Acta Scientific NUTRITIONAL HEALTH (ISSN:2582-1423)

Volume 7 Issue 4 April 2023

Review Article

Phytotherapeutic Potential of Super Seeds: An Overview

Divya Jain, Tamanna Kohli* and Saloni Chauhan

Department of Food and Nutrition, College of Community Science, Punjab Agricultural University, Ludhiana, India

***Corresponding Author:** Tamanna Kohli, Department of Food and Nutrition, College of Community Science, Punjab Agricultural University, Ludhiana, India.

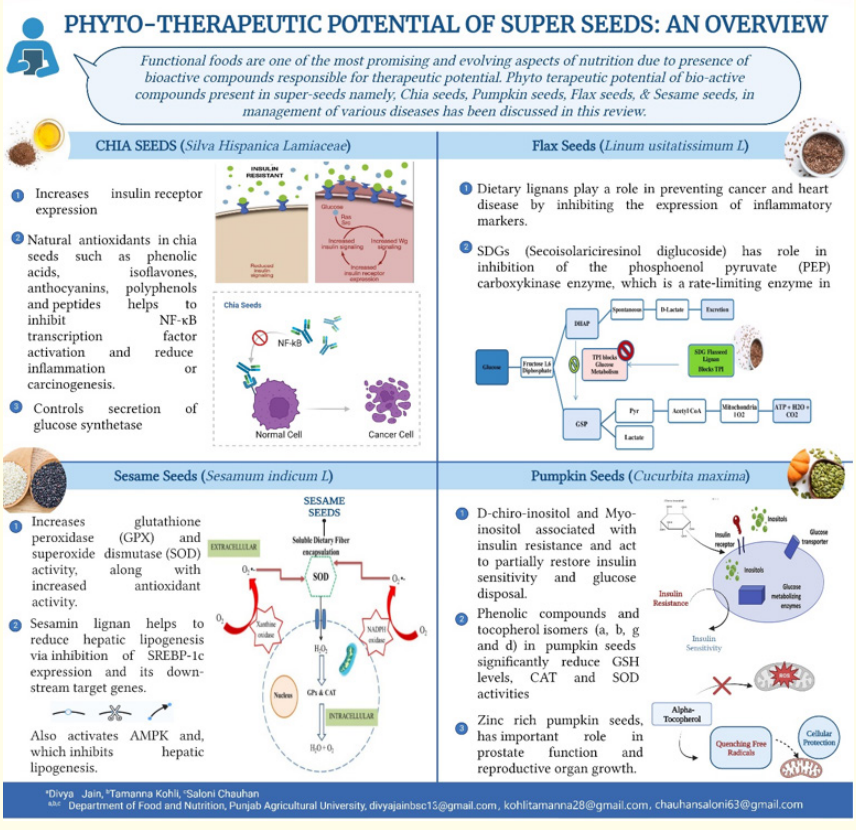
DOI: 10.31080/ASNH.2023.07.1222

Received: March 06, 2023

Published: March 22, 2023

Abstract

The burden of chronic non-communicable diseases (NCD) is increasing worldwide. Epidemiological evidence supports the claim that the consumption of functional food ingredients and reduction in the risk of NCDs has a positive correlation resulting in increasing demand for foods with phytochemicals can be observed. The review discusses the potential role of the edible 'Super seeds' namely Chia, Flaxseed, Sesame and Pumpkin seeds. These seeds are rich source of potential phytochemicals resulting in excellent therapeutic benefits. The study also included an overview of their mechanism in controlling various diseases.



Keywords: Super-Seeds; Therapeutic Effect; Non-Communicable Disease; Phytochemicals; Functional Foods

Highlights

- Functional foods are one of the most promising and evolving aspects of nutrition due to presence of bioactive compounds responsible for therapeutic potential.
- Edible seeds, other than calorie dense, are one of the functional foods known for their phytotherapeutic properties due to the presence of phytocomponents.
- Natural antioxidants present in chia seeds (*Silva H L)* such as phenolic acids, isoflavones, anthocyanins, polyphenols and peptides help inhibit NF-κB transcription factor activation and reduce inflammation.
- Dietary lignans found in flaxseed (*Linumusitatissimum L*) play a role in preventing cancer and heart disease by inhibiting the expression of inflammatory markers.
- Sesamin, sesamolin, and sesamol, present in sesame seeds (*Sesamum indicum L.)* are known to reduce oxidative stress.
- Pumpkin seeds (*Cucurbita maxima)* contain mediators of insulin action, such as D-chiro-inositol, trigonelline and nicotinic acid, which play a role in controlling diabetes.

Introduction

Rapid global urbanization and changing living conditions have been linked to the growing burden of non-communicable diseases (NCDs). NCDs, are typically long-lasting and results from a combination of genetic, physiological, environmental and behavioral factors. Globalization has increased lifestyle risk factors for NCD's related to unhealthy dietary patterns, tobacco use, harmful alcohol use and physical inactivity. Therefore, becoming a leading threat to human health and development [1].

According to the WHO report (2021), about 41 million people each year dies due to NCD's, accounting for 71% of all deaths worldwide. Cardiovascular diseases are responsible for the most deaths (17.9 million people annually), followed by cancer (9.3 million), respiratory diseases (4.1 million) and diabetes (1.5 million). In India, nearly 5.8 million people die from non-communicable diseases (heart and lung diseases, stroke, cancer and diabetes) every year [2]. Most estimates suggest that NCDs are an economic burden of 510 percent of GDP in India, which is significant and is slowing down GDP, thus hampering development. The management and treatment of these diseases impose both direct and indirect costs on the community. The disproportionate allocation of health resources among communities worldwide places a major burden on health facilitators to provide a cost-effective approach. Reducing the burden of NCDs requires reducing intermediate and modifiable risk factors. However, it is very difficult for individuals to make healthy choices throughout life when the underlying environments continue to encourage the unhealthy choices.

Numerous therapies use conventional medications based on an arduous single-dose regimen that lasts patients almost their entire lives, most of the time exhibiting side effects such as diarrhea, bloating, or bloating [3]. Although a call for alternative approaches to Seeking treatments for these diseases that differ from conventional medicines and bring us back to traditional disease management strategies. The role of diet in NCDs has been well documented in recent years by epidemiological and social studies. Lifestyle and dietary changes associated with economic development and globalization have favored the consumption of foods high in energy, fats, free sugars and sodium at the expense of reduced intakes of fruits, vegetables and whole grains, implying lower fiber intakes. A stable lifestyle requires a balanced diet that reduces high levels of fat, cholesterol and sugar, which has a beneficial effect on health, especially in people with a predisposition to non-communicable diseases [4]. The emergence of food components with health benefits offers an excellent opportunity to improve public health and therefore this category of components has received much attention from the scientific community, consumers and food manufacturers in recent years. The list of dietary ingredients (vitamins, probiotics, bioactive peptides, antioxidants) is endless, and the scientific evidence supporting the concept of health-enhancing food ingredients is growing.

Significant dietary changes in humans have become a major socio-economic concern in recent decades [5]. There is a growing global interest in identifying novel functional foods that can operate on a variety of biochemical targets with minimal toxicity. "Functional foods" have seen a lot of coverage in recent years as part of healthier lifestyle improvements [6]. The Food and Nutrition Board of the National Academy of Sciences has suggested that a functional food is "any modified food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains." In other words "functional" refers to a food substance which has essential nutritional functions and is routinely ingested to provide physicological benefits. Bioactive compounds are found in functional foods such as fiber, oligosaccharides, essential fatty acids, phytochemicals and antioxidants that have protective effects on human well-being and may play a role in minimizing the risk of chronic degenerative diseases [7]. The global rise in public health awareness has necessitated the search for functional foods with various health benefits. Edible seeds and nuts are traditionally used as a base or main course and in the ancillary supplements, thickeners, spices and food flavorings. They are a rich source of phytocomponents, macronutrients and micronutrients such as proteins, fatty acids, polyphenols, carbohydrates, fiber, vitamins and minerals. These seeds and nuts are part of the cultural and genetic heritage of different regions of the world, either directly or after processing.

