Research Article

# Preclinical Study of Nephroprotective Properties of Flarosukcin, New Urolitholytic Drug

**Tamara Iermolenko[1*], Igor Zupanetz[2], Vladimir Lesovoy[3]**

1. Tamara Iermolenko (PhD) – Assistant Professor at the Department of Pharmacology, Kharkov National Medical University, Kharkov, Ukraine.
2. Igor Zupanetz (PhD,MD) – Professor, Chairman of the Department of Clinical Pharmacology and Pharmaceutical Guardianship, National University of Pharmacy, Kharkov, Ukraine.
3. Vladimir Lesovoy (PhD,MD) – Professor, Chancellor at Kharkov National Medical University, Kharkov, Ukraine.

*Corresponding author's E-mail: ermolenko_tamara@mail.ru

**Accepted on:** 21-01-2013; **Finalized on:** 31-03-2013.

**ABSTRACT**

The paper describes results of urolitholytic drug Flarosukcin effect on filtration-reabsorption renal function on modeled experimental renal insufficiency. Use of 2.0 ml/kg Flarosukcin increases diuresis in rats, reduces endogenous creatinine level in the blood and increases its excretion in urine reducing glomerular filtration and normalizing tubular reabsorption. Also the studied drug positively affects renal function of nitrogen excretion in rats, increases excretion of urea, endogenous creatinine, uric acid and consequently decreases their level in animals' blood. Flarosukcin is shown to provide complex diuretic, spasmolytic and cytoprotective action on modeled experimental renal insufficiency and is believed to be promising for the further studying as a nephroprotective and urolitholytic drug.

**Keywords:** Filtration-reabsorption function of the kidneys, urea, uric acid, nephrolithiasis, succinate buffer complex.

## INTRODUCTION

Medications differed both by form and by quality depending on society development at different times, but always they were used for treatment and prophylaxis of various diseases. New drug development is one of solutions for adequate treatment of chronic diseases, on the basis of rational drug use in the treatment, balanced therapeutic tactics based on estimation of efficiency, drug safety and treatment costs.

These days chronic kidneys illness is a socially significant problem around the world. Water and electrolyte imbalance and nitrogenous exchange disorder are the main pathogenetic factors of renal insufficiency.

So, kidneys are a body involved into regulation of stability of organism's internal environment. Renal function is closely connected with support of electrolyte concentration in body fluid and with water excretion and reabsorption. The most important renal function is excretion from the organism of nitrogen metabolism products - urea and creatinine, uric acid[1].

Damages of the kidneys structural and functional system are always accompanied by disordered renal functions, such as excretory, ionic-, osmo-, volume-, metabolic, acid regulation, and etc. Thus all disorders have no selective action and are caused by tubular and glomerular activity of the kidneys[2].

Pharmacological correction of these disorders remains the major task of medicine and stimulates searching for new approaches to treatment. No negative influence of medicamentous factors on kidneys should be provided in conservative methods of renal insufficiency therapy. Medications stimulating nitrogen metabolism product excretion from an organism, increasing kidneys resistance to ischemia, characterizing by anti-inflammatory and diuretic action, are believed to be perspective[3].

Urolithiasis is considered a significant reason for renal insufficiency development. Urolithiasis and nephrolithiasis can be related to chronic diseases tended to be recurred and quite often characterised by aggressive, complicated current, they affect life quality and may lead to patient's disability. The relevance of social and economic and general medical aspect of urolithiasis is that this disease is one of the most common urological diseases and takes the second place in the disease structure after inflammatory nonspecific diseases of kidneys and urinary tracts and observed in almost 3% population[4].

