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Common Applications of Black Cumin Seed (*Nigella sativa*) Oil in Folk Medicine

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ABSTRACT

Objectives: The seasonal plant *Nigella Sativa* (black cumin seed) has a broad range of medicinal effects. Black cumin seed oil (BCSO) has been found to have a range of advantageous effects as therapeutic or preventive therapy in varieties of diseases including hypertension, diabetes, obesity, and reproductive difficulties. **Methods**: the review collects potential medicinal applications and mechanisms for BCSO in the period between 1994 to 2022 from internationally accepted databases and scientific journals. **Results**: The oil also has been found to be a potent antioxidant and anti-inflammatory agent that renewed its interest as a low-risk dietary supplement. Additionally, it was shown that combinatorial therapy with other conventional chemotherapeutic medicines has a great synergistic effect allowing the reduction in the dosage of concurrently administered drugs while maintaining the optimal efficacy and minimizing or eliminating the global toxicity. **Conclusion**: The most prevalent substance of this volatile oil is thymoquinone (TQ), which is also the ingredient to which most of this herb's benefits are related. The current study shed light on the most valuable characteristics as well as traditional medicinal and biological principles of BCSO.

***Keywords**: BCSO, Thymoquinone, Antioxidant, Traditional, Dietary supplement.*

INTRODUCTION

Cumin seeds are used as common food spices and aromatic plants. They are extensively spread in nations bordering the Mediterranean Sea, central Europe, and western Asia. The seeds are also employed in folk medicine in Saudi Arabia, India, China and the nations surrounding the Mediterranean Sea. In India, cumin (Cuminum cyminum), black cumin (Nigella sativa), and bitter cumin (*C. nigrum*) are the three different types of cumin [1]. These previous types of mentioned cumin have common uses such as antioxidant activity through effect on lipid peroxidation and free radical scavenging mechanisms due to their higher phenolic content [1]. Black cumin seed oil (BCSO) is rich in highly active compounds such as fixed and volatile oils; fixed oil contains unsaturated fatty acids such as arachidonic, eicosadienoic, linoleic, linolenic, palmitic and myristic acid [2], while the volatile oil consists of saturated fatty

acids as nigellone, thymoquinone (TQ), thymohydroquinone (THQ), dithymoquinone, thymol, carvacrol, α- and β-pinene [2].

BCSO has been used as a food and medicine for a very long time in India as a remedy for a number of illnesses and conditions including asthma [3], cancer [4,5], diabetes [6,7], hypertension [8,9], obesity [10,11], inflammation[12,13] and hepatitis[14,15]. Thymoquinone (TQ) is the most common ingredient in the volatile oil of black cumin seed and is the primary factor in the herb's advantages. Many investigations have shown that crude black seed or its main active component TQ have varieties of biological activities include anti-cancer [16-18], anti-oxytocic [19], anti-tussive [20], anti-inflammatory [21,22], antipyretic [23], analgesic [21,24] and anti-oxidant [25,26] outcomes. Additionally, the oil has wide spectrum of microbiological uses [27] such as antimicrobial activity [28,29], anti-viral[30,31], anti-parasitic [32-34]and anti-fungal [35] applications. BCSO has also been shown to alleviate the symptoms of different disorders including hypertension, dyslipidemia, diabetes [18,36,37], asthma [19], convulsions [38,39], natural and chemical toxicities [40,41]. Moreover, the oil has protective effect against renal [42] and liver [43] complications. The current review demonstrates the possible medicinal uses of BCSO.

MATERIALS AND METHODS

Authors collected all possible information about "phytochemical, pharmacological significance of BCSO" in the period from 1994 to 2022 that were published in all resources (journals, books,.....etc.) and found in different internationally recognized databases such as PubMed Central, Google scholars,.....etc. The collected data were selected, correlated to the main review objectives, and explained using potential documented mechanisms and different pathways.

RESULTS AND DISCUSSION

A. Safety profile of BCSO

After administering black cumin seed oil (5 mL/day) for 8 weeks to healthy individuals, no significant liver, renal, or gastrointestinal side effects were encountered [44,45]. A clinical trial has been performed on 39 significantly obese males and found that receiving three grams of black cumin seeds per day for three months had no discernible adverse effects [46]. Also, the treatment with black cumin seeds (2 gram per day for six weeks) showed no effect on serum parameters such as alanine aminotransferase (ALT) and creatinine levels in adult individuals [46]. Another clinical study found that consuming black cumin seed as supplement powder for 40 days had no effect on total leukocyte or platelet counts [47].

