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Nutraceutical Value of Sesame Oil

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ABSTRACT
Nutrients, herbals and dietary supplements are major constituents of nutraceuticals which make them active in maintaining health, act against various disease conditions and thus promote the quality of life. Drug as dietary supplements play a major role to alleviate all type of disease. The sheer number and type of dietary supplements available is overwhelming, and it's hard to know which offer health benefits and which are merely giving false promises - often the information about supplements is confusing or unclear. From ancient time globally the peoples were using the sesame oil as dietary source. Sesame oil is known dietary source having putative antioxidant property. In this review we summarized the medicinal value of sesame oil with respect to phytochemistry and pharmacological activity. This article must provide the data for the researcher to develop the molecule from sesame oil to treat many type life threatening diseases.
KEYWORDS : Sesame oil, Antioxidants, Dietary supplements, *Sesamum indicum*, Oxidative stress

INTRODUCTION

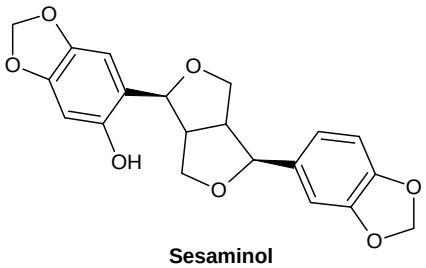
SESAME OIL

Sesame has been part of the human diet since ancient times. Sesame oil is one of the major dietary oils in Asian countries. Sesame seeds and oil contain several kinds of sesame lignans that may contribute to improved human health. Sesame oil, derived from the seeds of plant species of *Sesamum indicum* Family *Pedaliaceae,* consists of various fatty acids and nonfat antioxidants, including tocopherol, sesamin, sesamolin, and sesamol (1). Sesame seed believed to be indigenous to tropical Africa and cultivated in India, China and Nigeria (2). Sesame oil is obtained by refining the expressed or extracted oil from the seeds of *Sesamum indicum.* The oil consists of glycerides of oleic, linoleic, palmitic, stearic and myristic acids and also contains a crystalline substance, sesamine, and a phenolic substance sesamol, which gives the red colour with 1% solution sucrose in strong hydrochloric acid (2).

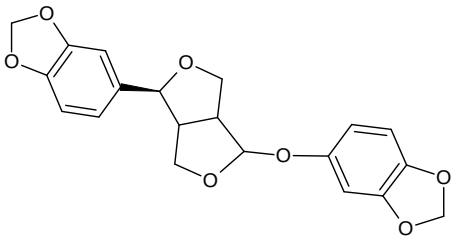
PHYTOCONSTITUENTS FROM SESAME OIL

Sesamum indicum seed has been an important oil seed since ancient times. It contains protein, oil & many other bioactive compounds. Lignans and lignin glycosides have been most intensively studied due to their antioxidative properties. On the other hand, napthoquinones and anthraquinones have been isolated from the roots, an unutilized part of sesame. Chlorosesamone, hydroxysesamone and 2, 3-epoxysesamone has been isolated from the roots and their antifungal activities reported. Anthrasesamones A-E has been isolated from the roots, and other two anthraquinone derivatives have been isolated from a hairy root culture of sesame (3). Sesamin and sesamolin are the most abundant lignans of sesame seeds and the major fat soluble lignans (4). Sesamin and sesamolin are comprised of benzene and furofuran rings. The structural difference between them is that sesamolin contains oxygen between its benzene and furofuran rings (5). Sesamin is absorbed via the lymph, incorporated into the liver, and then transported to the other tissues such as lung, heart, kidney, and brain (6). Sesamin is removed from serum and tissue within 24 hours after oral administration in rats (6), sesamin metabolite is mostly excreted and disappeared in urine within 24 hours (7). Sesamin is metabolized by cytochrome P450 in rat liver which results in conversion of the methylenedioxyphenyl to dihydrophenyl (catechol) moiety in structures. The dihydrophenyl (catechol) moiety has been reported to possess strong radical scavenging activities (8).

