

**COMPARATIVE CHARACTERISTICS OF STREPTOZOTOCIN-
INDUCED DIABETIC NEPHROPATHY AND ADRIAMYCIN
NEPHROPATHY MODELS IN SCREENING OF
NEPHROPROTECTIVE PHYTOPREPARATIONS**

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Abstract: *Chronic kidney disease (CKD) is a global health burden with a steadily increasing prevalence, particularly due to the rise of type 2 diabetes mellitus. The prevalence of CKD worldwide reaches 13.4%, and the number of patients requiring renal replacement therapy increases by 5–7% annually. In Uzbekistan, there is a steady increase in the number of patients with diabetic nephropathy, which is associated with the high prevalence of type 2 diabetes mellitus. Modern nephrology has a limited arsenal of agents capable of slowing the progression of CKD, which explains the interest of researchers in natural compounds. However, scientific substantiation of the effectiveness of phytopreparations requires experimental studies on adequate animal models. The choice of an adequate model is a critical step that determines the reliability of the obtained results and the possibility of their extrapolation to clinical practice. This thesis compares two widely used CKD models: streptozotocin*

(STZ)-induced diabetic nephropathy and adriamycin-induced nephropathy. The STZ model is characterized by selective damage to pancreatic β -cells, leading to persistent hyperglycemia and subsequent diabetic nephropathy. It allows the study of metabolic disturbances, oxidative stress, and protein glycation, which are key in the pathogenesis of diabetic kidney injury. In contrast, adriamycin-induced nephropathy is a model of podocyte injury, with massive proteinuria developing within 5–7 days after a single injection. Its clinical value lies in the possibility of studying podocytoprotective properties of phytopreparations and preserving the integrity of the glomerular filtration barrier. The STZ model is recommended for screening antioxidants and anti-inflammatory agents, while the adriamycin model is optimal for evaluating podocytoprotection.

Keywords: *chronic kidney disease, streptozotocin nephropathy, adriamycin nephropathy, phytopreparations, nephroprotection, experimental models, podocytoprotection.*

Introduction

Chronic kidney disease (CKD) represents a progressive condition in which irreversible loss of nephrons and decreased filtration function of the kidneys occur. According to global epidemiological studies, the prevalence of CKD in the world reaches 13.4%, and the number of patients requiring renal replacement therapy increases by 5–7% annually. In Uzbekistan, as in many countries of the region, there is a steady increase in the number of patients with diabetic nephropathy, which is associated with the high prevalence of type 2 diabetes mellitus.

Modern nephrology has a limited arsenal of agents capable of slowing the progression of CKD. Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and sodium-glucose cotransporter-2 inhibitors have proven their effectiveness in large clinical trials, but even their use does

not allow completely stopping the process of fibrosis of renal tissue. In this regard, the interest of researchers in natural compounds that have been used in traditional medicine for centuries to treat kidney diseases is natural.

Uzbek traditional medicine has a rich arsenal of medicinal plants used for kidney pathology. However, scientific substantiation of their effectiveness requires experimental studies on animal models that reproduce the key links in the pathogenesis of CKD. The choice of an adequate model is a critical step that determines the reliability of the obtained results and the possibility of their extrapolation to clinical practice.

Objective and Methodology

The aim of this work is to analyze the clinical significance of the main experimental models of CKD and to determine optimal approaches to their use in studying the nephroprotective properties of phytopreparations. The work used methods of systematic literature analysis, comparative evaluation of experimental CKD models, and generalization of data from our own studies conducted in Uzbekistan.

The streptozotocin (STZ)-induced diabetic nephropathy model occupies a special place in research, since diabetes mellitus is the leading cause of CKD worldwide. Streptozotocin selectively damages pancreatic β -cells, which leads to persistent hyperglycemia and subsequent development of diabetic nephropathy. The clinical value of this model is determined by the fact that it allows studying the effect of phytopreparations on metabolic disorders, oxidative stress, and protein glycation, which play a key role in the pathogenesis of diabetic kidney damage.

Adriamycin nephropathy is a model in which the main damage is localized at the level of podocytes. A single administration of adriamycin causes selective damage to these cells, which leads to massive proteinuria already 5–7 days after injection. The clinical significance of this model lies in the possibility of studying drugs aimed at protecting podocytes and preserving

the integrity of the glomerular filtration barrier. Considering that podocyte damage is an early event in the pathogenesis of many forms of nephropathies, this model is of particular interest for screening phytopreparations with podocytoprotective properties.

Results

Table 1 presents the comparative characteristics of the two most commonly used CKD models according to the main methodological and pathophysiological parameters.

Table 1. Comparative characteristics of 5/6 nephrectomy and streptozotocin-induced diabetic nephropathy models

Parameter	5/6 nephrectomy	STZ-nephropathy
Mechanism of induction	Surgical	Chemical (STZ 55–65 mg/kg)
Animal species	Rats (Wistar, Sprague-Dawley)	Rats, mice
Time to proteinuria	3–4 weeks	4–8 weeks
Time to glomerulosclerosis	6–8 weeks	12–16 weeks
Hypertension	Pronounced	Moderate
Hyperglycemia	Absent	Pronounced (>20 mmol/L)
Reproducibility	High	Medium

Parameter	5/6 nephrectomy	STZ-nephropathy
Cost of creation	Medium	Low
Perioperative mortality	10–20%	Absent
Applicability for phytopreparations	High	High

Table 2 presents the comparative characteristics of two models reproducing different mechanisms of glomerular damage.

Table 2. Characteristics of adriamycin nephropathy and C-BSA-induced membranous nephropathy

Parameter	Adriamycin nephropathy	C-BSA membranous nephropathy
Inductor	Adriamycin (10 mg/kg)	C-BSA (immunization)
Animal species	C57BL/6 mice	Wistar rats
Time to proteinuria	5–7 days	4–6 weeks
Predominant lesion	Podocytes	Glomerular basement membrane
Immune deposits	Absent	IgG, C3

Parameter	Adriamycin nephropathy	C-BSA membranous nephropathy
Mechanism of damage	Oxidative stress	Immune complexes
Applicability for phytopreparations	Podocytoprotection	Immunomodulation

Extract of licorice (*Glycyrrhiza glabra*) demonstrated the ability to reduce proteinuria and reduce oxidative stress in the streptozotocin nephropathy model. Similar results were obtained in the study of ginger extract (*Zingiber officinale*), which reduced the expression of proinflammatory cytokines TNF- α and IL-6. These data confirm the prospects of using plant extracts for the correction of metabolic and inflammatory disorders in diabetic nephropathy.

Conclusions

Experimental models of chronic kidney disease are the most important tool for preclinical study of nephroprotective properties of phytopreparations. Each of the considered models has its advantages and limitations that determine its applicability for solving specific research tasks. The STZ-nephropathy model provides an opportunity to study metabolic and inflammatory mechanisms, adriamycin nephropathy focuses on podocyte protection, and the ureteral obstruction model allows evaluating antifibrotic action. For studying phytopreparations used in Uzbek traditional medicine, it is advisable to use a combination of several models, which will allow obtaining a more complete picture of their nephroprotective action. At the same time, it is necessary to take into account the criteria of reproducibility, economic efficiency, and ethical acceptability. Evaluation of effectiveness should include a complex of

functional, biochemical, and morphological methods, as well as toxicological studies. Further research in this direction will allow scientific substantiation of the use of traditional plant remedies for kidney diseases and create prerequisites for the development of new nephroprotective drugs based on Uzbek plant raw materials.

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