B. Medical application of BCSO

1. Hypertension

The term "hypertension" means a 140 mmHg or higher increase in systolic blood pressure and/or 90 mmHg or higher increase in diastolic blood pressure [48]. Hypertension is a substantial risk element for heart disorders, stroke, and renal disease [49]. By the year 2025, about 15–25% of people, or around 1.5 billion people worldwide are expected to have hypertension [50]. About 29.5% of Egyptian individuals have hypertension [51].The increase in the lipid peroxidation and oxidative stress have been shown to play key a role in the etiology of essential hypertension and the arterial damage associated with it [52,53]. *In-vivo* study was also conducted on 24 male rats which were treated with oral nicardipine once a day at a dose of 3 mg/kg and BCSO at a dose of 2.5 mg/kg respectively, for eight weeks, concurrently with L-NAME administration. In the L-NAME-treated rats, the results demonstrated that BCSO reduced the increase in systolic blood pressure [54]. BCSO also inhibits Rho-associated-kinase (ROCK), a critical mechanism in aortic relaxation, by limiting extracellular Ca^{+2} entrance[55]. Huseini *et al.* found that after administering black cumin seed oil (5 mL/day) as a crude dietary supplement to hypertensive patients for 2 months ,their systolic and diastolic blood pressure decreased considerably when compared to the placebo and their baseline levels [56]. The positive impact was attributed to thymoquinone's antioxidant action against N-γ-nitro-L-arginine methyl ester (L-NAME)-induced hypertension and kidney injury [57]. The blood pressure-lowering impact of BCSO and its cardiovascular depressant effects may be attributed to indirect and direct mechanisms mediated centrally in the brain stem [58]. Studies have found beneficial correlation between blood pressure, percent consumption of some components in BCSO as linoleic acid (57.71%) and oleic acid (24.46%)[59-62] that were detected and measured in the BCSO [63]. Total polyphenols as quercetin [64] and various flavonoids were also discovered and quantified in BCSO [56] that were responsible for blood pressure-lowering action due to their antioxidant properties as well as endothelium-dependent vasorelaxation [65,66]. Additionally, studies have shown that *N. Sativa's* antioxidant activity may be contributed to its major components of thymoquinone, dithymoquinone, and thymol [57,67]. Thymol is a singlet oxygen chelator, whereas thymoquinone (TQ) and dithymoquinone are free radical scavengers with Superoxide Dismutase (SOD)-like activity [32,68,69]. The free radical trapping activity of TQ is maintaining a harmony in the renin-angiotensin system and decreasing heart diseases via muscarinic and serotonin receptor dependent pathways[70-72].Furthermore, the combinatorial effect of BCSO with sunflower oil in 2.5 mL twice daily for 8 weeks respectively in 26 treated patients with hypertension and 29 placebo showed a significant

reduction in diastolic blood pressure level, proving that using BCSO as a supplement to other oils had additional antihypertensive action [73]. The diuretic characteristics of *N. sativa* may be also responsible for its blood pressure-lowering effects [72].

2. Obesity

Obesity means having a body mass index of 30 kg/m2 or more [74]. Obesity has become so widespread cause for many infectious diseases [75] and other illness such as diabetes [76,77], coronary heart diseases (CHD) [78], certain types of cancer [79], and sleep-breathing problems[80,81]. The worldwide prevalence was 14.0% in 2019 [82] and about four million Egyptian individuals in 2020 suffered from obesity [83]. *In-vivo* studies revealed a decrease in appetite and food intake After utilizing *N. sativa* supplements as well as an increase in energy consumption, which could be the powerful anti-obesity mechanism of BSCO [84,85]. The soluble fiber content of BCSO may be a substantial factor to the sense of satiety and fullness [84]. After administering black cumin seed oil (*2000 mg /day)* to healthy *obese women that underwent a 4-week washout period between two 8-week periods of supplementation, improvements in anthropometric and body structure measures were found and a notable reduction in hunger indicating that N. sativa supplements can help with obesity improvement* [86]. Many studies suggested that *N. Sativa*'s hypolipidemic impact was due to its antioxidant capabilities, particularly TQ, which reduced lipid peroxidation and improved lipid metabolism [87-89]. After administering black cumin seed oil (*3 g /day)* to 50 obese women given a poor-calorie diet for 8 weeks , loss of weight in the black cumin group compared to the placebo group was observed [90]. Another clinical study conducted using 90 obese women to investigate the effect of BCSO combined with a poor-calorie diet on cardiometabolic risk variables in obese women [84]. Both the weight and waist circumference in the Black cumin seed oil group were considerably lower than placebo group with notable reduction in triglyceride and VLDL level. The major components of TQ, thymol, lipase, and unsaturated fatty acids, including arachidonic, linoleic, oleic, linolenic and eicosadienoic acids, unsaturated fatty acids, particularly *polyunsaturated fatty acids* (PUFA), have abilities to combat obesity and modify the link between the Lipoprotein lipase (LPL) rs320 gene and obesity [91,92]. After administering black cumin seed oil (*1 g /day)* to patients with hypercholesterolemia for 2 months , hypotriglyceridemic effect of BCSO on lipid profile was reported as it decreased the total cholesterol (TC), *triglycerides (TG)*, LDL-C and increased HDL-C concentrations [93,94]. Unsaturated fatty acids modify the levels of TG and VLDL and have an impact on the production and catabolism of TG-rich lipoproteins. [93,94]. Hypotriglyceridemic effect of BCSO improves insulin resistance and fatty liver by reducing lipolysis and fat accumulation in adipocytes which reduce free fatty acid influx to the liver [95].

