

# Comprehensive Review of Seven Plant Seed Oils: Chemical Composition, Nutritional Properties, and Biomedical Functions

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# Comprehensive Review of Seven Plant Seed Oils: Chemical Composition, Nutritional Properties, and Biomedical Functions

Agata Sumara <sup>a</sup>, Anna Stachniuk <sup>a</sup>, Magdalena Montowska <sup>b</sup>, Klaudia Kotecka-Majchrzak <sup>b</sup>, Ewelina Grywalska <sup>c</sup>, Przemysław Mitura <sup>d</sup>, Lara Saftić Martinović <sup>e</sup>, Sandra Kraljević Pavelić <sup>f</sup>, and Emilia Fornal <sup>a</sup>

<sup>a</sup>Department of Bioanalytics, Medical University of Lublin, Lublin, Poland; <sup>b</sup>Department of Meat Technology, Poznan University of Life Sciences, Poznan, Poland; <sup>c</sup>Department of Experimental Immunology, Medical University of Lublin, Lublin, Poland; <sup>d</sup>Department of Urology and Urological Oncology, Medical University of Lublin, Lublin, Poland; <sup>e</sup>Department of Biotechnology, University of Rijeka, Rijeka, Croatia; <sup>f</sup>Faculty of Health Studies, University of Rijeka, Rijeka, Croatia

## ABSTRACT

A suitable and balanced diet is a major factor determining human health and should comprise unprocessed food enriched with oilseed products containing bioactive components and fatty acids. This paper reviews the chemical compositions and biomedical functions of plant seed oils extracted from black cumin, evening primrose, hemp, milk thistle, sesame, flax, and pumpkin seeds. The review provides a comprehensive overview of current oil extracting techniques and of the composition and content of bioactive components, including fatty acids, phytosterols, tocopherols, phenols, and carotenoids. Moreover, we describe research findings on the medical applications, benefits and limitations of treatment with plant seed oils for diverse diseases such as mastalgia, premenstrual syndrome, menopause, diabetes, metabolic syndrome, cancer, and urinary tract and liver disease, as well as their use in dermatology and chemotherapy. The use of plant seed oils as topical agents and their anti-bacterial properties are reviewed, as well as important precautions in their medical applications. The information provided in this review is intended to serve as a compendium for medical professionals in the field of integrative medicine, nutrition, and dietetics, and to help consumers make the best use of plant seed oils in accordance with their medical and health needs. The review is also addressed to food control laboratories, as it provides detailed tabularised data on the components and their contents in the above-mentioned seven plant seed oils. These data are highly useful for the development of new analytical methods for testing the quality and authenticity of oils.


## KEYWORDS

Edible oil; fatty acid; bioactive compound; medicinal plant; medical application; oil composition

## Introduction

Plant oils play an important role in the human diet globally, accounting for over 75% of the total lipids consumed daily.<sup>[1]</sup> Edible plant oils, such as black cumin (*Nigella sativa* L.), evening primrose (*Oenothera biennis* L.), flax (*Linum usitatissimum*), hemp (*Cannabis sativa* L.), milk thistle (*Silybum marianum*), pumpkin (*Cucurbita* spp.), and sesame (*Sesamum indicum* L.) oils are extracted from non-traditional seeds. The food industry also obtains oils from nuts, fruits, and beans. In comparison to major oilseed crops, such as sunflower or rapeseed, the above-mentioned species are not grown on a large scale, and thus the market for these non-conventional oils is smaller and their production cost

**CONTACT** Emilia Fornal  [emilia.fornal@umlub.pl](mailto:emilia.fornal@umlub.pl); [efornal@poczta.onet.pl](mailto:efornal@poczta.onet.pl)  Department of Bioanalytics, Medical University of Lublin, ul. Jaczewskiego 8b, Lublin, 20-090, Poland

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is higher. Consequently, they are not as widely available to consumers as the major plant oils, and they are more prone to adulterations. Plant seed oils are used mostly because of their biological activity and unique health properties<sup>[1]</sup> and they are a source of many significant phytochemicals such as carotenoids, tocopherols, sterols, and phenolic compounds, as well as vitamins and minerals<sup>[2, 3]</sup> Plant oils also contain essential fatty acids required for the proper development and function of the human body, which must be supplied by the diet because they cannot be synthesised by the body<sup>[4, 5]</sup> Many plants and plant oils have been used as medicines since antiquity, and they are still used in the food, pharmaceutical, and cosmetics industries<sup>[6]</sup> Numerous studies have confirmed the effectiveness of plant oils in the treatment of liver disease<sup>[7]</sup> atopic dermatitis<sup>[8]</sup> mastalgia<sup>[9]</sup> and diabetes<sup>[10]</sup> among others. The presence of bioactive compounds in plant oils depends on the plant species, origin, and method of cultivation. These factors affect the health-promoting properties and quality of the oils<sup>[11]</sup> as well as their plant metabolite content. To satisfy market demand, edible oils are obtained using various methods. Oils used for health purposes are typically obtained through cold pressing to prevent the degradation of bioactive compounds and fatty acids<sup>[12]</sup> and there is growing interest in pressing methods that use supercritical CO<sub>2</sub>. This safe and environmentally friendly technique ensures high-quality products<sup>[13]</sup> Residues obtained after oil extraction are often reprocessed and used as additives in food or as an animal feed.

From the analytical and pharmaceutical perspective, plant oils are an extremely complex matrixes owing to the high content of chemical compounds of varying concentration and originating from different groups of compounds. As the oils have beneficial health effects, which result from the presence of bioactive compounds in oils, the interest in the pressing of oils from not-typical oil plants is growing, and their consumption increases. Yet the research on correlations between oil composition and health effects, although many research groups undertake studies on biomedical applications of oils, are far from comprehensive. To support researchers in their efforts and endowers to strengthen our knowledge on the use of oils in prevention and treatment of disease and assist patients and consumers in the selection of oils best fitting their dietary and medical needs the review of research papers presenting the findings on chemical composition, nutritional properties, and biomedical functions was undertaken.

