Chapter 8

Conclusion and Scopes for Future Studies
8. Conclusion and scopes for future studies

Knowledge about the cellular mechanisms responsible for insulin resistance and endothelial dysfunction in chronic renal failure is of clinical and scientific relevance to identify targets for the development of novel therapeutics to treat CRF. This thesis describes the mechanisms by which oxidative stress could induce insulin resistance in CRF. This thesis work provides the first evidence that the decreased in phosphorylation of IRS-1 in response to insulin stimulation in animal models of both oxidative stress and CRF could be the main culprit in causing insulin resistance. Further, alteration of redox sensitive stress kinases seems to have a major hand in decreasing IRS-1 tyrosine phosphorylation. In addition, we have identified new strategies to prevent insulin resistance by use of green tea and taurine. Overall, we can conclude oxidative stress via the activation of stress sensitive kinases (JNK, p38 MPAK and NF-κB) plays an important role in causing insulin resistance in CRF. Therefore, oxidative stress along with stress sensitive kinases should be considered as potential target in treatment of CRF along with conventional therapy.

Although, our results are in supportive of above conclusion, further studies are clearly warranted to firmly establish the link between oxidative stress, redox sensitive serine kinase 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 through more light on our understanding of mechanism of insulin resistance.
2. We though decrease in IRS-tyrosine phosphorylation has been studied, the role of IRS-1 serine phosphorylation needs to identified in both the model of oxidative stress and CRF. 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 experimental results show the beneficial effect of antioxidants against insulin resistance, protein glycation and dyslipidemia, clinical trials with antioxidants are warranted in patients with CRF.