7. SUMMARY

The present study demonstrates that naringin administration to diabetic rats attenuates the cardinal symptoms of diabetes. Increase in serum insulin level indicates the insulinotropic effect of naringin. In addition, results of the present study indicate that naringin administration corrects not only disturbances in the glucose metabolism but also disturbances in protein and lipid metabolism. This improvement in the protein and lipid metabolism prevents further deterioration of the condition and occurrence of diabetic complications like nephropathy and coronary artery disease. Further, naringin treatment reduces lipid peroxidation and improves the enzymatic and non-enzymatic antioxidant status of pancreatic tissue, which arrests the progression of the disease leading to complications.

Naringin administration to diabetic rats up-regulates the mRNA expression of Pdx-1, FoxM1 and Insulin genes. Further, immunohistochemical and immunoblot analyses show that it also up-regulates the protein expression of PDX-1 and FoxM1. Immunostaining against PDX-1 and FoxM1 demonstrates the nuclear localization of these proteins in the beta cells occupying the central portion of the islets. Nuclear localization of PDX-1 and FoxM1 indicates the availability of these transcription factors to up-regulate their downstream targets.

The increased mRNA and protein expressions of PDX-1 observed in naringin treated diabetic animals corroborate well with increase in expression of Insulin mRNA and serum insulin levels. These findings suggest that increased expression of PDX-1 following naringin administration up-regulates the Insulin gene expression that in turn leading to increased insulin biosynthesis and secretion. Expression of both insulin and PDX-1 in beta cells elucidates that these are functionally mature beta cells.

Similarly, in beta cells of naringin treated diabetic animals, increased expression of FoxM1 mRNA and protein suggests that the beta cells are proliferating. Increased insulin immunostaining and serum insulin levels establish that these proliferated cells are functionally mature beta cells. Further, expression of FoxM1 was noticed only in the islets and not around the pancreatic ductal tissue. This affirms
the well-accepted notion that beta cells proliferate from pre-existing beta cells. Thus, in the present study, ductal progenitors are not playing a role in the naringin-mediated proliferation of beta cells.

Histopathological and ultrastructural changes in naringin treated diabetic animals endorse the process of regeneration occurring in the islets and beta cells of diabetic animals. Moreover, the results of group VII, which were much improved than the results of group VI animals, suggest the need for prolonged use of naringin to achieve better therapeutic results.

The beneficial effect of naringin observed in animal model should be tested in humans by clinical trials in order to develop naringin as a new pharmacological agent for the treatment of diabetes.