The aim of this study is to review the current status of our understanding of bioactive compounds, fatty acids, various extraction techniques, medical uses, and precautions in the medical applications of black cumin, evening primrose, flax, hemp, milk thistle, pumpkin, and sesame seed oils. The paper presents detailed information about oil products obtained using different extraction techniques from these seven non-traditional (niche) seeds cultivated globally. Tables summarising the groups and individual concentrations of bioactive compounds, including polyphenols, tocopherols, phytosterols, saturated, monounsaturated, and polyunsaturated fatty acids contained in those oil products, forms an important part of this paper. The medical applications, benefits and limitations of treatment with plant seed oils for diverse diseases including mastalgia, premenstrual syndrome, menopause, diabetes, metabolic syndrome, cancer, and urinary tract and liver disease, as well as their use in dermatology and chemotherapy are discussed. The use of plant seed oils as topical agents and their anti-bacterial properties are reviewed.

## Oil extraction techniques

The high demand for plant oils has led to the development of various oil extracting techniques. Plant oil production requires efficiency, high pressing speed, and a high-quality product<sup>[14]</sup> Several techniques are currently used to extract plant oils, including mechanical cold pressing<sup>[15]</sup> extraction with organic solvents<sup>[16]</sup> supercritical fluid extraction<sup>[14]</sup> ultrasound-assisted extraction<sup>[17]</sup> microwave-assisted extraction<sup>[18]</sup> and enzyme-assisted extraction<sup>[19]</sup>

Cold pressing is conducted in continuous screw presses at temperatures not exceeding 50°C in accordance with the provisions of the Codex Alimentarius. After collecting and washing, the seeds are dried to achieve a maximum water content of 7%, cleaned with a magnetic cleaner, and ground and

pressed. The obtained oil is then collected and transferred to dark containers to protect the final product from light. Mechanical extraction is an ecological, energy-saving, facile process<sup>[4]</sup> A low extraction temperature ensures high levels of bio-compounds, contributing to the high quality of the oils<sup>[15]</sup>

However, cold pressing is inefficient as it extracts only 60%–80% of the seed oil (5%–15% yield by weight)<sup>[20]</sup> Furthermore, the oxidation stability of cold-pressed oil is lower than that of oil extracted with organic solvents<sup>[15]</sup> such as *n*-hexane, *n*-hexane/ethanol, or isopropanol. The choice of an appropriate solvent, the ratio of solvent volume to seed weight, and the extraction temperature all affect the efficiency of the extraction process<sup>[16, 21]</sup>

The use of CO<sub>2</sub> in supercritical fluid extraction is a recent alternative to organic solvent and ultrasound-assisted extraction. The use of CO<sub>2</sub> as a solvent in supercritical fluid extraction processes is advantageous due to its low critical temperature (31.1 °C) and non-toxicity. Moreover, it is easy to completely remove the CO<sub>2</sub> from the product but the equipment required is expensive<sup>[22]</sup>

Ultrasound-assisted extraction operates in the frequency range >18–20 kHz, part of the frequency range (20–100 kHz) used in the food industry. The power density used for ultrasound-assisted extraction techniques is in the low-to-high range, from .01 to .1 and from 1 to 10 W/mL. Extraction efficiency is affected by the extraction time, temperature, and solvent composition. Ultrasound-assisted extraction helps obtain oils with greater efficiency and requires less energy and water compared with cold pressing, making it an environmentally friendly process<sup>[17]</sup>

## Oilseed plants

### *Black cumin seeds*

*N. sativa L.* is a small, grassy, annual plant and a member of the *Ranunculaceae* flowering plant family. Its common names are black onion seed, black cumin, and nutmeg flower<sup>[23]</sup> The species originated from Southern Europe, Asia, and North Africa, and it is now cultivated worldwide<sup>[24]</sup>

*N. sativa* reaches a height of 20–40 cm, has green leaves 2.5–5.0 cm long, and white, pale blue, or blue flowers with 5–10 petals<sup>[23]</sup> It is cultivated mainly for its small (1–5 mm), flattened, funnel-shaped seeds that become black upon exposure to air<sup>[25]</sup> The seeds contain 26%–34% oil and 20%–85% protein, and they are a rich source of minerals (K, P, Ca, Mg, S, Zn, Fe, Cu, Mn, and B)<sup>[24, 26]</sup>

The seeds have a unique, bitter taste, and they are usually added to bread, cooked dishes, and cheese or used to flavour beverages. In some regions, the seeds are ground and used to replace pepper<sup>[27]</sup> The seeds are used as a preservative additive to extend product shelf life<sup>[28]</sup> Oil extracted from *N. sativa* seeds has a characteristically strong smell and a dark yellow colour<sup>[29]</sup> The most important naturally occurring phenolic compounds in black cumin seed oil are the dark yellow compound thymoquinone and its dimer dithymoquinone, which helps protect the skin against UV radiation<sup>[30, 31]</sup>

### *Evening primrose*

Evening primrose (*O. biennis L.*) is a biennial plant belonging to the *Onagraceae* flowering plant family. The herb originated from North America, but it is now cultivated in Europe and some regions of Asia, Australia, and South Africa<sup>[32]</sup> The name ‘evening primrose’ refers to the tendency of the yellow flowers to open partially or totally in the evening when moths and butterflies can drink the nectar<sup>[33]</sup> Other names for the plant are ‘night willow herb’ and ‘King’s cure-all’<sup>[34]</sup> Evening primrose prefers sunny areas with average moisture conditions, but it can also grow in less favourable conditions.

