International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 06 Issue: 04 | April - 2022 Impact Factor: 7.185 ISSN: 2582-3930

AN INSIGHT INTO SESAMOL: PHARMACOLOGICAL ACTIVITIES, AND FUTURE RESEARCH PROSPECTS

Shabana Khatoon[1]

Assistant Professor, Department of Pharmacology, Faculty of Pharmacy, Integral University, Lucknow-226026, Uttar Pradesh, India,

Corresponding author:

Dr.Mohammad Khushtar*

Associate Professor, Department of Pharmacology, Faculty of Pharmacy, Integral University, Lucknow-226026, Uttar Pradesh, India,

Dr. Mohd.Afroz[1]

Department of Pharmacology, Faculty of Pharmacy, Integral University, Lucknow, India

Dr. Shazia usmani[1]

Department of Pharmacology, Faculty of Pharmacy, Integral University, Lucknow, India

Md. Arshad[2]

Department of Zoology, Aligarh Muslim University, Aligarh, India

Abstract

In the current review, most of the pharmacological effects (in vivo and in vitro) of sesamol are summarized as, hepatoprotective activity, anti-microbial, neuroprotective, cardio protective, anti-inflammatory, anticonvulsant, anti-anxiolytic, wound healing, cosmetic (skin whitening), anti-cancer, antioxidant, and other biological effects. Here compile the proposed mechanism behind these pharmacological effects. The present work summarizes the most interesting in vitro and in vivo studies on the biological effects of sesamol. Another Sesamol work summarizes data available from Pub med and Scopus databases.

Keyword: Medicinal uses of sesamol, Pharmacological properties of Sesamol, Bioavailability, Combination Therapy of Sesamol with Other Drugs, Doses, Metabolism and Excretion of Sesamol, The Important Role of Sesamol in the Treatment of osteoporosis Disease

Introduction

Sesame is an important traditional health food and has been used to improve nutritional as well as prevent various diseases. Sesame seeds are not only rich in oil and protein, but also rich in lignans like sesamin and sesamolin [1, 2]. Sesame (*Sesamum indicum* L.) seeds have been authenticated for their medicinal value in both Indian and Chinese other countries systems of medicine [3]. Its numerous potential nutritional benefits are attributed to its main bioactive constituents; sesamol [4].Sesame seed also contains lignans like aglycones in oil and lignans like glucosides. Sesame seed is rich in oil, contains increased amounts of [83-90%], unsaturated fatty acids, mainly linoleic acid [37-47%], oleic acid [35-43%], palmitic [9-11%] and stearic acid [5-10%] with trace amount of linolenic acid. [5, 6]

Sesame seeds have been widely used in culinary as well as traditional medicines for their preventive, nutritive, and curative properties. Sesame seed is an important source of phytonutrients such as omega-6 fatty acids, flavonoid phenolic anti-oxidants, vitamins, and dietary fiber with potential anti-cancer, as well as health promoting properties. Sesame oil extracted from *Sesamum indicum* seeds has been employed in the food and pharmaceutical industries due to the high lipids and protein content and its flavor [7, 8].

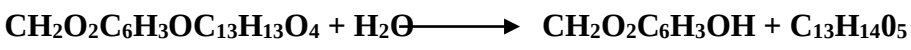
The active constituents of *Sesamum Indicum*

Sesame seed is nutritional components with beneficial effects along with health promotion for the humans. The bioactive components present in the seed like vital minerals, vitamins, phytosterols, polyunsaturated fatty acids, tocopherols, and others bioactive components like lignans such as sesamin and sesamolin [9].

These bioactive components enhance the stability and keeping quality of sesame oil along with numerous health benefits. Sesame seeds are considered valuable foods as they enhance the diet with the pleasing aroma and flavor and offer nutritional and physiological benefits. Recent studies on the antioxidant and anti-carcinogenic activities of sesame seed have greatly increased its applications in health food products that assert liver and heart protection and tumor prevention[10].It has various pharmacological effects like anti-inflammatory, immunosuppressant, analgesic, anti-oxidant, hypolipidemic, wound healing, anti-hypertensive, ulcer protective, and anti-cancer [11-13].

Mechanism of action

Sesame oil is yellow non crystallizable oily substance obtained this color reaction was due to a phenolic compound. Although that substance name is sesamol. Synthesized sesamol by the reaction of piperonal with peracetic acid. Sesamol was obtained in the form of the acetate, combination with formic acid. The acetate was saponified with alkali, the alkaline solution acidified, and the sesamol recovered by vacuum distillation [14].



(Sesamolin) (Sesamol) (Samin)

Common Ethno botanical Use

Seeds are tonic, laxative, emollient, demulcent, diuretic, nourishing, galactagogue, and aphrodisiac; removes constipation, thus helpful in piles. Powdered seeds are used in applied to burns and scald. Oil is widely used in pharmaceutical products; believed to promote the growth of hair. Infusion of the leaves is much used as a demulcent, also given as a remedy for disease of the respiratory tract. Every part of the plant is used as a diuretic in Cambodia. In Madagascar, every part of the plant is considered emollient and laxative [15, 16, 17].
Sesame oil possesses excellent emollient properties. Sesame oil is a natural antibacterial, antiviral and anti-inflammatory agent, and for these reasons it has been used to treat acne [18, 19]. Other medicinal uses of sesamol in the present investigation, several pharmacological effects of sesamol are investigated like, antioxidant, anti-cancer, neuroprotective, cardio protective, anti-inflammatory, hypolipidemic, radio protective, anti-aging, anti-ulcer, anti-dementia, anti-depressant,antiplatelet, anticonvulsant, anti-anxiolytic, wound healing, cosmetic (skin whitening), anti-microbial, matrix metalloproteinase (MMPs) inhibition, hepatoprotective activity, and other biological effects[20].

Pharmacological properties of Sesamol

Antioxidative Activity

Other experiment confirmed the sesamin, sesamolin and sesamol three sesame lignans prevent melanin synthesis through 2 stages: a) by blocking melanin-induction and b) by interrupting melanogenic enzyme production. To investigate that sesamol, sesamin and sesamolin are potential for antimelanogenesis agents [24]. Other study confirmed the sesamolis able to alleviate cognitive impairments in (Chronic intermittent hypoxia) CIH-exposed rats, with its neuroprotective effects likely inhibiting oxidative stress and inflammation. A study was carried out to find the antioxidants effect with sesamol derivatives were computationally designed in a rational way, using a computer [25]. Other study demonstrates that the antioxidant effects of sesamol might inhibit cataract formation [26].