3. Diabetes

Diabetes is an endocrine system disorder and one of the most common and quickly expanding diseases in the world characterized by unusually high blood glucose levels [96]. The risk of heart disease, dyslipidemia, infection, morbidity, and mortality can all rise as complications of metabolic disorders in diabetes [97,98]. World Health Organization (WHO) encourages researchers to explore the potential therapeutic characteristics and adverse effects of medicinal herbs in management of diabetes to avoid severe side effects of some chemical medications [99]. The International Diabetes Federation (IDF) estimates that there are currently more than 537 million diabetics worldwide [100] and about 15.2% in the adult individuals in Egypt had diabetes in early 2020[101]. It was confirmed by *In-vitro* investigation on the isolated pancreatic Islets of Langerhans that BCSO stimulated insulin secretion [102] and reduced the severity of degenerative and necrotic alterations[103,104]. A study demonstrated the hypoglycemic impact of BCSO in streptozotocin plus nicotinamide diabetic hamsters and data showed that it caused stimulatory influence on β-cell perform with a subsequent elevation in serum insulin concentration , and repairing activity of the pancreatic damage [105]. In type 2 diabetes animal model, findings showed that black seed oil has insulin tropic characteristics [106,107]. Kanter *et al*. also proved that BCSO has a pharmacological protective role against diabetes by decreasing oxidative stress and maintaining pancreatic β-cell integrity in diabetic animal model [103,108,109] with reduction in hepatic gluconeogenesis [110]. This was hypothesized because of TQ inhibits the expression of gluconeogenic enzymes and the generation of hepatic glucose by activating the adenosine monophosphate-activated protein kinase (AMPK) in muscles and liver, in addition to its capacity to reduce glucose absorption in the intestine [111,112]. Also, the administration of BCSO as 2 mL/kg to diabetic rats resulted in a significant increase in liver glycogen content due to increased pancreatic insulin production, which stimulates the glycogen synthase enzyme and lowers circulating glucose levels [113]. These findings supported a previous study that found that daily stomach treatment by 80 mg/kg thymoquinone for 45 days elevated the insulin levels in streptozotocin (STZ)-induced diabetic rats [114]. A clinical study conducted on 60 patients showed that BCSO improved insulin resistance as an adjuvant therapy compared to administering 10 mg Lipitor with 500 mg metformin only per day [115]. Additionally, BCSO resulted in a significant reduction in fasting plasma glucose and an elevation in insulin concentration when compared to

contemporaneous control concentration, with adequate renal and hepatic safety [116] The effect of BCSO was also investigated on lipid profile and glucose metabolism in patients with diabetes type 2 and data showed that fasting glucose, glycated hemoglobin, triglyceride, and low density lipoprotein–cholesterol (LDL-C) levels were all significantly reduced compared to placebo [117,118].

