Improving The Methods Of Diagnosis And Treatment Of Patients With Chronic Kidney Disease

Umarova Z.F.

Abstract: This article presents data on the effect of Ganoderma Lucidum on the state of the Tamm-Horsfill protein in chronic kidney disease. It is noted that the use of Ganoderma Lutsidum improves the condition of patients, positively affects uromodulin, creatinine and glomerular filtration rate. So, under the influence of the Ganoderma Lucidum, the Tamm-Horsfill protein normalizes, which cannot be achieved using traditional treatment methods. The results are presented, the corresponding conclusions are made.

Key words: uromodulin; Tamm-Horsfill protein; creatinine; chronic kidney disease; Ganoderma Lucidum

1. INTRODUCTION

Relevance. Uromodulin (Tamm-Horsfall protein), a glycoprotein with a molecular weight of 95-105 kDa, is a specific renal protein synthesized in cells of the thick ascending part of the Henle loop. This uromodulin was first described by Morner in 1895 and subsequently isolated from the urine of I.Tamm and F.L. Horsfall is a glycoprotein that inhibits viral hemaglucination. Although a number of studies have shown the presence of Tamm-Horsfall protein in the pancreas, salivary glands, ileum, and glial cells of the human brain, mRNA of this protein was found only in renal tissue [1]. The Tamm-Horsfall protein belongs to the family of glycosylphosphatidylinositol-linked (GPI) membrane proteins, which includes the sperm GPI membrane protein, GP2 protein - a precursor of pancreatic enzymes, veta-glycan. The proteins of this family lack transmembrane and cytoplasmic domains and bind to cell membranes by covalent bonds through GPI, being released from the membranes under the action of specific phospholipases. After traffic and maturation inside the epithelial cells, the Tamm-Horsfall protein exits through the apical membrane and combines in the urine into polymers, forming gel-like structures. Part of the glycoprotein is secreted basolaterally, penetrates the interstitium and then enters the systemic duct [2]. Traditionally, this protein is considered as one of the main factors preventing stone formation and ascending urinary tract infection. There are also few studies on the involvement of the Tamm-Horsfall protein in the formation of tubulointerstitial fibrosis, the development of arterial hypertension and the progression of chronic kidney disease. In experimental studies, it was found that an increase in the production of uromodulin is associated with the development of salt-sensitive hypertension, since the Tamm-Horsfall protein activates Na, K, 2Cl, a transporter in the thick ascending section of the Henle loop [3,5].

- *Umarova Zamira Fakhrievna – PhD, Associate Professor of the faculty and hospital therapy department №2 of the Tashkent Medical Academy, e-mail: zamiraumarovadoctor@gmail.com, tel: +998909954151*
- *Tashkent Medical Academy*
- *For corresponding author: pulatabilov1985@mail.ru*

It is also known that changes in calcium and magnesium transport are associated with the activating effect of uromodulin on TRPV5 (increase in Ca reabsorption) and TRPV6 (increase in Mg reabsorption) [4]. Research Wu X.R. (2012) showed that this uromodulin plays the role of a signaling molecule to trigger mechanisms of damage to renal tissue. On the other hand, studies by Liu M. et al., 2016 showed that Tamm-Horsfall protein is a powerful nephroprotective factor. At the same time, a recent study by Khasun Muhammad (2019) proved that, as the renal dysfunction worsens, the excretion and production of this protein decreases. This protein can modulate not only apical, but also basolateral transport of divalent cations. At the same time, there are no drugs that can control the level of this uromodulin, then we are offered the opportunity to use Ganoderma Lutsidum for Tamm-Horsfall protein indicators. Ganoderma Lucidum is an effective natural adaptogen used to treat various diseases since the time of emperors. At the same time, despite the numerous works on Ganoderma in the SCOPUS and Web of Sciense abstract databases, there is no information [6–20] about the effect of this fungus on the indices of the most common urine protein, so we found it relevant to conduct a similar study. Purpose of the study. To evaluate the effect of Ganoderma Lucidum on Tamm-Horsfall protein indicators in chronic kidney disease. Materials and research methods. To achieve our goals, we examined 57 patients with varying severity of chronic kidney disease on the basis of the 1-city clinical hospital. The control group consisted of 11 healthy people. Patients of the main group were divided into 2 subgroups: 1 subgroup - 24 patients with varying degrees of severity of chronic kidney disease who took, in addition to traditional therapy (corticosteroids and immunosuppressants) and Ganoderma Lucidum in the form of Reishi GOLD and Excellium GOLD capsules in a dosage of 1-2 capsules 3 times per day for 1 month, subgroup 2 - 33 patients with varying degrees of severity of chronic kidney disease who took only traditional therapy. The age of the patients at the time of the examination was 32.5-57 years, the average age was 41.5 ± 12.5 years. After signing an informational consent to participate in the experiment, all patients underwent a full range of clinical and biochemical research methods. Clinical research methods included a routine method of determining the diagnosis. Biochemical research methods included: determination of a clinical blood test, general urinalysis. Levels of uromodulin and

