
Antioxidants have valuable effects on the process of spermatogenesis, particularly with diabetes mellitus (DM). Therefore, the present study investigated the impact and the intracellular mechanisms by which thymoquinone (TQ) works against diabetes-induced testicular deteriorations in rats. Wistar male rats (n = 60) were randomly allocated into four groups; Control, Diabetic (streptozotocin (STZ)-treated rats where diabetes was induced by intraperitoneal injection of STZ, 65 mg/kg), Diabetic + TQ (diabetic rats treated with TQ (50 mg/kg) orally once daily), and TQ (non-diabetic rats treated with TQ) for 12 weeks. Results revealed that TQ significantly improved the sperm parameters with a reduction in nitric oxide (NO) and malondialdehyde (MDA) levels in testicular tissue. Also, it increased testicular reduced glutathione (GSH) levels and superoxide dismutase (SOD) activity. Interestingly, TQ induced downregulation of testicular inducible nitric oxide synthase (iNOS) and nuclear factor kappa-B (NF-kappaB) and significantly upregulated the aromatase protein expression levels in testicles in comparison with the diabetic rats. In conclusion, TQ treatment exerted a protective effect against reproductive dysfunction induced by diabetes not only through its powerful antioxidant and hypoglycemic effects but also through its downregulation of testicular iNOS and NF-kappaB along with upregulation of aromatase expression levels in diabetic rats.