The factors affecting urolithiasis growth are both of exogenous and endogenous character. The disease growth is known to be associated with influence on a human body of environment adverse factors, modern life features, various climatic, geographical, inhabited, occupational conditions, hereditary factors. All the listed conditions allow naming this disease as "disease of civilization". The reasons and mechanisms of nephrolithiasis appearance still remain actual and unresolved problems. Influence of exogenous, endogenous, genetic factors and their various combination disturb metabolic processes in an organism accompanied by increase of level of substances involved into kidney stone formation, imbalance between inhibitor crystallization (citrate ions, magnesium, zinc, manganese, cobalt, hippuric acid, xanthine, inorganic pyrophosphate, glycosaminoglycan, nephrocalcine, Tamm-Horsfall protein, and etc.) and promoters (calcium ions, uric acid, etc). Even in insignificant quantity inhibitors suppress crystallisation, thus most of patients with nephrolithiasis have none of them or in insufficient quantity. So, for

example, if in normal conditions magnesium ions bind up to 40% of oxalic acids in urine, their lack is observed as formation of calcium oxalate crystals. Certainly, other factors are important in nephrolithiasis development, they are associated with urinary tracts infection, pathological changes in the upper segments that may lead to urino- and haemodynamics disorder, stable urine pH shift[5,6].

Consequently, kidney stone formation in the urinary tracts is resulted due to many complex and interrelated processes.

Treatment methods of patients suffering from nephrolithiasis can be divided into two main groups - operative and conservative. The method choice depends on patient's general state, age, clinical illness, concrement size and localisation, kidneys anatomy and functions[7].

Renal calculus removal is important in urolithiasis treatment. But it only creates conditions for urodinamics improvement, urinary tracts inflammation correction because renal calculus removal does not positively affect the metabolic processes in patient's organism. Therefore neither modern early diagnostics, nor modern low invasive treatment methods relieve a patient from urolithiasis or possible kidney stone reformation. It's really important to apply therapy focused upon prophylaxis of recurrent kidney stone formation after urinary tracts clearance from kidney stones or its fragments – urolithiasis methaphylaxis[8].

Numerous metabolic disorders in nephrolithiasis require for various medications. At the same time, despite permanent increasing of drug range, herbal drugs are considered important in methaphylaxis. They are characterized by such advantages, as direct effect on kidney stone formation, urine ionic strength stabilization and kidney stone formation inhibitors, fast removal of kidney stones, fragments and sand after successful destruction by remote lithotripsy, increasing kidneys resistance to ischemia, and characterized by anti-inflammatory, diuretic action, stimulating metabolism product excretion from organism, providing a possibility of long-term application without serious side-effects[9].

Their efficiency is proved by scientifically grounded methods. Range widening of medications containing biological phytogenesis components is an actual problem as their demand quickly growths[10].

Long-term trials have proved herb value for treatment of many pathological disorders. Certain advantages of herbal drugs before synthetic medications are a wide selection of therapeutic active components in herbs, a possibility of combination, and lower frequency of side-effects promoting their wide use in clinical practice as supplementary to the main treatment. The main advantages of herbal drugs are that they do not cause any essential side-effects[11,12].

The extended spectrum of pharmacological correction of kidneys disorder remains the main task of medicine and pharmacy and makes searching of new approaches and medications for conservative therapy of patients with chronic renal diseases necessary.

Therefore, a perspective direction in conservative treatment of nephrolithiasis is development by Joint-Stock Company Scientific Production Center "Borshchagovsky Chemical-Pharmaceutical Plant" (Kiev) of a new original combined drug, Flarosukcin syrup. It contains in the compound a summarized plant extract of Astragali falcati, Betulae verucosae leaves, Tiliae cordatae flowers and buffer succinate complex[13,14].

Astragali falcati contained in summarized plant extract makes the greatest share - 6 parts, according to the paper data the chemical compound of above-ground part of Astragali falcati is presented by flavonoids, nitrogen-containing compounds, alkaloid, phenolic carboxylic acids, triterpenoids and vitamins. The main flavonoid component is robinin characterized by diuretic and hypoazotemic action[15].

In connection with the above, the purpose of our research is to study features of pharmacological influence of succinic acid salts and herbal components on filtration-reabsorption renal function, content of creatinine, urea and uric acid in experimental renal insufficiency. Phytolyzin paste containing plant extracts was used as a reference drug[16].