biomarkers were determined in blood serum and daily urine taken in the morning. The biomaterial was collected according to the standard method adopted during laboratory tests, centrifuged at 1500 rpm for 10 minutes, after which studies were carried out, stored at a temperature of –80 ° C until the study. Serum uromodulin (Sumo) and urine (Uumo) concentrations were measured by enzyme immunoassay using the Uromodulin Human ELISA Assay kits (BioVendor, Brno, Czech Republic). Also, all patients underwent X-ray research methods, which included: ultrasonography of the kidneys on the apparatus My Sono-U6 (Samsung, South Korea). Statistical data processing was carried out using the program Statistica 6.0 for Windows 10.

2. RESEARCH RESULTS.

The presence of mannose in the carbohydrate chain of the Thomas-Harsfill protein promotes binding to mannosensitive fimbriae of E. coli, preventing the colonization of world organisms on uroepithelium. Since the initial and ischemic damage to the kidneys enhances the synthesis and secretion of the Thomas-Harsfill protein, stimulating its release from the cell surface by activation of specific phospholipases. At the same time, the physiological concentration of the Thomas-Harsfill protein completely prevents the binding of mannosensitive E. coli fimbriae to uroplakins 1A and 1b, the two main urothelial receptors for type 1 fimbriae.

According to the clinical and laboratory research method, all patients were distributed as follows (table. 1)

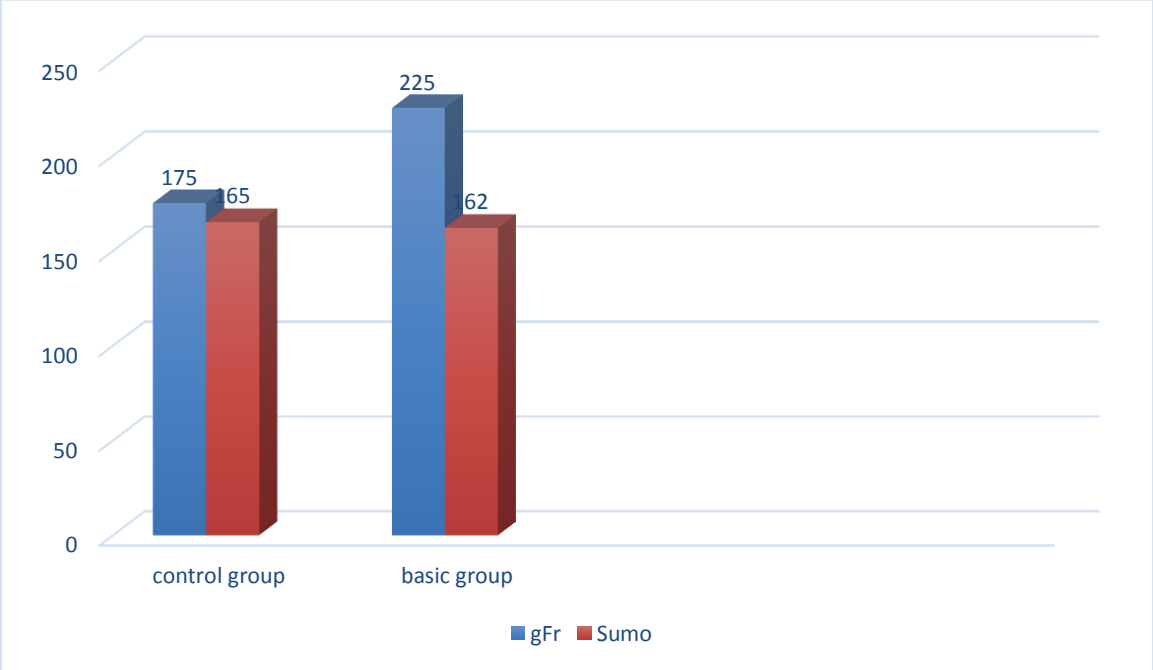
***Table 1**. General urine analysis and daily proteinuria depending on the main clinical diagnosis (Mann-Whitney test).*