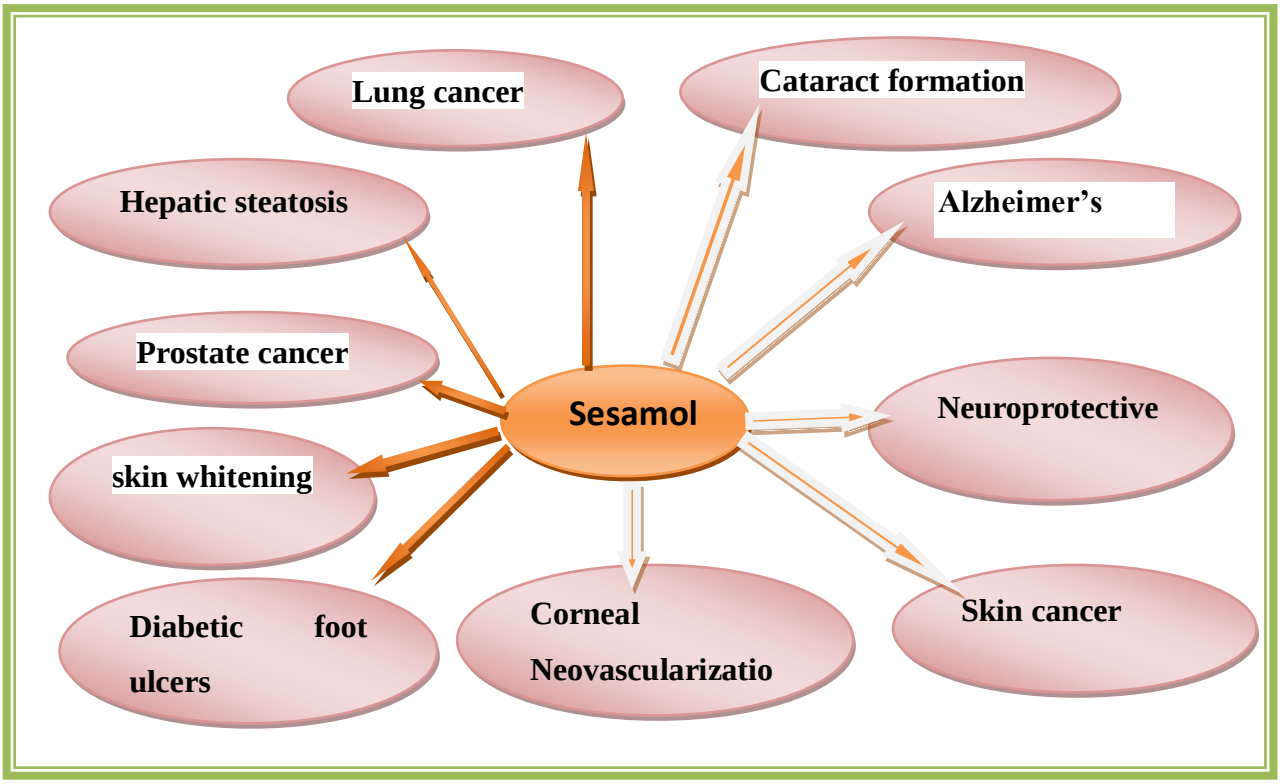


Fig.1

Neuroprotective

Another study confirmed the chronic intermittent hypoxia (CIH) could be a major feature of obstructive apnea, which may cause oxidative stress and inflammation which may further impair the system nervosum.Sesamol

improved learning and memory impairment in (CIH) Chronic intermittent hypoxia exposed rats. Additionally, sesamol also reduced the degree of TNF-α and IL-1β within the hippocampus. Partly right that sesamol can alleviate cognitive impairments in (CIH) Chronic intermittent hypoxia exposed rats, with its neuroprotective effects likely inhibiting oxidative stress and inflammation [27]. Another study reported that sesamol as a protective agent from Alumina nanoparticles-induced (neurodegenerative disorders) neuroprotective activity [28].Other studies demonstrate that Sesamol treatment (25, 50, and 100 mg/kg) significantly attenuated oxidative stress markers, augmented the protective mechanisms, prevented hippocampal CA1 neuron loss, and neuronal infarction in rats and it showed a neuroprotective effect of sesamol can be attributed to its antioxidative potential [29].

Alzheimer's diseases

Sesamol, an antioxidant lignan obtained from sesame oil and it possesses neuroprotective bioactivities. Cognitive deficits possible link between gut and brain sesamol shown the protective effects. Wild type and (ApoE) *apolipoprotein E* mice were treated with a high-fat diet and sesamol could only improve cognitive deficits and anxiety behaviors in wild type. Sesamol prevented dietary-induced gut barrier damages and systemic inflammation and inhibited Aβ accumulation in an (ApoE) *apolipoprotein E*-dependent beneficial effect on gut microbiota/metabolites could be translated into neurodegenerative diseases treatment [30].

Another study reported that black sesame pigment antioxidant and heavy metal-binding properties with potential as a food supplement. These properties open new perspectives toward the use of black sesame pigment as an ingredient of functional food or as a food supplement for the prevention of Alzheimer's diseases [31].

Anti-Cancer Activity

Anticancer nanoparticles were fabricated by linking the nanoparticles of two name anticancer agents, sesamol and selenium, using as polyethylene glycol. Sesamol- polyethylene glycol selenium nanoparticles effectively inhibited the human liver cancer cell line (HepG2 cells). Sesamol- polyethylene glycol -selenium nanoparticles indicated the synergistic inhibition between sesamol and selenium nanoparticles and Sesamol nanoparticles beneficial effects of anticancer agents [32].

Prostate cancer

Benign prostatic hypertrophy patients reflect an increased Glutathione S-transferases (GST) activity and malondialdehyde (MDA) levels. Sesamol and derivatives have manifest efficacy in protecting against

testosterone-induced BPH (Benign prostatic hypertrophy). The antioxidant potential of sesamol was claimed to be responsible for Prostate cancer [33].

Hepatic steatosis

Sesamol alleviated chronic high-fat diet HFD (Chronic high-fat diet) induced hepatic steatosis by reducing oxidative stress and inflammation in the liver. The positive effects mediated by Sesamol might be through the activation of nuclear factor erythroid 2-related factor 2 (Nrf2 transcription). Sesame seed extract to obtained sesamol it developed into a new functional compound or even a potential therapeutic agent extracted from common food. In the future, human intervention studies or clinical trials may support the utilization of SEM to prevent the progression of (NAFLD) Non-alcoholic fatty liver disease [34].

Diabetes

Sesamol noticeably abate the body weight gain of obese mice and suppressed lipid accumulation in adipose tissue and liver. Sesamol also improved serum and hepatic lipid profiles and increased insulin sensitivity. Sesamol treatment decreases the level of ALT &AST significantly. Furthermore, after sesamol treatment, the hepatic sterol regulatory element-binding protein-1 decreased, while the phosphorylated hormone-sensitive lipase, the creatinine palmitoyltransferase 1α, and the peroxisome proliferator-activated receptor coactivator-1α increased, which were responsible for the fatty acid synthesis, lipolysis, and fatty acid β-oxidation, respectively. Sesamol might serve as a beneficial drug to treat obesity [35].

Obesity is the imbalance between energy intake and expenditure, and it is a serious risk factor of non-communicable diseases. Recently many studies have shown that browning of white adipose tissue to increase energy consumption has a great therapeutic potential for obesity. Sesame oil shown potential beneficial functions on obesity treatment. Sesamol promoted the browning of white adipocytes. This pre-clinical data promised the potential to consider sesamol as a metabolic modulator of HFD-induced obesity. Obesity is one of the global public health concerns. The current study found that sesamol treatment decreased the content of body fat and reduced serum TG and TC levels in HFD-induced mice [36].

Respiratory disorder

Fourier transform infrared microscopy (FTIR) novel technique in the field of cancer therapy can distinguish apoptosis induction by sesamol from cisplatin in the mimic physiological condition in the SK-LU-1 cell line.

Sesamol and cisplatin induce apoptosis in SK-LU-1 (Human lung adenocarcinoma cisplatin-sensitive) cells by causing DNA damage [37].