They are able to reduce the risk of various diseases and help reduce oxidative stress. Thus, they prevent the development of chronic diseases, including diabetes, cancer, cardiovascular disease, neurogenesis, and inflammation. This review aims to discuss some edible seeds used as functional foods, their nutrients (micro- and macromolecules), phytochemical composition, biological activities, and role in the prevention of non-communicable diseases. This article provides the mechanism of action of Super Seeds namely Chia Seeds, Flax Seeds, Sesame Seeds and Pumpkin Seeds in combating various non-communicable diseases.

Search Methodology

The search was performed in the Google Scholar, Pubmed and Science Direct databases using the key terms Seeds, Super-Seeds, Disease Prevention and Therapeutic Effect. The review focused on the functional and therapeutic effects of seeds, supported by at least two or more *in vivo* and *in vitro* studies describing their phytotherapeutic potential.

Results

Seeds with Phytotherapeutic Potential

Chia Seeds

Chia, scientifically referred to as *Silva Hispanica Lamiaceae*, is a mint-like perennial herb. It is grown locally in parts of southern Mexico and northern Guatemala. According to the historical accounts, chia seeds were used as one of the staple foods of the Mayan and Aztec civilizations [8]. In pre-Columbian times, the seeds of the species Salvia hispanica l., also known as chia sage and Spanish sage [9]. The word chia seed refers to its fruitlessness rather than a seed. Chia seeds are oval and gray with black and white spots, about 2 millimeters in diameter, and mottled with brown, gray, black, and white. The seeds are hygroscopic, absorbing up to 12 times their weight in liquid when soaked, and developing a slimy coating that gives chia-based foods and beverages a distinctive gel texture [10].

The seeds are high in omega-3 fatty acids, protein, carbohydrates, and soluble and insoluble fiber, both of which show promise as useful ingredients [11]. Fiber has long been recognized as an essential part of a balanced diet. They are rich in monounsaturated and polyunsaturated fats as well as many vitamins, minerals and antioxidants. They make valuable contributions to our normal diet in a variety of ways. Because of their defensive, versatile, and antioxidant properties, chia seeds are now consumed by many people as a superfood. Chia seeds are one of the most commonly used functional foods and are said to protect the cardiovascular system, have an anti-inflammatory effect and regulate blood sugar and lipid metabolism [12].

Chemical composition

Because of its nutritional and therapeutic potential, chia has received a lot of interest in recent years. Chia seeds are known for their high levels of antioxidants, minerals, and soluble fiber. It has a high percentage of alpha-linolenic acid (60%) compared to other oilseeds [13]. Chia seeds can be used as a good source of protein with exceptional thermal stability. Nutritionally, chia seeds contain protein (15-25%), lipids (30-33%), carbohydrates (26-41%), fiber (18-30%), and minerals (4-5%) [14].

Therapeutic properties

Chia seeds are high in antioxidants, fiber, and protein, making them a powerful therapeutic agent [15]. Chia seeds are currently used for their nutritional and therapeutic properties, such as: Chia seeds exert effects such as reducing postprandial glycemia, appetite, waist circumference and cardiovascular risk factors [16]. Chia seeds are a good source of antioxidants such as polyphenols, chlorogenic and caffeic acids, myricetin, quercetin, kaempferol, and essential fatty acids that help prevent heart disease and cancer [17]. Fiber intake increases fecal bolus formation and intestinal output, which helps reduce obesity and colon cancer.

Antioxidant activity

The presence of phenolic compounds such as phenolic acids, isoflavones, anthocyanins, vitamins, polyphenols and peptides help inhibit NF-κB transcription factor activation, reduce inflammation and carcinogenesis, and protect against attack by reactive oxygen and nitrogen species. Natural antioxidants found in chia seed extract may work together more effectively than a single dietary antioxidant to reduce active oxygen species [18]. Antioxidant effects may protect the body from diseases such as neurological disorders, inflammation, immune deficiency, ischemic heart disease, stroke, Alzheimer's and Parkinson's diseases and cancer [19].

Antidiabetic effect

In previous studies, chia seeds have been shown to increase glucose uptake, oxidation and tissue restoration of insulin sensitivity, and modulation of gene expression associated with lipogenesis and mitochondrial function, the main effects of chia on health status [20]. Symptoms of insulin resistance and dyslipidemia were reversed when chia seeds were added to the diet [21]. Enes., *et al.* (2020) reported the effect of different fractions of chia (Salvia hispanicaL.) on glucose metabolism. The effect of chia on glucose homeostasis by controlling AKT activation, gluconeogenesis, and glycolytic pathways. Chia oil has been shown to increase insulin receptor expression, which helps insulin bind to it, which signals for phosphorylation of AKT. P-AKT blocks FOX01 to migrate to the cell nucleus and initiate transcription of gluconeogenetic enzymes, thereby controlling glucose synthetase. Chia-hydrolyzed phenols help decrease the gluconeogenic pathway. Chia flour and chia oil increased AMPK expression, which increases glucose uptake and oxidation and glycolytic enzymes, resulting in improved glucose

tolerance [22]. Another study evaluated the effect of supplementing chia seeds (40g/day for 12 weeks) on blood pressure in type 2 diabetics. The observation showed a significant reduction in the patients' systolic blood pressure [23].

Anti-hyperlipidemic effect

Chia contains a high amount of fiber and omega-3 unsaturated fatty acids, chia seed intake has shown promise in lowering serum cholesterol levels and inhibits key indicators of cholesterol synthesis, such as 3-Hydroxy-3-methylglutaryl coenzyme A reductase [24]. Due to its high fiber and low carbohydrate content, chia has been shown to improve satiety and reduce appetite for food [25]. In addition, the soluble fiber helps reduce the risk of cardiovascular disease, gastrointestinal disease and the prevention of metabolic syndrome. The essential biochemical compounds prostaglandins, leukotrienes and thromboxane are formed from alpha-linolenic acid and eicosatetraenoic acid, which are used in a variety of physiological functions. Parasympathetic speech, heart rate variability and ventricular arrhythmia are all improved by omega-3 fatty acids [26].

Flaxseeds

Linum usitatissimum L, also known as flaxseed or linseed, is a blue-flowering annual herb believed to have originated in Egypt and belongs to the genus Linum in the family Linaceae [27]. Flaxseed is a member of the Linaceae family. It is one of the oldest crops, cultivated since the dawn of civilization and used as a traditional Indian food and medicinal, playing an important role in nutrition and disease prevention [28]. Flaxseed has been used in the diet for the benefits associated with some of its biologically active components, which are nutritionally important due to the availability of fatty acids and often have health benefits for consumers.

Flax is grown in many countries, particularly in the northern hemisphere, such as Canada, the United States, Russia, China, and India. The color of the seeds varies from a mild reddish brown to light gold. Flaxseed is crunchy in color, chewy texture with a good nutty flavor [29]. Flaxseeds come in two basic varieties/colors: brown or yellow (golden flaxseed). Most species Yellow flaxseeds, called solin, have a similar oil profile to brown flaxseeds and both are very high in omega-3 fatty acids (especially, ALA) [30].

Flaxseed is increasingly recognized as a functional food as it is an important source of phytochemicals, particularly polyunsaturated fatty acids (PUFA). In India, flaxseed has a long history of use and flaxseed preparations are valued for their nutritional and therapeutic properties. Flaxseed is a rich source of phenolic compounds such as lignans, phenolic acids, flavonoids, phenylpropanoids and tannins [31]. These antioxidants have the potential to affect cell growth and viability and numerous studies have shown that these antioxidants have pharmacological properties such as antidiabetic, hypotensive, immunomodulatory, anti-inflammatory and neuroprotective effects. Flaxseed has been shown to have powerful antioxidant and anti-inflammatory properties in both animal and clinical studies [32].