## MATERIALS AND METHODS

Flarosukcin pharmacodynamics was investigated on experimental renal insufficiency in rats modeled by daily (for 14 days) intragastric administration of water solution of 1% ethylene glycol of 8 ml/kg[17-20].

96 white rats of both genders of weight 220-250g were used, randomized into 4 groups by 24 animals each: 1st group - intact control, 2nd group - pathology control, 3rd group - animals administered with Flarosukcin of 2.0 ml/kg, 4th group - animals administered with comparative drug Phytolyzin of 1.3 g/kg (considering a specific sensitivity factor according to Yu.R.Rybolovlev's method)[21].

At Phytolyzin paste dosing, 1 table spoon was dissolved in 10 ml of salt solution and administered as 2.0 ml/kg dose.

All experiments were conducted according to the European convention for the protection of vertebrate animals used for experimental and other scientific purposes[22].

Glomerular filtration, tubular reabsorption, and alkaline phosphatase level were studied; blood urea, creatinine, uric acid values as well as calcium and phosphorus content in animals' blood were estimated.

Research results were processed by variation statistics methods using Fisher-Student criteria by computer programs[23,24].

## RESULTS AND DISCUSSION

Ethylene glycol administered to animals in not toxic concentration is known to be exposed in an organism to oxidation to carbonic acid and water, thus forming intermediate products - glycol aldehyde, ethylene glycol, glyoxylic, oxalic acid toxic compounds. Mainly glycol intoxication is observed as renal insufficiency development with primary diffuse lesion of proximal tubules. Biochemical disorders at this intoxication are characterized by disorder of glomerular filtration and tubular reabsorption, considerable accumulation of nitrogen metabolism products - urea, creatinine, uric acid[25,26].

### Flarosukcin influence on filtration-reabsorption renal function

Table 1 showed that experimental renal insufficiency development was accompanied by reduction by 1.7 times of daily urine volume in animals by 14 Day comparing to the intact control group. Flarosukcin use in renal insufficiency development increased diuresis practically by 3 times comparing to the pathology control, thus increasing the intact group values by 1.7 times. Comparative drug Phytolyzin increased diuresis comparing to the pathology control group by 3.2 times and by 1.8 times exceeding the intact group values. Studied drug Flarosukcin increased (by 11 times) glomerular filtration comparing to the pathology control, and reabsorption in tubules was completely restored. Phytolyzin use increased glomerular filtration by 8.5 times comparing to the control group and resulted in normalization of glomerular reabsorption.

### Anti-inflammatory action of Flarosukcin

One of kidneys inflammation markers is Alkaline Phosphatase (ALP). High ALP activity in urine is evidently connected with renal tubules disorder at inflammation[27]. According to the papers herbal components of the studied drug provide expressed anti-inflammatory action, besides succinic acid and metabolites are characterized by cytoprotective properties, participating in oxidation-reduction cycle of dicarboxylic acids (Krebs cycle) and provide normal vital activity of cells[28-30].

In connection with the above Flarosukcin influence on ALP activity in experimental renal insufficiency was studied.

Table 2 showed that ALP in intact animals' blood made at the average 82.88 nmol/d·l, in urine – 52.88 nmol/d·l. At experimental renal insufficiency ALP level increased by 3.7 times in rats' blood, in urine – by 1.7 times comparing to the intact group. The specified changes conformed the paper data on change of ALP activity in blood and urine in rats with experimental renal insufficiency[27].

Flarosukcin administration at pathology development decreased ALP activity in animals' blood by 3.7 times and in urine by 2 times. Comparative drug Phytolyzin was characterized by similar action, reducing ALP activity in animals' blood by 3.3 times, in urine - by 1.8 times comparing to the pathology control and practically leading its level to intact animals' values. Anti-inflammatory activity of compared drugs was comparable and had no reliable differences.

### Flarosukcin influence on nitrogen excretion renal function

In renal insufficiency nitrogen catabolism products (urea, creatinine, uric acid) are accumulated in an organism reflecting intoxication level.