4-Pain

There are numerous studies demonstrated the analgesic effect of BCSO as a miracle pain relieving natural product [119-121]. *In-vivo* study confirmed this activity as the oil had a good significant effect against pain generated by injections of 7% acetic acid in dosages of 0.05 ml, 0.1 ml, and 0.2 ml in dependent doses in animal model, respectively [120]. Furthermore another study on an animal model of neuropathic pain demonstrated that BCSO can inhibit neuropathic pain progression and manage hyperalgesia[121]. Mastalgia is the clinical word for a breast ache, which is one of the most annoying things along with many women between the ages of fifteen and fourty [122]. It's a deep, painful pain in the breast tissue that some women experience as heaviness, stiffness, irritation, or burning [122]. For women with cyclic Mastalgia, application of BCSO is safe and more effective through administrating of 600 mg twice daily for two months as a topical analgesic compared to topical diclofenac [119]. Another clinical study has been carried out to investigate the pain relieving effect of BCSO on geriatric patients with pain in their knees and results proved its significant efficacy as knee pain analgesic [123].

5-Skin Disorders

Vitiligo is a skin disorder that results in the loss of skin pigment cells, resulting in white areas **[124]**. In vitiligo, the skin's melanocytes (pigment-producing cells), mucous membrane, and retina are damaged, resulting in white spots in various locations of the skin**[125]**. According to estimates, vitiligo affects between 0.1 and 8% of the world's population **[126]** ,while its prevalence in Egypt is around 0.4 and 2% **[127].** BCSO was shown to be more effective when combined with others than traditional vitiligo treatments or supplements such as fish oil in reducing size of vitiligo lesions since thymoquinone can mimic the function of acetylcholine and stimulates cholinergic receptors and induces the release of melanin and skin darkening **[128]**. A cream containing BCSO was effective in sensitive skin areas like the genital region, hands and face when given twice a day for six months to vitiligo patients **[129]**. Acne vulgaris is another common type of skin disorder caused by chronic inflammatory mechanism **[130]**. Studies have shown effective response of the acne lesions to BCSO given two times daily for two months **[130,131]**. The most probable mechanisms for BCSO for management of skin disorders include the anti-inflammatory effect of BCSO and/or thymoquinone that inhibit *cyclooxygenase* (COX) and 5-lipoxygenase pathways of arachidonate processing and downregulate leukotriene biosynthesis **[132,133]**. Furthermore, the immunomodulatory and the antimicrobial properties of BCSO that contains α-pinene against *P. acnes* which play a significant role in acne pathogenesis play a key role in acne treatment **[22,134,135]**

6- Infertility

Male infertility is a condition that can be caused by a variety of factors, such as abnormal spermatogenesis related to pituitary disorders, testicular cancer, germ cell aplasia, varicocele, and environmental factors, as well as faulty sperm transportation due to birth defects or immunological and neurogenic causes [136]. Infertility affects 8–12% of couples worldwide with male factor infertility (MFI) accounting for 40–50% of the causes [137] , while the exact prevalence of infertility in Egypt is unknown owing to a lack of registration and well-performed studies[138]. A dose of BCSO (1mL/Kg) increased testicular antioxidants and reduced testicular oxidative stress [139]. Smaller doses of BCSO (0.4mL/Kg) boosted sperm concentration, decreased lipid peroxidation and increased glutathione peroxidase, but hadn't any effect on sperm movement and level of testosterone in serum [140]. BCSO acts as a potential protective factor in infertility through stimulation of spermatogenesis, increasing spermatids' quantity and the seminal vesicles weight [141]. Furthermore, co-administration of BCSO with acetamiprid (ACMP) counteracted the negative effects of ACMP-induced reproductive toxicity on reproductive organ mass, semen quality, testosterone, and lower levels of thiobarbutiric acid-reactive substances (TBARS) level [141,142]. Alcoholic extract of BCSO particularly at high doses, might raise male rats' reproductive potential, LH, and testosterone levels [143]. After administration of 2.5 mL BCSO twice daily to infertile patients for 60 days, an enhancement in their aberrant sperm morphology, movement and quality without causing any side effects was detected [144]. Additionally, the combination of BCSO (0.5 mL/Kg) with metformin has been improved sperm parameters, blood testosterone levels, mitochondrial membrane potential, and overall body weight in obese individuals with fertility issues [145,146]. BCSO improves sperm quality through several mechanisms including increasing the amount of spermatids and spermatocytes in the cauda epididymis and testicular ducts [147].