Evening primrose seeds sprout in the summer or autumn. The plant can reach a height of 2 m, with rosette leaves 5–30 cm long and 1–7 cm wide. Its yellow flowers are 1.0–2.5 cm in diameter and have four petals that wither and turn orange. The seeds are 1.3–1.6 mm long and contain approximately 20%–30% oil<sup>[33, 34]</sup> and 2893 mg/100 g dry mass minerals (K, Na, Ca, Mg, Fe, Mn, Cu, and Zn)<sup>[35]</sup>

### Flax

Flax (*L. usitatissimum*) is an annual herb belonging to the *Linaceae* flowering plant family. It is one of the oldest cultivated plants and was used in Egypt before 6000 BC, as well as in Mesopotamia, Rome, and Greece, to make textiles. Flaxseed oil was used for embalming the Pharaohs and as a medicine. Today, flax is cultivated worldwide, especially in Kazakhstan, Russia, China, and India, but also in South and North America, Europe, and Africa<sup>[36]</sup>

Flax is also known as linseed and is a major oil seed plant globally<sup>[37]</sup> The plant reaches a height of 30–120 cm, with greyish-green leaves and small blue flowers. The seeds are 4–7 mm long, smooth, flat, and light brown<sup>[38]</sup> They usually contain 41% oil, 28% dietary fibre, and 20% protein<sup>[39]</sup> Every part of the flax plant has value; for example, flax fibre is used in the textile industry as a natural and ecological fabric, and waste fibre is an important ingredient in the production of high-quality paper such as air mail envelopes, cigarette papers, and currency notes<sup>[38]</sup>

### Hemp

Hemp (*C. sativa L.*) is an annual herb belonging to the *Cannabaceae* flowering plant family. Hemp was first used in China as a textile fibre and as food and medicine. It is one of the oldest cultivated plants. Hemp was distributed to Europe between 1000 and 2000 BC, and to South and North America in the 16<sup>th</sup> and 17<sup>th</sup> centuries. Today, it is cultivated at most altitudes, ranging from sea level to alpine foothills.

Depending on the growth conditions, the plant can reach a height of a 2.5–3.5 m<sup>[40]</sup> The leaves are alternate or opposite on the stem<sup>[41]</sup> The seeds contain 25%–35% oil, 20%–25% protein, and 20%–30% carbohydrates<sup>[42]</sup> Hemp can be cultivated either indoors or outdoors. The crop is affected by many factors, such as temperature, soil moisture, and light. Hemp is currently cultivated to meet the needs of the textile, food, and pharmaceutical industries<sup>[40]</sup> Hemp and hemp seed oil contain phytocannabinoid compounds, namely cannabidiol (CBD), tetrahydrocannabinol (THC), cannabichromene (CBCA), and tetrahydrocannabinolic acid (THCA), with CBD and THC having the highest concentrations. Extensive cannabinoid profiling was conducted by Citti et al. (2019)<sup>[43]</sup> CBD does not show psychoactive properties, unlike THC<sup>[44]</sup> Accordingly, the maximum THC content allowed by the European Parliament in food products is .2%<sup>[45]</sup>

### Milk thistle

Milk thistle [*S. marianum (L.) Gaertn*] is an annual or biennial plant and an important member of the *Asteraceae* flowering plant family. It has been known since antiquity as a detoxifying agent and a remedy for liver diseases<sup>[46]</sup> Milk thistle is currently studied for its hepatoprotective, neuroprotective, nephroprotective, and cardioprotective activities<sup>[47, 48]</sup> Silymarin comprises around 1.5%–3.5% of the fruit weight, and more than 50% of silymarin is silybin. The plant originated from the Mediterranean, and it is now cultivated in Europe, Asia, and Northern Africa, especially in warm and dry regions<sup>[49]</sup>

The plant ranges from .7 to 2 m in height, depending on moisture, soil composition, and weather conditions. The flowers are purple, and the leaves are dark green with characteristic spiny edges; the leaves exude milk sap<sup>[49]</sup> The fruits are small (6–7 mm) and grey to dark brown in colour<sup>[51]</sup> Milk thistle pericarp and seed coat are rich in the silymarin flavonoids silybin A and B, isosilybin A and B, silydianin, and silychristin taxiofolin<sup>[48, 52]</sup>

In addition to these bioactive components, the fruit contains 20%–30% oil, 25%–30% protein, and has a high copper content (17 mg/g). The roots, flowers, leaves, and stalks are used as forage for animals.<sup>[46, 53]</sup>

## **Pumpkin**

Pumpkin (*Cucurbita spp.*) is an annual plant and a member of the *Cucurbitaceae* family. The usefulness of this plant was recognised in ancient times in Central and North America, and it became widespread in Europe in the 16<sup>th</sup> century owing to its beneficial effects on human health<sup>[54, 55]</sup> Pumpkin is a common and well-known plant in traditional medicine, and it is used as an antioxidant, in the treatment of diabetes and high cholesterol levels, as a diuretic, as an anti-helminth agent, and in benign prostatic hyperplasia treatment.<sup>[55]</sup>

Pumpkin is a round orange fruit containing a large amount of pulp and oval, flat seeds that are green to red and contain a dark red fluorescent oil.<sup>[2, 54]</sup> The seeds comprise 24%–40% protein and 22–64% oil, and they are a source of vitamins (especially A, C, E, and the B group vitamins) and minerals (K, P, Mg, Ca, Na, Mn, Zn, Cu, and Fe).<sup>[11, 56]</sup> Pumpkin pulp is used to produce syrups, jams, juice, purees, and fruit cocktails. The seeds are roasted and salted as snacks<sup>[57]</sup>

## **Sesame**

Sesame (*S. indicum L.*) is an annual plant from the *Pedaliaceae* flowering plant family. Sesame was first cultivated over 5000 years ago in Asia, and it is now grown in over 50 countries, including the subtropical and tropical regions of South America, Asia, and Africa. Asia and Africa are the leading producers of sesame<sup>[59]</sup>

Sesame can reach a height of 1–2 m. The seeds are small (2–4 mm long and 1.5–2.0 mm wide), oval, and their colour ranges from yellow to black. The seeds contain 37%–63% oil, 10%–25% protein, 3%–14% carbohydrates, and 3%–5% ash, and they are used as a food additive, especially to improve the taste and aesthetic values of baked goods<sup>[60]</sup>

