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File: ■ Black Cumin (*Nigella sativa*, Ranunculaceae)
■ Gastric Ailments

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RE: Black Cumin Seed's Regenerative Effects on Gastric Ailments

Khan SA, Khan AM, Karim S, Kamal MA, Damanhouri GA, Mirza Z. Panacea seed "nigella": a review focusing on regenerative effects for gastric ailments. *Saudi J Biol Sci*. July 2016;23(4):542-553.

Black cumin (*Nigella sativa*, Ranunculaceae), a seed-bearing shrub common to the Mediterranean coasts of Saudi Arabia, Africa, and Asia, is a traditional food spice and medicine. Known in Ayurvedic, Unani, and herbal medicine, black cumin seeds (BCSs) have been researched since the 1970s. BCSs contain more than 100 compounds, many still uncharacterized, but including nigelline, nigellone, thymoquinone (TQ), phytosterols, fatty acids, vitamins including tocopherols, and minerals. While the composition of BCS essential oil (BCSEO) varies according to seed characteristics and method of distillation, nearly 88% is made up of monoterpenes like *p*-cymene, carvacrol, α-thujene, γ-terpinene, and α- and β-pinene and their oxygenated derivatives; the remainder is sesquiterpenes and their derivatives. BCSEO contains 74.4-82.5% unsaturated fatty acids (UFAs) including arachidonic, eicosadienoic, oleic, linoleic, and linolenic acids.

BCS is used in traditional medicines worldwide and is especially prized in the Middle East. It is antihistaminic, antioxidative/antiperoxidative, and immunomodulating and has been used in an array of chronic and/or degenerative conditions. It may have antiviral effects. Oils rich in α- and γ-linolenic acid have been found to exert both antisecretory and antiulcerative effects. BCSEO has been reported to have numerous anticancer activities, affecting cell cycle regulatory protein expression and cancer cell development, growth, and proliferation. The authors also note benefit to patients with bronchial asthma, as well as a chelating effect, reducing free radical damage.

Gastric ulcers, prevalent worldwide, are caused by an imbalance of harmful and protective factors in the gastric mucosa. Constantly exposed to harmful agents including gastric and bile acids as well as drugs, microbes, and food ingredients, ulceration may occur along with excess gastric acidity, inflammation, cell proliferation, and reduced gastric motility and blood flow. Stress is a prime factor in ulcer progression. Treatment options either counteract factors such as pepsin, acid, active oxidants, and other endo- and exogenous irritants or stimulate mucosal defenses. Gastric lesions may be healed with antioxidant therapy, proton pump inhibitors, and drugs that reduce gastric secretions; however, there is currently no economically feasible treatment and prevention regimen. In many forms of traditional medicine, spices with strong antioxidant potential and herbs with antiulcerative effects are used to address this disease.

BCS has been found to lower gastric acidity and increase mucosal content. In vivo, TQ significantly reduced acute gastric lesions induced by ethanol. In vitro experiments found that aqueous BCS extracts lowered histamine- and bethanechol-induced gastric acid secretion but not pentagastrin-induced secretion. BCS extract acts against Gram-positive bacteria more so than Gram-negative strains, and one study found it to inhibit pathogenic yeast. It is a more potent antimicrobial than tetracycline, cefuroxime, and ciprofloxacin, and a stronger antifungal than clotrimazole.

Helicobacter pylori is a causative agent in peptic ulcers, gastric cancer, and chronic gastritis. It is increasingly resistant to antibiotics. BCSs act in vitro against this organism comparably to conventional triple therapy and, again in vitro, act synergistically with several antibiotics. Anti-inflammatory effects of BCS are primarily credited to its component of UFAs and polyunsaturated fatty acids (PUFAs) through a variety of mechanisms. BCS's antioxidant capacity, comparable to that of Trolox, is a key factor in its benefits in gastric ulcers and in preventing cancer. BCS flavonoids stimulate the gastric mucus and strengthen the mucosal immune system by scavenging superoxide and hydroxyl free radicals. BCSEO inhibits lipid peroxidation; TQ has this effect and also boosts cellular antioxidant capacity.

In vivo, supplementation with BCSEO significantly elevated gastric glutathione (GSH), superoxide dismutase, and glutathione S-transferase activity while accelerating ulcer healing. While these antioxidant effects are seen with raw BCS or BCSEO, they do not occur when the seed or oil has been boiled, possibly due to alterations in the chemical composition. Antihistaminic and anti-allergic properties of BCS are also well documented and exert specific benefits in the gastrointestinal tract. Low concentrations of nigellone effectively inhibit histamine release from mast cells. This also indicates a possible role for BCS in asthma and other histamine-related allergies, borne out in vitro and in vivo. Finally, BCS, BCSEO, and TQ all boost natural killer cell- and T cell-mediated immunological responses, again through a variety of biological pathways and mechanisms including reducing neutrophil infiltration, acid secretion, and, most recently reported, proton pump inhibition. In vitro, TQ acts synergistically with 5-fluorouracil in a dose- and time-dependent manner to boost apoptosis and inhibit cancer cell growth. While not discussed further in this otherwise quite detailed report, the authors state that another BCS compound, α-hederin, possesses "remarkable" healing activities in vitro and in vivo.

BCSs are associated with very low toxicity; however, smaller doses are recommended medicinally because doses as high as 50-100 mg/kg have been reported to drastically lower GSH, with resulting mortality in vivo. While reporting that nigelline can have a paralytic effect in large doses, and another BCS compound, melanthin, is toxic in large doses, the authors do not address these toxicities in their discussion of BCS. Contact dermatitis after prolonged topical use at a high dose has been reported, but oral administration in recommended doses seems quite safe.

As with many herbal medicines and medicinal foods, clinical trials of BCS and BCSEO are lacking.

—Mariann Garner-Wizard

Referenced article can be accessed at
http://www.sciencedirect.com/science/article/pii/S1319562X14001302.