Table 3 showed that endogenous creatinine in blood of intact animals made at the average 212.4 mcmol/l, 58.54 mmol of creatinine was excreted per day. In the pathology control group a quantity of creatinine daily excreted through the kidneys decreased by 3 times, and its blood level increased by 1.7 times testifying renal insufficiency development.

**Table 1:** Flarosukcin influence on glomerular filtration and filtration reabsorption in experimental renal insufficiency

| Groups of animals | Dose, ml/kg | Urine Volume, ml | Glomerular filtration, ml/min | Tubular reabsorption, % |
|---|---|---|---|---|
| Intact control (n=24) | – | 6.66 ± 0.61 | 0.193 ± 0.037 | 97.20 ± 0.34 |
| Pathology control (n=24) | – | 3.90 ± 0.30 * | 0.034 ± 0.006 * | 90.24 ± 1.50 * |
| Flarosukcin (n=24) | 2.0 | 11.63 ± 1.45 */** | 0.384 ± 0.044 */**/*** | 97.86 ± 0.18 ** |
| Phytolyzin (n=24) | 2.0 | 12.38 ± 0.80*/** | 0.290 ± 0.043 ** | 96.64 ± 0.48 ** |

* - difference reliability relating to intact control (p≤0,05); ** - difference reliability relating to pathology control (p≤0,05); *** - difference reliability relating to comparative drug (p≤0,05).

**Table 2:** Flarosukcin influence on alkaline phosphatase (ALP) level in rats in experimental renal insufficiency

| Groups of animals | Dose, ml/kg | Blood ALP, nmol/d·l | Urine ALP, nmol/d·l |
|---|---|---|---|
| Intact control (n=24) | – | 82,88 ± 4,90 | 52,88 ± 4,93 |
| Pathology control (n=24) | – | 310,0± 23,44* | 93,0 ± 5,22* |
| Flarosukcin (n=24) | 2.0 | 83,0 ± 10,32* * | 46,75 ± 4,08* * |
| Phytolyzin (n=24) | 2.0 | 92,5 ± 10,80* * | 49,75 ± 5,84* * |

* - difference reliability relating to intact control (p≤0,05); ** - difference reliability relating to pathology control (p≤0,05);

**Table 3:** Flarosukcin influence on nitrogen excretion values in rats in experimental renal insufficiency

| | Intact control (n=24) | Pathology control (n=24) | Flarosukcin (n=24) | Phytolyzin (n=24) |
|---|---|---|---|---|
| Dose, ml/kg | - | - | 2.0 | 2.0 |
| Cr in the blood mmol/l | 212.4±11.1 | 360.8±16.4 * | 214.5±28.0 * * | 278.8±22.4 / * * |
| Cr excretion, mmol/day | 58.54 ± 1.25 | 18.14 ± 1.05 * | 115.14 ± 0.44 ** | 113.65 ± 1.22** |
| Urea in the blood, mmol/l | 6. 27 ± 0.29 | 11.63 ± 0.60 * | 6.72 ± 0.28 **/*** | 9.57 ± 0.78 */** |
| Urea excretion, mmol/day | 413. 60 ± 35.42 | 134.16 ± 15.34 * | 493.55 ± 44.98 **/*** | 369.87 ± 30.61 ** |
| Uric acid, mmol/l | 145.26 ± 7.68 | 212.87 ± 2.58 * | 159.88 ± 7.03 **/*** | 210.19 ± 14.30 * |
| Uric acid excretion, mmol/day | 10.73 ± 1.28 | 5.36 ± 0.83 * | 21.40 ± 1.82 */** | 16.69 ± 1.67 */** |

* - difference reliability relating to intact control (p≤0,05); ** - difference reliability relating to pathology control (p≤0,05); *** - difference reliability relating to comparative drug (p≤0,05).

