Chapter 8

Conclusion and Scope for Future Studies
8. Conclusion and scope for future studies

The present study for the first time investigated the role of oxidative stress and antioxidants on redox sensitive serine kinase pathways (NF-kB, p38MAPK and JNK) and insulin action in invitro and invivo models. Our results clearly demonstrate oxidative stress induced activation of redox sensitive serine kinase pathways and increased IRS-1 serine phosphorylation as potential molecular mechanisms of insulin resistance. The present data also help us to understand the molecular basis of insulin sensitizing property of antioxidants. In conclusion, identification of therapeutic strategies which will specifically inhibit these redox sensitive serine kinase pathways and IRS-1 serine phosphorylation will open novel objectives to prevent or delay the onset of insulin resistance and its related complications.

Although, our results are in support of above conclusion, further studies are clearly warranted to firmly establish the link between oxidative stress, redox sensitive serine kinases and insulin resistance.

1. The role of redox sensitive serine kinase pathways in the pathogenesis of insulin resistance needs to be studied thoroughly. The effect of specific natural / synthetic inhibitors of redox sensitive serine kinase pathways on insulin action must be studied. Moreover, apart from oxidative stress other specific signals which activate these pathways and their effect on insulin action need to be investigated. Further studies with gene knockout / over expression of these redox sensitive kinases (cell lines/animals) and the effect of oxidative stress on insulin action in these models will throw more light on our understanding of mechanism of insulin resistance.
2. The specific inhibitory serine phosphorylation sites of IRS-1 molecule need to be identified. Essentially recognition of the specific signals and kinases which phosphorylate the specific serine residues will be more helpful to develop effective novel drugs.

3. Although our results show the beneficial effect of antioxidants in insulin resistance, several clinical trials with antioxidants yield disappointing results. We believe research needs to be carried out on several fronts. First, antioxidant therapy needs to be improved. Either older antioxidants such as vitamin E, LA, and vitamin C need to be reformulated or newer antioxidants need to be identified. At this juncture, the use of antioxidant mixtures may be more useful. Moreover, screening tests to monitor oxidative stress to initiate antioxidant therapy or other therapeutic strategies need to be organized.