4. SUMMARY AND CONCLUSION

Cardiovascular disease remains the major cause of mortality in the world, typically claiming a third of all deaths. The primary cause of CVD is atherosclerosis, which refers to the hardening of arteries. Atherosclerosis is the disease of the heart, a chronic inflammatory condition, in which there is overproduction of reactive oxygen species (ROS) and endothelial cell activation. Statin therapy is used as a drug in the treatment of atherosclerosis. But causes adverse side effects, mostly affecting muscles and the liver and the most severe forms of myotoxicity and rhabdomyolysis. So the present study has focused on the drugs having the dual property of lowering lipid level and antioxidant activities together. The combination of CoRNS and Eo has been used in the present study in controlling atherogenic disturbances in the experimental animals.

In the present study, a significant gain in the body weight was noted in HCD fed animals which was restored in CoRNS and Eo treated animals.

The biochemical parameters such as urea, uric acid, creatinine and albumin were also studied. There was increase in the urea, uric acid and creatinine and decrease in the albumin level in the HCD fed animals. This shows that renal and cardiovascular damage occurs in these animals. Further, there was increase in the homocysteine level. Treatment with CoRNS and Eo has shown significant modulatory changes with restoration of all these parameter.
The lipid levels were altered in the HCD fed animals. There was a significant increase in TC, TG, free cholesterol, F.F.A and PL in the HCD fed animals. There was also marked increase in the serum lipoprotein such as LDL and VLDL and decrease in HDL with decrease in the activity of the lipid metabolizing enzymes such as LPL, CEH and LCAT. On treatment with CoRNS and Eo, restoration of all the lipid profile has been achieved. There was enhanced level of HDL with decrease in the activity of LDL and VLDL. The activities of the lipid metabolizing enzymes such as LPL, CEH and LCAT were increased with decrease in the activity of CES. This shows the hypolipidemic activity of CoRNS and Eo.

In hypercholesterolemic condition, marked histological changes were noted in the liver and aorta. Increased lipid accumulation was seen in the aorta of HCD fed rats which was confirmed by transmission electron microscopic studies. The abnormal morphological changes were reduced due to the treatment with CoRNS and Eo.

There was a significant alteration in the marker enzymes in the plasma and tissues. The marker enzymes such as LDH, ALP, AST and ALT were significantly increased in HCD fed animals. On treatment with CoRNS and Eo, the activities of these enzymes were decreased significantly. There was significant increase in the activity of CPK in the serum and the tissue such as liver and heart. The activities of all these enzymes were restored to normal levels on treatment with CoRNS and Eo. This shows the cytoprotective role of CoRNS and Eo.

Supplementations of HCD to the animals have caused increased production of ROS. There was increased production of free radicals in the HCD fed animals. This causes increase in the lipid peroxidation which damages the membranes. There was increased production of lipid peroxides in the membrane of
erythrocytes and in the tissues such as liver and heart. This causes damage to the membranes and leakage of the membrane bound proteins. Hence, there was decreased activity of the ATPases in the cardiac and hepatic tissues indicating alteration in the membrane integrity. Treatment with CoRNS and Eo has reverted the condition to normal state.

There was a decrease in the antioxidant status in the HCD fed animals. The activities of enzymatic and non-enzymatic antioxidants were lowered in the HCD fed animals. On treatment with CoRNS and Eo, the activity of enzymatic antioxidants such as SOD, CAT and GPx and non-enzymic antioxidants such as vitamin C and vitamin E were significantly increased providing defense against free radicals. The HCD fed rats showed abnormal glutathione metabolism through alteration in the activities of glutathione metabolizing enzymes along with the decline in the thiol level in the cardiac and hepatic tissues. On treatment with CoRNS and Eo, a significant regulatory action in glutathione metabolism has been imparted.

A marked elevation in the activity of lysosomal enzymes indicates lysosomal disturbances in the atherogenic condition. This indicates severe inflammatory response. Supplementation with CoRNS and Eo prevented lysosomal disruption on account of which the activities of lysosomal enzymes have been restored.

The HCD fed animals showed marked increase in the level of protein bound carbohydrates in the plasma and tissues which alters the vascular cell membranes integrity particularly sialic acid elevation which is more indicative of cardiovascular disease. CoRNS and Eo treatment prevented the abnormal increase in the protein bound carbohydrates in plasma and tissues, indicating cardioprotective role.
Increase in the production of peroxides in the high lipid status in HCD fed rats disturbs the mitochondrial complex enzymes. The activities of the mitochondrial complexes were significantly decreased in the HCD fed rats. This would damage the mitochondria due to accumulation of free radicals. Treatment with CoRNS and Eo has significantly enhanced the activity of complex enzymes which indicate protection rendered to mitochondria from damage.

There were increased levels of CRP and fibrinogen in the HCD fed animals. Moreover, the level of TNF-α was also significantly increased. The increase in the levels of inflammatory markers confirms cardiovascular disease. Treatment with CoRNS and Eo has significantly restored the levels of these markers.

The cardioprotective role of CoRNS and Eo has further reduced the oxidation of DNA thus preventing DNA fragmentation which is has been registered in DNA fragmentation studies. Thus, CoRNS and Eo has proved to be an excellent therapy in controlling atherogenic disturbances. These nutraceuticals seem to possess more effective antiatherogenic effect when given in combination to the HCD fed experimental animals. The expression of IL-10, an anti-inflammatory marker was studied. Treatment with CoRNS and Eo has elevated IL-10 and thus, inhibiting TNF-α. This confirms the anti-inflammatory role of CoRNS and Eo.

The present work shows that the combination of Coenzyme Q₁₀, Riboflavin, Niacin, Selenium and *Emblica officinalis* exhibits a better antioxidant, hypolipidemic and anti-inflammatory functions. This combined drug exert potential role in mitigating various biochemical changes characteristic of atherosclerosis reverting the alterations to near normal state.