Intragastric administration of Flarosukcin of 2.0 ml/kg in pathology development increased by 6.3 times creatinine excretion by the kidneys comparing to the pathology control group testifying intensive excretion by the kidneys of nitrogen metabolism products accumulated at pathology. Thus endogenous creatinine level in rats' blood decreased by 1.7 times and was at level of intact animals' values.

Reference drug Phytolyzin also stimulated creatinine excretion by the kidneys by 6.3 times, endogenous creatinine in the blood of the study group decreased by 1.3 times comparing to the pathology control group. But thus it considerably differs from the intact animal values.

Therefore Flarosukcin normalizes the endogenous creatinine level in blood and urine of the animals with experimental renal insufficiency. Studied drug Flarosukcin reliably exceeds by action expressiveness comparative drug Phytolyzin.

One of important renal functions is excretion of urea formed in an organism. Urea is excreted by the kidneys so that it passes from plasma into glomerular filter whereas it is partially reabsorbed in tubules, based on diffusion principle[31].

The urea content in the blood depends on speed of its synthesis and release, and is one of the main biochemical markers of normal or broken renal function.

The data given in table 3 testifies that urea content in intact animals' blood made at the average 6.3 mmol/l, 413.6 mmol of urea was excreted per day. Urea level excreted by the kidneys per day in the pathology control group decreased by 3 times, and its level in blood increased by 1.9 times testifying renal insufficiency development.

14 day use of Flarosukcin increased by 3.7 times urea excretion by the kidneys compared to the pathology control group, its content in the urine increased by 19% even comparing to the intact animals that testifies intensive excretion by the kidneys of nitrogen metabolism products accumulated at pathology. Thus urea level in blood decreased by 1.7 times and reached the intact control values.

Comparative drug Phytolyzin also increased urea excretion by the kidneys by 2.8 times, but did not reach intact animals values (lower by 11%). Urea content in blood in the group decreased by 1.2 times comparing to the control pathology group, however did not reach intact animals values (lower by 53%).

Thus Flarosukcin normalized urea content in the blood and excretion in urine more effectively, exceeding Phytolyzin action by 30% and 34% (accordingly in blood and urine).

Uric acid as well as urea is one of end-products of proteometabolism. Uric acid is filtered in glomerule, up to 80% is reabsorbed, and partly uric acid is sercreted. Increase of uric acid in the blood can be resulted by fast synthesis, glomerular filtration reduction, tubular reabsorption increasing. Besides, blood uric acid increase is observed in renal insufficiency and is applied as one of diagnostics tests. Increase of blood uric acid and its simultaneous decrease in urine cause formation of arthrolith in interstisium of medullary substance of kidney and so-called urate kidney[32,33].

Table 3 shows research results confirming that intragastric administration of 1% solution of ethylene glycol to rats increased by 1.5 times blood uric acid by 14 Day. Thus daily uric acid excretion by the kidneys decreased twice comparing to intact animals. Increase of blood uric acid and decrease of excretion confirm renal insufficiency development, namely parenchymatous kidneys disease usually observed in intoxication by ethylene glycol[34].

Flarosukcin use in renal insufficiency development reduced blood uric acid level by 1.3 times that practically reached the intact control values. Uric acid excretion increased by 4 times comparing to the pathology control group. It should be noted that daily uric acid excretion in urine in these animals exceeded twice the intact group values confirming increased uric acid excretion by the kidneys and accordingly, decreased uraemia.

Comparative drug Phytolyzin comparing to the pathology control group reduced daily uric acid level in urine by 3 times, exceeding intact animals' values by 1.6 times. However uric acid level in animals' blood increased by 1.4

times comparing to the intact group, reliably not differing from the pathology control values.

Hence, Flarosukcin stimulates decreasing of blood uric acid in experimental animals with renal insufficiency, intensively excreting its surplus in urine. By the specified action Flarosukcin is reliably more effective than comparative drug Phytolyzin.

## CONCLUSION

2.0 ml/kg of Flarosukcin in use on modeled experimental renal insufficiency increased diuresis in animals, endogenous creatinine level in blood decreased and excretion in urine increased raising glomerular filtration and normalizing tubular reabsorption.

