

# Traditional Chinese Medicine Approaches in the Context of Diabetic Kidney Disease

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## Abstract

Diabetic Kidney Disease (DKD) is a major microvascular complication of diabetes mellitus (DM), which can lead to renal failure in diabetic patients. With rising global prevalence and limited conventional therapeutic efficacy, traditional Chinese Medicine (TCM) has emerged as a complementary and holistic approach, provides a unique perspective on DKD pathogenesis and treatment. This review highlights the potential of TCM to complement conventional therapies, advocating for interdisciplinary collaboration to optimize DKD management.

## Introduction

DKD is a significant complication of diabetes characterized by microvascular lesions that lead to kidney dysfunction and increased blood glucose levels. It is a major contributor to end-stage renal disease and poses serious morbidity and mortality risks for diabetes patients.

Prevalence	10.5% of the adult population (age 20 - 79) has diabetes; approximately 783 million adults will suffer diabetes in 2045; DKD as the major complication of diabetes is a global health concern
Signs	Declined renal functions due to renal structural changes; the two major indicators are albuminuria and declined glomerular filtration rate.
DM to DKD	Vascular complications resulted from diabetes lead to microvascular lesion. This leads to significant kidney malfunctioning and thus DKD, the major cause of end-stage renal diseases
Stages	DKD is diagnosed when the patients are in the third stage diagnosis according to Mogensen classification
Strategies	Anti-hypertension, anti-hyperglycemia, anti-oxidation, anti-inflammation, metabolism regulations, anti-fibrosis etc.

Table 1 – Summarize of basic background, definition, and current management towards DKD

## Understanding DKD in TCM

In TCM, DKD is seen as a progression of chronic hyperglycemia leading to kidney *Yin* deficiency and various imbalances in *Qi*, *Yang*, and *Blood*. This condition manifests through symptoms like thirst and edema, with advanced stages reflecting complex patterns of *damp-heat accumulation*. Treatment aims to restore balance among *Yin* and *Yang*, using herbs that resolve dampness and improve fluid metabolism.

## TCM clinical application for DKD

**Liuwei Dihuang Pill:** Reduce UAER in early DKD.

**Shenqi Dihuang Decoction:** Reduce proteinuria, alleviate kidney chronic inflammation.

**Qiju Dihuang Pills:** lower levels of serum IGF-1, TGF- $\beta$ 1, and IL-8.

**Qizhi Jiangtang Capsule:** Regulate blood sugar and blood lipid content, reduce insulin resistance combined with Sitagliptin.