Distribution Patients in groups	n	RDu gr/l	WbcUc, /p.m.	RbcUc, / p.m.	DP, gr/d
Control group	11	1015,5 [1012,0-1020,0]	5,0 [2,0-14,0]	17,50 [7,0-30,0]	2,06 [1,14-3,27]
Basic group	11	1015,5 [1012,0-1020,0]	5,0 [2,0-14,0]	17,50 [7,0-30,0]	2,06 [1,14-3,27]

* -p≤0,0028

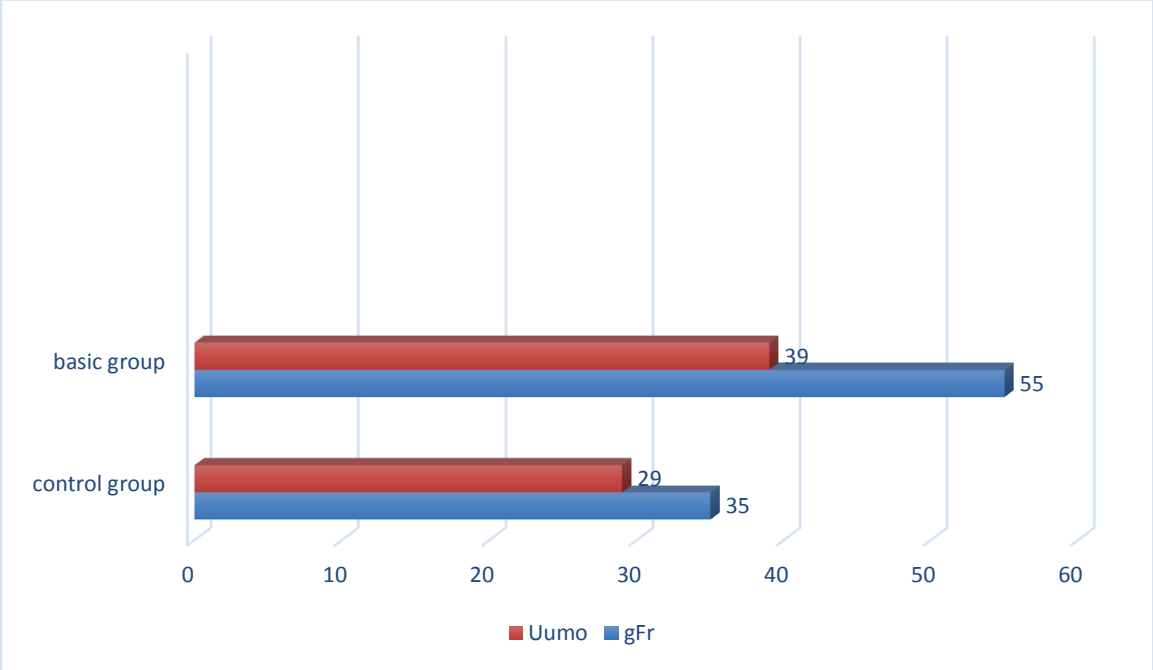
RDu - relative density of urine
WbcUc - urinary white blood cell count
RbcUc – urinary red blood cell count
DP – daily proteinuria

***Fig. 1**. The concentration of uromodulin in serum in the examined patients.*



gFr - glomerular filtration rate according to the formula CKD-EPI based on the concentration of serum creatinine, ml / min
Sumo - the concentration of uromodulin with serum, mmol / l

***Fig. 2**. The concentration of uromodulin in urine in the examined patients*



gFr - glomerular filtration rate according to the formula CKD-EPI based on the concentration of serum creatinine, ml / min
Uumo - uromodulin concentration in urine, mmol / l