Also the drug positively affects nitrogen excretion renal function, by action is not inferior to the comparative drug by all studied parameters.

Flarosukcin is a promising object for the further experimental studying as an urolitholytic and nephroprotective remedy.

## REFERENCES


1. Smirnov A.V., Petrishchev I.Yu. et al. Glomerular Filtration Speed - an indicator of endothelium functional condition at early stages of chronic kidneys disease. Therapeutic archive, 79(6),2007, 25-29
2. Tareyeva Ye.M. Nephrology Principles. Moscow, Medicine, 1, 1972, 551
3. Taran O. I. Conservative Treatment of Chronic Renal Insufficiency. Doctor, 2, 50-53
4. Dzeranov N.K., Beshliev D.A. Urolithiasis Treatment - Complex Medical Problem. Urology, 6,2003, 18-22
5. Alyaev Yu.G., Rapoport L.M., Rudenko V. I. Urolithiasis. Relevant Issues of Diagnostics and Treatment. Vrachebnoye Sosloviye, 4, 2004, 4-9
6. Udiniy Yu.G., Dziurak V. S., Zheltovskaya N.I. Proteolysis-Ionic Theory of Nephrolithiasis Pathogenesis. Urology and Nephrology, 6, 1989, 37-40
7. Gorchakova N.O., Poliakova I.F., Biletskaya T.O. Pharmacological Methods of Urolithiasis Treatment. Pharmaceutical Magazine, 5,1990, 37-40
8. Cherepanova E.V., Dzeranov N.K. Urolithiasis Metaphylaxis in Out-Patient Conditions. Experimental and Clinical Urology, 3, 2010, 39-39
9. Tkachuk V. N., Al-Shukri S.H., Rizan A. Herbal Therapy Use in Patients with Nephrolithiasis after Remote Stroke-Wave Lithotripsy. Urology, 5,2011, 8-10.
10. Ospanova T.S., Semidotskaya Z.D., Halansky O. A. Flavonoid Drugs in Pathogenetic Therapy of Chronic Gromeluronephritis. Liky, 6, 1996, 19-26
11. Ostapchuk N.F. Herbal Therapy of Kidney and Urinary Tract Diseases. Kiev, 1991, 32.
12. Gurevich K.G. Herbal Drugs in Urology. Pharmateka, 15, 2003, 71-75
13. No.99024 Ukraine, MPK A61K 36/481. Herbal Remedy for Treatment and Prophylaxis of Kidney and Urinary Tract Diseases, No. a201014906; applied on 12/13/2010; issued on 07/10/2012, Bulletin No.13.
14. Smirnov A.V., Nesterova O.B., Golubev R. V. et al. Cardioprotective Effects of Succinate Dialysis Solution. Nephrology, 16(2), 2012, 69-78.
15. Vasilchenko Ye.A., Sokolova Ye.V. Study of Robinin Influence on Diuretic Renal Function of Kidneys and Uropoiesis Partial Processes. Modern Problems of Pharmacology. III congress of pharmacologists of the USSR. - K, 1971, 50.
16. Milevskiy Ye. Medical properties of Phytolyzin. Pharmacy and Medicine News, 19(2), 1985, 60-62.
17. Liubartseva L.A., Sokolov V. Ye., Angarskaya M.A. Combined Herbal Drug Renolyt on experimental nephrolithiasis in rats. Pharmacology and Toxicology, 10, 1975, 79-82.
18. Romendik L.M. To Technique of Model of Chronic Nephro-Nephrite in Rats. Pathological Physiology and Experimental Therapy, 3, 1964, 84-86.
19. Liy J., Cao Z., Zhang Z. A comparative study on several models of experimental renal calcium oxalate stones formations in rats. J. Huazhong Univ. Sci. Technolog. Med. Sci, 27, 2007, 83-87.
20. Debray Ch., Vaille Ch., Martin Et. L'intoxication par l'ethylene-glycol. Un contrepoison: l'ion citrate. Semaine hopitaux Paris, 44, 67, 1968, 3301-3309.
21. Rybolovlev Yu. P., Rybolovlev R. S. Dosage of substances for mammals by constants of biological activity. Reports AH the USSR, 6, 1979, 1513-1516.
22. European convention for the protection of vertebrate animals used for experimental and other scientific purpose. Council of Europe, Strasbourg, 1986, 52.
23. Lapach S.N., Chubenko A.V., Babich P.N. Statistical Methods in Medical and Biologic Trials using Excel. K, Morion, 2000,320.
24. Rebrova O. Yu. Statistical Analysis of Medical Data. STATISTICA Application use. M, Media Sphere, 2006, 312
25. Kamyshnikov V. S. Clinic and Biochemical Laboratory Diagnostics. M., Interpresservis, 2, 2003, 463.
26. Papayan A.V., Arhipov V. V, Beresneva Ye.A. Markers of Renal Function and estimation of renal insufficiency progressing. Therapeutic Archive, 4, 2004, 83-90
27. Petrun N.M. Activity of Acid and Alkaline Phosphatase in Kidneys, Blood and Urine at Different Stages of Sublimate Intoxication. Pharmacology and Toxicology, 10, 1975, 155-158.
28. Guliaev V.G. Hypoazotemic Properties and Mechanism of Action of Bioflavonoids and Antihypoxanths in Treatment of Acute and Chronic Renal Insufficiency [dissertation]. Kiev Medical University, 1989, 72-105.
29. Guliaev V.G. Hypoazotemic and Diuretic Action of Lespeflan in Acute Renal Insufficiency. Urology and Nephrology, 4, 1993, 32-34.

