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Editorial

Thymoquinone, a constituent of prophetic medicine-black seed, is a miracle therapeutic molecule against multiple diseases

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The seeds and oil of *Nigella sativa*, commonly known as black cumin, have been in use for a very long time to cure various ailments. In a Hadith, one of the sayings of Prophet Muhammad about the black cumin was mentioned that states "hold on to use the black cumin, because it can heal every disease except the death."[1] It has been mentioned as a curative black seed in the "Holy Bible" and is described as the Melanthion by Hippocrates and Dioscorides and as the Gith by Pliny.[2] Ibn Sina, a Persian physician, recommended its use to cure fever, wounds, skin diseases, fungus, parasites, and worms, as well as against bites and stings of poisonous animals. Thymoquinone (TQ), an active constituent of *N. sativa* seeds, has shown a wide range of pharmacological actions including antioxidant and anti-inflammatory, antidiabetic, anticancer, antimicrobial, hepatic, and renal protective effects.[3] TQ has shown an anti-inflammatory activity by downregulating the expression of pro-inflammatory and proliferative mediators such as tumor necrosis factor-α (TNF-α), inducible nitric oxide, cyclooxygenases-2, 5-lipoxygenase, and cyclin D1. TQ also possesses an antiglycation activity and protects the enzymatic activity of superoxide dismutase (SOD) against glucose- or methylglyoxal-induced glycation.[4] Recently, TQ was shown to inhibit peroxynitrite-induced oxidative damage of histone-H2A protein.[5]

TQ possesses a broad anticancer activity by altering p38 mitogen-activated protein kinase and peroxisome proliferator-activated receptors-γ pathways[6] TQ also induces the inhibition of spindle formation in carcinoma cells through the induction of G2/M cell-cycle arrest. Moreover, TQ decreased the expression of antiapoptotic proteins including Bcl-2 and Bcl-xL, whereas increased the expression of proapoptotic protein Bax. It also increases the levels of Phosphatase and tensin homolog (PTEN) in doxorubicin-treated MCF-7 cells and inhibits their proliferation through the activation of p53. TQ also inhibits the growth of colon cancer cells by arresting at G1 phase of the cell cycle.

TQ has been shown to possess the hepatic and renal protective effects against drug-induced toxicity by reducing the levels of aspartate transaminase, lactate dehydrogenase, alanine transaminase, blood urea, and creatinine.[7] TQ also demonstrated an ability to bind to free bilirubin and prevented the binding of bilirubin to erythrocytes that facilitated the increased detoxification and elimination of the toxic bilirubin.[7] Moreover, TQ showed immunomodulatory effects by downregulating the gentamicin-induced functional expression of cytokines including interleukin (IL)-6, IL-18, IL-1β, and TNF-α.[8] TQ has shown nephroprotective role against lipopolysaccharide-induced renal fibrosis and corrected the parameters of SOD and catalase in *Escherichia coli*-induced pyelonephritis.[3] The protective effect of TQ is largely mediated through its antioxidant potential including the reactive oxygen species scavenging ability, the lipid peroxidation inhibition, the protection of hepatic antioxidant enzymes, the suppression of oxidative stress, and hepatic inflammation.[3]

In recent years, the use of TQ was explored against a wide range of infectious diseases. TQ has been shown to prevent the biofilm formation in a number of bacteria including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis,* and *Pseudomonas aeruginosa*.[9] Thus, TQ seems to be an important part of antimicrobial armory, particularly against the pathogens that use the biofilm formation as an important part of their virulence strategy. Interestingly, TQ inhibited the activity of the drug efflux pumps in *P. aeruginosa*, *S. aureus,* and *Bacillus cereus*.[9] TQ has shown activity against both the drug-susceptible and drug-resistant *M. tuberculosis* by specifically targeting the intracellular locations of the pathogens.[10] We showed that a liposomal formulation of TQ can effectively cure fluconazole-resistant *Candida albicans*.[11]

In addition to above-mentioned actions, TQ also showed beneficial effects against respiratory disorders including asthma, emphysema, and pulmonary fibrosis. It ameliorated an allergic airway inflammation through the inhibition of Th-2 cytokines such as IL-4, IL-5, and IL-13.[12] TQ showed cardioprotective effect by reducing the hepatic steatosis in hyperlipidemic rabbits by virtue of its strong free radical scavenging and antioxidant activity.

TQ, a principal bioactive compound of *N. sativa* seeds, is a hydrophobic molecule that shows poor solubility in an aqueous solution. A variety of TQ formulations have been developed to increase its bioavailability and pharmacological activity.[3] Majority of them showed superior therapeutic activity to free TQ.

Recently, various TQ formulations have been investigated to treat multiple diseases including cancer, inflammatory and autoimmune disorders, and infections. We are still not able to use the full potential of TQ as a chemotherapeutic agent due to its reduced solubility in an aqueous milieu. To progress TQ from the bench to the bedside, major efforts should be made to prepare TQ formulations that can conquer the problem of poor solubility and bioavailability associated with the chemical nature of the drug. Thus, due to its multitargeting nature, TQ may be proved a very effective chemotherapeutic agent in the treatment of multiple diseases.

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