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Pharmacological activity of *Helianthus annuus* seeds: A review

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Abstract
The use of biofertilizers in developing environmentally friendly agriculture as an alternative to chemical-based fertilizers in enhancing food production is promising in sustainable agriculture for the improvement in the yield of some commercial crops such as sunflowers and other oilseed crops in terms of quality and quantity. Sunflower is an important oilseed crop native to South America and currently cultivated throughout the world. Generally, the sunflower is considered important based on its nutritional and medicinal value. Sunflower seeds, a nutrient-dense food have been found to have a potential role in chronic inflammatory conditions, bacterial and fungal infections, cardiovascular diseases, skin diseases, and even cancers. Sunflower contains mineral elements and phytochemicals such as dietary fiber, manganese, vitamins, tocopherols, phytosterols, triterpene glycosides, α-tocopherols, glutathione reductase, flavonoids, phenolic acids, carotenoids, peptides, chlorogenic acid, caffeic acid, alkaloids, tannins, and saponins; and these compounds contribute to their functional and nutraceutical development. This article is to give an overview about a wide array of uses of sunflower seeds and to enlighten the therapeutic potential of cheap, accessible, and easily available oil seed crop 'Sunflower' in human beings.

Keywords: *Helianthus annuus*, environmentally friendly agriculture, tocopherols, phytosterols

Introduction

The continuous rising in the human population and high demand for foods has resulted in hunger, disease outbreaks, and even starvation to death; therefore, there is a need to intensify more on agricultural practices for maximum food production for the human populace Food production for human nutrition is essential for healthy living (El-Hamidi & Zaher, 2018) [8]. Over time, many farmers have engaged in conventional agricultural practice using chemical fertilizers for better crop yields and productivity and these in a systemic way adversely affect crop yield, physical and chemical properties of soil, and water as a result of surface runoff, and microbial ecological imbalance. The persistent use of chemical fertilizers through plants has been channelled into a plant-food chain system, causing disease symptoms in humans. It is imperative to critically devise biotechnologically modern approaches needed, suitable in the agricultural system in improving crop yields, and productivity devoid of threats to the environment (Grieve *et al.*, 2019) [40]. The exploitation of microbial resources in formulating bio inoculants (biofertilizers and biopesticides) has contributed to safe food product delivery in the agronomic system sustainably (Mahanty *et al.*, 2017) [3, 23]. The soil amended with microbial-based formulated fertilizer (biofertilizers) promotes plant health and crop yield with intents of proffering long-lasting solutions to the problems associated with the continuous use of chemical fertilizers in enriching soil fertility for crop productivity The use of biofertilizers as applied to some crops such as maize, legumes, tubers, and oilseeds crop has been reported (Babalola & Glick, 2012; Igiehon & Babalola, 2017) [4, 15]. Thus, growing of plant-based high-quality foods such tuber crops, oilseed crops (sunflower, rapeseed, safflower, and soybeans), fruits, and vegetables have been domesticated as a source of diet for humans and raw materials for industry. Sunflower (*Helianthus annuus*) is an oilseed crop native to North America. It is cultivated throughout the world, and most of its products have been commercialized as culinary or livestock feed. The adaptation of sunflowers to different climatic and soil conditions has enhanced its cultivation as an oilseed plant throughout the world (Forleo, Palmieri, Suardi, Coaloa, & Pari, 2018) [10].

The growth of sunflower requires fertile soil, moderate rainfall, viable seeds, etc. Among the three leading oilseed crops, that is, soybean, rapeseed, and sunflower in the world today, sunflower has been recognized as a major source of high-quality edible oil importantly used for culinary purposes. Sunflower is one of the important oilseed crops grown throughout the world as a source of premium oil and dietary fiber that significantly contributes to human health (Khan, Choudhary, Pandey, Khan, & Thomas, 2015) [19]. In some countries like India and South Africa, growing of sunflowers might be more competitive to other crops like maize, soybean, and sorghum (Vijayakumar *et al.*, 2016) [39]. Due to the continuous increase in the human population, the demand for edible sunflower seeds, oil, and by-products has also increased, and to meet the demand, there is a need to intensify efforts to expand sunflower output (Taher, Javani, Beyaz, & Yildiz, 2017) [37]. Today, the international oilseed market is dominated mainly by sunflowers and other oilseed crops such as soybean, rapeseed, peanut, cottonseed, etc.