Chemical composition

Flaxseeds are high in calories, fiber and protein, but low in carbohydrates. Nutritionally, flaxseed contains 30-41 percent fat, 20-35 percent fiber, and 20-30 percent protein [33]. Flaxseed contains a high proportion of polyunsaturated fatty acids such as ALA and linolenic acid and a moderate amount of monounsaturated fatty acids such as oleic acid. Because of its favorable combination of polyunsaturated and monounsaturated and saturated fatty acids, flaxseed lipid is the most nutritionally attractive chemical component of flaxseed. Flaxseed contains 40% lipids (70-73% polyunsaturated), with alpha-linolenic acid making up more than half of this fat. Flaxseed contains approximately 30% alpha-linolenic acid (ALAs), 17% linolenic acid, 19% oleic acid, 3% stearic acid and 5% palmitic acid, resulting in an excellent n-6:n-3 fatty acid ratio of approximately 0.3:1 [34].

Aside from that, flaxseeds also contain phytoestrogens, lignans, vitamin E, and carotenoids, all of which are linked to cardiovascular health. It also contains most of the secoisolariciresinol diglucose (SECO), a lignan that is metabolized to enterodiol and enterolactone [35]. SECO is used in flaxseed as a diglucoside, which is part of an ester-linked complex or oligomer containing 3-hydroxyl-3-methylglutaric acid and is a rich source of omega-3 fatty acids. Because it contains alpha-linolenic acid, lignans, and polysaccharides, flax is considered a healthy food. It contains over 800 times the amount of dietary lignan found in most other foods, which is why it has attracted interest as a possible functional food [36].

Therapeutic properties

Because of its nutritional benefits, flaxseed holds promise for many chronic diseases. Flaxseed has been found to help with coronary disease, atherosclerosis, asthma, cancer, obesity, osteoporosis, autoimmune diseases, developmental disabilities, brain growth and function, and hormonal status. In epidemiological and laboratory studies, consumption of ALA from flaxseed has been shown to prevent cardiovascular disease. Flaxseed has more than three times the amount of omega-3 fatty acids as omega-6 fatty acids, resulting in an omega-6/omega-3 (n-6/n-3) fatty acid ratio of 0:3:1. The use of flaxseed in the diet can increase the absorption of omega-3 fatty acids and thus improve the fatty acid ratio.

Omega-3 fatty acids are abundant in flaxseeds, which are known to help prevent cardiovascular disease, high blood pressure, cancer, skin conditions, kidney dysfunction, rheumatoid arthritis, and

multiple sclerosis, to name a few of the diseases [37]. Flaxseed proteins are used as sources of bioactive peptides such as angiotensin converting enzyme inhibitors and free radical scavengers, in addition to their nutritional benefits [38]. The multifunctional nature of peptides derived from flaxseed proteins is also reflected in studies that have shown potential health-promoting functions such as antimicrobial, antihypertensive, calmodulin-inhibiting, anti-inflammatory, antioxidant, and antidiabetic properties [39].

Antioxidant activity

Flaxseed plays an important role in the field of nutrition and disease research due to its potential health benefits associated with R-linolenic acid (57%) and an important lignan, secoisolariciresinol diglucoside (SDG), which is 600-700 times higher than in other edibles plant sources. Flaxseed has the potential to improve lipid peroxidation and thus oxidative damage. Flaxseed has a high concentration of the lignan SDG. A study by Rajesha., *et al.* (2006) evaluated the antioxidant activity of flaxseed at 5 and 10 percent measured by feeding weaned albino rats for 14 days. The 10 percent flaxseed treated group showed 95, 182, and 136 percent recovery of catalase, SOD, and peroxidase, respectively, indicating the beneficial effect of flaxseed components as an antioxidant, as seen by the recovery of liver enzymes [40].

Anti-proliferative action

During ischemia-reperfusion, flaxseed can impede arrhythmogenesis. It also protects against atherogenesis as well as vascular dysfunction in hypercholesterolemic states. A study by Mandasescu., *et al.* (2005) reported that flaxseed showed antiatherogenic activity in mice after 24 weeks of supplementation. Compared to mice fed dietary cholesterol alone, supplementation of the high-cholesterol diet with 10% (w/w) ground flaxseed reduced plasma cholesterol and saturated fatty acids, increased plasma ALA, and prevented plaque formation in the aorta and the aortic sinus [41]. It has been repeated that 20-50g per day of flaxseed in healthy subjects has been shown to reduce circulating total and LDL cholesterol levels while having no effect on HDL levels [42].

Silva and Alcorn (2019) reviewed the role of flaxseed lignans as important dietary polyphenols in cancer prevention and treatment. The authors discussed the mechanism of action of lignans to prevent the formation of cancer cells. Flax lignans block carcinogenesis by inhibiting pro-carcinogen activation into electrophilic species and their subsequent interaction with DNA. Alternatively, lignans can stimulate the detoxification of carcinogens and their subsequent elimination from the body. Ultimately, it suppresses cancer by interfering with cancer promotion through non-genetic changes and regulating cancer progression. Flax lignans can act as blocking and suppressive agents to modulate autophagy, cell cycle and differentiation, thereby affecting cancer cell proliferation [43].

Anti-diabetic effect

The presence of phytic and soluble fiber in flaxseed plays a role in lowering blood sugar levels. SDG derived from flaxseed has been shown to be beneficial in preventing both type 1 and type 2 diabetes. It has been suggested that SDG's hypoglycemic role in type 2 diabetes is attributed to its antioxidant function. It is conceivable that the hypoglycaemic role of the SDGs in type 2 diabetes is due to inhibition of the phosphoenol pyruvate carboxykinase enzyme, which is a rate-limiting enzyme in glucose metabolism [44]. The ALA found in flaxseed also plays a role in insulin sensitivity and glycemic regulation.

In obese individuals, flaxseed reduces insulin resistance by controlling oxidative stress. Flaxseed can dramatically lower postmeal blood sugar levels [45]. According to Wang., *et al.* (2013), -linolenic acid has the potential to improve peripheral insulin sensitivity in obese people, which contributes to the prevention and cure of type 2 diabetes and atherosclerotic vascular disease. In obese patients with glucose intolerance, flaxseed affects glycemic management and inflammatory biomarkers [46]. In addition, flaxseed contains soluble viscous fiber, which delays gastric emptying and glucose uptake and lowers the glycemic response to carbohydrate-containing foods [47].

Cardio-protective effect

Flaxseed has been shown to counteract atherogenic effects through its cellular action. There are three possible mechanisms of action. It is well known that antioxidants can suppress atherogenesis in animals and reduce it in humans. In addition, flaxseed contains omega-3 fatty acids, which have anti-inflammatory effects and inhibit atherogenesis. In addition to its anti-atherogenic potential, flaxseed also contains powerful antioxidants in its lignans [48]. After 24 weeks of dietary intervention, researchers discovered that flaxseed (0.4g/day) effectively inhibited the expression of inflammatory markers such as interleukin (IL)-6, mac-3 and vascular cell adhesion molecule-1 (VCAM-1) in vascular atherosclerotic tissue from mice [49]. Likewise, about 20grams of ground flaxseed per day for 60 days has been shown to reduce TG (by 36%) and cholesterol (by 17%) in mildly hypercholesterolemic adult [41]. According to studies Including 40g (approx. 4.5 tablespoons) of ground flaxseed in a low-fat, low-cholesterol diet is feasible, well tolerated and a good source of soluble fiber and ALA.

Sesame seeds

Sesame, scientifically known as *Sesamum indicum L.*, is a member of the Pedaliaceae family. One of the oldest oilseeds ever discovered, sesame seeds are traditionally used for their antioxidant properties, mainly due to the presence of vitamin E (alpha-tocopherol) and lignans, including sesamin, sesamolin, and sesamol [50]. It ranks ninth among the oilseeds in the world. Sesame dates back

to 1600 BC. and is said to have originated in the Central African savannah and then spread across western Asia to India. India, China, Sudan, Ethiopia, Uganda and Pakistan are the top producers of sesame [51].