## **Oil components**

### **Fatty acids**

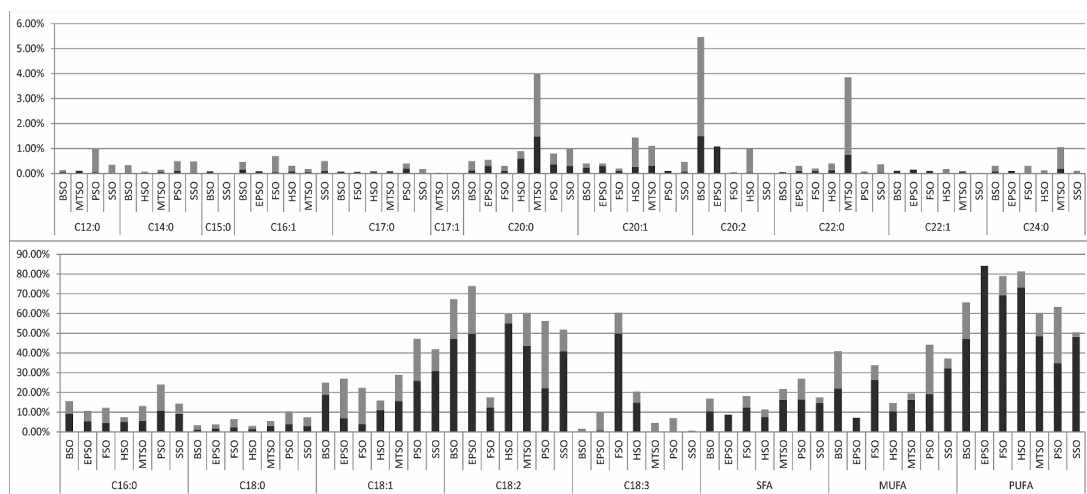
Depending on the plant species, growth conditions, and pressing process, plant oils can differ qualitatively and quantitatively, which affects the taste, colour, health-promoting properties, and antioxidant properties of the oils. Naturally occurring fatty acids are a large group of compounds, and their content affects the health-promoting properties of the final oil product substantially. The most important components of oils are saturated fatty acids (SFAs) and unsaturated fatty acids. SFAs are compounds with an even number of carbons and no double bonds, with palmitic (C16:0) and stearic (C18:0) fatty acids being the most common in plant seed oil. The highest concentration of SFAs in the oils discussed in this review are in pumpkin seed oil (16.4%–27.06%)<sup>[61, 62]</sup> and milk thistle seed oil (16.26%–21.67%)<sup>[63, 64]</sup> and the lowest is in evening primrose seed oil (8.65%)<sup>[65]</sup> Of the naturally occurring SFAs, palmitic acid was the most abundant fatty acid in the seven seed oils discussed in this paper, with pumpkin seed oil having the highest concentration of palmitic acid (10.74%–23.9%)<sup>[14, 66]</sup>

Monounsaturated fatty acids (MUFAs) contain one double bond and are another fatty acid group. Of the seven types of oil reviewed here, the largest amounts of MUFAs are found in pumpkin seed oil (19.06%–44.12%)<sup>[61, 67]</sup> and black cumin seed oil (21.93%–40.86%)<sup>[68]</sup> The most common MUFA is oleic acid (C18:1), with the highest concentrations found in pumpkin and sesame seed oils, at 18.14–44.11% and 30.8–41.9%, respectively<sup>[61, 67, 69, 70]</sup>

The third group of fatty acids are polyunsaturated fatty acids (PUFAs), which have two or more double bonds. Essential fatty acids are an important subgroup of PUFAs because they cannot be synthesised by the human body and must be supplied by the diet. Essential fatty acids include omega-3 (e.g.,  $\alpha$ -linolenic acid) and omega-6 (e.g., linoleic acid) fatty acids<sup>[5, 71]</sup> High concentrations of PUFA have been recorded in all seven oils, with the highest concentration in evening primrose seed oil (84.16%) and the lowest in sesame seed oil (48.2%–50.5%)<sup>[65, 72, 73]</sup> Fig. 1 shows the min–max range of fatty acids. Information on all seven plant seed oils (compound concentration, origin, and extraction technique) is presented in Tables S1 to S7 in the supplementary materials.

## Phenols

Phenols are a large, ubiquitous group of plant secondary metabolites. These compounds have an aromatic ring and one or more hydroxyl groups in their structure. Their effect on human health depends on their metabolism and bioavailability<sup>[74]</sup> Primarily, phenols act as strong antioxidants and can inhibit lipid oxidation. Therefore, phenols protect PUFA-rich oils against degradation of their health-promoting and olfactory and gustatory properties<sup>[75]</sup> Enriching the diet with products containing high amounts of phenolic compounds helps the prevention of neurodegenerative disorders or cardiovascular diseases<sup>[76]</sup> The results collected from different research articles show that the phenol concentrations in different oils range from 51 mg/kg in sesame seed oil<sup>[73]</sup> to 8120 mg GAE/kg (GAE: gallic acid equivalent) in milk thistle seed oil<sup>[64]</sup> The total phenolic contents in the seven plant seed oils are presented in Table 1, and detailed data are listed in Tables S1 to S7.



**Figure 1.** Min–max ranges of fatty acid contents in seven edible plant seed oils. BSO – Black Cumin seed oil; EPSCO – Evening Primrose seed oil; FSO – Flax seed oil; HSO – Hemp seed oil; MTSO – Milk Thistle seed oil; PSO – Pumpkin seed oil; SSO – Sesame seed oil. Lauric acid (C12:0); Myristic acid (C14:0); Pentadecanoic acid (C15:0); Palmitoleic acid (C16:1); Heptadecanoic acid (C17:0); Cis-Heptadecanoic acid (C17:1); Arachidic acid (C20:0); Cis-11-Eicosenic acid (C20:1); Cis-11,14, -Eicosenic acid (C20:2); Behenic acid (C22:0); Erucic acid (C22:1); Lignoceric acid (C24:0); Palmitic acid (C16:0); Stearic acid (C18:0); Oleic acid (C18:1); Linoleic acid (C18:2); Alpha linolenic acid (C18:3); SFA – Saturated fatty acid; MUFA – Monounsaturated fatty acid; PUFA – Polyunsaturated fatty acid.