After treatment with Ganoderma Lutsidum in the 1st subgroup of the main group, positive moments are determined in the normalization of the concentration of uromodulin in both blood serum and urine. So, already from 2-3 weeks of using the Ganoderma, Lucidum gFr reached the value of 183.0 ± 0.5 (p≤0.05) mmol / l, and Sumo reached the value of 64.5 ± 0.05 (p≤0.01) . Whereas in the 2nd subgroup of the main group, after applying traditional therapy, by the end of 3-4 months, a slight shift of gFr was observed in the positive direction and reached 217.0 ± 0.5 (p≤0.05), and Sumo remained unchanged (p≤ 0.01).
After treatment with Ganoderma Lutsidum in 1 subgroup of the main group, positive moments are determined, already by 2-3 weeks of use, gFr also decreases to 36.5 ± 0.05 (p≤0.01), and Uumo reaches 30.0 ± 0 01 (p≤0.001). Then, as in the comparison group, where traditional methods of treatment were used, gFr reached values of 50.0 ± 0.05 (p≤0.01), and the concentration of uromodulin in urine Uumo had slight shifts of 35.0 ± 0.05 (p≤0,01).

***Fig. 3**. The results of treatment with Ganoderma Lutsidum and conventional treatment based on the concentration of uromodulin in blood serum (based on data on gFr).*

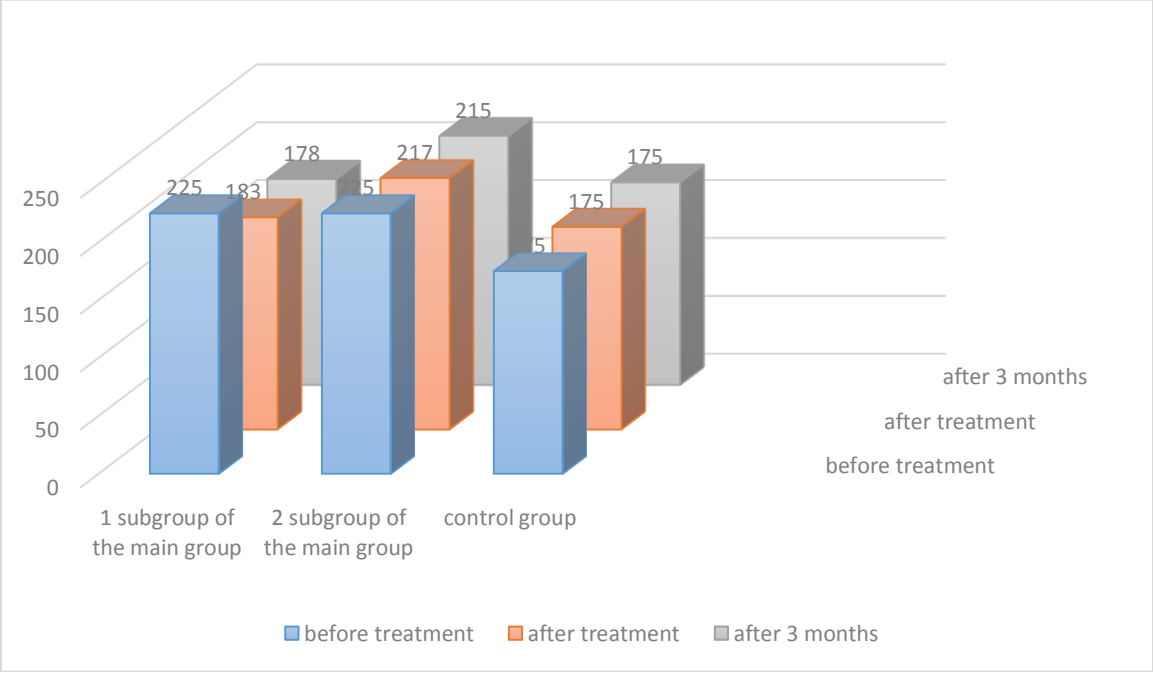


Fig. *4. The results of treatment with Ganoderma Lutsidum and traditional treatment based on Sumo.*