Lung cancer

Inhibition of COX2 expression enhanced the antitumor activity of sesamin via the (Akt-PI3K) intracellular signal transduction pathway and phosphorylated protein kinase B (pAkt) and phosphoinositide 3 kinase (PI3K) signaling pathway in lung cancer cells. Phosphoinositide 3 kinases (PI3K) expression was observed to be under the control of COX2, possibly forming a negative feedback loop. In addition, phosphoinositide 3 kinase (PI3K) depletion induced apoptosis and G1-phase arrest in human alveolar epithelial cells (A549) cells. Sesamin blocked the phosphorylated protein kinase- phosphoinositide 3 kinase (pAkt-PI3K) signaling pathway by down regulating the expression of COX2, therefore causes in cell cycle arrest and increased apoptosis in vitro. Sesamin and COX2 inhibitor may promote the development of potential treatment for lung cancer may be promoted for the development [38].

Diabetic foot ulcer

Reveal the SM-PLGA Sesamol poly (lactic-co-glycolic acid) nanosuspension is capable of controlled release of sesamol which significantly accelerated the healing process in foot ulcers. Evidence demonstrates that SM-PLGA nano-formulation is a promising healing agent for use in the treatment of non-healing chronic wounds. Sesamol-PLGA poly (lactic-co-glycolic acid) nanosuspension significantly boost the acceleration of wound healing in diabetic foot ulcers by restoring the altered wound healing process in diabetic condition[39].

Corneal Neovascularization

In this experimental and comparative study, the right eyes of 56 Wistar Albino rats were chemically cauterized to produce corneal neovascularization. When compared to the control group, all treatment groups demonstrated statistically significant differences (P0.001). When compared to subconjunctival sesamol, topical sesamol was shown to be more efficacious (P=0.003). When compared to topical bevacizumab, topical sesamol+ bevacizumab was found to be more efficacious (P=0.018). For the prevention of corneal neovascularization, topical sesamol monotherapy or sesamol coupled with bevacizumab may be an alternative. Sesamol stopped melanin production by inhibiting the melanocortin 1 receptor (MC1R)[40].

Radio protective effect

Ionizing radiations induce damage to the bone marrow and blood cell. comparison with the only-irradiated group, oral consumption of sesamol 2 h and 7 days as 54.5% and 70.4% ($P < 0.0001$), and micro-nucleated nucleated polychromatic erythrocytes (mnPCE) as 49% and 66% ($P < 0.001$).To investigate PCE/NCE polychromatic erythrocytes/ normochromic erythrocytes ratio increased as 47% and 83.6% ($P < 0.0001$) compared to the irradiated group. The percentage of DNA in the tail and apoptotic comets decreased significantly with oral consumption of sesamol (daily or single dose) compared to the irradiated group ($P < 0.005$). These variations were greater in the 7-day continuous pre-irradiation method. Sesamol as a radio protector can reduce the effects of gamma irradiation on mice bone marrow and blood cells [41].

Anti-tumor activity

Sesamol antitumor effect was studied in solid Ehrlich carcinoma (SEC) mice to check its ability to potentiate along with doxorubicin (DOX) [42].

Skin cancer

Sesamol was screened for its skin cancer properties and findings represent that the seeds possess Skin cancer activity using various administration (both in a free and encapsulated form) considerably decreased the tumor burden and lipid peroxidation level and increased anti-oxidant levels, down regulation of (B-cell lymphoma 2) BCL-2 and stimulation of bax (BCL2 Associated X, Apoptosis Regulator) (BAX BCL2 Associated X, Apoptosis Regulator is a Protein coding gene. Protein expression on treatment with both free and encapsulated sesamol was responsible for the induction of apoptosis in tumor cells [43].

Neuroprotective activity

Alumina nanoparticles (SNPs) are widely used causing neurobehavioral impairment in intoxicated animals and humans. The Concentrations of 8-hydroxydeoxyguanosine (8-OHdG) and malondialdehyde (MDA) were increased the level of lipid peroxidation and oxidative DNA damage. (GSH) Glutathione depletion with inhibited activities of Superoxide dismutase (SOD), catalase (CAT) was investigated. Serum levels of IL-1β and IL-6 were increased. Finding Histopathologically, Alumina nanoparticles (AlNPs) induced hemorrhages, edema, neuronal necrosis, and/or apoptosis in the medulla oblongata. The cerebellum showed loss of Purkinje cells, and the cerebrum showed per vascular edema, neuronal degeneration, necrosis, and neuronal apoptosis. Sesamol (SML) with Alumina nanoparticles (AlNPs) consider as antioxidant, anti-inflammatory, and anti-

apoptotic effects of Sesamol (SML). Since sesamol could be an assuring phytochemical with neuroprotective activity [44].

Cosmetic (skin whitening)

Sesamol inhibited melanin synthesis through the inhibition of the melanocortin 1 receptor (MC1R)/MITF/tyrosinase pathway in B16F10 cells. Sesamol is a potent depigmenting agent. Sesamol reduced the melanin and elevates the brightness of the mouse skin. Sesamol may be used in skin whitening products [45].

Anti-inflammatory

Sesamol is a redox inhibitor. It inhibits lipoxygenase through its radical scavenging activity and it shows a potential anti-inflammatory agent. [46].

Leishmanicidal effect

Visceral leishmaniasis caused by the protozoan parasite Leishmania donovani (L. donovani), is the most severe form of leishmaniasis its effect of sesamol was mediated by apoptosis-like cell death mechanism as evidenced by cell cycle arrest, and loss of mitochondrial membrane potential. Hence, sesamol was used as therapeutic herbal for the treatment of visceral leishmaniasis after further validations [47].

Atherosclerosis

Sesamol shows protective effects against nonalcoholic steatohepatitis (NASH) and atherosclerosis [48].

