the alkali refining of rice bran oil. Further research work is required to extract oryzanol from other refining by-products and also to understand completely the benefits of γ-oryzanol.

Squalene

This is another very important nutraceutical present in rice bran oil, olive oil, wheat germ oil, palm oil, etc. in minor quantities. This is a hydrocarbon used in the synthesis of cholesterol [16]. Squalene is known for its ability for oxygen quenching and regarded as antioxidants. Another important source of squalene is marine animal oil, particularly shark liver oil. However, due to stringent restrictions for the protection of marine animals, scientists are looking for alternative sources, specifically from plant sources [155]; (Figure 4). Squalene is known for its significant contribution to weight loss and cholesterol control [156]. Squalene also has tremendous scope for use in the cosmetics industry, more specifically for skincare products [157]. Squalene is projected as a hydrating agent for skin and it helps in regenerating healthy skin cells.

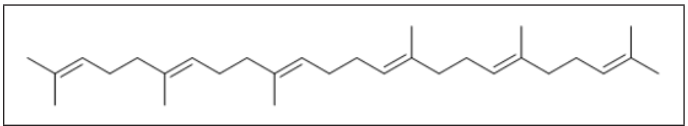

Figure 4: Squalene.

It also prevents premature aging. This is used in the formulation of treatment in various skin diseases [16]. It is also projected to have anti-cancer activities [158]. Rao et al reported that squalene intake may reduce the development of tumours [159]. Smith also proposed a mechanism for anti-cancer properties shown by squalene [160]. Some other reports also suggested low evidence of cancer and degenerative diseases by using squalene rich diet [161,162]. More importantly, an emulsion based on squalene and other surfactants were prepared as an effective stimulant to the immune system. In the post-COVID -19 scenario, the importance of squalene has been increased tremendously. It is effectively used in several vaccines for malaria, hepatitis B and C, HIV, and H1N1 viruses [163,164]. It may even have an important role in developing vaccines against the COVID-19 virus. World production of squalene is around 6000 tons with a commercial value of around 112 million USD. It is expected that the demand of squalene will be increased significantly, and technologies are to be developed for the extraction of squalene from various plant and animal sources. Supercritical carbon dioxide extraction is showing promises as a preferred method as no traces of solvents is detected [165].

Carotenoids

Carotenoids are fat-soluble isoprenoid group of molecules with more than 500 varieties. They are widely available in fruits, flowers and are found as pigments in oils and fats. It is found in various oils like corn oil, groundnut oil, soybean oil, rapeseed oil, sunflower oil, cotton-seed oil, olive oil etc. at a concentration less than 100ppm [166-172]. However, it is most widely found in palm and palm kernel oil at a concentration of nearly 500-700ppm in crude oil [173]. The major composition of carotenoids includes phytofluene, β-carotene, δ-carotene, lycopene, β-zeacarotene, etc. [174] of which β -carotene is of special importance to human health. β-carotene is the precursor of retinol, popularly known as vitamin A. β -carotene is converted to retinol by the action of enzyme carotene deoxygenase which is present in human liver and intestinal mucosa following cleavage at the central double bond of the molecule [16]. However, the rate of conversion is very low [175]. Carotenoids also serve various health benefits as it strengthens the immune system, reduces the risk of degenerative diseases [176], shows antioxidant properties by quenching of singlet oxygen. Carotenoids like α -carotene, lycopene, and β -carotene also showed antiobesity/hypolipidemic activities [174,177]. α -carotene is reported to exhibit appreciable activity as an anti-cancer agent [174]. Though present in crude oils, carotenoid is removed almost completely during bleaching and thus is obtained as a refinery by-product. Recovery of the same is important owing to its importance as a nutraceutical.

Conclusion

It is quite evident from the discussion that oils and fat can be regarded as one naturally occurring major source for various types of nutraceuticals having varied health benefits. Though oils and fats are considered to be responsible for weight gain and a higher level of serum cholesterol, judicious uses of this commodity and prescribed uses of nutraceuticals present in the oils and fats can help to control the serum cholesterol levels. The antioxidant properties of some of these nutraceuticals help in maintaining general health. These nutraceuticals serve specific functional properties and are used in food, cosmetics, and pharmaceutical applications. However, the awareness level of common people about these nutraceuticals has to be improved. On the other hand, technologies are to be developed for commercial exploitation of these oils and fats-based nutraceuticals.

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