From literature, it has been reported that consumption of processed sunflower as a source of a meal is therapeutically important in reducing the risk of chronic organs-associated diseases in humans (Sarwar, Sarwar, Sarwar, Qadri, & Moghal, 2013) [32] and this necessitates more intensification in its agricultural production and research as promising oilseed crops with multifunctional attributes. Therefore, the daily consumption of sunflower oil can be recommended to boost human immunity for healthy living. The health benefits of sunflower oil, meal, and other products are limitless, as they possess anticancer, antioxidant, antihypertensive, anti-inflammatory, hypocholesterolemic, skin-protective, analgesic, and antibacterial activities. Their effects on the muscles, blood vessels, and nerves are also known. Sunflower oil is also efficient in the treatment of colds, coughs, dysentery, constipation, and diseases like urinary, bronchial, pulmonary, and laryngeal infections. Some of the pharmacological and health benefits of sunflower are described below:

Antioxidant benefits

Oxygen is one of the vital elements that involve in various aerobic processes in humans. Antioxidants functions are to protect body cells from damage caused by reactive oxygen species and reduce the risk of developing severe disease conditions such as Pharmacological and health benefits of sunflower cataracts, carcinoma, chronic inflammation, atherosclerosis, cardiovascular disease, neurodegenerative diseases, and premature aging (Jiraungkoorskul, 2016) [18]. Examples of natural antioxidants from sunflowers, as shown above can help retard or inhibit or prevent oxidation, scavenge free radicals, and thus prevent disease proliferation within the cell (Guo *et al.*, 2017) [13]. The use of synthetic antioxidants is limited due to toxicity. Thus, research interest in the discovery of novel antioxidants from plants with currently ongoing might be promising as a source of dietary antioxidants.

Anti-inflammatory and cardiovascular benefits

Sunflower is characterized by anti-inflammatory activity. The seeds of sunflowers are known to be rich in vitamin E and magnesium that serve as an excellent source of fat-soluble antioxidant to the body (Kumar, Sharma, & Vasudeva, 2017) [20]. The antioxidant properties displayed by vitamin E neutralize the free radicals that may cause damage to the fat-containing structures and molecules, such as cholesterol, brain cells, and cell membranes (Nowicka & Kruk, 2017) [27]. The oxidation of cholesterol and attachment of cholesterol particles to the blood vessel walls can cause atherosclerosis, thus resulting in blockage of arteries, stroke, or heart attack. Vitamin E and magnesium exhibit anti-inflammatory effects, protect bio molecular components, and reduce symptoms like osteoarthritis, rheumatoid, and asthma by scavenging the free radicals tendencies of causing such effects (Bashir, Zahara, Haider, & Tabassum, 2015) [5]. The consumption of foods rich in vitamin E and magnesium importantly helps to reduce risk of atherosclerosis, lower blood pressure, rheumatoid arthritis, asthma, osteoarthritis, colon cancer, diabetes, sudden heat sensation in women at menopause, high blood pressure, stroke, heart attack, and cardiovascular disease and migraine headaches (Bashir *et al.*, 2015) [5]. The anti-inflammatory and inhibition effects of chemical compounds triterpene glycosides obtained from the methanol extract of sunflower petals that cause ear edema in induced experimental mice have been reported (Bashir *et al.*, 2015) [5]. Studies have revealed that people who consume more foods rich in vitamin E have a low risk of heart attack than people who inadequately feed on the less vitamin E diet. Poor supply of magnesium can pose high-risk factors to muscle spasms, high blood pressure, fatigue, soreness, and migraine headaches (Vijayakumar *et al.*, 2016) [39]. Therefore, it is recommended that the consumption of sunflower and associated products would greatly reduce the risk of organ diseases and other human infections. Furthermore, sunflower seeds have also proven efficient in the treatment of stomach and esophagus cancers. The research findings on guinea pigs according to (Berquin *et al.* 2007) [6] had revealed that the stem marrow and bottom of sunflower flowers containing hemi cellulose functionally block sarcoma and Ehrlich ascites carcinoma. In some cases, the relationship between cancer development and consumption of oil-rich food is usually complex and sometimes depends on the characteristics relating to the oil and fat composition in foods.