**Zishen Tongluo:** Improve metabolism and renal function, reduce UAER

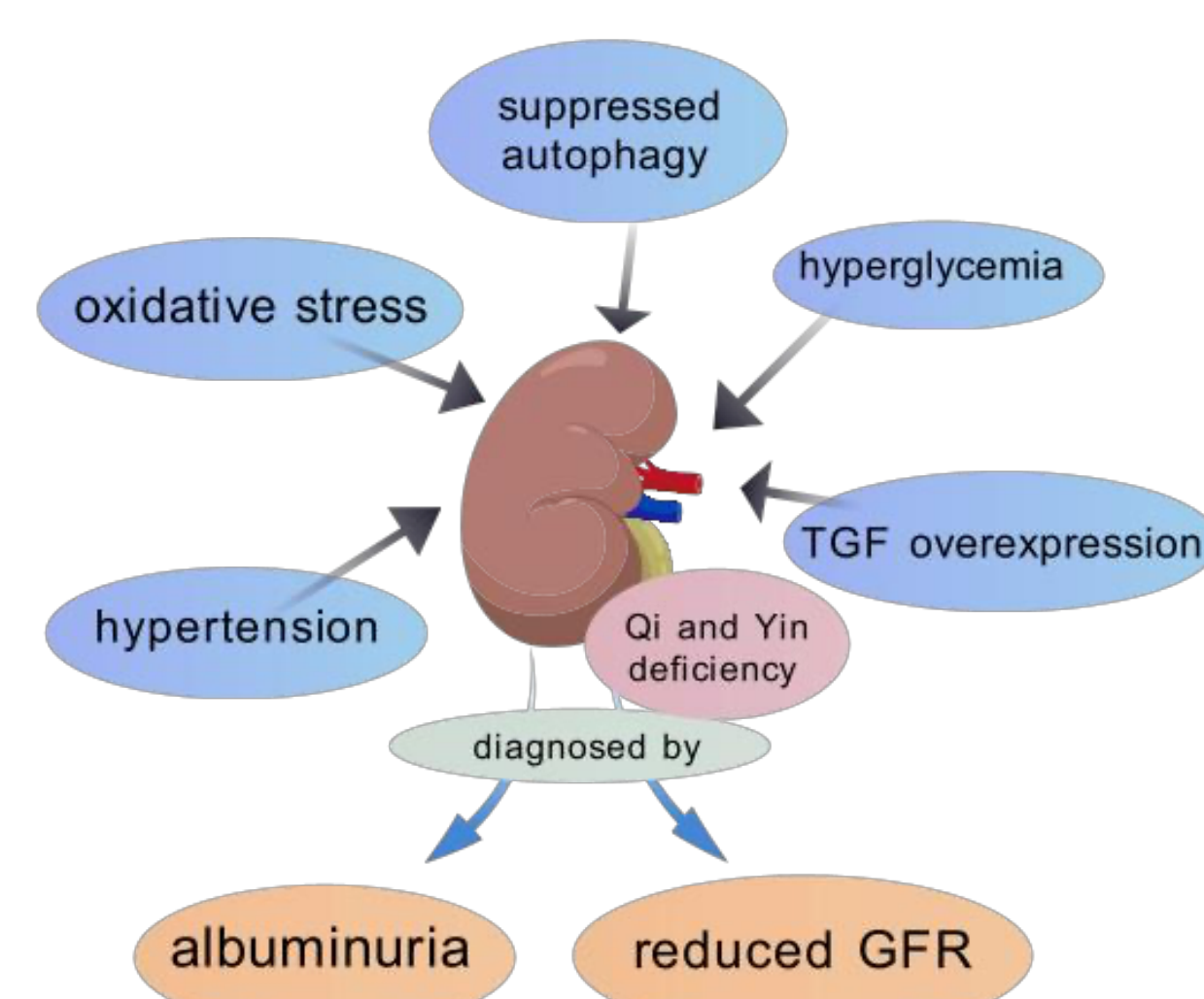


Fig 1 – Pathophysiology of DKD with its contributing factors

TCM Preparation	Sources	DKD staging	Study Period	Sample Size (Intervention: Control)
Liuwei Dihuang Pill	Song et al. (2004)	3	3 months	41:31
Shenqi Dihuang Decoction	Du et al. (2021)	3-4	3 months	80:80
Qiju Dihuang Pills	Chen et al. (2023)	3	2 months	40:40
Qizhi Jiangtang Capsule	Guo et al. (2014)	3	6 months	81:80
Zishen Tongluo	Ma et al. (2013)	3	3 months	25:20

Table 2 – Summarize of selected clinical RCT of using different TCM to treat DKD

## Key mechanisms involved in the protective effects of TCM against DKD

### Anti-inflammation:

Renal inflammation highly correlate the progression of DKD. Liuwei Dihuang Decoction, Tangshen Formula, and Danggui-Shaoyao-San possess anti-inflammatory effect by inhibit the expression of NF- $\kappa$ B; Jiangtang decoction inhibit NF- $\kappa$ B while activates the PI3K/Akt pathway; Melatonin, as a natural hormone, effectively inhibits the TLR2/MyD88/NF- $\kappa$ B pathway; Paeoniflorin, key compound from Paeonia lactiflora, inhibit both TLR2 & TLR4 pathways, result in reduced expression of inflammatory marker.

### Anti-fibrosis:

Inhibit fibrotic progression is a key to manage DKD. TGF- $\beta$ /SMAD pathway is a central mediator of renal fibrosis. Chaihuang Yishen Capsules & Liuwei Dihuang Decoction inhibit such pathway by increase SMAD7 expression & decrease SMAD2/3 phosphorylation respectively; JAK/STAT signaling dysregulate DKD. Other than the ant-inflammatory effect, Tangshen Formula also possess negative feedback regulation of the JAK/STAT/SOCS pathway

### Antioxidation:

Emodin, derived from *rhubarb*, and moringa isothiocyanate, derived from *moringa oleifera*, and the Liuwei Dihuang Decoction have all exhibited antioxidation and possess great prospective for DKD treatment. Emodin reactivate NRF2, regulates various antioxidant enzymes to practice antioxidation, reducing oxidative.

### Metabolism Regulation:

TCM formulas including Huangqi Decoction, Yiqi Jiedu Decoction, and Xiaokeyinshui have all demonstrated potential in DKD management through metabolism. Yiqi Jiedu Decoction, regulates glucose metabolism through increasing glucose uptake by promoting the AMPK/GLUT4 signaling pathway.