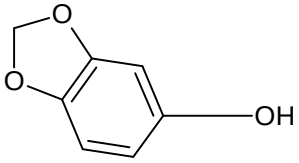
A new chlorinated red naphthoquinone pigment having antifungal activity, named chlorosesamone, was isolated from the roots of *Sesamum indicum.* Its structure was cherecterized as 2-chloro-5, 8-dihydroxy-3-(3-methyl-2-butenyl)-1, 4-naphthoquinone (9). Two anthraquinone derivatives, named anthrax sesamone D and E, were isolated from the roots of *Sesamum* indicum. Their respective structures were determined to be 1, 2, 4-tetrahydroxy-3-(4-methylpent-3-enyl) anthrax quinone and 1, 2-dihydroxy-3- (4-methylpent-3-enyl) anthrax quinone (10). 2-Geranyl-1, 4-naphthoquinone was isolated from the hairy root culture of *Sesamum indicum.* The structure was determined to be 2-[(*e*)-3, 7-dimethylocta-2, 6-dienyl]-1, 4-naphthoquinone (11). A new anthraquinone derivative, named anthrasesamone F, was isolated from the seeds of *Sesamum indicum.* Its structure was determined to be (Z)-6, 7-dihydroxyl-2-(6-hydroxy-4-methyl-3-pentenyl) anthraquinone (3).

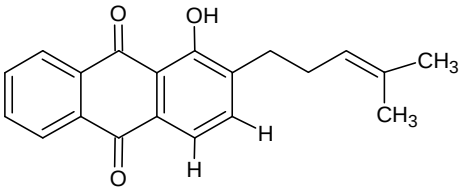


Sesaminol



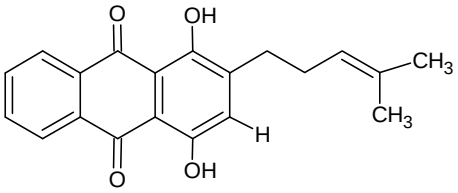
Sesamolin

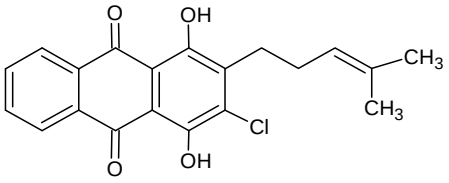




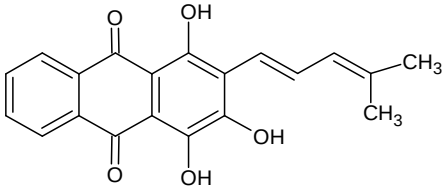
Anthrasesamone A

Sesamol

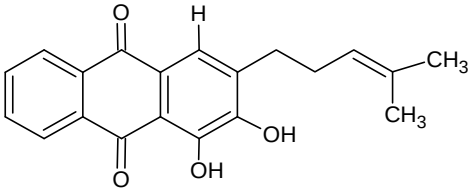




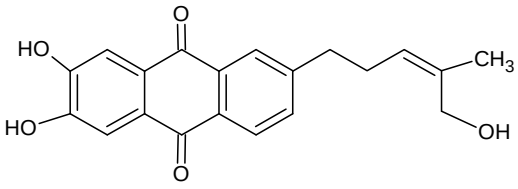
Anthrasesamone B



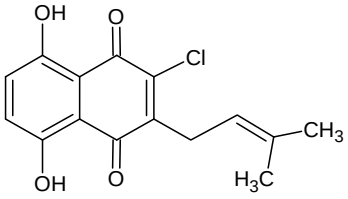
Anthrasesamone C



Anthrasesamone D

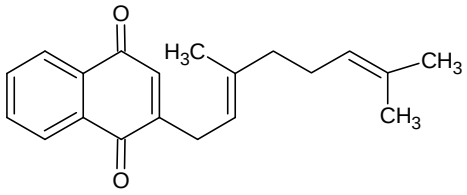


Anthrasesamone E



Anthrasesamone F

Chlorosesamone



2 - geranyl - 1, 4 - naphthoquinone

MEDICINAL VALUE

Sesamum indicum is used as external poultice, emenagogue, lactagogue, diuretic, tonic and demulcent (12). Sesamin and sesaminol are the major phenolic constituents of sesame oil which have been reported to possess a broad spectrum of pharmacological effects including anti-mutagenic, antioxidant, antihypertensive, anti-inflammatory antithrombotic and cardio protective effects (13).

