shown to exert significant anti-cancer effects on a great variety of neoplasms [43]. For *N. sativa* anti-cancer effects, different mechanisms such as utilization of free radicals, effects on enzyme activity, inhibition of cell proliferation [85], changes in intracellular glutathione, anti-oxidant activity, trapping free radicals [59, 86] and induction of apoptosis in cancer cells through a pathway dependent and inon-dependent ofon pP53 have been proposed [87]. Also for TQ anti-cancer mechanism, its effects on colon cancer cells awere growth inhibition, morphological changes, and increased apoptosis of cancer cells. TQ inducesd apoptosis by increasing the expression of the target gene mRNAs of P53 and, p21WAF1, and significant inhibition of anti-apoptotic proteins (BCL-2) [88]. In a study, the methanol extract of *N. sativa* had shows a strong cytotoxic action against *Ehrlich ascites* carcinoma cells and Dalton's ascitic lymphoma cells and a minimal cytotoxicity to normal lymphocytes [89]. Cytotoxic and apoptotic effects of *N. sativa* ethanol extract on ACHN line of renal cancer cells in comparison to normal L929 cells have been reported [90]. *N. sativa* seed extract with less toxicity on normal lymphocyte cells, had has a potent anti-cancer effects on sarcoma and lymphoma-180 cells, with less toxicity on normal lymphocytes [91]. Also topical application of *N. sativa* extract inhibitsed early stages of skin cancer in mice [92]. Moreover, TQ anti-tumor and anti- angiogenic effects on osteosarcoma *in vitro* and *in vivo* were have been investigated and the. tRe-sults demonstratceed that TQ inducesd a higher percentage of growth inhibition and apoptosis in the human osteosarcoma cell line SaOS-2, and in a dose-dependent manner considerably blocksed constitution of human umbilical vein endothelial cell tube in a dose-dependent manner. It iwas observed that TQ significantly downregulatesd NF-κB DNA-binding activity, XIAP, survivin, and VEGF in SaOS-2 cells. Also, Ttreatment with TQ upregulatesd the expression of cleaved caspase-3 and SMAC in SaOS-2 cells. Findings showed that TQ effectively inhibitsed tumor angiogenesis and tumor growth both *in vitro* and *in vivo*. As a result, inhibition of NF-κB and downstream effector molecules was is a possible mechanism of action for TQ's in anti-tumor and anti-angiogenic activity in osteosarcoma [92]. Also, theThe inhibitory effects of TQ were identifiedare reported *in vitro* and *in vivo* on benzopyrene induced stomach cervical cancer in rats [93]. Another study showsed that induced fibrosarcoma can be inhibited by TQ *in vitro* and. tThe mechanism of for this effect is was not clear, but may be related to interference with DNA synthesis, which was is probably related to glutathione reduction and storage, lipid peroxides, and the activity of some enzymes [94-95].

Anti-diabetic activity

N. sativa usages hasve been recommended by many traditional medicine experts to treat diabetes [96]. Significant effects of *N. sativa* on blood sugar reduction have been confirmed, which is. This effect was probably due to the presence of essential oil [42]. It iwas thought that many the anti-diabetic properties of *N. sativa* were are induced by activation of adenosine monophosphate kinase (AMPK), a glucose and lipid affecting cellular uptake of proteins with hypolipidemic and anti-diabetic properties [97-98]. Oral administration of volatile oil of black cumin (2 mg·kg^{-1}·BW^{-1}) in Balb/c mice, showed shows a significant reduction in blood glucose in Balb/c mice [44]. Intraperitoneal injection of NSO (50 mg·kg^{-1}) caused considerable hypoglycemic effect in fasting normal rabbits and alloxan-diabetic rabbits. BAlso because of no change in basal insulin levels in all groups, it appears that *N. sativa* reducesd blood glucose by an insulin-independent mechanism [99]. *N. sativa* extract showed an insulin-sensitizing action by enhancing ACC phosphorylation, a major component of the insulin-independent AMPK signaling pathway, and by enhancing muscle Glut4 content [100].

Moreover, *N. sativa* extract in vitro and in streptozotocin diabetic rats causesd regeneration and relative proliferation in beta cells and a decrement in free radicals production in streptozotocin-diabetic rats [101-102]. Treatment of rats with *N. sativa* extract and oil and TQ, significantly decreasesd tissue MDA and serum glucose and increasesd serum insulin and tissue SOD levels in rats. These findings demonstrated that *N. sativa* and TQ could be clinically useful in the treatment of diabetes and in the protection of β-cells against oxidative stress [103]. In another research, *N. sativa* powder (mixed with edible food) and TQ (in drinking water) were given to rats for 25 days and. hHematologic parameters analysis demonstrated that TQ and *N. sativa* induced a significant decrease in blood sugar in normal rats [104]. Also, *N. sativa* extract consumption for two months in rabbits causesd a considerable reduction in blood gloucose and ceruloplasm and also improvesd histological and biochemical signs of liver injury. These beneficial effects can be attributed to its anti-oxidant properties [105]. *N. sativa* regulates activity of glucose metabolism liver enzymes and thereby reducesd the gluconeogenesis. It inhibitsed the activity of "glucose 6-phosphatase and fructose 1.6 bisphosphatase," which is involved in gluconeogenesis. Furthermore, *N. sativa* increases the enzyme activity of "glucose 6- phosphate, which is involved in the pentose phosphate pathway in cells [106-107].

Cardiovascular-protective activity

In a study, the protective effect of *N. sativa* on the thoracic aorta contractile response was is evaluated in an experimental model of diabetes mellitus in rat. The results showed that treatment of diabetic rats with this plant causesd maximum reduction in contractile response to non-specific KCL agonist and specific noradrenaline agonist. Probably long-term oral administration of *N. sativa* could reduce vascular contractile responsiveness and the number of cardiovascular complications in diabetes [108].

In another study, the effect of *N. sativa* iswas studied on cardiac activity in diabetic rabbits and t. The results showed that *N. sativa* extract modulatesd irregular heart activity in diabetic rats [109]. Also, Tthe protective effects of TQ and acute (at 4 and 18 hours) effects of diesel exhaust particles