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Edible plants from traditional Chinese medicine is a promising alternative for the management of diabetic nephropathy

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ABSTRACT

Diabetic nephropathy (DN) is a serious microvascular complication in diabetes mellitus patients and 30–45% of DN patients progresses to end-stage renal disease, imposing a heavy burden on the society. Unfortunately, the pathogenesis of DN remains unclear, and effective and safe therapies are in great demand. Rather than conventional medicines that concentrate on delaying renal failure by controlling blood sugar and/or ameliorating microalbuminuria, traditional Chinese medicine (TCM) emphasize on the patients' whole inner system and devote to repair the kidney with consideration of overall health. Since many TCM herbs are edible, edible plants from TCM as diet therapy would be a promising alternative for DN management. To date, remarkable progresses have been made on the therapeutic effects of TCM edible plants for DN. In this review, the pathogenesis and experimental models of DN are firstly discussed. Thereafter, the structures of active components from TCM edible plants are summarized followed by discussion of recent research on TCM edible plants as functional food for diet therapy. Additionally, the necessity for safety evaluation of TCM edible plants for DN treatment is addressed.

Contents

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1. Introduction

According to the updated epidemiological data from the International Diabetes Federation, diabetes mellitus (DM) is a notorious chronic metabolic disease with high morbidity and mortality afflicting 382 million people in 2013 globally, and the diabetic population will approach 592 million by 2035 (Guariguata et al., 2014). Miserable suffering of the diabetic patients is attributed not only to the hyperglycemic state, but also to life-threatening complications associated with the disease. Microvascular (retinopathy and nephropathy) and macrovascular (atherosclerotic) disorders will develop if long-term diabetes is not effectively controlled (Musabayane, 2012).

Diabetic nephropathy (DN) is a serious microvascular complication in patients with insulin-dependent DM both type 1 or type 2. The prevalence of DN is increasing at an alarming rate in both developing and developed countries (Zelmanovitz et al., 2009). It progresses to end-stage renal disease (ESRD) with a rate of 30–45%, and is the major cause of cardiovascular mortality imposing a heavy burden on the society (Pugliese, 2014). Current therapies for the management of DN mostly rely on the application of drugs such as anti-hyperglycemic agents, antihypertensive agents, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and dihydropyridine calcium channel blockers (Tripathi & Yadav, 2013). Recently, toll-like receptor-4 antagonist CRX-526 has become a new emerging treatment (Lin et al., 2013). However, side effects and unexpected conditions of these therapeutic approaches may arise after long term administration. For instance, although statins have been shown to possess lipid lowering, cardiovascular, and antiproteinuric benefits in DN patients, a recent research concludes that data reporting the renoprotective effects of statins may be relatively sparse and biased, and the related side effects of statins in DN patients should be taken into consideration (American Diabetes Association, 2004). Moreover, serum potassium levels should also be carefully monitored during the administration of ACE inhibitors or ARBs to avoid the development of hyperkalemia (Strippoli et al., 2008). Given the complex nature of DN pathogenesis and the limitations of conventional drugs, more effective and safe novel therapies are in great demand.

Under this situation, many researchers have focused their attention on natural products with renoprotective effects in recent years. WHO also recommends herbal medicines as an adjuvant therapy for diabetes and its associated complications (Dirks, 2004). As a holistic and combinational approach, the use of traditional Chinese medicine (TCM) in the management of DN has its superior advantage. Dietary therapy has been part of TCM for several thousand years. Recent evidence indicates that TCM edible plants such as *Panax notoginseng*, *Cinnamomum zeylanicum* and *Astragalus membranaceus* have significant potential to modulate DN progression (Chen et al., 2008; Gao et al., 2012; Liu, Xu, Shen, & Wu, 2012; Tang et al., 2011; Tu, Dong, & Lu, 2011; Tu, Qin, Dong, Lu, & Guan, 2011). Moreover, many TCM edible plants such as mushroom, grape, hawthorn etc., demonstrate a preferable benefit for DN patients (Chen et al., 2008; Li et al., 2009; Mooradian, Failla, Hoogwerf, Maryniuk, & Wylie-Rosett, 1994). Since many TCM herbs are edible and the concept of diet therapy is widely accepted, the introduction of edible plants from TCM as dietary therapy would be a promising alternative for DN management. In order to provide scientific evidence for the use of dietary therapy derived from TCM edible plants as a complementary approach for DN treatment, the present review herein aims to classify anti-DN bioactive components and summarize the beneficial effects of TCM edible plants against DN models with emphasis on their underlying mechanisms. Further, the safety and toxicity concerning the consumption of TCM edible plants are evaluated.

2. DN development and experimental models in TCM edible plants study

2.1. *Kidney structure and pathogenesis of DN*

Structurally the kidneys make urine by filtering blood and metabolic wastes. There are millions of structural units inside the kidney, which are called nephrons. Glomerulus is the primary part of nephron, contributing to the selective filtration of blood and metabolic wastes to form urine. Podocytes, the glomerular basement membrane (GBM), and endothelial cells constitute the filtration barrier of the glomerulus. The electrical charges of the barrier and pores inside allow the filtration of water and small substances, while preventing proteins from being filtered (Zelmanovitz et al., 2009).

Pathologically, DN is a functional progression from hyperfiltration to microalbuminuria, and then to macroalbuminuria, finally to renal failure (Somania, Singhai, Shivgunde, & Jain, 2012). In 1983, Mogensen defined five stages in the development of renal changes in diabetes. The first one is characterized by hyperfunction and hypertrophy, which is at least partially reversible; next morphologic lesions take place with an increase in glomerular filtration rate (GFR); then the decisive stage comes with microalbuminuria, which manifests as