CHAPTER 7

CONCLUSION
7. CONCLUSION

Rationale behind selection of rutin was that in our previous work, we found that Urtica Dioica leaf extract had neuroprotective effects in diabetes and depression. The extract contained a high quantity of rutin in it. Therefore we selected rutin for its neuroprotective effects against diabetes induced neurological complications. To evaluate the effect of rutin on long standing diabetes, we used multiple low dose STZ induced diabetes model. After STZ injections, animals developed significant hyperglycemia, glucose intolerance and hypoinsulinemia. Rutin treatment showed potential anti-diabetic effects by significantly improving the glycemia, and glucose tolerance and increasing the insulin levels. We observed that diabetes led to polyphagia, polydipsia and reduced body weight. Rutin treatment efficiently rescued all of these complications in diabetic animals. Further we observed that diabetes led to impaired neurobehavioral outcomes like anxiety, depression and cognitive decline. Rutin treatment was effective in preventing these complications thereby serving its neuroprotective role efficiently.

The neuroanatomical basis of the neurological complications of diabetes were associated with severe hippocampal neurodegeneration. Hippocampal neurons in diabetes had reduced dendritic arborization and spike density. Rutin treatment significantly prevented this damage and neurons appeared healthy. To understand the molecular basis of the central diabetic complications, we evaluated the insulin signalling in brain and whether or not it correlates with the disease pathology. We studied protein expression analysis of insulin, InR and GLUT4 via western blot (hippocampus), and InR and GLUT4 via immunofluorescence (in CA3 region of hippocampus). Our results revealed that the neuroprotective effects of rutin and its anti-diabetic potential could be attributed to its ability to up-regulate insulin, InR and GLUT4.

To better mimic the natural ways of diabetes induction, we employed the CUS led depression-induced diabetes model. CUS led to development of hyperglycemia (pre-diabetes), increased serum insulin, and insulin resistance (HOMA-IR index). Rutin treatment effectively prevented the hyperglycemia, reduce insulin levels and prevented the development of insulin resistance. CUS led to neurological complications like anxiety, depression and cognitive deficits, which didn’t occur in rutin treated stressed animals. Rutin treatment also prevented the CUS induced hippocampal neurodegeneration and central insulin resistance. To conclude, rutin’s anti-diabetic properties and neuroprotective effects against the central complications could be attributed to its ability to modulate hippocampal insulin signalling.
With significant advances in healthcare management and diabetes therapeutics, life expectancy in diabetic patients, continuous therapy, social stress and increased lifespan of the diabetic population have modified the spectrum of diabetic complications and associated morbidity. Therefore, besides traditional diabetic complications, a new set of unexpected complications have started to emerge which includes cancer, physical disability, cognitive dysfunction, depression etc. Diversification of diabetic complications and increased lifetime spent in the diabetic state has led to increased financial burden, intensification of disease and life monitoring quality system. Therefore we need to critically assess the current diabetic therapeutics, and search for suitable alternatives that could halt the diabetic progression as well as reverse the central complications that have already set in. With, insulin resistance being the major hurdle in diabetes, use of naturally occurring compounds like rutin, that circumvent the insulin resistance, could really change the dynamics of current diabetic therapeutics.