30. Guliaev V.G. Use of New Herbal Drug Lespeflan in Nephrology. Medical aid, 1994, 2, 47-49

31. White A, Hendler F. Biochemistry Principles, M, World, 1982, 1978

32. Shiuk O. Functional Trials of Kidneys. Prague, Avitsenum, 1975, 133-134

33. Lazarov N.I. Importance of Uric Acid Clearance in Uropathy Diagnostics. Urology and Nephrology, 1974, 6, 31-32

34. Vaile Ch., Debray Ch., Martin Et. Sur la lithiase renale experimentale a l'ethylene-glycole chez le rat male et femelly. Ann. Pharmac. Frans., 1963, 21, 2, 111-116

**Source of Support:** Nil, **Conflict of Interest:** None.

**Corresponding Author's Biography: Ms. Tamara Iermolenko**

Ms. Tamara Iermolenko has graduated from and finished a postgraduate at National University of Pharmacy, Kharkov, Ukraine. She has 8 year experience of teaching activity. Currently she works as assistant professor at the Pharmacology Department of Kharkov National Medical University.

**Co-Author's Biography: Prof. Igor Zupanetz**

Prof. Igor Zupanetz has finished doctoral candidacy at Kharkov Medical University. He has 27 year experience of teaching and scientific activity at National University of Pharmacy. Since 1993 he has worked as Chairman of the Department of Clinical Pharmacology and Pharmaceutical Guardianship. He is involved into principle researches over chondrotropic properties of biologically-active substances. He has prepared 3 doctors of sciences, 17 Candidate sciences. He is co-developer of 13 original medications, author of 476 scientific papers, including 18 monographs, 12 textbooks, and 39 manuals.

**Co-Author's Biography: Prof. Vladimir Lesovoy**

Prof. Vladimir Lesovoy**,** Rector of Kharkiv National Medical University, Director of the Regional Clinical Centre of Urology and Nephrology named after V.I. Shapoval, a Corresponding Member of the National Academy of Medical Sciences of Ukraine, Doctor of Medical Science, Professor.

He is one of the leading Ukrainian scientists in urology. The scope of his scientific interests comprises the issues of diagnosis optimization and treatment of Oncourological and Andrological Pathology, specific and non-specific diseases of urogenital organs.