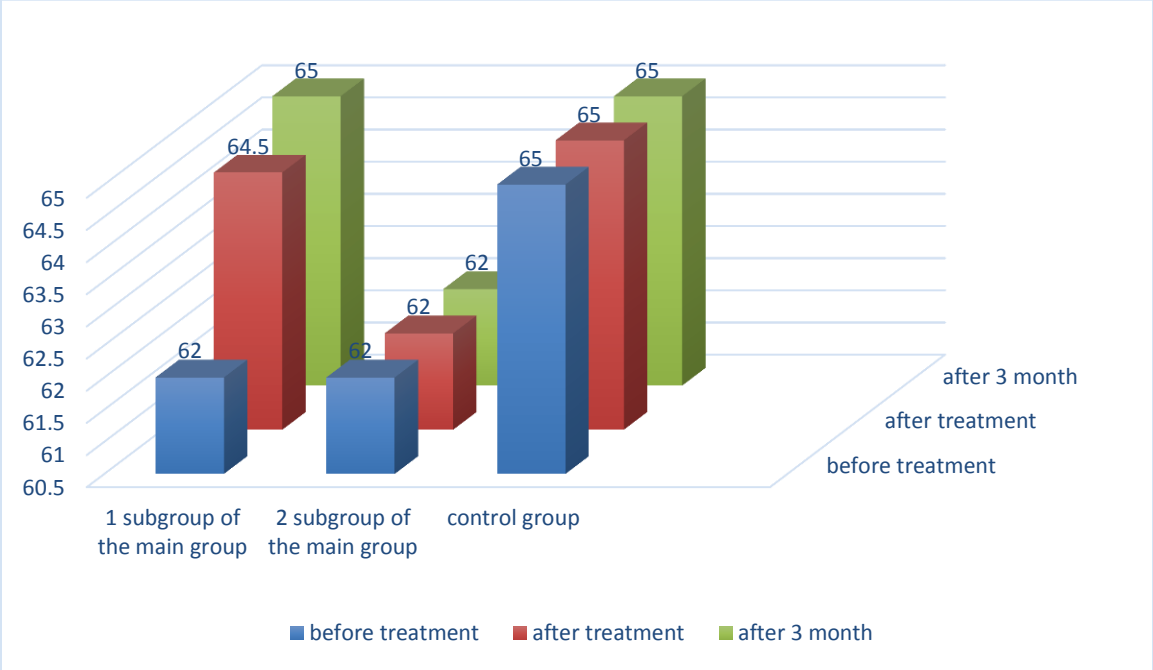


Fig. 5*. The results of treatment with Ganoderma Lutsidum and traditional treatment based on the concentration of uromodulin in the urine (based on Uumo data).*