Sesamum Indicum is an annual shrub with white bell-shaped flowers that belongs to the Pedaliaceae family. Sesame is grown primarily in tropical, subtropical, and southern temperate climates around the world, with most production occurring in India, China, South America, and Africa [52]. Due to the presence of a good amount of protein and unsaturated fatty acids such as linoleic acid, lignans such as sesamin, sesaminol, sesamol, sesamolinol and sesamolin, phytosterols and tocopherol content, sesame is one of the most common medicinal plants with high nutritional value [53]. In addition to the great therapeutic potential, sesame oil is very stable. Sesame seeds are small (3-4 mm long and 1.5-2 mm wide), flattened, ovate, smooth or reticulated. Sesame seeds can be seen in different colors like white, yellow, green, red, brown and black. Among the most valuable oilseeds, sesame seed is primarily a commercial export product [54]. Black and white sesame seeds are identical, however, black sesame seeds have a higher nutritional calcium content because they retain their husk portion. In addition to iron, both seeds are a good source of zinc, riboflavin, niacin and thiamin.

Chemical composition

Sesame seeds are known to be used in many medicinal products as they contain various bioactive components (including essential nutrients): polyunsaturated fatty acids, tocopherols, phytosterols, flavonoids and an extraordinary class of phenylpropanoids. Various alkaloids, saponins, tannins, cardiac glycosides, carbohydrates, terpenoids, flavonoids and sterols are present in these seeds. Even good lignin content is present as it contains both oil-dispersed and glycosylated lignans. Chemically, sesame oil seeds are made up of 17-19 percent protein and 16-18 percent carbohydrates [55].

The sesame seed fat content, which contains about 300 ppm sesamin & sesamolin, has a higher proportion of 50-60 percent. The phenolic antioxidants namely sesamol (3,4-methylenedioxyphenol), sesaminol and sesamolinol are produced during refining [56]. Sesame seeds are a good source of minerals like potassium, phosphorus, magnesium, calcium and sodium. Phosphorus is present in large amounts because it is important for the production of amino acids. Due to the presence of a balanced amino acid composition, especially the sulphur-containing amino acid methionine, which is really unusual in other plant proteins [57].

Therapeutic properties

Sesame seeds have many potential health benefits and have been used in folk medicine for thousands of years. The health-promoting properties are due to the presence of bioactive compounds such as lignans and phenol. Recent research has found that phenolic phytochemicals have potent antioxidant activity, as well as antidiabetic and antihypertensive effects. Sesame seeds have been shown to reduce oxidative stress through the activities of vitamin E and lignans such as sesamin, sesamolin, and sesamol [58]. The phytosterols contained in sesame seeds have anti-cancer, anti-atherosclerotic, anti-inflammatory and antioxidant properties. Similarly, the lignans present in sesame seeds have a variety of pharmacological activities, including antioxidant activity, antiproliferative activity, increasing the antioxidant activity of vitamin E in lipid peroxidation processes, lowering cholesterol levels etc. Sesamin is the most abundant lignan found in sesame, which has anti-obesity, antihypertensive, antioxidant and lipid-lowering properties [59].

Anti-hyperlipidemic effect:

The hyperlipidemic effect of sesame seeds is due to the presence of phytosterols, which help to lower plasma levels of fat-soluble vitamins, since fat-soluble vitamins circulate with LDL, causing a drop in circulating LDL levels. Studies have shown that consumption of dietary sesame seed powder reduces plasma total cholesterol, LDL cholesterol, and the ratio of LDL to HDL cholesterol in postmenopausal women. Ingestion of a healthy diet along with a 40g white sesame seed supplement in patients with hyperlipidemia for 3 months demonstrated a significant reduction in serum levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and TC/HDL-C ratio. Sesame seed supplementation showed a reduction in lipid peroxidation (TBARS) while activities of glutathione peroxidase (GPX) and superoxide dismutase (SOD) were increased, along with increased antioxidant activity in hyperlipidemic patients [60].

A study by Tsai-Sung., *et al.* (2019) discussed the mechanism of action of sesamin, a naturally occurring lignan, in inhibiting ligand-induced lipogenesis. Sesamin has been selectively shown to reduce hepatic lipogenesis via inhibition of SREBP-1c expression and its downstream target genes. It plays a role in activating AMPK and increases recruitment of SMILE to the SREBP-1c promoter, which inhibits hepatic lipogenesis. However, these effects were opposite in gut cells, where there is no SMILE recruitment but competitively increased SRC-1 binding to the ABCG1 promoter region. Researchers suggested that sesamin might alleviate drug-induced lipogenesis via suppression of LXR and PXR signaling [61].

Anti-diabetic effect:

Sesame seeds have a reducing effect on plasma glucose concentration. Sesame seeds, especially its oil, contain magnesium and other minerals that have been shown to help manage diabetes [62]. In hypertensive diabetics, the use of sesame oil as the only cooking oil has a convincing effect on reducing blood pressure and plasma glucose [63]. Sankar and his co-researchers discovered

that sesame oil increases the effectiveness of the oral antidiabetic drug glibenclamide in type 2 diabetics. The combination therapy of sesame oil and glibenclamide demonstrated an improved anti-hyperglycaemic effect with a 36 percent reduction in glucose levels and a 43 percent reduction in HbA_1c at endpoint [64].

Anti-inflammatory effect:

Haghighian., *et al.* (2015) investigated the protective effect of a sesame seed supplement (40g for 2 months) in patients with osteo-arthritis, which showed significant inhibition of inflammatory biomarkers. A significant decrease in serum MDA and hs-CRP was reported after the 2-month study ($P < 0.05$). Serum IL-6 was also significantly reduced. Sesame may also increase nutrients that may protect against cardiovascular disease [65].

Anti-carcinogenic effect

In addition to containing an anti-cancer compound called phytate, sesame seeds also contain magnesium, which has anti-cancer properties. According to Wark., *et al.* (2012) 100 mg of magnesium reduced the risk of colon tumors by 13% and the risk of colon cancer by 12% [66]. Consuming sesame seeds tends to increase plasma gamma-tocopherol and vitamin E activity, all of which are thought to help reduce cancer and heart disease [67].

Pumpkin seeds

Pumpkin (Cucurbita sp.) is a fruiting vegetable native to the western hemisphere and easily grown in tropical countries of Asia such as Indonesia, Malaysia and the Philippines. Although the gourd itself has various benefits, its seeds have been the focus of interest in the field of nutrition and disease research in recent years due to the emerging various active compounds [68]. Until now, pumpkin seeds have long been considered agricultural waste, although the presence of some specific bioactive compounds and their nutraceutical properties are used to treat and ward off a variety of diseases. This well-known traditional crop is native to the warm-temperate regions of South America and belongs to the Cucurbita genus, which is generally grown in spring and harvested in autumn [69].

Cucurbita maxima belongs to the genus Cucurbita. Pumpkins probably come from Central and South America. The seeds are tiny, flat, green edible seeds known as pepitas [70]. Pumpkin seeds have been used as an ingredient in a variety of dishes because, after salting and roasting, pumpkin seeds are eaten directly for human consumption as a snack in many cultures around the world.

Chemical composition

Pumpkin seeds are becoming increasingly popular as nutraceuticals. The therapeutic and nutritional importance of pumpkin seeds is mainly due to the presence of unsaturated fatty acids, including palmitic, stearic, oleic and linoleic acids, as well as other nutraceutical components such as phytoestrogens and vitamin E, all of which have medicinal, nutraceutical and cosmeceutical potential [71]. Because it is high in unsaturated fatty acids, sterols, and tocopherols, it shows excellent potential for preventing certain diseases.