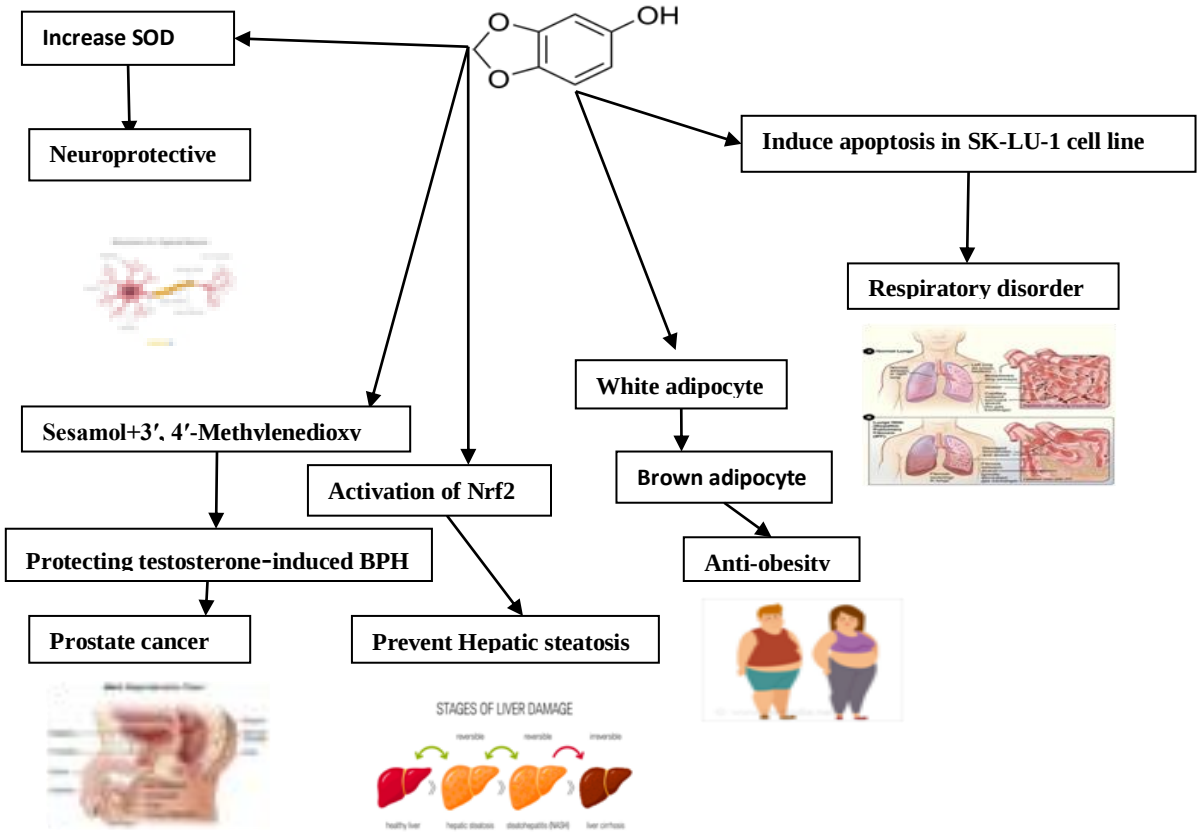

Increase SOD
OH
Neuroprotective
Induce apoptosis in SK-LU-1 cell line
Respiratory disorder
White adipocyte
Sesamol+3′, 4′-Methylenedioxy
Activation of Nrf2
Brown adipocyte
Protecting testosterone-induced BPH
Anti-obesity
Prostate cancer
Prevent Hepatic steatosis
STAGES OF LIVER DAMAGE

Fig.2

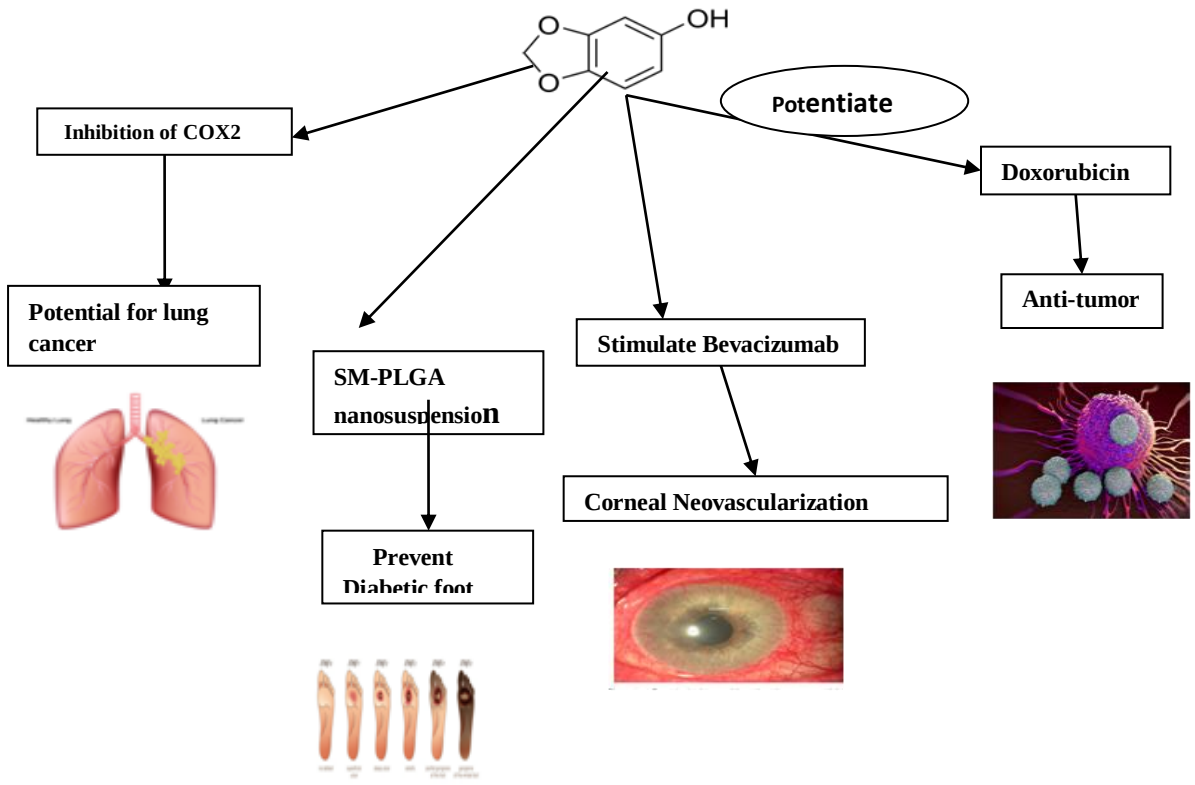

OH
Potentiate
Inhibition of COX2
Doxorubicin
Potential for lung cancer
Anti-tumor
SM-PLGA nanosuspension
Stimulate Bevacizumab
Corneal Neovascularization
Prevent Diabetic foot

Fig.3

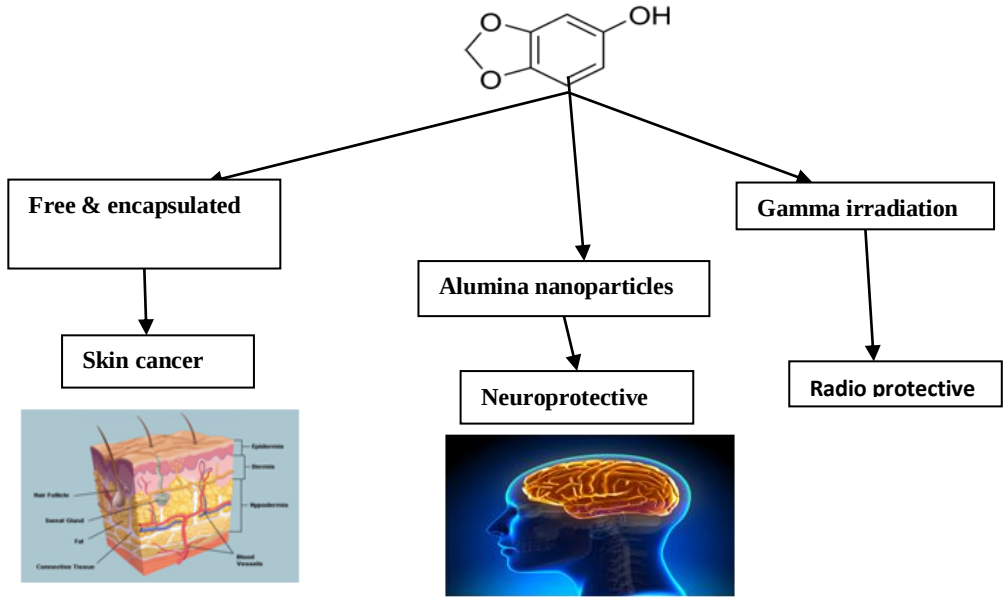

OH
Free & encapsulated
Alumina nanoparticles
Gamma irradiation
Skin cancer
Neuroprotective
Radio protective

Fig.4

Bioavailability

Sesamol has low bioaccessibility, which could be enhanced by encapsulation in 425 phosphatidylcholine mixed micelles. Sesamol in phosphatidylcholine mixed micelles 426 showed enhanced bioavailability along with improved anti-inflammatory activity [49].