**Table 1.** Total phenolic, tocopherol, and sterol contents of the seven studied plant seed oil..

Oil	Total Phenolic Content <sup>[Ref.]</sup>	Total Tocopherol Content <sup>[Ref.]</sup> [mg/kg]	Total Sterol Content <sup>[Ref.]</sup> [mg/kg]
Black Cumin	15.19–1140.4 <sup>a[18, 31]</sup>	91.5–279.2 <sup>[129]</sup>	812–2887.28 <sup>[29, 129]</sup>
Evening Primrose	55.49 <sup>b[124]</sup>	186.33 <sup>[65]</sup>	9149.21–9573.24 <sup>[65, 124]</sup>
Flax	768–3073 <sup>c[125]</sup>	271–788 <sup>[130, 131]</sup>	4722–7554 <sup>[130]</sup>
Hemp	440–2675 <sup>a[15, 126]</sup>	114.04–802.8 <sup>[15, 42]</sup>	2793.73 <sup>[42]</sup>
Milk Thistle	1160–8120 <sup>b[64, 127]</sup>	49.57–1015 <sup>[64, 132]</sup>	1816–6273.3 <sup>[63, 132]</sup>
Pumpkin	24.71–58.2 <sup>a[12, 128]</sup>	263.4–4420 <sup>[14, 79]</sup>	127.88–167400 <sup>[67, 82]</sup>
Sesame	51.0 <sup>b[73]</sup>	161.7–647 <sup>[73, 78]</sup>	5400–6376 <sup>[70, 133]</sup>

gallic acid equivalent (mg GAE/kg).

mg/kg.

ferulic acid equivalents (mg/kg).

## Tocopherols

The term ‘tocopherol’ encompasses various derivatives of vitamin E. These compounds are essential for human and animal health, as they have antioxidant, antiproliferative, pro-apoptotic, anti-angiogenic, and anti-inflammatory properties. They consist of a hydrophilic chromanol head and a hydrophobic isoprenoid side chain. The tocopherol family comprises four groups ( $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$ ), which differ in the number of methyl substituents on the aromatic ring.  $\alpha$ -Tocopherol, the main vitamin E derivative, has the highest biological activity<sup>[77]</sup>

Of the seven plant seed oils discussed here, the lowest concentrations of tocopherols were found in evening primrose seed oil and sesame seed oil (186.33 mg/kg and 161.7–647.0 mg/kg, respectively)<sup>[65, 73, 78]</sup> and the highest concentration was reported in pumpkin seed oil: 263.4–4420 mg/kg<sup>[14, 79]</sup> The total tocopherol contents in the seven plant seed oils are presented in Table 1, and detailed data are provided in Tables S1 to S7.

## Phytosterols

Phytosterols are plant-derived sterols and members of the triterpene family. The structure and function of phytosterols is very similar to cholesterol in vertebrates. Phytosterols are a ubiquitous group of compounds necessary for proper functioning of the plant. Campesterol, stigmasterol, and  $\beta$ -sitosterol are among the most common phytosterols. The concentrations of these compounds generally vary depending on the type of plant, with the highest concentrations found in seed oils<sup>[80]</sup> Phytosterols are found in high concentrations in plant food products, but only 1%–5% of the phytosterols ingested are absorbed in the digestive tract.<sup>[81]</sup> The high content of sterols in plant oil makes plant oils an important part of a balanced diet. Phytosterols lower LDL-cholesterol levels and intestinal cholesterol absorption, and they have anti-atherogenic and immunomodulating effects.<sup>[183]</sup> Phytosterols can cross the blood–brain barrier and accumulate in the brain. Thus, phytosterols could be metabolic modulators in neurodegenerative diseases such as Alzheimer’s disease.<sup>[184]</sup> Of the seven oils discussed here, the lowest concentration of phytosterols was recorded in hemp seed oil (2793.73 mg/kg)<sup>[42]</sup> and the highest concentration was reported in pumpkin seed oil (127.88–167400 mg/kg)<sup>[67, 82]</sup> The total phytosterol contents in the seven plant seed oils are presented in Table 1, and detailed data are collected in Tables S1 to S7.

## Medical applications of plant seeds oils

Plant seed oils are commonly used in alternative medicine or in addition to medical therapy using an integrative medicine approach. The health-promoting properties of seed oils have been demonstrated in numerous studies, as presented in the following sections.

### **Applications in treating mastalgia, premenstrual syndrome, and menopause**

Topical use of black cumin seed oil decreases pain in women suffering from cyclic mastalgia, with an efficacy comparable to a commercial painkiller<sup>[83]</sup> and the same efficacy as diclofenac<sup>[84]</sup> Similarly, a study conducted on a group of women aged 21–30 showed that after ingesting evening primrose seed oil at a dose of 1 g per day for one month, the reduction in mastalgia was comparable to that obtained with ormeloxifene<sup>[9]</sup> Evening primrose seed oil at a dose of 1 g twice a day helped to reduce premenstrual syndrome-related complaints compared with the placebo group<sup>[85]</sup> and helped control menopausal hot flushes<sup>[86]</sup> Pumpkin seed oil supplementation (3 g per day for 6 weeks) decreased hypertension in postmenopausal women, reducing brachial and central systolic blood pressure and improving arterial haemodynamics<sup>[87]</sup> The same oil (2 g per day for 12 weeks) increased the concentration of high density lipoprotein cholesterol and decreased diastolic blood pressure in postmenopausal women and significantly improved postmenopausal symptoms<sup>[88]</sup>