Pumpkin seeds are rich in protein (25-37%), vitamins and oil (35-45%), especially omega-6 fatty acids (40-55%). Along with these seeds, they are an important source of crude fiber (31.48 percent) and other bioactive compounds such as tocopherols and carotenoids, which have important antioxidant, anti-inflammatory, and hypolipidemic properties [72]. Certain amino acids such as arginine, glutamine, tryptophan, lysine, methionine and aspartic acids are found in abundance in pumpkin seeds [73]. The pumpkin seed oil contains a high concentration of sterols such as secoisolariciresinol (21 mg/100g dw) and lariciresinol are also present. The high concentration of phytosterols (265-289 mg/100g) in pumpkin seeds allows controlling hypercholesterolemia [74]. The presence of protein, fiber, minerals such as iron, zinc, calcium, magnesium, manganese, copper and sodium makes pumpkin seeds an essential food ingredient for the food industry.

Therapeutic properties

Researchers have so far particularly focused on the bioactive components mainly fatty acids, phytoestrogens and tocopherol in pumpkin seed oil, which have attracted attention for their antioxidant, anti-inflammatory, anti-diabetic, anti-cancer, anti-cardiovascular, anti-hyperlipidemic and estrogen-like effects. However, the widespread use of pumpkin seeds is gaining positive acceptance not only as an edible oil but also as nutraceuticals. Nutrients such as antioxidant phenolic compounds, tocopherols, triterpenes, saponins, phytosterols, lignans and carotenoids contained in pumpkin seeds have also demonstrated their great antioxidant ability [75]. Bioactive compounds found in pumpkin seeds, such as D-chiro-inositol, trigonelline, and nicotinic acid, serve as mediators of insulin action. Pumpkin seeds contain fiber that helps with constipation, diabetes, intestinal transit, cholesterol levels, and satiety [76].

The essential fatty acids found in pumpkin seeds, which belong to the omega-6 and omega-3 families, have significant nutritional properties as well as important roles in a variety of metabolic pathways [77]. Consuming pumpkin seeds in your diet may help prevent prostate testosterone-induced hyperplasia. Its high mineral content such as magnesium and phosphorus, which help maintain bone health and prevent osteoporosis. Pumpkin seeds also contain the phytoestrogen compounds secoisolariciresinol and lariciresinol, which have estrogen-like effects in menopausal women, e.g. B. to prevent hyperlipidemia and osteoporosis. The phytoestrogens found in pumpkin seeds may also be linked to a lower risk of hormone-dependent tumors [78]. The tryptophan found in pumpkin seeds helps regulate mood due to its antidepressant properties [79].

Anti-oxidant effect

Due to the existence of phenolic compounds and tocopherol isomers (a, b, g and d), it has been confirmed that raw pumpkin seeds have antioxidant capacity and thus can help reduce the risk of diabetes mellitus [80]. Another study found that the diet supplemented with flaxseed and pumpkin seed mixture produced a significant reduction in GSH levels, CAT and SOD activities (57, 27 and 60% respectively) in plasma and kidneys (34, 34 and 25% respectively) [81].

Abou-Zeid., *et al*. (2018) discussed the antioxidant mechanism of action of pumpkin seed oil against emamectin-induced toxicity in mice. Treated mice received dietary emamectin benzoate at 75 ppm, while another group of animals received emamectin in addition to pumpkin seed oil at a dose of 4 mL/kg for 8 weeks. Administration of emamectin induced oxidative stress in liver and kidney as shown by increased levels of MDA and percentage of DNA fragmentation with suppression of GSH level and CAT and SOD activities. The brain showed an increase in MDA levels with inhibition of SOD activity. However, administration of pumpkin seed oil along with emamectin resulted in significant liver and kidney protection and complete brain protection. It was concluded that the protective effect of pumpkin seed oil against toxic effects is due to its lipophilicity, which makes it easy to penetrate cell membranes and produces a significant improvement in the toxic burden of emamectin in mice [82].

Cardio-protective effect:

Seed oil extracted from two types of pumpkin, namely *Cucumeropsis mannii* and *Citrullus lanatus* (oil-rich variety), is known for its reducing effects on lipid levels. The high content of unsaturated fatty acids in pumpkin seeds prevents heart disease and promotes good health. Phytoestrogen components play the key role in inhibiting cardiovascular outcomes and balancing plasma lipid levels such as total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides [83]. Pumpkin seeds showed cardio-protective benefits by lowering blood pressure and causing a modest improvement in endothelial function in postmenopausal women. In a randomized controlled trial, the effect of seeds and seed oil on blood pressure and menopausal symptoms in non-hypertensive postmenopausal women was compared with pumpkin seed oil (PSO) supplementation (1 teaspoon/4.1grams per day) versus pumpkin seed oil (PSO) (2g/Day). After a 12-week trial, systolic blood pressure in both groups showed a 3% reduction [79].

Anti-carcinogenic effect

The pumpkin seed oil reduces the risk of cancer because it contains the high amount of the different carotenoid pigments [84]. These seeds show low androgenic activity and are considered safe in the treatment of prostate cancer. Cell growth inhibition for fast-growing cells along with cell growth inhibition of prostate, breast and colon cancer cells supports the ethnomedical use of pumpkin seeds to treat benign prostatic hyperplasia. Pumpkin seeds contain compounds like cucurbitacins and moschatin that have anti-cancer properties. Pumpkin seeds are used to minimize hormonal damage to prostate cells and reduce the risk of prostate cancer. Richter., *et al.* (2013) evaluated the effect of pumpkin seed extract (PSE) on estradiol production and estrogen receptor (ER)/ER/progesterone receptor (PR) status on MCF7, Jeg3 and BeWo cells. The bioactive components contained in the pumpkin seed extract showed a significant impact on cancer prevention and treatment. The study showed a concentration-dependent increase in estradiol production. Significant ER down-regulation and significant PR up-regulation were also observed [85].

Anti-diabetic effect:

Pumpkin seed extract intake has been shown to lower blood sugar levels and increase insulin levels in diabetic rats [86]. Major bioactive compounds in pumpkin seeds such as trigonelline (an alkaloid that of niacin), nicotinic acid and D-chiro-inositol, exerts a hypoglycemic effect. These seeds are effective in preventing diabetes-related complications due to the presence of phytochemicals. Trigonelline, D-chiroinositol, and nicotinic acid, known as insulin action mediators or insulin sensitizers, are among the phenolic antioxidants present in pumpkin seeds. The possible mechanism affects pancreatic cell qualification along with insulin release, glucose metabolism and enzyme activity [75]. Consumption of pumpkin seed oil can reverse the risk of developing diabetes by reducing the elevated levels of the enzymes plasma alanine aminotransferase (ALT) and aspartate aminotransferase. Regular consumption of pumpkin seeds in meals could be useful in preventing diabetes and its related complications [87].

The phyto-compounds present in above functional super-seeds, shown to have therapeutic potential in controlling various diseases, work through different prevention mechanisms. A summarized content of the seed's major therapeutic properties and their mode of action resulting in disease management has been discussed in table 1.

Discussion

Changing lifestyles and dietary habits have taken a toll on the health of people worldwide, ultimately increasing the prevalence of non-communicable diseases. Coping with these diseases creates a demand for dietary changes. Functional foods are one of the most promising and evolving aspects of nutrition. Bioactive compounds in functional foods such as fiber, oligosaccharides, essential fatty acids, phytochemicals and antioxidants that have protective effects on human well-being and may play a role in minimizing the risk of chronic degenerative diseases. Edible seeds are one of the functional foods known for their phytotherapeutic properties due to the presence of phytocomponents in them that help in the treatment of various NCDs.

