Chapter # 11: SUMMARY AND CONCLUSIONS

Hyperglycemia is a critical factor in the development of diabetic nephropathy. Hence, glycemic control could slow the development of diabetic nephropathy. Traditional herbal medicines have been widely used for the treatment of various diseases in the world. Citrus fruits are considered to have renal protective activity. After thorough analysis, founds that Naringenin was the major active ingredient in the citrus fruits.

The levels of urine creatinine, kidney weight to body weight ratio, serum creatinine as well as BUN, urea, uric acid and albumin which are considered as markers of renal function, were higher in diabetic nephropathy rats than those of normal rats. Proteinuria led to a very early renal endothelial dysfunction in diabetes and accelerated the occurrence of tubular cell damage. Therefore, reduction of proteinuriamay be beneficial for kidney function and is able to prevent progression of DN. Continuous treatment with NARN (50 mg/kg b.wt/day) for 15 days obviously ameliorated all of those renal dysfunctions of DN progression in diabetic rats.

The most common histopathological alterations on DN rats occur in glomerulus. The administration of NARN provided a well improvement in the renal morphology, it’s indicated that NARN has nephroprotective effects against DN. Inflammatory cytokines, primarily IL-1, IL-6, IL-18 and TNF-α are involved in the development and progression of DN. Abnormal levels of immunoglobulins are very common in diabetic nephropathy. Metabolic alteration of collagen IV occurs in micro- or macro vascular basement membrane of diabetic nephropathy.
Oxidative stress has been considered to be a common pathogenetic factor of complications including nephropathy. Hyperglycemia is suggested to promote oxidative stress through both non-enzymatic and enzymatic mechanisms. The inhibitory effects of NARN on expressions of TNF-α and collagen IV and oxidative stress diabetic rat imply its potential efficacy in preventing the progression of DN.

In addition, hyperlipidemia participates in the progression of glomerular injury and a more rapid decline of renal function was observed in animals with DN. NARN has an impact on lipid metabolism in experimental animals (DN) inhibit the elevations in serum total cholesterol, triglycerides, VLDL-cholesterol and LDL-cholesterol levels, but it also reduced the increase in the blood glucose level, suggesting that NARN improves both carbohydrate and lipid metabolism. The decreased levels Na’K’-ATPase may cause disturbance of intracellular ion balance and thereby acceleration of cellular ageing. This further leads to an increase in cell size and osmotic fragility, which contribute to the disturbances in micro-vascular circulation observed in DN. Oral administration of NARN to these DN animals prevented the alterations in red cell fragility and the activity of membrane bound Na’K’-ATPase, which indicates the role of NARN in maintaining the structural integrity of erythrocytes during DN.

This study revealed that the NARN administered at a dose of 50mg/kgbwt was effective. Further, concurrent administration NARN successfully prevented renal damage associated with diabetic nephropathy, explored by various biochemical and histological examinations. Alteration in mean body weight, blood urea nitrogen, creatinine and uric acid associated with DN were reduced by treating animals simultaneously with NARN. In conclusion, the results of the present study indicate
that NARN may emerge as a putative antihyperglycemic, nephro protective antilipidperoxidative, antihyperlipidemic agent against diabetic nephropathy. Further studies need to be undertaken in order to confirm these findings and its extrapolation in humans.