### **Applications in treating diabetes and metabolic syndrome**

A four-week treatment with black cumin seed oil helped increase insulin secretion and decrease blood glucose levels. The addition of black cumin seed oil to the diet was conducive to weight loss and weight maintenance and helped treat symptoms associated with obesity and insulin resistance<sup>[89]</sup> Supplementation with 10 g per day of flaxseed oil for 12 weeks by patients with type 2 diabetes mellitus and coronary heart disease showed beneficial metabolic changes, such as reduction in insulin and C-reactive protein levels<sup>[10]</sup> Another study showed that the inclusion of flaxseed oil in the daily diet may prevent or delay the onset of metabolic syndrome. In addition, patients with metabolic syndrome showed reduced oxidative stress biomarkers and reduced systolic and diastolic blood pressure after consuming flaxseed oil<sup>[90]</sup> Research conducted on type 2 diabetes mellitus patients showed that white sesame seed oil can regulate glucose metabolism by reducing glucose and glycosylated haemoglobin levels and increasing insulin levels after 90 days of consumption<sup>[91]</sup>

### **Anti-bacterial activity**

Black cumin seed oil helps inhibit the growth of pathogens that occur in food, such as *Staphylococcus aureus*, *Escherichia coli*, and *Listeria monocytogenes*<sup>[92]</sup> Black cumin seed oil also inhibits *Bacillus subtilis* and *Bacillus cereus*, yet is not cytotoxic<sup>[93]</sup> Flaxseed oil inhibits the growth of and biofilm formation by methicillin-resistant *S. aureus*, *Klebsiella pneumoniae*, and *Staphylococcus epidermidis*, and it aids the healing of wounds caused by infection by these bacteria<sup>[94, 134]</sup>

### **Applications in dermatology and as topical agents**

Evening primrose seed oil used as an adjuvant in the treatment of atopic dermatitis patients resulted in decreased symptoms<sup>[8]</sup> Topical treatment with evening primrose oil alleviated molluscum contagiosum in children and improved their skin after three months of treatment<sup>[95]</sup> Milk thistle seed oil is an ingredient in anti-aging preparations, and a four-week treatment with facial cream containing this oil improved skin condition, including a reduction in wrinkles and improved skin elasticity<sup>[96]</sup> The lipids in pumpkin seed oil form nanostructures that are used in the production of sun protection cosmetics. These topical sunscreens have strong antioxidant properties and may help delay photoaging and protect against skin cancer<sup>[97]</sup> In addition, a significant difference in hair loss was observed between men with androgenic alopecia treated with placebo and pumpkin seed oil. The mechanism of action of pumpkin seed oil is well documented: it inhibits the conversion of testosterone into more the potent compound dihydrotestosterone. Thus, androgens were partially inhibited in the group treated with

pumpkin seed oil.<sup>[56]</sup> Flaxseed oil showed some interesting effects on carpal tunnel syndrome when applied as a topical gel formulation and was more effective than using a hand splint in a controlled randomised clinical trial.<sup>[98]</sup>

### **Applications in cancer and chemotherapy**

A study on the anticancer action of hemp seed oil showed an inhibitory effect on cancer cell proliferation and an enhanced effect on cancer cell apoptosis.<sup>[99]</sup> A preliminary study conducted on melanoma in a murine model confirmed that cannabinoids from hemp seed oil affect the length and quality of life of mice with melanoma, suggesting that supplementation of the diet with hemp seed oil can affect the quality of life of patients undergoing radiotherapy and chemotherapy.<sup>[100]</sup> Preliminary research on patients with severe pain following chemotherapy shows that massaging the site of phlebitis with sesame seed oil helps reduce pain.<sup>[101]</sup>

### **Other specific applications in medicine**

Sesame seed oil has been used to treat patients with multiple sclerosis, and preliminary studies show that it can help improve their quality of life.<sup>[102]</sup> Clinical trials demonstrate that pumpkin seed oil is useful in the treatment of lower urinary tract symptoms connected with overactive bladder and the early stage of benign prostatic hyperplasia. Evening primrose seed oil can be used as a safe and non-invasive alternative in the treatment of chronic nonbacterial prostatitis.<sup>[103]</sup>

Black cumin seed oil shows promising results in the treatment of non-alcoholic fatty liver disease: it reduces liver steatosis and injury significantly and alters triglyceride, LDL-C, and HDL-C levels in the blood.<sup>[104]</sup> Moreover, the same oil shows promising results in the treatment of male infertility by improving semen quality significantly after two months usage at a dose of 5 ml/day.<sup>[105]</sup> Black cumin seeds can alleviate the negative effects of aflatoxin B1 in quails by increasing the levels of lactic acid bacteria and spore-forming bacteria while concomitantly decreasing the *E. coli* population.<sup>[106]</sup> Furthermore, in aflatoxin B1-intoxicated rats, thymoquinone, which is the main component of black cumin seeds, had a protective effect against aflatoxin B1-induced hepatotoxicity in mice.<sup>[107]</sup> A honey-based formulation of black cumin seed oil was effective in lowering the systolic and diastolic blood pressure in healthy volunteers in a placebo-controlled clinical trial<sup>[108]</sup> and when used for 8 weeks at a dose of 5 ml/day, it showed promising results in the treatment of functional dyspepsia.<sup>[109]</sup> Black cumin seed oil supplements were also tested for their effectiveness in regulating liver enzymes and lipid profiles in patients with non-alcoholic fatty liver disease: supplementation reduced inflammation markers.<sup>[110]</sup> Black cumin seed oil (500 mg twice a day for one month) also lowered the number of swollen joints and the duration of morning stiffness in rheumatoid arthritis patients.<sup>[111]</sup>

In a clinical trial conducted on relapsing remitting multiple sclerosis patients, a combined therapy of hempseed and evening primrose oils with a hot nature diet improved clinical symptoms after six months by altering the activity of delta-6-desaturase and secretory phospholipase-A2.<sup>[112]</sup> The authors also revealed that this combination improved erythrocyte membrane fatty acid composition in the same group of patients.<sup>[113]</sup>

Supplementation with flaxseed oil (1 g twice a day for 120 days) has a beneficial effect on chronic inflammation in dialysis patients by significantly decreasing C-reactive protein levels.<sup>[114]</sup> This effect may be correlated with the proven antioxidative properties of flaxseed oil in rats exposed to ultraviolet C radiation by preventing photoreactive damage.<sup>[115]</sup> A recently published meta-analysis showed the usefulness of various flaxseed supplements in controlling blood pressure, as evidenced in randomised controlled trials.<sup>[116]</sup> This finding is especially important considering the high rate of death associated with cardiovascular pathologies, where controlling blood pressure is a critical parameter correlated with life expectancy in cardiovascular patients.