The oxidation stability and bioactivity of a nanoemulsion incorporating tocopherol and sesamol highly depended on the oil saturation. A nanoemulsion with a high degree of unsaturated oil (flaxseed oil) was more susceptible to oxidation, and the addition of tocopherol and sesamol could retard the lipid oxidation. Sesamol exhibited better in vitro and in vivo bioactivity in our experiment compared with tocopherol. The lipid-lowering effects of tocopherol and sesamol were superior in the low saturation oil (olive oil) group. The antioxidant activities of tocopherol and sesamol were better in the high saturation oil (flaxseed oil) group. Overall, this study could be used for the design and application of a specific nanoemulsion system fortified with lipophilic nutraceuticals [50].

Combination Therapy of Sesamol with Other Drugs

The combined effect of sesamol as an add-on drug along with the available therapy to control hyperlipidemia and ischemic heart diseases [51]. Sesamol has been documented to posses

Sesamol with crocin, an approach that could not only abolish the toxic effects of sesamol on platelets, but also enhance the quality of treatment due to their synergistic action, on the lines of combinatorial drug therapy [52]. Investigated the neuroprotective actions of dietary flavonoids (sesamol and naringenin) involve a number of effects within the brain, including a potential to protect neurons against injury induced by neurotoxins, rotenone. The flavonoids, inhibited caspase activation and reduced cell death in brain and muscle regions with their anti apoptotic property [53].Notably, Sesamol has been documented to sesamol was successful where the cytotoxicity of this drug on MCF-7 breast cancer cell lines was not only maintained but also augmented due to the particles better uptake and internalization. These novel formulations in the treatment of the subcutaneous and the skin proximal solid tumors such as the breast cancer solid masses. Evaluating the developed formulations in animals or humans is thus warranted. [58]. Another study demonstrated the estrogen receptor (ER) is an important member of the nuclear receptor super family, including the ERα (ESR1 gene) and ERβ (ESR2 gene) subtypes. Indeed, ERα takes part in the uncontrolled proliferation and invasion of breast carcinoma sesamol shows that this agent is helpful for the clinical adjuvant treatment of patients with ERα-negative breast cancer. Sesamol may not be immediately applied to clinical practice. Novel research direction and potential option for the adjuvant treatment of ERα-negative breast cancer [59]. Investigated the combination effect of sesamol, sesamin, and sesamolin in SK-MEL-2 cells. Intracellular uptake of sesamol,

sesamin, and sesamolin compounds in SK-MEL-2 cells was higher than in Vero cells (sesamol < sesamin < sesamolin).Sesamol was able to reduce cell viability and tumor volume of SK-MEL-2 cells with less damage to Vero cells. Sesamol was able to induce late-stage apoptosis and necrosis cell death even at a relatively low intracellular concentration compared to sesamin and sesamolin [60]. Recently, sesamol has been documented to found that sesame phytoestrogen lignanscan stimulate testosterone aromatization to estradiol, or convert it to Dihydrotestosterone. High level intake of liquorice root extract or sesame oil caused hormonal disturbance and decreases sperm count [61].

Dose use

Most clinical studies use Sesamol at 300 to 100 mg per day in divided doses [62]. Based in animal study of Cataract condition intraperitoneally administered 50 mg/kg/day saline solution and 50 mg/kg/day sesamol [63]. Based on animal studies of sesamol (50 mg/kg B.W) aked into the circulation as a result of hepatocellular injury. In this study, level of AST in 300 mg/kg group was comparable to normal control, while ALT was insignificantly increased ($P > 0.05$), indicative of possibly low hepatoxicity [64]. Sesamol reported dose 100 mg/kg or 200 mg/kg per day hepatocellular carcinoma *in vitro* and *in vivo* chemotherapeutic opportunities [65]. **Metabolism and Excretion of Sesamol**

Examined the Sesamol was able to reduce both triacylglycerol and cholesterol at both dosages (50 and 100 mg/kg), implying that it might reduce the absorption and increase the excretion of cholesterol as well. Sesamol treatment can be beneficial in preventing hyperlipidemia and related disorders [67]. Amin F et al. identified the Sesamol metabolites (glucuronides and sulfates) were detected in all tissues, with the highest concentrations in the plasma, lungs, and liver. It was concluded that sesamol is first incorporated and metabolized by the liver, and its metabolites are subsequently transported to other tissues, its metabolites were still detected in the intestines. The authors argued that organs of the gastrointestinal tract serve as the major metabolic pathway with enzymatic conversions (sulfation and/or glucuronoconjugation) of sesamol metabolites showed that sesamol-conjugated metabolites were excreted in urine after elimination from the plasma via the kidneys by active tubular secretion and sesamol-conjugated metabolites get rapidly eliminated in urine and feces within 4 h of sesamol administration [68].

The Important Role of Sesamol in the Treatment of osteoporosis Disease

Esculentoside A (EsA) inhibits cartilage inflammation, matrix catabolism and osteoclastogenesis by restraining the NF-κB and MAPK signalling cascades, thereby reducing the degeneration of the cartilage and its matrix and osteoclast formation. Esculentoside A (EsA) may be a potential therapeutic agent for the treatment of osteoarthritis [71]. Another study conducted on components of sesame oil (SO) and rice bran oil (RBO)

possesses a significant degree of an anti-arthritic effect thus indicating a potential role for anti-arthritic [72]. The consumption of diets supplemented with soybean oil (SbO) or sesame oil (SO) might be useful for preventing bone loss caused by estrogen deficiency in ovariectomy status [73]. **Conclusion**

Sesamol is a non-toxic drug that inhibits the expression of inflammatory indicators such cytokines, redox status, protein kinases, and enzymes that cause inflammation. Sesamol also activates caspase cascades and promotes apoptosis in cancer cells through mitochondrial and receptor-mediated mechanisms. Sesamol's pleiotropic biological effects have been described via several molecular pathways. It has been shown to have significant therapeutic effects in the treatment of oxidative and inflammatory diseases, metabolic syndrome, and mental disorders. Furthermore, significant data demonstrated sesamol's potential to limit inflammatory cell proliferation, invasion prevention, and angiogenesis by impacting several molecular targets and downstream processes. Sesamol has been studied for a variety of purposes and has been found to be effective in the majority of investigations. The pharmacological profile revealed that it is a powerful antioxidant, making it useful for diabetic complications, liver disorders, neuroprotection, and anticancer activity.

Reference:

[1]Che PR, Chien KL, Su TC et al. Dietary sesame reduces serum cholesterol and enhances antioxidant capacity in hypercholesterolemia:Nutr Res 2005; 25: 559–67.

[2]Shasmitha R,et al. Health benefits of Sesamum indicum: A short review. Asian Journal of Pharmaceutical and Clinical Research: 2015; 8(6):1- 3.

[3]D Bedigian. Webbia. 2015; 70(1):1-42.

[4]KP Suja, A Jayalekshmy, C Arumughan.et al. J Agric Food Chem: 2004; 52(4):912-5.

[5]Isha D, Milind P et al. Eat til and protect dil. IRJP: 2012; 3(11):2230-8407.