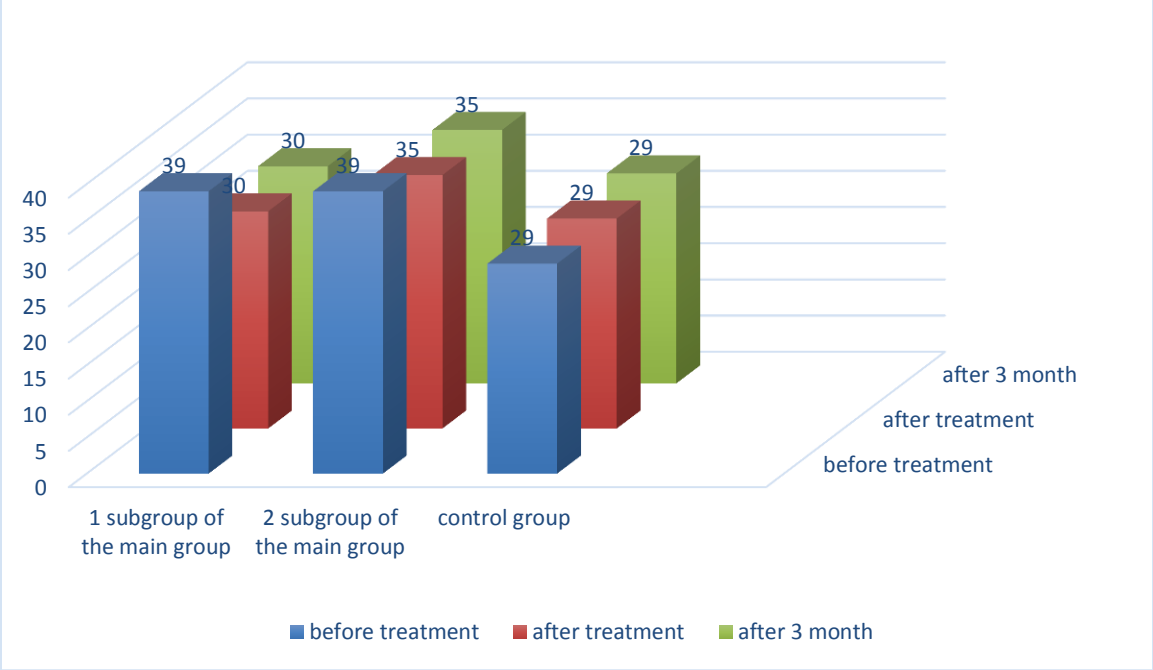
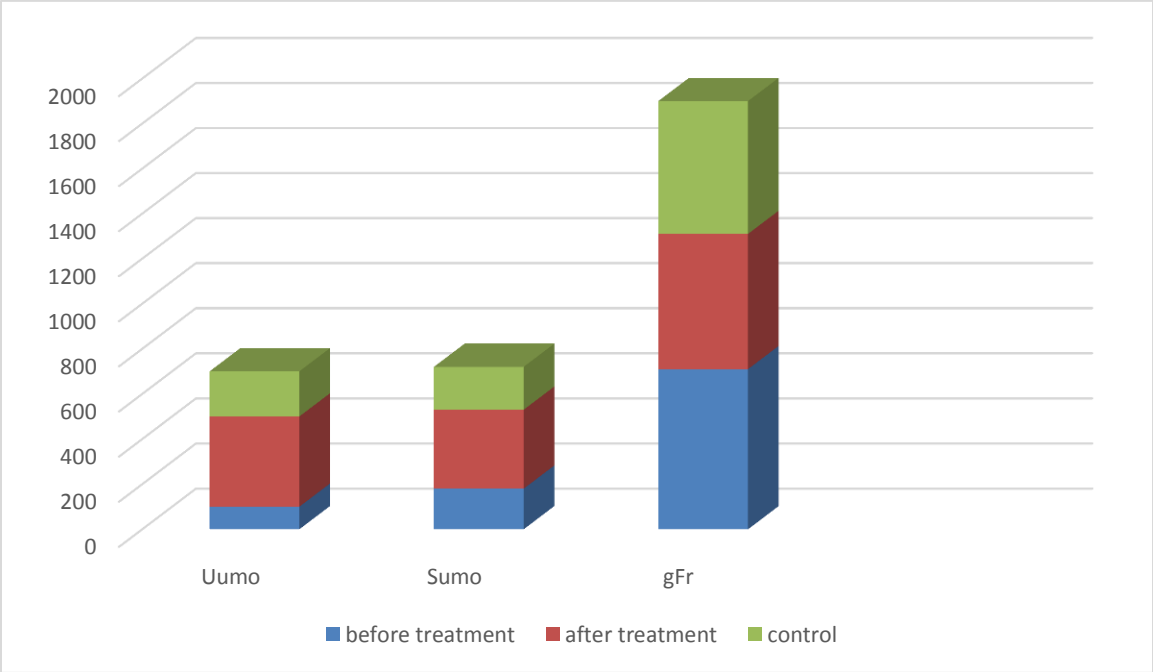


***Fig. 6**. The concentration index Uumo / Sumo before and after treatment with Ganoderma Luizdum in comparison with traditional treatment.*



Thus, the use of Ganoderma Lucidum for kidney diseases is justified, since it allows you to normalize creatinine clearance and uromodulin in both blood serum and urine. Since Tamm-Horsfall protein plays a role in the progression of chronic kidney disease, a decrease in its concentration leads to an improvement in the clinical course of this disease. The mechanism of action of Ganoderma Lucidum can be explained by the fact that when exposed to this drug, the effect of uromodulin on the reabsorption of Ca and Mg decreases. Since the Tamm-Horsfill protein is an early biomarker for the development of tubular atrophy and fibrosis, glomerular intrusion at relatively safe glomerular filtration rates, its determination is an important diagnostic sign of the presence or absence of chronic kidney disease. So, the use of Ganoderma Lucidum improves the basolateral traffic of uromodulin, which leads to an increase in the concentration of this glycoprotein in the blood serum with relatively safe urinary secretion. Since uromodulin is able to modulate not only apical, but also basolateral ion transport in the cells of the renal tubules, its normalization will help reduce side effects of patients with chronic kidney disease.

CONCLUSIONS:

The positive effect of Ganoderma Lucidum on the course and prognosis of a disease with chronic kidney disease can be characterized as a normalization of the ratios of creatinine and uromodolulin in both blood serum and urine, as evidenced by the studies. The study allows us to recommend the use of Ganoderma Lutsidum for kidney diseases, namely for chronic kidney disease, as it reduces pain symptoms, improves the clinical symptoms of the disease and improves the prognosis of this disease.

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