Super Seeds (Scientific Name)	Therapeutic Properties	Mode of Action	Reference
Chia Seeds (*Silva Hispanica Lamiaceae*)	Anti-inflammatory effect	Inhibits NF-κB transcription factor activation. Reduce inflammation and carcinogenesis. Protect against attack by reactive oxygen and nitrogen species.	[18,19]
	Anti-diabetic effect	Effect on glucose homeostasis by controlling AKT activation, gluconeogenesis, and glycolytic pathways. Increases insulin receptor expression. Controls secretion of glucose synthetase	[20,21,22]
	Anti-hyperlipidemic effect	Omega -3 rich seeds helps to inhibit key indicators of cholesterol synthesis	[24]
Flaxseeds *(Linum usitatissimum L.*)	Anti-oxidant activity	R-linolenic acid (57%) and (Secoisolariciresinol diglucoside) SDG lignan are responsible for anti-oxidant potential Improve lipid peroxidation	[40]
	Anti-inflammatory effect	Probiotics, SFA, PUFAs and n-3 fatty acids found in flaxseed has role in down-regulating inflammatory cytokines such as IFN- and TNF-	[88]
	Anti-proliferative effect	Flax lignans block carcinogenesis by inhibiting pro-carcinogen activation into electrophilic species and their subsequent interaction with DNA, thus affect cancer cell proliferation.	[43]
	Anti-diabetic effect	SDGs (Secoisolariciresinol diglucoside) has role in inhibition of the phosphoenol pyruvate carboxykinase enzyme, which is a rate-limiting enzyme in glucose metabolism. ALA found in flaxseed also plays a role in insulin sensitivity and glycemic regulation. Soluble fiber delays gastric emptying and glucose uptake and lowers the glycemic response to carbohydrate-containing foods	[44,45,47]
	Cardio-protective effect	Omega-3 rich flaxseeds show cardio-protective response by inhibiting atherogenesis. Lignans inhibit the expression of inflammatory markers such as Interleukin (IL)-6, mac-3 and vascular cell adhesion molecule-1(VCAM-1)	[48,49]
Sesame Seeds (*Sesamum indicum*)	Anti-hyperlipidemic effect	Phytosterols, which help to lower plasma levels of fat-soluble vitamins, since fat-soluble vitamins circulate with LDL, causing a drop in circulating LDL levels Reduction in lipid peroxidation (TBARS) Increases glutathione peroxidase (GPX) and superoxide dismutase (SOD) activity, along with increased antioxidant activity. Sesamin lignan helps ito reduce hepatic lipogenesis via inhibition of SREBP-1c expression and its down-stream target genes. Sesamin activates AMPK and, which inhibits hepatic lipogenesis.	[60,61]
Pumpkin seeds *(Cucurbita sp.)*	Anti-diabetic effect	D-chiro-inositol and Myo-inositol associated with insulin resistance and act to partially restore insulin sensitivity and glucose disposal	[86]
	Anti-oxidant effect	Phenolic compounds and tocopherol isomers (a, b, g and d) in pumpkin seeds significantly reduce GSH levels, CAT and SOD activities	[81,82]
	Cardio - protective effect	Phytoestrogen components play the key role in inhibiting cardiovascular outcomes and balancing plasma lipid levels such as total cholesterol, low- density lipoprotein (LDL), high- density lipoprotein (HDL) and triglycerides.	[79,83]
	Reproductive effect	Zinc rich pumpkin seeds, has important role in prostrate function and reproductive organ growth	[83]

Table 1: Major therapeutic properties of Super-seeds and their mode of action.

Chia seeds (*Silva H L)* are rich in antioxidants, fiber and protein, making them a powerful therapeutic agent. Natural antioxidants in chia seeds such as phenolic acids, isoflavones, anthocyanins, polyphenols and peptides help inhibit NF-κB transcription factor activation and reduce inflammation and carcinogenesis. Flaxseed (*Linumusitatissimum L*), which is an excellent source of PUFA, plays an important role in the prevention of inflammatory diseases by improving disease severity by down-regulating inflammatory cytokines such as IFN- and TNF-. Dietary lignans found in flaxseed play a role in preventing cancer and heart disease by inhibiting the expression of inflammatory markers. The presence of phytic and soluble fiber in flaxseed helps in lowering blood sugar levels. Sesame seeds (*Sesamum indicum L.)* are known for their antidiabetic and antihypertensive effects due to the presence of phenolic phytochemicals. Phytosterols and sesamin lignan are naturally present in sesame seeds and play a role in the treatment of hyperlipidemia and inflammatory diseases. Other lignans like sesamin, sesamolin, and sesamol are known to reduce oxidative stress. Pumpkin seeds (*Cucurbita maxima)* contain mediators of insulin action, such as D-chiro-inositol, trigonelline and nicotinic acid, which play a role in controlling diabetes. Phytoestrogen components play the key role in inhibiting cardiovascular outcomes and balancing plasma lipid levels. Seeds are a good source of zinc and low androgenic activity, so they are considered safe in treating prostate cancer. The main bioactive compounds in pumpkin seeds such as trigonelline (a niacin-derived alkaloid), nicotinic acid and D-chiro-inositol exert hypoglycemic effects.

Although the multifactorial pathogenicity of NCDs requires a multi-model therapeutic approach, using these superseeds discussed above as a phytotherapeutic approach is practical and inexpensive. The nutritional aspects of these seeds can be improved to increase their consumption in the daily diet for both international commodities and rural populations.

Declaration

Ethical Approval and Consent to Participate

Our institute do not require review based studies to be undergone Ethical approval or any consent.

Consent for Publication

All the authors have given their consent for publication of review article in your journal.

Conflict of Interest

There is no conflict of interest.

Author's Contribution

This work was done as collaborative effort of all the authors. Divya Jain guided during designing stage of the review and supervised at each step including data collection and, analysis and writing of manuscript.

Tamanna Kohli* performed the task of data collection, wrote the protocol of this manuscript, and managed the analysis of this study. Saloni Chauhan helped and supervised during planning of this review article, helped in review writing and critically revised the manuscript.

Funding

No funding was taken for this research project.

Data Availability

Data sharing is not applicable to this article as no new data were created or analyzed in this study as it is a review paper.

Acknowledgements

Nil.

Bibliography

1. Juma K., *et al.* "Non-Communicable Diseases and Urbanization in African Cities: A Narrative Review" (2019).

2. WHO. Report on non-communicable diseases (2021).

3. Araleimath VR and Bhise SB. "Antidiabetic effect of *Gymnema Sylvestre* extract on reptozotocin induced diabetic rats and possible β-cell protective and regenerative evaluation". *Digest Journal of Nanomaterials and Biostructures* 7.1 (2012): 135-142.

4. Thakur JS., *et al.* "Social and Economic Implications of Non-communicable diseases in India". *Indian Journal of Community Medicine* 36.1 (2011): S13-S22.

5. Adams S., *et al.* "Does dietary fiber affect the levels of nutritional components after feed formulation". *Fibers* 6.2 (2018): 29.

6. Ayerza R., *et al.* "Chia seed *(Salvia hispanica L.)* as an n-3 fatty acid source for broilers: influence on fatty acid composition, cholesterol and fat content of white and dark meats, growth performance, and sensory characteristics". *Poultry Science* 81 (2012): 826-837.

7. Al-Sheraji SH., *et al.* "Prebiotics as functional foods: A Review". *Journal of Functional Foods* 5 (2013): 1542-1553.

8. Chicco AG., *et al.* "Dietary chia seed *(Salvia hispanica L.)* rich in alpha-linolenic acid improves adiposity and normalises hypertriacylglycerolaemia and insulin resistance in dyslipaemic rats". *British Journal of Nutrition* 101.01 (2009): 41-50.

9. Nieman DC., *et al.* "Chia seed does not promote weight loss or alter disease risk factors in overweight adults". *Nutrition Research* 29.6 (2009): 414-418.

10. Capitani M., *et al.* "Rheological properties of aqueous dispersions of chia *(Salvia hispanica L.)* mucilage". *Journal of Food Engineering* 149 (2015): 70-77.

11. Munoz LA., *et al.* "Chia Seed *(Salvia hispanica):* An Ancient Grain and a New Functional Food". *Food Reviews International* 29.4 (2013): 394-408.

12. Marcinek K and Krejpcio Z. "Chia Seeds *(Salvia hispanica):* Health Promoting Properties and Therapeutic Applications - A Review". *Rocz Panstw Zakl Hig* 68.2 (2017): 123-129.