Research studies on the therapeutic potential of seed oils are summarised in [Table 2](#).

**Table 2.** Studies of the medical applications of plant seed oils.

Oil	Disease <sup>[Ref.]</sup>	Organism
Black cumin	Type 2 diabetes <sup>[137]</sup>	human
	Osteoarthritis <sup>[135]</sup>	human
	Bronchial asthma <sup>[23]</sup>	mice
	Behcet's disease <sup>[136]</sup>	human
	Non-alcoholic fatty liver disease <sup>[110]</sup>	human
	Phlebitis induced by chemotherapy <sup>[138]</sup>	human
Evening primrose	Rheumatoid arthritis <sup>[139]</sup>	human
	Mastalgia <sup>[9]</sup>	human
	Premenstrual syndrome <sup>[85]</sup>	human
	Mild atopic dermatitis <sup>[8]</sup>	human
	Multiple sclerosis <sup>[140]</sup>	human
	Type 2 diabetes <sup>[141]</sup>	human
	Polycystic ovary syndrome <sup>[142]</sup>	human
	Menopausal hot flashes <sup>[86]</sup>	human
	Gestational diabetes mellitus <sup>[143]</sup>	human
Flax	Diabetic foot ulcer <sup>[144]</sup>	human
	Non-alcoholic fatty liver disease <sup>[7]</sup>	human
	Type 2 diabetic with coronary heart disease <sup>[10]</sup>	human
	Metabolic syndrome <sup>[90]</sup>	human
	Ethanol-induced liver injury <sup>[145]</sup>	mice
	Dry eye disease <sup>[146]</sup>	human
	Multiple sclerosis <sup>[147]</sup>	human
Hemp	Atopic dermatitis <sup>[148]</sup>	human
	Hepatic steatosis <sup>[48]</sup>	mice
Milk thistle	Metabolic syndrome <sup>[58]</sup>	mice
	Overactive bladder <sup>[149]</sup>	human
Pumpkin	Aspiration pneumonitis <sup>[54]</sup>	rat
	Alcohol-induced hepatotoxicity <sup>[150]</sup>	rat
	Chronic nonbacterial prostatitis <sup>[103]</sup>	human
	Antinociceptive and anti-inflammatory activities <sup>[151]</sup>	rat
Sesame	Osteoarthritis <sup>[152]</sup>	rat
	Myocardial injury <sup>[153]</sup>	rat
	Small bowel obstruction <sup>[154]</sup>	human
	Osteoarthritis <sup>[155]</sup>	rat
	Hypertensive <sup>[156]</sup>	human
	Chemotherapy-induced phlebitis <sup>[101]</sup>	human
	Knee osteoarthritis <sup>[157]</sup>	human

## Precautions in medical applications of plant seed oils, and perspectives

Despite the proven benefits of using plant seed oils in various medical applications<sup>[50]</sup> especially to support patient well-being and recovery, some general precautions must be noted. Clinical evidence-based data should be considered when designing the optimal treatment regimen and thus more research in this area is required. The product safety label should also be taken into account. In particular, in medical preparations based on natural sources, special attention should be paid to the heavy-metal content, as the contamination of foodstuffs and medical products with heavy metals is recognised by regulatory agencies to be potentially harmful to human health. Such contamination is mainly due to anthropogenic activity that has disrupted the balance in the heavy metal content of the Earth's crust, resulting in their accumulation in various plants, including plant seeds. These contaminants include lead (Pb), cadmium (Cd), aluminium (Al), chromium (Cr), nickel (Ni), mercury (Hg), arsenic (As), chromium (Cr), copper (Cu), selenium (Se), and silver (Ag)<sup>[117]</sup> The ingestion of contaminated plants or products of plant origin can lead to the build-up of these metals in the body, which may have deleterious effects on human health. As plant seed oils can also be contaminated with heavy metals, oils should be tested carefully before consumption or use in medical applications. Currently, inductively coupled plasma–mass spectrometry (ICP–MS) is the gold standard for the monitoring of heavy metals.<sup>[118]</sup> For example, it is important to assess the heavy metal content in Ayurvedic preparations<sup>[119, 120]</sup> and World Health Organization (WHO) guidelines now stipulate that

the heavy metal content of such preparations should be measured and compared with permissible limits<sup>[117]</sup> Studies on seed oils have demonstrated the capacity of plants to absorb and accumulate heavy metals from contaminated soil. For example, the seed oil of *Solanum melongena L.* (eggplant) in a study conducted in India showed unacceptably high concentrations of Cd and Pb (39.32 µg/L for Cd and 20.05 µg/L for Pb)<sup>[121]</sup> Acceptable heavy metal levels in edible oils are set out by WHO in the Codex Alimentarius, in which the maximum permissible concentration for Pb and As is .1 mg/kg.<sup>[122]</sup> The heavy metal content decreases in the course of food processing, as demonstrated by Lee et al. for oilseeds obtained from sesame, perilla, and flax seeds.<sup>[123]</sup> Nonetheless, the globalisation of the food market requires stringent measures for monitoring the heavy metal content in food, including seed oils.<sup>[185]</sup>