7- Inflammatory disorders

Exaggerated inflammatory cells such as neutrophils, eosinophils, basophils, and mast cells are the main cause for the development of several inflammatory disorders [148]. The activation of mucous glands, vasodilation and increased vascular permeability are all

the physical signs of inflammation, and they are all responsible for common symptoms like itching, sneezing, runny nose, and nasal congestion [149]. *In-vivo* studies testing the anti-inflammatory effect of BCSO in different inflammatory animal models using carrageenan-induced paw oedema, croton oil-induced ear oedema and acetic acid-induced writhing showed that BCSO has a substantial painkiller impact in formalin test and light tail flick tests [150,151]. Allergic rhinitis is one example of the prevalent chronic and allergic condition, particularly among children, and its incidence in populations is rising as a result of industrial work [152]. Clinical studies were performed on allergic rhinitis patients, and clinical findings revealed that BCSO reduced nasal mucosal congestion, itching, runny nose, and sneezing episodes [153-155]. Similar clinical research was performed on 68 volunteers with allergic rhinitis who received BCSO in the form of nasal drops for six weeks , results showed a significant improvement in tolerance of exposure to the active allergen group compared to placebo [156]. Topical use of the BCSO was found to be more successful than systemic treatment in reducing the effect of aggravating variables, which could be owing to BCSO's stronger antihistamine membrane stabilizing effects than the systemic approach probablymdue to inhibition of Leukotrienes release [157-159]. Another serious common immune-mediated chronic inflammatory skin diseases is psoriasis which is characterized by highly proliferative keratinocytes, dilated blood vessels in the dermis, and a large infiltration of leukocytes [160]. *In-vivo* study showed that topical application of BCSO every day has significantly reduced imiquimod (IMQ)-induced psoriasis-like inflammation and reversed all skin abnormalities [160]. Moreover, a newly developed locally applied combination containing herbal extracts traditionally used in skin problems, such as olive oil, tea tree oil, cocoa butter, and rich source of vitamins with BCSO was found to be a promising remedy for psoriasis due to strong antioxidant properties of BCSO [159,161-163]. Furthermore, the main mechanisms for anti-inflammatory characteristics of BCSO in psoriasis management is inhibiting leukotriene production [164] and histamine production [164], superoxide scavenger [165], immunomodulatory effect [22] by increasing T cell-mediated and natural killer cell-mediated immune responses [166].

Rheumatoid arthritis (RA) is another chronic inflammatory condition that can result in permanent joint damage and severe disability[167]. Patients usually have symmetrical polyarthritis of the tiny joints in their hands and feet, as well as early morning tightness and, on rare occasions, neurological symptoms [168]. The usefulness of BCSO in RA patients was explored and results demonstrated a significant improvement in disease activity [169]. The possible explanation for such activity is due to inhibition of Eicosanoid production and membrane lipid peroxidation, 5-lipoxygenase and cyclooxygenase by BCSO main components such as TQ [170]. On other side, the antinociceptive actions of BCSO or thymoquinone are mediated by indirect kappa- and mu(1)-opioid receptor activation in the supraspinal nervous system, so supplementing with disease-modifying antirheumatic drugs (DMARD) therapy for rheumatoid arthritis could be considered a cost-effective supplemental therapy [170].

8-Osteoporosis

Osteoporosis is a common illness that results in fragility fractures as a result of a widespread loss of bone mass and microarchitecture [171] with prevalence of 200 million people affected worldwide[172] and 20 millions of Egyptian adults [173].*In-vivo* study showed BCSO has reversed osteoporosis in ovary-ectomized animals due to its high content of unsaturated fatty acids and antioxidants as well as its anti-inflammatory characteristics [174]. As it was proved that BCSO has a greater degree of unsaturation with linoleic acid and oleic acid [175]. Linoleic acid helps in reducing bone loss by improving calcium absorption in animals [176]. Furthermore, oleic acid raises Ca^{+2} levels [177] and promotes nutrient absorption in the body, which helps to maintain bone health and reduce calcium loss [178]. Moreover, BCSO contains useful amounts of calcium, making it a natural origin of calcium supplement for pregnant and nursing women, as well as youngsters and the aged people, which could help to explain the elevated Ca^{+2} levels [175].

