

## Chapter 13

# New Herbal Approaches for the Treatment of Diabetic Kidney Diseases and Its Therapeutic Implications

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### ABSTRACT

*Diabetic Kidney Diseases (DKD) is a very serious complication of diabetes. There is recent steep rise in the prevalence of metabolic syndrome and DKD worldwide. Factors responsible for intraglomerular hypertension include activation of various vasoactive systems, polyol pathway, oxidative stress, inflammation and protein kinase C. Sodium-Dependent Glucose Co-Transporter (SGLT-2) inhibitors, DPP-IV (Dipeptidyl peptidase-4) inhibitors are being developed to manage the hyperglycemia and oxidative stress induced inflammatory cascade. Herbal drugs have gained increasing popularity; are complex mixtures of polyphenols and phytochemicals from any raw or processed part of a plant, including leaves. Herbal drugs in this modern era are preferred due to its lesser side effects. Various preparations are presently used for ameliorating the effect of DKD. Since, medicinal plants have been reported to affect various metabolic receptors, enzymes and signaling cascade. Above book chapter explains the involvement of different phytochemicals in biological pathway associated with the kidney damage.*

### INTRODUCTION

Diabetes is a metabolic syndrome which now becomes a growing epidemic in most of the developed and developing countries. Diabetes is of two types; Type 1 diabetes i.e. if individual's body is not able to make enough insulin. It usually starts when the person is a child or young, but it can happen to anyone. It is treated by taking daily insulin shots or using an insulin pump and by following a restricted diet plan

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with care. About 5-10% of cases of the diabetes are Type 1. Type 2 diabetes; body makes some insulin but cannot use it properly. It is partially preventable and is typically brought on by poor diet and lack of exercise. Heredity may be one of the reasons; but it usually starts when the person is above the age of 40, but it can happen earlier also. It is treated with exercise, weight loss and meal planning. People with Type 2 diabetes generally requires insulin, but oral medications are given (called hypoglycemics) are prescribed if diet and exercise alone do not control the disease. Type 2 is the most common type of diabetes.

Diabetic kidney diseases (DKDs) are one of the serious and common complications of diabetes and part of the chronic kidney diseases (Tripathi & Yadav, 2013). Presently modern medicine is using diabetic kidney diseases (DKD) instead of diabetic nephropathy for which cure has not been yet found. Much research has been conducted in both basic sciences and clinical therapeutics, enhancing our understanding of the pathophysiology of diabetic nephropathy and expanded horizon of the potential therapies available. A better understanding of the pathogenesis of DKDs is therefore necessary to develop more effective therapies.

## **EPIDEMIOLOGY**

The recent steep rise in the prevalence of metabolic syndrome and of Type 2 diabetes worldwide is extremely pronounced in Asian nations and is particularly dramatically increasing in India. This gave India the dubious distinction of the “diabetes capital of the world”. In urban Indians, the overt nephropathy and microalbuminuria was found to be 2.2 and 26.9%, respectively (Ritz & Zeng, 2011). Diabetic kidney diseases are the most common causes of chronic kidney failure and end-stage kidney diseases in the United States (Mehdi & Toto, 2009).

Factors responsible for intraglomerular hypertension include activation of various vasoactive systems, such as endothelial systems and the RAAS. Polyol pathway, oxidative stress, inflammation and PKC pathways which are involved in making it a syndrome; with serious complications. These changes results to high secretion of fibrotic cytokines such as transforming growth factor  $\beta$  resulting to furtherance of haemodynamic changes (Sharma & Sharma, 2013). The earliest clinical evidence of nephropathy is an increase in microalbuminuria (defined as  $>30$  mg/day) into the macroalbuminuria range ( $>300$  mg/day) (Toth-Manikowski & Atta, 2015). Renal function is compromised even prior to the onset of initial damage to the kidney. There occurs several oxidation and reduction changes that appears early and continue as chronic damage progresses, highlighting the complexities of the disease. Besides the classical anti-diabetic drugs such as sulfonyl urea, biguanides,  $\alpha$ -glucosidase inhibitors, PPAR- $\gamma$  agonists (Peroxisome proliferator activated receptor), Sodium dependent glucose co-transport (SGLT-2) inhibitors, aldose reductase inhibitors, DPP-IV (Dipeptidyl peptidase-4) inhibitors etc are being developed to manage hyper-glycemia (Pathak and Bridgeman, 2010).

Increasing evidence from both experimental and clinical studies suggests that there is a close relationship between hyperglycemia and oxidative stress induced inflammatory cascade. People with diabetes are at higher risk of vascular, peripheral and cardiovascular diseases. Evidence of kidney damages are albuminuria, proteinuria, haematuria, decrease in creatinine clearance and structural abnormalities found on the kidney imaging tests. AGEs cause thickening of extracellular matrix, decrease in function of glomerulus. An estimated GFR  $< 45$  mL/min/  $1.73$  m<sup>2</sup> is associated with higher risks of renal, cardiovascular and other clinical manifestations irrespective of the age. Herbal drugs in this modern era are preferred

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