Another concern is the contamination of plants with mycotoxins-producing fungi and their secondary metabolites, mycotoxins.<sup>[186, 187]</sup> The vast majority of mycotoxins are potentially teratogenic, carcinogenic, nephrotoxic, tremorogenic, haemorrhagic, or immunotoxic.<sup>[186]</sup> Seeds are mostly prone to fungal contamination during pre- and post-harvest, posing a significant danger to human health. Fungal contamination can be invisible to the naked eye and produce mycotoxins, even in extreme conditions such as low moisture and water levels. Climatic and storage conditions (high temperature and humidity) are crucial to the growth of mould. Mycotoxins are present in infected seeds and their oils and are heat stable. The toxigenic fungi *Aspergillus niger*, *A. flavus*, *A. ochraceus*, *A. tamarii*, *Penicillium citrinum*, *Fusarium spp.*, and *Alternaria* species have been shown to be associated with sesame seeds.<sup>[186]</sup> Aflatoxin B1 (the most toxic mycotoxin, causing hepatitis, haemorrhage, oedema, immunosuppression, and hepatic carcinoma) was detected at up to 20.45 µg/kg in 37 of 100 sesame paste samples.<sup>[188]</sup> Precautions taken include proper timing and method of harvesting (without damaging the product), suitable storage conditions, proper transportation, premarket storage in dry conditions, preventing insect infestation, monitoring mycotoxins levels, and educating producers and consumers.<sup>[186]</sup> Products should be stored in ventilated and dry sites in disinfected, sterilised, and moisture-proof containers.<sup>[189]</sup>

Various chemical components can be detected in edible plant oils, apart from biological contamination. Hu et al. quantified seven phthalic acid esters in 124 samples of 16 types of oilseeds from China.<sup>[190]</sup> Phthalic acid esters are lipophilic chemicals that are widely used in plastic manufacturing.<sup>[191]</sup> Research conducted on animals has shown that phthalic acid esters have a detrimental effect on the liver and endocrine systems by exhibiting a hormone-disrupting effect. Some esters are also classified as human-cancer agents.<sup>[190, 192]</sup> Plants can absorb esters from atmospheric particles, soil, and irrigation water, as well as from packaging materials and during manufacturing processes.<sup>[190, 192]</sup> Pesticide residues are also found in oil seeds.<sup>[189]</sup>

The storage and proper usage of plant oils by consumers are crucial for maintaining quality. Consumers should store sealed containers of oil in the dark at cool temperatures to prevent lipid oxidation, isomerisation, decomposition, nutrient degradation, decreased edibility value, and the synthesis of harmful compounds.<sup>[193]</sup> Improper thermal treatment of oils may result in the synthesis of undesirable forms of fatty acids.<sup>[194]</sup>

To address concerns over the quality and safety of plant seed oils, strict monitoring and quality control is required during cultivation, processing, transportation, and storage.<sup>[189]</sup> The production of safe edible oil requires that producers pay attention to each step in the process and take proper safety measures to monitor each process.<sup>[189]</sup> New, inexpensive, and fast methods of detecting contamination in oilseeds are increasing. International establishment of and compliance with strict limits on the content of various compounds are necessary to ensure the correct and safe production, distribution, and trade of seed oils.<sup>[189]</sup> Reliable guidelines on the proper dosage and use of edible plant oils are needed to maximise their health benefits and ensure user safety. More systematic research on the medical applications of plant oils is likely in the next decade, given current direct links between new niche oils and their health benefits. The chemical composition of oils should be characterised as completely as possible, allowing their biomedical evaluation and providing an

understanding of the molecular basis of the health benefits of consuming plant oils and of the role of lipids in physiological and pathological processes<sup>[195]</sup> Standardised methods and assays for studying the chemical compositions and antioxidant and biomedical properties of oils should be developed and implemented to allow better comparison of published findings. Cold pressed niche oils are important components of a diet rich in nutrients. The popularity of such diets is increasing quickly, making such oils prone to adulteration. The development of methods for testing the authenticity of plant oils and detecting fraud is also very important. Research in the medical applications of plant seed oils would be facilitated and accelerated by establishing a curated database of research findings on the chemical compositions, biomedical properties, and medical applications of oils, as well as methods for testing plant seed oils.

## Conclusions

Plant seed oils are widely used in food, pharmaceutical, and cosmetics products, and they are important in the diets of people worldwide<sup>[189]</sup> In this study, we discussed the characteristics of seven common plant oils: black cumin seed oil, evening primrose seed oil, hemp seed oil, milk thistle seed oil, sesame seed oil, flaxseed oil, and pumpkin seed oil. In particular, we covered the methods used in plant oil production, the bioactive constituents of the obtained oils, and their biomedical properties. The increasing consumption of these oils has led to research on their possible pharmaceutical and medical applications, as evidenced by scientific publications. The present study provided a comprehensive overview of published scientific data on the properties of seven plant oils. These data provide important evidence-based information for medical professionals. Further research on the bioactivity and medical applications of plant seed oils is highly encouraged to guide medical professionals and consumers in the choice of oils for specific health-promoting or medical applications. Seed oil products have a place in integrative medical approaches, and their use can be additionally fostered by careful product quality controls.










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## ORCID

Agata Sumara  <http://orcid.org/0000-0001-8677-7379>  
Anna Stachniuk  <http://orcid.org/0000-0001-6384-1999>  
Magdalena Montowska  <http://orcid.org/0000-0002-6331-5726>  
Klaudia Kotecka-Majchrzak  <http://orcid.org/0000-0001-5109-6776>  
Ewelina Grywalska  <http://orcid.org/0000-0002-0451-4741>  
Przemysław Mitura  <http://orcid.org/0000-0002-2021-4490>  
Lara Saftić Martinović  <http://orcid.org/0000-0001-5637-4659>  
Sandra Kraljević Pavelić  <http://orcid.org/0000-0003-0491-673X>  
Emilia Fornal  <http://orcid.org/0000-0002-0503-0706>

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