[6]S Devarajan, B Chatterjee, H Urata, B Zhang, A Ali, R Singh, et al. Am J Med: 2016.

[7] Abou-Gharbia HA, Shahidi F, Shehata AA, Youssef et al. Effect of processing on oxidative stability of sesame oil extracted from intact and dehulled seed: J Am Oil Chem Soc1997;74:215-21.

[8] Abou-Gharbia HA, Shehata AA, Shahidi et al. Effect of processing on oxidative stability and lipid classes of sesame oil. Food Res Int 2000; 33:331-40

[9]Katsuzaki H, Kawakishi S, Osawa et al. Sesaminol glucosides in sesame seeds. Phytochemistry 1994; 35:773-6.

[10]Devarajan S, Singh R, Chatterjee B, Zhang B, Ali et al.. J clin lipidol. 2016; 10(2):339-49.

[11] S Devarajan, B Chatterjee, H Urata, B Zhang, A Ali, R Singh, et al. Am J Med. 2016.

[12]DZ Hsu, PY Chu, IM et al. Food nutr res. 2016;60:29807.

[13]Hemalatha S, Ghafoorunissa et al. Lignans and tocopherols in Indian sesame cultivars. J Am Oil Chem Soc 2004; 81:467-70.

[14]PIERRE BUDOWSI, K. S.et al.THE CHEMICAL AND PHYSIOLOGICAL PROPERTIES OF SESAME OIL: 1960 September 6,

[15] Ghani, et al. Medicinal plants of Bangladesh: chemical constituents and uses: 1998 Asiatic society of Bangladesh.

[16]Bosebabu, Bellamkonda & Cheruku, Sri Pragnya & Rao, Chamallamudi & Nampoothiri, Madhavan & Shenoy, Rekha & Nandakumar, Krishnadas & Parihar, Vipan & Kumar, Nitesh, An Appraisal of Current Pharmacological Perspectives of Sesamol: A Review. Mini-Reviews in Medicinal Chemistry: 2020 page no.20. 10.2174/1389557520666200313120419.

[17]Furumoto, T. and Hoshikuma, et al. Biosynthetic origin of 2-geranyl-1, 4-naphthoquinone and its related anthraquinone in a Sesamum indicum hairy root culture: Phytochemistry 2011; 72, 871-874.

[18]Hu, Y., Ye, W., Yin, Z. and Zhao, et al. Chemical constituents from flos Sesamum indicum L: Yao xue xue bao Acta pharmaceutica Sinica 2007; 42, 286- 291.

[19]https://www.brenntag.com › textron_natural_oils

[20] Monteiro, É.M.H., Chibli, L.A., Yamamoto, C.H., Pereira, M.C.S., Vilela, F.M.P., Rodarte, M.P., de Oliveira Pinto, M.A., da Penha Henriques do Amaral, M., Silvério, M.S. and de Matos Araújo, A.L.S. (2014) Antinociceptive and antiinflammatory activities of the sesame oil and sesamin. Nutrients, 6, 1931- 1944.

[21] J.M. Nzikou, 1L. Matos, 1G. Bouanga-Kalou, 1C.B. Ndangui, 1N.P.G. Pambou-Tobi, 1A. Kimbonguila, 2Th. Silou, 3M. Linder and 3 S. Desobry, Chemical Composition on the Seeds and Oil of Sesame (Sesamum indicum L.) Grown in Congo-Brazzaville. Advance Journal of Food Science and Technology 1(1): 6-11, 2009

[22]Salunke, D.K., J.K. Chavan, R.N. Adsule and S.S. Kadam, 1992. World oil seeds: Chemistry, technology and utilization. pp: 170-173.

[23]Elleuch, M., Besbes, S., Roiseux, O., Blecker, C. & Attia, H. (2007). Quality characteristics of sesame seeds and by-products. Food Chemistry 103 (2): 641 – 650

[24]Akinoso, R, Aboaba, S A & Olayanju, T.M.A. (2010) Effects of Moisture Content and Heat Treatment on Peroxide Value and Oxidative Stability of Un-Refined Sesame Oil. AJFAND 10 (10): 4268- 42850

[25]Bo Ren, Tian Yuan, Zhijun Diao, Chenxi Zhang, Zhigang Liu and Xuebo Liu, Protective effects of sesamol on systemic oxidative stress-induced cognitive impairments via regulation of Nrf2/Keap1 pathway†. Food Funct., 2018, 9, 5912–5924

[26]Anusha Chennuru and Mohamed T. S. Saleem, Antioxidant, Lipid Lowering, and Membrane Stabilization Effect of Sesamol against Doxorubicin-Induced Cardiomyopathy in Experimental Rats. BioMed Research International Volume 2013, Article ID 934239, 5 pages

[27]Premkumar Jayaraj, Chandrakala A. Narasimhulu,b Sanjay Rajagopalan,cSampath Parthasarathyb and Rajagopal Desikan Sesamol: a powerful functional food ingredient from sesame oil for cardioprotection.Food and Function issue 2, 2020

[28]MontraSrisayam1NatthidaWeerapreeyakul2KwanjaiKanokmedhakul3Inhibition of two stages of melanin synthesis by sesamol, sesamin and sesamolin. Biomedicine Volume, October 2017

[29]Laura M. Castro-Gonzalez, Juan Rau´ l Alvarez-Idaboy,´and Annia Galano* Computationally Designed Sesamol Derivatives Proposed as Potent Antioxidants. ACS Omega 2020, 5, 9566−9575

[30]Burak Turgut,1,* İrfan Ergen,2 and Nevin İlhan3,The Protective Effect of Sesamol in the Selenite-induced Experimental Cataract Model. Turk J Ophthalmol. 2017 Dec; 47(6): 309–314

[31]Zhang, Panpana,, b; Wang, Yanhuic; Wang, Hongyangb; Cao, Jie,,Sesamol alleviates chronic intermittent hypoxia-induced cognitive deficits via inhibiting oxidative stress and inflammation in rats. NeuroReport: January 13, 2021 - Volume 32 - Issue 2 - p 105-111

[32]Shimaa M. Abou-Zeid, Basma A. Elkhadrawey, Anis Anis, Huda O. Abu Bakr. E. El-Bialy, Hesham S. Elsabbagh & Nermeen B. El-Borai, Neuroprotective effect of sesamol against aluminum nanoparticle-induced toxicity in rats. Environmental volume 28, pages53767–53780 (2021)

[33]TejasSharmaVishalAiraoPrakrutiBuchDevendraVaishnavSachinParmar, Sesamol protects hippocampal CA1 neurons and reduces neuronal infarction in global model of cerebral ischemia in rats.PharmaNutrition,Volume 14, December 2020, 100217

[34]Tian Yuan 1, Chuanqi Chu 2, Rubing Shi 1, Tianlin Cui 1, Xinglin Zhang 1, Yihang Zhao 1, Xu Shi 1, Yan Hui 3, Junru Pan 1, Rui Qian 4, Xiaoshuang Dai 5, Zhigang Liu 1, Xuebo Liu 1 ApoE-Dependent Protective Effects of Sesamol on High-Fat Diet-Induced Behavioral Disorders: Regulation of the Microbiome-Gut-Brain Axis. J Agric Food Chem. 2019 Jun 5;67(22):6190-6201.