13. Ixtaina VY., *et al.* "Physical properties of chia *(Salvia hispanica L.)* seeds". *Industrial Crops and Products* 28.3 (2008): 286-293.

14. Segura-Campos., *et al.* "Chemical and functional properties of chia seed *(Salvia hispanica L.)* gum". *International Journal of Food Science* (2014): 241053.

15. Ayerza R and Coates W. "Composition of chia *(Salvia hispanica)* grown in six tropical and sub-tropical ecosystems of South America". *Tropical Science* 44 (2004): 131-135.

16. Capitani MI., *et al.* "Physicochemical and functional characterization of by-products from chia *(Salvia hispanica L.)* seeds of Argentina". *LWT-Food Science Technology* 45 (2012): 94-102.

17. Sowmya S., *et al.* "*In vitro* antioxidant activity*, in vivo* skin irritation studies and HPTLC analysis of Cayratia trifolia (L.) Domin". *International Journal of Toxicological and Pharmacological Research* 7.1 (2015): 1-9.

18. Aggarwal B and Shishodia S. "Molecular targets of dietary agents for prevention and therapy of cancer". *Biochemical Pharmacology* 71.10 (2006): 1397-1421.

19. Meyer B and Groot R. "Effects of omega-3 long chain polyunsaturated fatty acid supplementation on cardiovascular mortality: The importance of the dose of DHA". *Nutrients* 9.12 (2017): 1305.

20. Ayerza RJ and Coates W. "Effect of dietary alpha-linolenic fatty acid derived from Chia when fed as ground seed, whole seed and oil on lipid content and fatty acid composition of rat plasma". *Annals of Nutrition and Metabolism* 51.1 (2007): 27-34.

21. Sala-Vil A., *et al.* "Atherosclerosis" 214 (2011): 209-14.

22. Enes BN., *et al.* "Effect of different fractions of chia *(Salvia hispanicaL.)* on glucose metabolism,*in vivo* and *in vitro". Journal of Functional Foods* 71 (2020): 104026.

23. Alwosais EZ., *et al.* "Chia seed *(Salvia hispanica L.)* supplementation to the diet of adults with type 2 diabetes improved systolic blood pressure: randomized controlled trial". *Nutrition and Health* 27.2 (2021): 181-189.

24. Coelho MS., *et al.* "Peptides from chia present antibacterial activity and inhibit cholesterol synthesis". *Plant Foods for Human Nutrition* 73 (2018): 101-107.

25. Vuksan V., *et al.* "Comparison of flax *(Linum usitatissimum)* and Salba-chia *(Salvia hispanica L.)* seeds on postprandial glycemia and satiety in healthy individuals: A randomized, controlled, crossover study". *European Journal of Clinical Nutrition* 71.2 (2017): 234-238.

26. Alexander A and Miguel M. "Dietary fiber in the prevention and treatment of metabolic syndrome: A review". *Critical Reviews in Food Science and Nutrition* 48.10 (2008): 905-912.

27. NISCIR Report. National Institute of Science Communication and Information Resources, CSIR, New Delhi, India (2006).

28. Amin T and Thakur M. "*Linum usitatissimum L.* (Flaxseed) A Multifarious Functional Food". *Online International Interdisciplinary Research Journal* 4.1 (2014): 220-238.

29. Basch E., *et al.* "Flaxseed and flaxseed oil *(Linum usitatissimum):* A Review by the natural standard research collaboration". *Journal of the Society for Integrative Oncology* 5.3 (2007): 92-105.

30. Sargi SC*., et al.* "Antioxidant capacity and chemical composition in seeds rich in omega-3: Chia, Flax, And Perilla". Journal of Food Science and Technology 33.3 (2013): 541-548.

31. Shahzad HA., *et al.* "Physical and sensoric attributes of flaxseed flour supplemented cookies". *Turkish Journal of Biology* 30 (2006): 87-92.

32. Alu'datt MH., *et al.* "Distribution, antioxidant and characterization of phenolic compounds in soybeans, flaxseed and olives". *Food Chemistry* 139 (2013): 93-99.

33. Coskuner Y and Karababa E. "Some physical properties of flaxseed *(Linum usitatissimum L.)". Journal of Food Engineering* 78 (2007): 1067-1073.

34. Pellizzon MA., *et al.* "Flaxseed reduces plasma cholesterol levels in hypercholesterolemic mouse models". *Journal of the American College of Nutrition* 26.1 (2007): 66-75.

35. Pan AYuD., *et al.* "Meta analysis of the effects of flaxseed interventions on blood lipids". *The American Journal of Clinical Nutrition* 90 (2009): 288-297.

36. Rubilar M., *et al.* "Flaxseed as a source of functional ingredients". *Journal of Soil Science and Plant Nutrition* 10.3 (2010): 373-377.

37. Prasad K. "Flaxseed: a source of hypocholesterolemic and antiatherogenic agents". *Drug News and Perspectives* 13.2 (2000): 99.

38. Marambe HK., *et al.* "Release of angiotensin I-converting enzyme inhibitory peptides from flaxseed *(Linum usitatissimum L.)* protein under simulated gastrointestinal digestibility". *International Journal of Food Science and Technology* 48.3 (2011): 628-635.

39. Hwang C., *et al.* "Antioxidant and antibacterial activities of peptide fractions from flaxseed protein hydrolysed by protease from Bacillus altitudinis HK02". *International Journal of Food Science and Technology* 51 (2016): 681-689.

40. Rajesha J., *et al.* "Antioxidant Potentials of Flaxseed by *in vivo* model". *Journal of Agricultural and Food Chemistry* 54 (2006): 3794-3799.

41. Mandasescu S., *et al.* "Flaxseed supplementation in hyperlipidemic patients". *Revista Medico-Chirurgicala a Societatii de Medici si Naturalisti din Iasi* 109 (2005): 502-506.

42. Lucas EA., *et al.* "Flaxseed improves lipid profile without altering biomarkers of bone metabolism in postmenopausal women". *The Journal of Clinical Endocrinology and Metabolism* 87 (2002): 1527-1532.

43. Silva S and Alcorn J. "Review: Flaxseed lignans as important dietary polyphenols for cancer prevention and treatment: chemistry, pharmacokinetics, and molecular targets". *Pharmaceuticals* 12 (2019): 68.

44. Griel AE., *et al.* "An increase in dietary n-3 fatty acids decreases a marker of bone resorption in humans". *Nutrition Journal* 6 (2007): 2.

45. El-Tahir KE and Bakeet DM. "The black seed Nigella sativa Linnaeus-A mine for multi cures: a plea for urgent clinical evaluation of its volatile oil". *Journal of Taibah University Medical Sciences* 1.1 (2006): 1-9.

46. Wang DQ., *et al.* "Alpha-Linolenic acid improves insulin sensitivity in obese patients". *Zhonghua Yixueza Zhi* 93 (2013): 132-134.

47. Baranowski M., *et al.* "Dietary Flaxseed oil reduces adipocyte size, adipose monocyte chemoattractant protein-1 levels and T-cell Infiltration in obese, insulin-resistant rats". *Cytokine* 59 (2012): 382-391.

48. Prasad K. "Hypocholesterolemic and antiatherosclerotic effect of flax lignan complex isolated from flaxseed". *Atherosclerosis* 179.2 (2005): 269-275.

49. Dupasquier CM., *et al.* "Dietary flaxseed inhibits atherosclerosis in the LDL receptor-deficient mouse in part through antiproliferative and anti-inflammatory actions". *The American Journal of Physiology-Heart and Circulatory Physiology* 293.4 (2007): 2394-2402.

50. Duhoon SS., *et al.* "Sesame, Plant Genetic Resources: Oilseeds and Cash Crops" Narosa Publishing House, New Delhi, India (2004) 118-25.

51. Cooney RV., *et al.* "Effects of dietary sesame seeds on plasma tocopherol levels". *Nutrition and Cancer* 39 (2001): 66-71.