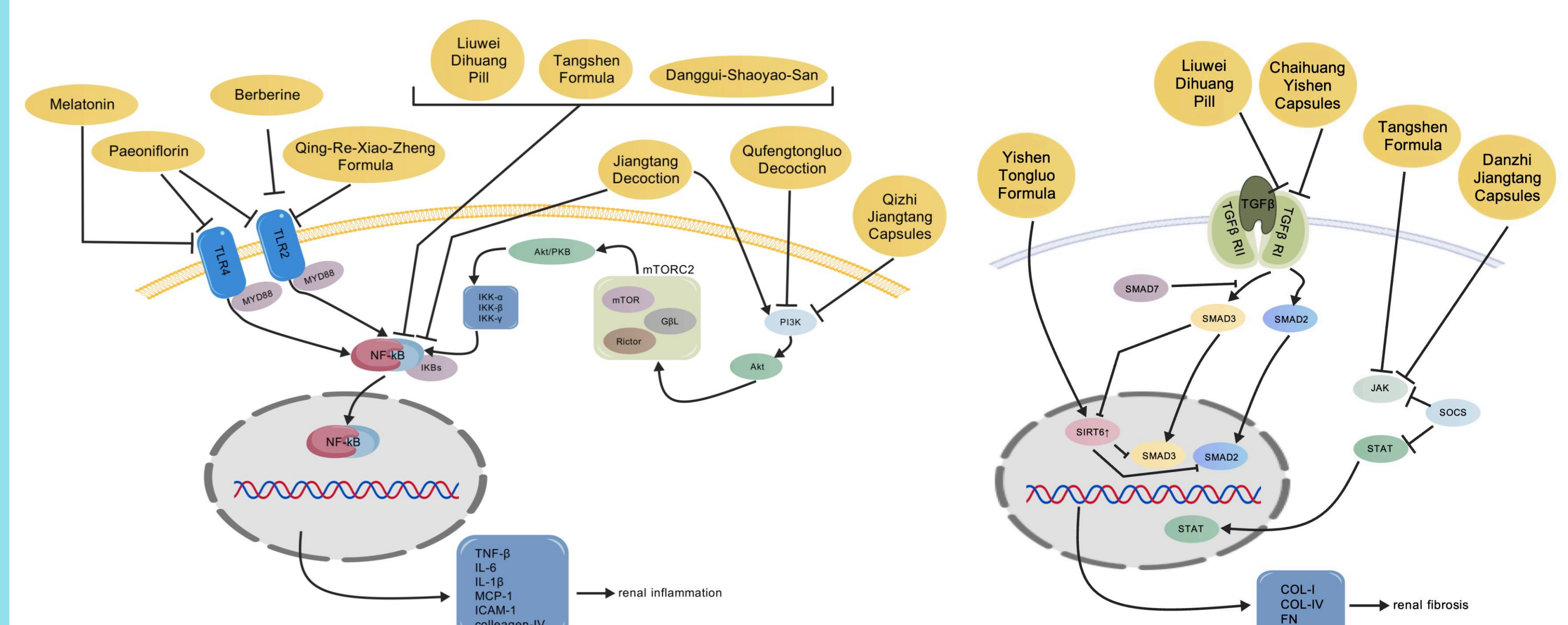


Fig 2 – Mechanism of TCM in suppressing renal inflammation

Fig 3 – Mechanism of TCM in suppressing renal fibrosis

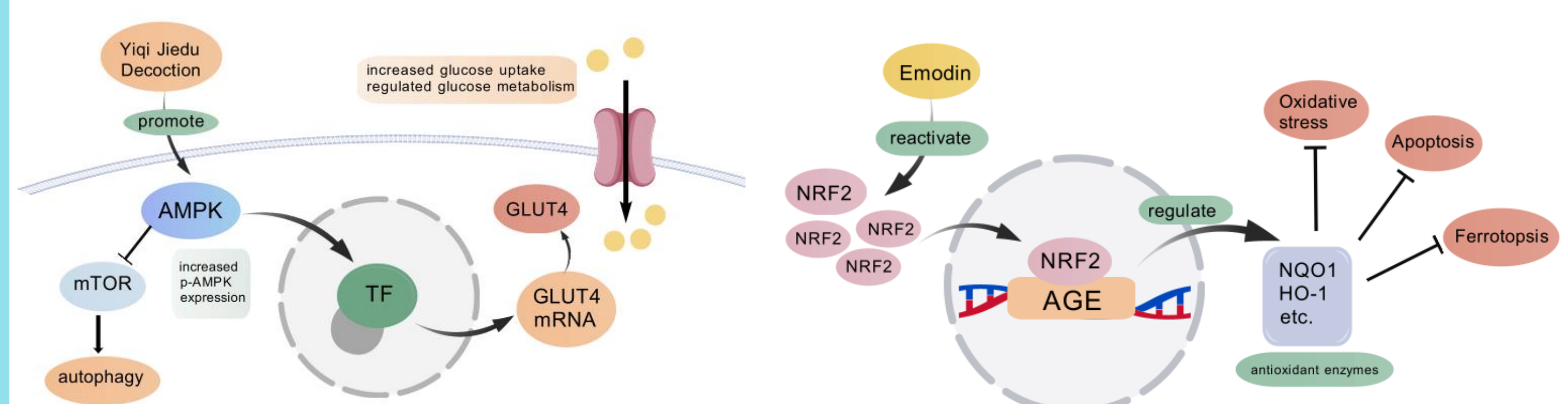


Fig 4 – Mechanism of Yiqi Jiedu Decoction in regulate glucose metabolism

Fig 5 – Mechanism of Emodin in regulate oxidative effect

## Conclusion

Driven by the rising prevalence of diabetes, DKD, presents significant health, economic, and societal challenges. Complementary strategies like TCM can improve clinical outcomes and patient's quality of life. However, inconsistencies in clinical trial designs complicate findings. Despite research on TCM mechanisms, translating these insights to human efficacy remains limited. Addressing drug-drug interactions and fostering interdisciplinary is essential. High-quality RCTs and mechanistic studies can support integrative care models and improve patient outcomes in DKD management.