Chapter 5

Summary and Conclusion
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- RBO with several physiochemical, nutritional and compositional properties is an important constituent of human diet.

- Systematic isolation from cRBO by a two-step crystallization technique, followed by identical spectroscopic/chromatographic results and melting point comparable to the literature reports and/or corresponding standard confirmed the isolated compound as OZ.

- Oral administration of OZ reduced the blood glucose level in normal and in STZ-induced diabetic rats in both single and multidose study.

- OZ supplementation ameliorated the severity of renal dysfunction and conferred marked protection against functional and morphologic injuries in the kidneys of diabetic rats by modulating renal alterations, and improving serum lipid profile.

- OZ supplementation significantly attenuated the behavioral as well as biochemical changes associated with diabetic neuropathy.

- OZ strongly inhibited the proliferation of colon and liver cancer cells by a mechanism that involved concentration dependent cytotoxicity. The predominant form of cell death was likely by the induction of apoptosis.

- Chronic supplementation of OZ (entire period) to carcinogen-exposed mice ameliorated the deleterious effects of DMH-mediated ACF development, crypt multiplicity, tumor occurrence, and ultrastructural changes in the colon.

- Oral administration of OZ caused regression of NDEA induced hepatocarcinogenesis in mice by restoring the activities of various liver injury and tumor markers, and suppressing the tumor-forming potential in a time-dependent manner.

- The underlying mechanism by which OZ acts on the pre-neoplastic cells in colon/liver tissue could be, at least partially, attributed to the inhibition of cell proliferation and induction of cell death by apoptosis.

- In various pathological conditions like diabetes, diabetic nephropathy and neuropathy, colorectal and hepatocellular carcinoma, OZ prevented lipid peroxidation and stabilized all components of the antioxidant defense system through scavenging of free radicals.

- OZ stimulated both cellular and humoral immune responses in experimental animal models of immunity. The effectiveness of OZ treated animals in overcoming the side
effects of drug-induced myelosuppression provides sufficient evidence in favor of the drug as a haematopoietic enhancer.

- The highly hydrophobic OZ was successfully incorporated into liposomes. The entrapment and loading capacity of the LEOs were dependent on the lipid bilayer composition and % OZ content added. Based on the physicochemical characterization, the LEOs were optimized to obtain the maximum OZ entrapment, loading and in vitro release. The formulation REV-1.10 with 5:1 (SPC:Chol) molar ratio and 10% OZ content, was identified as optimum and was stable in suspension form at 4°C for 90 days.

- In vivo pharmacokinetic studies revealed that oral administration of the optimized LEO (REV-1.10) in rats improves the gastrointestinal absorption and augments the oral bioavailability compared to free OZ.

Thus, the overall findings of the study are suggestive of the therapeutic potential of OZ in various oxidative stress mediated pathophysiological conditions. The effects could be attributed to the ability of OZ to promote the antioxidant defense system, inhibit cell proliferation, and induce apoptotic like changes. Given its superior pharmacokinetics and enhanced oral bioavailability, liposome encapsulation of OZ may be used as a novel improved oral nutrient delivery system.