Anti-cholesterol benefits

It is believed that certain chemical structures such as Phytosterols similar to cholesterol are found in sunflower seeds and the presence of Phytosterols in large amounts in the human diet tends to reduce blood levels of cholesterol, improve immune response, and risk factors to certain diseases such as cancers (Farahmandfar, Asnaashari, Pourshayegan, Maghsoudi, & Moniri, 2018) [9]. Aside from sunflower seeds, phytosterol is present naturally in oilseed crops such as soybean, pumpkin seeds, rapeseeds, safflower, palm oil, sesame seeds, and pine tree oil (Nagendra Prasad *et al.*, 2012) [26]. Their addition to processed foods such as butter, as an alternative food additive, is said to reduce lower cholesterol levels in foods. Phytosterols, sterols, and tocopherols represent major phytoconstituents in oilseed crops (Sujith-Kumar, Mawlong, & Singh, 2017) [36]. On ingestion, they underwent several mechanisms in lowering the cholesterol levels in the human body, and their appropriate use in and food industries has been recognized to play a major role in human health. Consumption of food with high Phytosterols enhances human immunity, proper functioning of the organs, lower cholesterol levels, and even protection against cancer (Moreau *et al.*, 2018) [25]. In the

real sense, Phytosterols can be extracted from plants and added to the processed oils and foods products based on their health and nutritious properties. The standard sunflower oil containing tocopherols and Phytosterols is interesting with therapeutic effects on human health as they reduce total plasma cholesterol and low-density lipoprotein (LDL) cholesterol levels (Rani, Sheoran, & Sharma, 2017) [29]. The major mechanisms by which Phytosterols found in sunflowers lower the LDL-cholesterol levels usually occur through the reduction (30%-50%) in the rate of cholesterol absorption in the intestine (Scolaro, de Andrade, & Castro, 2020) [34]. The reduction in the cholesterol levels may be achieved by some mechanisms through competition with cholesterol by the solubilization in mixed micelles in the intestinal lumen, thus cause a reduction in the absorbable cholesterol (Blanco-Vaca, Cedó, & Julve, 2019) [7]. Other mechanisms such as reduction of esterified cholesterol in the enterocyte, accelerated removal of cholesterol from the body through the trans-intestinal cholesterol secretion and modification in the expression of genes encoding proteins that carry sterols have been proposed. Furthermore, the expression of genes encoding proteins has been attributed with Niemann-Pick C1-like 1 (NPC1-L1) protein, reduction in the transport of cholesterol to the enterocyte, or ATP-binding cassette transporters (ABCG5 and ABCG8), and efflux of cholesterol from the enterocytes to the intestinal lumen (AbuMweis, Marinangeli, Frohlich, & Jones, 2014) [1]. Consequently, plant sterols function exerts a hypocholesterolemic effect that inhibits the intestinal actions in the absorption of the cholesterol (Jesch & Carr, 2017) [17]. The mechanisms of lowering the cholesterol level during the lipid digestion process have been described based on dynamic competition existing between plant sterols and free cholesterol by integrating into the mixed micelles (He *et al.*, 2019) [14]. The Phytosterols are hydrophobic as compared cholesterol which is believed to have more affinity for micelles than cholesterol thus, displacing cholesterol molecules from the mixed micelles, and then, the accreted dietary cholesterol is passed through the feces together with re-circulating self-biliary cholesterol, which in turn reduce the absorption and cholesterol level in the living organism. Nevertheless, it has been proposed that the consumption of Phytosterols-containing meals might not be necessary to present simultaneously with cholesterol in the intestinal lumen to inhibit cholesterol absorption. Hence, other anti-cholesterol mechanisms were suggested. Other mechanisms of anti-cholesterol include that the absorption of dietary and free cholesterol into the intestine is normally esterified by an enzyme acyl-coenzyme A cholesterol acyltransferase 2 (ACAT-2) prior absorption into the chylomicrons and later extravagated into the lymph (Xu, Du, Turner, Brown, & Yang, 2019) [40]. It is evident that Phytosterols are poor substances for ACAT-2 and their interference with esterified cholesterol inside enterocyte could competitively reduce the inhibition potential. Then, the esterified cholesterol can then be produced to the intestinal lumen by the ABCG5/8 along with free Phytosterols with the aid of heterodimer transporter. Therefore, the reduced ACAT activity could then decrease the cholesterol absorption from the intestinal lumen and mixed micelles, once ACAT activity within the enterocyte is regulated by substrate produced. The interaction of Phytosterols with intestinal cholesterol sensors (liver X receptor) has been reported to reduce cholesterol absorption in the intestine (Ma *et al.*, 2017) [22].