Sesame oil has long been regarded as a daily nutritional supplement for increasing cell resistance to lipid peroxidation (LPO) (14). Sesame oil decreases LPO by inhibiting the generation of reactive oxygen free radicals and also it attenuates multiple organ failure triggered by endotoxin lipopolysaccharide in rats (8, 15-17). A single dose of sesame oil attenuates oxidative stress and hepatic injury in rats and also reduces iron initiated oxidative stress in rats & mice (15, 18-21). Sesame oil attenuated hepatic injury and decreased LPO, hydroxyl radical, and superoxide anion, but not nitric oxide, in acutely iron-intoxicated mice. Furthermore, inhibiting the activity of xanthine oxidase might be involved in the sesame oil-associated protection against acute iron-induced LPO and hepatic injury in mice. Although, circulating antioxidants have been associated with the depletion of superoxide anion during oxidative stress. More investigation is needed to confirm this, however (21, 22). Besides sesamin and sesamolin, sesaminol also demonstrated the antioxidant properties on the in vitro oxidative modification of human low-density lipoprotein (LDL); furthermore, it was a more effective scavenger than either α-tocopherol or probucol in reducing the peroxyl radicals derived from 2,2'-azobis (2-amidinopropane) dihydrochloride (23). The findings suggest the potential effect of sesame oil to protect LDL against lipid peroxidation.

Sesame oil increasing the alpha-tocopherol concentration in the blood and tissue it was observed in rats fed an alpha-tocopherol containing with sesame seed or its lignans (24). Additionally sesame oil showed the significant free radical scavenging capacity (RSC) in the methanolic fraction due to the presence of phenolic compounds (25). Hypoglycemic effect of a hot water extract from defatted sesame seed on the blood glucose level in genetically diabetic KK-A^y mice has been reported earlier, the results indicate that the extracts had a reductive effect on the plasma glucose concentration of KK-A^y mice, and this effect is suggested to have been caused by the delayed glucose absorption (26).

In addition to decrease lipid peroxidation and generation of reactive oxidative species, sesame oil increased the activities of antioxidative enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase in rodents under various conditions of oxidative stress (20, 21, 27, 28). A study in hypertensive patients indicated that sesame oil consumption remarkably reduced oxidative stress and simultaneously increased GPx, SOD, and catalse activities (29). These results support the hypothesis that sesame oil consumption may help to enhance antioxidant defense system in humans.

The potential antioxidant property and antihypertensive effect were reported earlier. The investigators suggested that sesamine is a useful prophylactic treatment in hypertension and cardiovascular hypertrophy (23, 30, 31). Administration of sesame oil at a dose of 5 ml/Kg before doxorubicin (DOX) treatment clearly attenuated the cardio toxicity. The oxidative damage to the heart contributes to the myocardial toxicity induced by DOX in male rats. These effects might be limited by the use of sesame oil. The protective effect of sesame oil may be due to its antioxidant properties (13).

Sesamin has been reported to inhibit desaturase activity, an enzyme that converts dihomo γ-linolenic acid (DGLA, 20:3, n-6) to arachidonic acid (AA, 20:4, n-6) (32). The inhibition of Δ5 desaturase activity results in accumulation of dihomo γ-linolenic acid whereas arachidonic acids are decreased, which also reduces the formation of pro-inflammatory mediators including prostaglandin PGE2, Tumor Necrosis Factor- α (TNF-α), Interleukin-6 and Interleukin-10 in mice (33). Thus, these studies imply that sesame lignans may affect the inflammatory pathway.

Animal studies have suggested that sesame lignans reduce cholesterol levels by both by inhibiting absorption and by decreasing synthesis of cholesterol (34, 35). Sesamin supplementation significantly reduced the concentration of serum cholesterol in rats fed a cholesterol-enriched diet; moreover, a significant reduction in the activity of liver microsomal 3-hydroxy-3-methylglutaryl Coenzyme A reductase (HMG-CoA reductase), the rate limiting enzyme of cholesterol synthesis in liver was observed (35). Additionally, sesamin can play a role as a transcriptional factor that regulates gene expression, sterol regulatory element binding proteins (SREBPs) which are membrane-bound transcriptional factors of the basic-helix-loop-helix-leucine zipper family, relating to cholesterol biosynthesis and LDL receptors, as well as fatty acid synthesis (34-36). SREBP-1 is mainly involved in the gene expression of enzymes in fatty acid synthesis and SREBP-2 regulates the gene expression of enzymes involved in cholesterol synthesis and the LDL receptor (36, 37). Dietary sesamin remarkably decreased not only mRNA of HMG-CoA reductase and LDL receptor, but also mRNA level and protein content of SREBP-1 in rat liver (34).