9-Epilepsy

Epilepsy is a neurological disorder affecting around 70 million people worldwide [179] and involves the occurrence of at least one or more epileptic seizures [180]. Gamma-aminobutyric acid (GABA) is a neurotransmitter that helps to keep the inhibitory tone in the brain and prevents neuronal stimulation [181]. Seizures can occur when the equilibrium between inhibitory and excitatory neurotransmission is disrupted [181]. Functional abnormalities in the central nervous system during epilepsy and seizures have long been known to cause oxidative damage and lipid peroxidation in brain tissues [182]. BCSO was shown to lessen pentylenetetrazol's (PTZ) convulsive and deadly effects in kindled mice and reduce PTZ-induced oxidative toxicity in the tissue of mice brain [183,184]. The combination of BCSO (10 mL/Kg) with sodium valproate (100 mg/kg) and phenytoin sodium (25 mg/kg) as standard medicines in PTZ-induced convulsion has potentiated antioxidant activity and enhanced the level of GABA in the brain, increased neuroprotective effects and prevent episode development [184,185]. Similarly, in another investigation, BCSO in a dose of 10 mL/kg orally for 7 days was shown to

improve malonaldehyde (MDA) level as well as a decrease in glutathione peroxidase and superoxide dismutase levels in the brains of mice who had a PTZ-induced seizure [4].

10- Cancer

The uncontrolled division and proliferation of cells invading healthy tissues is the primary issue triggering the genesis of all cancer types [186]. There were 18 million new cases of cancer diagnosed in 2018, with lung, breast, and prostate cancers accounting for the majority of cases (2,09 million, 2,09 million, and 1,28 million, respectively)[187]. Cancer is triggered by a number of causes, including aberrant DNA methylation [188], histone deacetylation [189] as well as genetic abnormalities [190]. Different tumor suppressor genes (TSGs) are silenced in cancer as a result of these epigenetic alterations [191]. Another carcinogenic causes is the free radicals build up in the body which produce oxidative stress and inducing carcinogenesis [192]. An earlier investigation revealed that TQ-rich BSCO prevented cancer cells from proliferating and caused them to undergo apoptosis. The interplay between TQ and downregulation of the epigenetic regulators which typically promote cell proliferation and shield cells from apoptosis by blocking the expression of a variety of tumor suppressor genes could be the underlying mechanism[193]. In human adeno- and ductal carcinoma cells including Michigan Cancer Foundation-7 (MCF-7), TQ demonstrated antiproliferative effects by promoting apoptosis through p38 phosphorylation, reactive oxygen species (ROS) production, activating caspases, and Bax while decreasing Bcl-2 [4,194]. Moreover, TQ mediated apoptosis in human colon adenocarcinoma HCT116 cells as it inhibited STAT3 pathway[195]. In addition, it significantly inhibited phase-I CYP1A1 enzyme synthesis in hepatic cancer and raised glutathione (GSH) levels in HepG2 cells[196]. Additionally, there is only one *In-vivo* study on TQ in lung cancer, which found that it dramatically boosted tumor apoptosis and blocked pulmonary arterial remodeling in rats given monocrotaline (MCT) treatment[197]. The ability of TQ to induce apoptosis through pro-oxidant effects in tumor xenograft nude mice was demonstrated in a renal cancer *In-vivo* investigation [198]. In a clinical study showed that administration of BCSO (80 mg/kg/day) for seven days after each methotrexate dose was able to reduce methotrexate induced liver toxicity and improved survival in Egyptian children with acute lymphoblastic leukemia as an adjuvant therapy in patients having methotrexate therapy [199]. The proposed mechanisms of anti-cancer activity of BCSO are related to its components such as thymoquinone, carvacrol, t-anethole, and 4-terpineol that all have noteworthy donating hydroxyl radical scavenging characteristics for free radicals scavenging properties [54]. Moreover, BCSO caused a considerable reduction in malonaldehyde (MDA) level in rats treated with carbon tetrachloride [159,200], and LPS-treated rats [201] as compared to preclinical investigations.

CONCLUSION

The use of *N. sativa* seed oil and its active ingredient thymoquinone demonstrate varieties of benefits in the management of different diseases such as hypertension, diabetes, obesity, osteoporosis, and other inflammation related diseases linked with oxidative stress. There are different proposed mechanisms of activity for BCSO and main components such as antioxidant, analgesic, modulate glucose and lipid metabolism and serum profiles. Additionally, BCSO can be used in combination therapies with different drugs and supplements for management of many different diseases such as diabetes and cancer. The collective data in the present review is good source for scientists looking for the potential use of medicinal plants such as BCSO and its pure components for future clinical applications on wide screen of diseases since most of its significant consequences have been proved to be positive with minimal side effects. Further clinical and animal studies are required to explore more applications of this magic seed in traditional herbal medicine.

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Conflict of interest

The authors declare that they have no conflicts of interest regarding the publication of this paper.

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