Anticancer benefits

The health benefits of sunflower are not exclusive to antioxidant, anti-inflammatory, or cardiovascular effects, and the sunflower is also known to possess anticancer properties. Sunflower seeds are known to be an excellent source of a trace element, selenium. This element is of fundamental importance in improving human immunity against cancerous cells (Roy, Hossan, & Rahmatullah, 2015) [31]. The intervention trials of inverse correlation between selenium intake and cancer development using animal models have been reported in many research studies. The presence of selenium in sunflowers has instigated DNA repair and production in degenerated cells, inhibition of growing cancer cells, and induction of apoptosis, self-destruction of sequence in the body to remove unwanted or worn-out cells. Furthermore, the incorporation of selenium to the protein active sites such as glutathione peroxidase protects body cells against cancer (Pisoschi & Pop, 2015) [28]. Glutathione peroxidase is one of the antioxidant enzymes that support liver function in the detoxification of harmful molecules. At a low concentration of glutathione peroxidase, the toxic molecules found in contact with the cells are not destroyed; hence causing impairment to the cellular DNA and ensuring the growth of cancer cells (Issam, Nawel, & Yassine, 2015) [16]. It is believed that due to the selenium richness in sunflower seeds, it can be used as composite foods in the production of good snacks and another domestic diets. Furthermore, the use of sunflower seeds in traditional medicine as an alternative in the treatment of cancer or malignant growth is known (Bashir *et al.*, 2015) [5]. However, studies on sunflower seed extract have proven to display anticancer activities against cancer cells.

Anti-asthmatic, antidiabetic, and antimicrobial benefits

The use of sunflower in the treatment or reduction in the risk factors of asthma and diabetes has revealed their health benefits. The antiasthmatic and antidiabetic efficacy of sunflower extracts has been reported (Gad & El-Ahmady, 2018) [11]. The oral administration of ethanolic extracts of sunflower seeds extract in rats with antihyperglycemic effects has been reported (Saini & Sharma, 2013) [33]. Also, the in vivo antiasthmatic assay of aqueous extract from sunflower on ovalbumin-induced mice and the assessment of their lungs by hematoxylin and eosin staining had revealed the extract potency in reducing asthma effect on the mice (Kim *et al.*, 2020) [21]. Similarly, the consumption of sunflower seed and oil would probably reduce major risk factors of asthma or diabetes in humans. The antimicrobial activity of methanolic sunflower seeds extracts against some pathogenic Gram-positive and Gram-negative bacteria, which include *Staphylococcus aureus*, *S. epidermis*, *Escherichia coli*, *Proteus vulgaris*, and *Pseudomonas aeruginosa* that might result in food-borne illness has been documented (Menzel *et al.*, 2019) [24]. It is, therefore, important that sunflower extract can be applied as natural food preservative agents (Thielmann, Kohnen, & Hauser, 2017) [38].

Conclusion

The rising human population and demand for food necessitate sustainable agricultural practices. Conventional farming with chemical fertilizers adversely affects soil, water, and human health. Therefore, biotechnological approaches, including biofertilizers and biopesticides, are essential for improving crop yields without environmental harm. Sunflower, a significant oilseed crop, offers numerous

health benefits, including antioxidant, anti-inflammatory, cardiovascular, and anticancer properties. The adoption of microbial-based fertilizers can enhance sunflower cultivation, contributing to food security and health. Continued research and application of these sustainable practices will support agricultural productivity and human well-being.

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