52. Kanu PJ., *et al.* "Nutraceutical importance of sesame seed and oil: A review of the contribution of their lignans". *Sierra Leone Journal of Biomedical Research* 2.1 (2010): 4-16.

53. Namiki M. "Nutraceutical Functions of Sesame: A Review". *Critical Reviews in Food Science and Nutrition* 47 (2007): 651-73.

54. Worako K., *et al.* "Analysis of Price Incentives for Sesame Seed in Ethiopia" 2005-2012". Ethiopia: FAO (2015).

55. Reshma MV., *et al.* "Extraction, separation and characterization of sesame oil lignan for nutraceutical applications". *Food Chemistry* 120 (2010): 1041-1046.

56. Tunde-Akintunde TY and Akintunde BO. "Some physical properties of sesame seed". *Biosystems Engineering* 88.1 (2004): 127-129.

57. Liao CD., *et al.* "Nano/sub-microsized lignan glycosides from sesame meal exhibit higher transport and absorption efficiency in Caco-2 cell monolayer". *Food Chemistry* 119 (2010): 890-896.

58. Kwon YI., *et al.* "Evaluation of clonal herbs of Lamiaceae species for management of diabetes and hypertension". *Asia Pacific Journal of Clinical Nutrition* 15.1 (2006): 107-118.

59. Wichitsranoi J., *et al.* "Antihypertensive and antioxidant effects of dietary black sesame meal in pre-hypertensive humans". *Nutrition Journal* 10 (2011): 82.

60. Alipoor B., *et al.* "Effect of sesame seed on lipid profile and redox status in hyperlipidemic patients". *International Journal of Food Sciences and Nutrition* 63.6 (2012): 674-678.

61. Tsai-Sung T., *et al.* "Sesamin, a Naturally Occurring Lignan, Inhibits Ligand-Induced Lipogenesis through Interaction with Liver X Receptor Alpha (LXRα) and Pregnane X Receptor (PXR)" (2019).

62. Takeuchi H., *et al.* "Hypoglycemic effect of a hot-water extract from defatted sesame *(Sesamum indicum L.)* seed on the blood glucose level in genetically diabetic KK-Ay mice". *Bioscience, Biotechnology, and Biochemistry* 65 (2001): 2318-2321.

63. Sankar D., *et al.* "Effect of sesame oil on diuretics or Betablockers in the modulation of blood pressure, anthropometry, lipid profile, and redox status". *Yale Journal of Biology and Medicine* 79.1 (2006): 19-26.

64. Sankar D., *et al.* "Sesame oil exhibits synergistic effect with antidiabetic medication in patients with type 2 diabetes mellitus". *Clinical Nutrition* 30.3 (2010): 351-358.

65. Haghighian MK., *et al.* "Effects of Sesame Seed Supplementation on Inflammatory Factors and Oxidative Stress Biomarkers in Patients with Knee Osteoarthritis". *Acta Medica Iranica* (2015).

66. Wark PA., *et al.* "Magnesium intake and colorectal tumor risk: a case control study and meta-analysis". *The American Journal of Clinical Nutrition* 96.3 (2012): 622-631.

67. Cooney RV., *et al.* "Effects of dietary sesame seeds on plasma tocopherol levels". *Nutrition and Cancer* 39.1 (2001): 66-71.

68. Lestari B and Meiyanto E. "A Review: The Emerging Nutraceutical Potential of Pumpkin Seeds". *Indonesian Journal of Cancer Chemoprevention* 9.2 (2018): 92-101.

69. Chen Q., *et al.* "Quality assessment and variety classification of seed-used pumpkin by-products: Potential values to deep processing". *Food Science and Nutrition* 7.12 (2019): 4095-4104.

70. Sarkar S and Guha D. "Effect of ripe fruit pulp extract of Cucurbita pepo Linn. in aspirin induced gastric and duodenal ulcer in rats". *Indian Journal of Experimental Biology* 46.9 (2008): 639-645.

71. Stevenson DG., *et al.* "Oil and Tocopherol Content and Composition of Pumpkin Seed Oil in 12 Cultivars". *Journal of Agricultural and Food Chemistry* 55.10 (2007): 4005-4013.

72. Barakat LA and Mahmoud RH. "The antiatherogenic, renal protective and immunomodulatory effects of purslane, pumpkin and flax seeds on hypercholesterolemic rats". *North American Journal of Medicine and Science* 3.9 (2011): 411.

73. Ristic-Medic D., *et al.* "Effects of dietary milled seed mixture on fatty acid status and inflammatory markers in patients on hemodialysis". *The Scientific World Journal* (2014).

74. Rajasree RS., *et al.* "Phytochemicals of Cucurbitaceae family - A Review". *International Journal of Pharmacognosy and Phytochemical Research* 8 (2016): 113-123.

75. Adams GG., *et al.* "The hypoglycemic effect of pumpkin seeds, Trigonelline (TRG), Nicotinic acid (NA), and D-Chiro-inositol (DCI) in controlling glycemic levels in diabetes mellitus". *Critical Reviews in Food Science and Nutrition* 54 (2014): 1322-1329.

76. Ratnam N., *et al.* "A review on Cucurbita pepo". *International Journal of Pharmacognosy and Phytochemical Research* 9.9 (2017): 1190-1194.

77. Miura Y. "The Biological Significance of w-oxidation of Fatty Acids". *Proceedings of The Japan Academy. Series B, Physical and Biological Sciences* 89.8 (2013): 370-382.

78. Patel D., *et al.* "Therapeutic Potential of Secoisolariciresinol Diglucoside: A Plant Lignan". *International Journal of Pharmaceutical Sciences and Drug Research* 4.1 (2012): 15-18.

79. Maiya M. "Effect of supplementation with pumpkin seed oil versus pumpkin seeds on blood pressure and menopausal symptoms in non-hypertensive postmenopausal women". Department of Nutrition and Food Sciences, College of Health Sciences, Texas Woman's University, Denton, Texas (2017).

80. Veronezi CM and Jorge N. "Bioactive Compounds in Lipid Fractions of Pumpkin (*Cucurbita sp*) Seeds for Use in Food". *Journal of Food Science* 77 (2012): 653-657.

81. Makni M., *et al.* "Flax and Pumpkin seeds mixture ameliorates diabetic nephropathy in rats". *Food and Chemical Toxicology* 48.8-9 (2010): 2407-2422.

82. Abou-Zeida SM., *et al.* "Ameliorative effect of pumpkin seed oil against emamectin induced toxicity in mice". *Biomed Pharmacotherapy* 98 (2018): 242-251.

83. Gossell-Williams M., *et al.* "Supplementation with Pumpkin Seed Oil Improves Plasma Lipid Profile and Cardiovascular Outcomes of Female Nonovariectomized and Ovariectomized SpragueDawley Rats". *Phytotherapy Research* 22.7 (2008): 873-878.

84. Jain D., *et al.* "Evaluation of antiulcer activity of ethanolic extract of Daemia extensa (jacq) R. Br. Seed". *Journal of Pharmacy and Pharmacology* 4.5 (2017): 41-44.

85. Richter D., *et al.* "Effects of phytoestrogen extracts isolated from pumpkin seeds on estradiol production and ER/PR expression in breast cancer and trophoblast tumor cells". *Nutrition and Cancer* 65.5 (2013): 739-745.

86. Xia T and Wang Q. "Antihyperglycemic effect of Cucurbita ficifolia fruit extract in streptozotocin-induced diabetic rats". *Fitoterapia* 77 (2006): 530-533.

87. Makni M., *et al.* "Antidiabetic effect of flax and pumpkin seed mixture powder: effect on hyperlipidemia and antioxidant status in alloxan diabetic rats". *Journal of Diabetes and its Complications* 25.5 (2011): 339-345.

88. Ibrahim A., *et al.* "Immunomodulatory and anti-angiogenic properties of *linum usitatissium* (flaxseed) seeds ethanolic extract in atherogenic diet treated rats". *Advances in Animal and Veterinary Sciences* 8.1 (2020).