[35]Lucia Panzella 1,*ID, Thomas Eidenberger 2 and Alessandra Napolitano 1 ID. Anti-Amyloid Aggregation Activity of Black Sesame Pigment: Toward a Novel Alzheimer's Disease Preventive Agent. Molecules 2018, 23, 676

[36]Fuguo Liu 1, Hua Liu 1, Runhua Liu 1, Chunxia Xiao 1, Xiang Duan 1, David Julian McClements 2, Xuebo Liu 1 delivery of sesamol using polyethylene-glycol-functionalized selenium nanoparticles in human liver cells in culture. J Agric Food Chem. 2019 Mar 13;67(10):2991-2998.

[37]Abhishek Shah1,Aarti Abhishek Shah2,4,Krishnadas Nandakumar2,Avinash Kumar3,
Aravinda Pai3.Richard Lobo1, In-silico and in vivo evaluation of sesamol and its derivatives for benign prostatic hypertrophy. 3 Biotech (2021) 11:411

[38]Wenya Zheng 1 , Ziyu Song 1 , Sha Li 2 , Minmin Hu 1 , Horia Shaukat 1 and Hong Qin 1,* Protective Effects of Sesamol against Liver Oxidative Stress and Inflammation in High-Fat Diet-Induced Hepatic Steatosis. Nutrients 2021, 13, 4484

[39]Hong Qin,1,* Haiyan Xu,1 Liang Yu,2 Lina Yang,1 Cui Lin,1 and Jihua Chen1,*Sesamol intervention ameliorates obesity-associated metabolic disorders by regulating hepatic lipid metabolism in high-fat diet-induced obese mice. Food Nutr Res. 2019; 63

[40]Hong Qin1 *, Haiyan Xu1 , Liang Yu2 , Lina Yang1 , Cui Lin1 and Jihua Chen1, Sesamol intervention ameliorates obesity-associated metabolic disorders by regulating hepatic lipid metabolism in high-fat diet-induced obese mice. Food & Nutrition Research 2019, 63: 3637

[41]Boondaree Siriwarin1, Waraporn Tanthanuch3∗, Natthida Weerapreeyakul2 , Kanjana Thumanu3, Biomolecular changes and DNA targeting effect of sesamol in human lung adenocarcinoma (SK-LU-1) cells by FTIR microscopy. Asian Pacific Journal of Tropical Biomedicine 2018; 8(8): 377-386

[42]QING FANG1, YUYIN ZHU1, QILAI WANG1, MEIJUN SONG2, GUOSHENG GAO3 and ZHIMING ZHOU1, Suppression of cyclooxygenase 2 increases chemo sensitivity to sesamin through the Akt-PI3K signaling pathway in lung cancer cells. INTERNATIONAL JOURNAL OF Molecular medicine 43: 507-516, 2019

[43] Karthik Gourishetti, Raghuvir Keni, Pawan Ganesh Nayak, Srinivas Reddy Jitta, Navya Ajitkumar Bhaskaran, Lalit Kumar, Nitesh Kumar, Nandakumar Krishnadas, Rekha Raghuveer Shenoy, Sesamol-Loaded PLGA Nanosuspension for Accelerating Wound Healing in Diabetic Foot Ulcer in Rats 23 November 2020 Volume 2020:15 Pages 9265—9282.

[44]Hüseyin Kaya 1, Gökhan Pekel, Aygün Yörükoğlu, Mehmet Can Hiraali, Barbaros Şahin, is Sesamol Effective in Corneal Neovascularization? Eye Contact Lens. 2018 Nov; 44 Suppl 2:S414-S419.

[45]Mehrsa Majdaeen 1, Amin Banaei 2, Razzagh Abedi-Firouzjah 3, Kourosh Ebrahimnejad Gorji 4, Gholamreza Ataei 5, Farideh Momeni 6, Hamed Zamani 7 Investigating the radio protective effect of sesamol oral consumption against gamma irradiation in mice by micronucleus and alkaline comet assays. Appl Radiat Isot. 2020 May;159:109091

[46]Nesma A Abd Elrazik 1, Mohamed El-Mesery 1, Amro El-Karef 2, Laila A Eissa 1, Amal M El Gayar 1Sesamol Upregulates Death Receptors and Acts as a Chemo sensitizer in Solid Ehrlich Carcinoma Model in Mice. Nutr Cancer. 2021 Jan 13;1-15

[47]Rishi Bhardwaj 1, S N Sanyal 1, Kim Vaiphei 2, Vandita Kakkar 3, Parneet Kaur Deol 3, Indu Pal Kaur 4, Tranum Kaur 5 Sesamol Induces Apoptosis by Altering Expression of Bcl-2 and Bax Proteins and Modifies Skin Tumor Development in Balb/c Mice. Anticancer Agents Med Chem. 2017; 17(5):726-733.

[48]Shimaa M Abou-Zeid 1, Basma A Elkhadrawey 2, Anis Anis 3, Huda O AbuBakr 4, Badr E El-Bialy 2, Hesham S Elsabbagh 2, Nermeen B El-Borai 2 Neuroprotective effect of sesamol against aluminum nanoparticle-induced toxicity in rats. Environ Sci Pollut Res Int. 2021 Oct; 28(38):53767-53780.

[49]Ya-Jhen You 1,† , Po-Yuan Wu 2,3,† , Yi-Jung Liu 1,4, Chien-Wei Hou 5 , Chin-Sheng Wu 1 , Kuo-Ching Wen 1 , Chien-Yih Lin 6,* and Hsiu-Mei Chiang 1,4,* Sesamol Inhibited Ultraviolet Radiation-Induced Hyper pigmentation and Damage in C57BL/6 Mouse Skin. Antioxidants 2019, 8, 207

[50]P. S. Yashaswini, A. G. Appu Rao, and Sridevi A. Singh, Inhibition of lipoxygenase by sesamol corroborates its potential anti-inflammatory activity. International Journal of Biological Macromolecules, S0141813016305864–. doi:10.1016/j.ijbiomac.2016.06.048

[51] Rahat Ali 1 , Shams Tabrez1 , Sajjadul Kadir Akand1 , Fazlur Rahman1 , Atahar Husein1 , Mohd Arish2 , Ali S. Alqahtani3 , Mohammad Z. Ahmed3 , Mohammad Husain1 and Abdur Rub1* Sesamol Induces Apoptosis-Like Cell Death in Leishmania donovani: Front. Cell. Infect. Microbiol, 28 October 2021

[52]Yang Yang, Yuan Qu, Xiaoqiang Lv, Ruijin Zhao, Jing Yu, Suying Hu, Jingqi Kang, Yaling Zhang, Ye Gong, Tingting Cui, Xin Zhang and Yaping Yan *,Sesamol supplementation alleviates nonalcoholic steatohepatitis and atherosclerosis in high-fat, high carbohydrate and high-cholesterol diet-fed rats: Food Funct. 2021 Oct 4;12(19):9347-9359.