Furthermore, sesame lignans increase peroxisomal and microsomal hepatic fatty acid oxidation through increased gene expression of hepatic fatty acid oxidation enzymes in vivo in animal models (38-42). The mechanism of peroxisome proliferators-activated receptorα (PPARα) regulation of gene transcription has been proposed (36, 43), which is that PPAR binds DNA at direct repeats as a heterodimer with retinoid X receptor (RXR). In the unliganded state, this complex binds co-repressor proteins while in the liganded state, the co-repressor complex is replaced by a co-activator complex. This leads to a conformational change and promotes gene activation. These findings indicate that sesamin or other sesame lignans may act as a ligand for SREBPs and PPARs.

PHYSIOLOGIC EFFECTS OF SESAME OIL

The consumption of sesame seed or pure sesame lignans has been shown in vitro and in vivo to have diverse physiological functions, which may include antihypertensive and hypocholesterolemic effects. Consumption of sesame lignans

or sesame oil has been shown to lower blood pressure in several types of hypertensive animals and humans. A clinical trial in hypertension patients on treatment with nifedipine, an antihypertensive drug has demonstrated that the group that consumed dietary sesame oil had significantly lowered blood pressure compared with a group with nifedipine alone or other dietary oils (29). This study indicates that sesame oil may have potential effects on drug metabolism in humans. Sesamin metabolites containing a dihydroxyphenyl (catechol) structures have potent radical scavenging activities in vitro (8). It has been suggested that sesamin metabolites modulate the vascular tone and contribute to the in vivo antihypertensive effect of sesamin by inducing an endothelial nitric oxide-dependent vasorelaxation (22). The study suggests that the enhancement of endothelium-dependent vasorelaxation induced by sesamin metabolites is one of the possible mechanisms of antihypertensive effects of sesamin (22).

Sesame lignans may affect blood lipids as well as lipid metabolism, acting a hypocholestrolemic agent. The absorption of lymphatic cholesterol and fatty acids was highly inhibited and liver cholesterol levels were significantly lower in rats fed sesame oil diet (44, 45). Furthermore, the sesame oil diet significantly decreased levels of serum total cholesterol and LDL-cholesterol in rats (44). Sesamin supplements had similar effects on reducing the absorption of lymphatic and serum cholesterol in rats; moreover, a significant reduction in the activity of liver microsomal HMG-CoA reductase was observed (35). Animal studies have demonstrated that dietary sesame lignans may decrease triacylglycerols (TG) and cholesterol concentrations in blood and liver presumably through decreasing HMG-CoA reductase and LDL receptor mRNA levels (34). A recent study in postmenopausal women also showed that the consumption of dietary sesame seed powder reduces plasma total cholesterol, LDL cholesterol, and the ratio of LDL to HDL cholesterol (46). Another study with hypertensive patients demonstrated that total cholesterol, LDL-cholesterol and triglyceride decreased, while HDL-cholesterol was elevated by sesame oil consumption (29). These findings support that sesame consumption may inhibit the absorption and synthesis of cholesterol, which can improve blood lipids levels in humans.

A number of studies in vitro and vivo have shown that the consumption of sesame seed or pure sesame lignan affects γ-tocopherol metabolism, resulting in increased plasma γ-tocopherol concentrations (46-50). In rat studies, dietary supplementation with sesame seeds or pure sesame lignans dramatically increased blood and tissue γ-tocopherol concentrations (51-56). Additionally, urinary excretion of γ-CEHC in rats fed sesame lignans significantly decreased (56). The effect of sesame on γ-tocopherol has been studied in humans. Women who ate unrefined sesame oil (22.5 g/d) for 4 weeks demonstrated a 42% increase in serum γ-tocopherol concentrations (50). Postmenopausal women who consumed sesame powder (50 g/day) for 5 wk also had increased serum γ-tocopherol concentrations (46).

The cytochrome P450 (CYP), a superfamily of heme-thiolate proteins is responsible for the detoxification of foreign compounds or xenobiotic chemicals such as drugs and carcinogens, as well as for metabolism of endogenous compounds such as steroids, bile acids, and fat soluble vitamins (57). In vitro studies in HepG2 cells and primary rat hepatocytes have suggested that CYP enzymes mediate ω-hydroxylation of the tocopherol side chain. Ketoconazole and sesamin, the inhibitors of CYP enzyme activity, inhibited α- and γ-tocopherol metabolism (47, 48).

Gastric mucosal lipid peroxidation plays a significant role in the pathogenesis of ethanol-induced gastric mucosal lesions. Pretreatment of sesame oil, but not mineral oil, significantly decreased acidified ethanol-induced mucosal ulcer formation and luminal hemorrhage. Sesame oil reduced mucosal lipid peroxidation, as well as glutathione and nitric oxide production in acidified ethanol-treated stomachs. Furthermore, both sesame oil and mineral oil did not affect serum ethanol concentration in acidified ethanol-treated rats (58).

Sepsis is a major cause of mortality in the intensive care unit. Oxidative stress plays an important role in the pathogenesis of organ failure during sepsis. Sesame oil decreases circulating oxygen free radicals in septic rats; however, its effect on hepatic oxidative status is unknown. Recent studies shown the evidence that sesame oil might attenuate hepatic lipid peroxidation by inhibiting superoxide anion and nitric oxide, at least partially, in experimental septic rats (59-61).

Acetaminophen (APAP) & lead-plus-lipopolysaccharide (Pb + LPS) overdose causes acute liver injury or even death in both humans and experimental animals. Both significantly increased aspartate transaminase, alanine transaminase, lipid peroxidation, and superoxide anion and hydroxyl radical generation levels; it also induced glutathione depletion. Sesame oil (8 mL/kg; orally) did not alter the gastric absorption of APAP, but it inhibited all the parameters altered by APAP & lead-plus-lipopolysaccharide and protected the rats against acute liver injury. Sesame oil maintained the intracellular glutathione levels, reduced reactive oxygen species levels, and inhibited lipid peroxidation in rats with APAP-induced acute liver injury. Sesame oil reduced Pb + LPS-induced tumor necrosis factor-alpha, interleukin-1beta, and nitric oxide production in serum and liver tissue. Furthermore, sesame oil decreased inducible nitric oxide synthase expression in leukocytes and liver tissue in Pb + LPS-treated mice. The inhibition of proinflammatory cytokines and nitric oxide might be involved in sesame oil associated protection against Pb + LPS-induced acute hepatic injury in mice (62-64).

cisplatin (cis-diamminedichloroplatinum) is an effective drug for the treatment of several solid tumors and has been used therapeutically for decades, several cisplatin-induced side effects have limited its therapeutic dosage in clinical studies. Sesame oil attenuates cisplatininduced hepatic and renal damage by at least partially inhibiting nitric oxide-associated LPO in mice. Sesame oil might be a new approach for preventing cisplatin-induced multiple organ injury during the treatment of tumors (65).

Endotoxin is a potent inducer of lipid peroxidation (LPO), which is associated with the development of endotoxemia.

3,4-Methylenedioxyphenol (sesamol) is one of the sesame oil lignans with a high anti-LPO effect. Sesamol dose dependently reduced serum LPO inendotoxin-challenged rats, decreased hydroxyl radical and peroxynitrite, but not superoxide anion counts, increased the activities of superoxide dismutase, catalase, and glutathione peroxidase in endotoxin-treated rats, reduced nitric oxide (NO) production and inducible NO synthase expression, and attenuated hepatic and renal injuries induced by endotoxin in rats. We concluded that sesamol might protect against organ injury by decreasing NO-associated LPO in endotoxemic rats (66).

CONCLUSION

Sesame seed oil, which is low in saturated fat and high in polyunsaturated and monounsaturated fats, is an ideal cooking medium for a heart saving diet plant. The antioxidants in sesame seed oil, viz., sesaminol, sesamolin and sesamolinol protect fats from being oxidized. Sesaminol maintains the so-called bad cholesterol low-density lipoproteins in an unutilized state which prevents arteriosclerosis. Sesamin also helps maintain Normal Blood Pressure. It helps regulate the body's immune and auto immune system balance. It inhibits a set of regulating compounds, which cause inflammation, clotting and other immune imbalances that contribute to disorders such as heart disease and autoimmune joint disorders. This review shows the evidence that the sesame oil was useful in the treatment of all acute and chronic diseases as dietary supplement. With the present evidence further research work is required to bring the sesame oil as neutraceutical drug.

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LIST OF ABBREVIATIONS

LPO-Lipid Peroxidation, LDL-Low Density Lipoprotein, RSC-Radical Scavenging Capacity, GPx-Glutathione Peroxidase, SOD-Superoxide Dismutase, DOX-Doxorubicin, TNF-α-Tumor Necrosis Factor- α, SREBPs-Sterol Regulatory Element Binding Proteins, HMG CoA-3-Hydroxy 3-Methyl Glutaryl Coenzyme, PPAR-Peroxisome Proliferator Activated Receptor, RXR-Retinoid X Receptor, HDL-High Density Lipoproteins, CYP-Cytochrome P450, APHP-Acetaminophen, Pb + LPS-Lead blus Lipopolysaccharide, NO-Nitric Oxide

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