[53]Xin Guo, Xiao-Tian Sun, Li Liang, Long-Kai Shi, Rui-Jie Liu, Ming Chang,* and Xing-Guo Wang, Physical Stability, Oxidative Stability, and Bioactivity of Nanoemulsion Delivery Systems Incorporating Lipophilic Ingredients: Impact of Oil Saturation Degree: J. Agric. Food Chem. 2021, 69, 5405−5415

[54]Nitesh Kumar,Jayesh Mudgal,Vipan K. Parihar,Pawan G. Nayak,N. Gopalan Kutty & C. Mallikarjuna Rao, Sesamol Treatment Reduces Plasma Cholesterol and Triacylglycerol Levels in Mouse Models of Acute and Chronic Hyperlipidemia: *Lipids* volume 48, pages633–638 (2013)

[55] Ram M. Thushara • Mahadevappa Hemshekhar • Manoj Paul • Mahalingam Shanmuga Sundaram • Rohith L. Shankar • Kempaiah Kemparaju • Kesturu S. Girish, Crocin prevents sesamol-induced oxidative stress and apoptosis in human platelets: J Thromb Thrombolysis (2014) 38:321–330

[56]Sonia Angeline M1 , Aditi Sarkar1 , Kushi Anand1, 2, Rashmi K Ambasta1 and Pravir Kumar*1,2,3,4, Sesamol and Naringenin reverse the effect of rotenone induced PD rat model: Neuroscience Volume 254, 19 December 2013, Pages 379-394

[57]Anil Kumar, Gurleen Kaur, Harikesh Kalonia, Puneet Rinwa, Evaluation of sesamol and buspirone in stress induced anxiety in mice: Indian Journal of Pharmacology | February 2013 | Vol 45 | Issue 1

[58]Fuguo Liu†1, Hua Liu†1, Ruihua Liu†, Chunxia Xiao†, Xiang Duan†, David Julian, Delivery of sesamol using polyethylene glycol-functionalized 2 selenium nanoparticles in human liver cells in culture: J. Agric. Food Chem., 19 Feb 2019:1-23

[59]Sara R. ElMasry1 , Rania M. Hathout1, 2*, Mohammad Abdel-Halim3 , Samar Mansour1,2, In Vitro transdermal delivery of sesamol using oleic acid chemically-modified gelatin nanoparticles as a potential breast cancer medication: Journal of Drug Delivery Science and Technology 15 August 2018,1-41

[60]Fuguo Liu a 1 , Xingze Li a 1 , Lin Wang b , Xiaojia Yan a , Dexue Ma a , Zhigang Liu a , Xuebo Liu a *, Sesamol incorporated cellulose acetate -zein composite nanofiber membrane: An efficient strategy to accelerate diabetic wound healing: International Journal of Biological Macromolecules 28 January 2020 1-42

[61]Xiao Ma,⊥ Juhong Wang,⊥ Guifen Hu, Yinggang Chen, Xiaoling Hu, Yijia Zhu, Linchao Ding,* and Shilong Ning*, Sesamol Epigenetically Induces Estrogen Receptor α Re-expression by Up regulating miR-370-3p in Estrogen Receptor α-Negative Breast Cancer: J. Agric. Food Chem. 2021, 69, 8737−8746

[62]Tarapong Srisongkram a,b , Natthida Weerapreeyakul a,b,* Route of intracellular uptake and cytotoxicity of sesamol, sesamin, and sesamolin in human melanoma SK-MEL-2 cells: Biomedicine & Pharmacotherapy 146 (2022) 112528

[63]Eman G.E. Helal1, Mohamed A. El-Aleem2, Shaimaa S. Ahmed1, Comparison between Sesame Oil and Glycyrrhizaglabra Effect as Phytoestrogen on Male Albino Rats: The Egyptian Journal of Hospital Medicine (April 2019) Vol. 75 (4), Page 2550-2555

[64] Burak Turgut*, İrfan Ergen**, Nevin İlhan, The Protective Effect of Sesamol in the Selenite-induced Experimental Cataract Model: Turk J Ophthalmol 2017;47:309-314

[65] Burak Turgut*, İrfan Ergen**, Nevin İlhan***, The Protective Effect of Sesamol in the Selenite-induced Experimental Cataract Model: Turk J Ophthalmol 47; 6: 2017

[66]Boondaree Siriwarin[a] Natthida Weerapreeyaku, Sesamol induced apoptotic effect in lung adenocarcinoma cells through both intrinsic and extrinsic pathways:Chemico-Biological interaction Volume 254, 25 July 2016, Pages 109-116

[67] Shahanshah Khana,b, Sandeep Choudharya, Arun Kumar a, Akanchha Mani Tripathi a, Amit Aloka, Jawahar Singh Adhikari a, Moshahid Alam Rizvi, Nabo Kumar Chaudhurya,Evaluation of sesamol-induced histopathological, biochemical, haematological and genomic alteration after acute oral toxicity in female C57BL/6 mice: Toxicology Reports 3 (2016) 880–894

[68]Zhigang Liu, Bo Ren,Yihui Wang, Chen Zou,Qinglian QiaoZhijun Diao, Yashi Mi, Di Zhu & Xuebo Liu, Sesamol Induces Human Hepatocellular Carcinoma Cells Apoptosis by Impairing Mitochondrial Function and Suppressing Autophagy:scientific reports 7:45728

[69]Nitesh Kumar • Jayesh Mudgal • Vipan K. Parihar • Pawan G. Nayak • N. Gopalan Kutty • C. Mallikarjuna Rao,Sesamol Treatment Reduces Plasma Cholesterol and Triacylglycerol Levels in Mouse Models of Acute and Chronic Hyperlipidemia: Lipids (2013) 48:633–638

[70] Amin F. Majdalawieh • Hyo-Sung Ro, Sesamol and sesame (Sesamum indicum) oil enhance macrophage cholesterol efflux via up-regulation of PPARc1 and LXRa transcriptional activity in a MAPK-dependent manner: Eur J Nutr (2015) 54:691–700

[71] remkumar Jayaraj a, Chandrakala A Narasimhulu b , Sanjay Rajagopalan c , Sampath Parthasarathy Rajagopal Desikan*a, Sesamol: A powerful functional food ingredient from sesame oil for cardioprotection. Food Funct., 6 jan.2020,1-23

[72]Bo Ren, Tian Yuan, Xinglin Zhang, Luanfeng Wang, Junru Pan, Yan Liu, Beita Zhao, Weiyang Zhao, Zhigang Liu, and Xuebo Liu, Protective Effects of Sesamol on Systemic Inflammation and Cognitive Impairment in Aging Mice: Journal of Agricultural and Food Chemistry. 18 Feb 2020, 1-42

[73]Nayana Venugopal Yadav1 · Sadashivaiah1 · Breetha Ramaiyan1 · Pooja Acharya1 · Lokesh Belur2 · Ramaprasad Ravichandra Talahalli1, Sesame Oil and Rice Bran Oil Ameliorates Adjuvant Induced Arthritis in Rats: Distinguishing the Role of Minor Components and Fatty Acids. Lipids (2016) 51:1385–1395

[74]Azza M. El Wakf • Hanaa A. Hassan • Nermin S. Gharib, Osteoprotective effect of soybean and sesame oils in ovariectomized rats via estrogen-like mechanism: Cytotechnology (2014) 66:335–343

[75]C. Mahendra Kumar a , U.V. Sathisha b , Shylaja Dharmesh b , A.G. Appu Rao a , Sridevi A. Singh a,* Interaction of sesamol (3,4-methylenedioxyphenol) with tyrosinase and its effect on melanin synthesis Biochimie 93 (2011) 562e569:

[76]Zhigang Liu, Qisen Xiang, Lihui Du, Ge Song, Yutang Wang, Xuebo Liu, The interaction of sesamol with DNA and cytotoxicity, apoptosis, and localization in HepG2 cells: Food Chemistry 141 (2013)289-296