



**1-3,**

where 1. R=H; 2. R=2-OCH<sub>3</sub>; 3. R=2-Cl

**Materials and methods.** The objects of our research – 5-nitro-9-hydrazinoacridine derivatives, which were synthesized at the department of medical chemistry of National University of Pharmacy.

**Results and discussion.** The prognosis was carried out using free online software pkCSM developed by the University of Cambridge. According to the results obtained the 5-nitro-9-hydrazinoacridine derivatives do not cause skin sensitization, are not hERG I inhibitor and are hERG II inhibitor. This indicates that the investigated substances probably are not allergenic and may be cardiotoxic with probability 50%. Results of computer prognosis showed that 5-nitro-9-hydrazinoacridine 1 are not hepatotoxic substance. Introduction in the 2 position of acridine cycle chlor or methoxy substituent leads to hepatotoxicity.

**Conclusions.** So, investigated 5-nitro-9-hydrazinoacridine derivatives are interesting objects for further research.

## THE EFFECT OF THE COMBINED USE OF VITAMINS C AND D ON THE MICROSCOPIC COMPOSITION OF RATS' URINE

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**Introduction.** The year 2019 witnessed the advent of a new severe acute respiratory syndrome coronavirus (SARS-CoV-2) that causes coronavirus disease 19 (COVID-19). The COVID-19 pandemic has spurred renewed interest in vitamin D to address viral replication and hyperinflammation that have a major role in the pathogenesis of severe COVID-19. The beneficial effects of vitamin D in COVID-19 were attributed to be mediated through its multiple actions on the immune system. Calciferol is known to enhance the production of various anti-microbial peptides by the immune cells and modulates the immune system according to the internal milieu. It reduces the dysregulated production of self-damaging pro-inflammatory cytokines and promotes the expression of anti-inflammatory cytokines by immune cells. The dynamic role of vitamin D can be of immense value in the context of immune dysfunction observed in COVID-19 patients with cytokine storm and acute respiratory distress syndrome.

Ascorbic acid represents an appealing option for clinicians to utilize in the context of the global COVID-19 pandemic due to its proposed clinical efficacy, relative safety, and low cost. Due to its known antioxidant effects and role in enhancing immune function, vitamin C was assumed to have a beneficial impact on COVID-19. This is mainly *via* supporting lymphocyte activity, stimulating interferon- $\alpha$  production, reducing inflammation, and improving endothelial function.

Considering all beneficial effects of vitamins D and C on COVID-19, most guidelines recommend these drugs for the treatment, especially in severe cases. However, the doses are very high. Since it is "*sola dosis facit venenum*", the side effects are not unexpected. Calciferol is very unlikely to cause severe symptoms of toxicity right away, and symptoms may take months or years to show up. High doses of vitamin D can cause hypercalcemia without toxicity symptoms but can also cause toxicity symptoms without hypercalcemia. Vitamin C is likely safe for most people. However, it is well known that large doses of ascorbic acid may cause acidification of the urine that promotes stone formation in the urinary tract. Thus, special care should be taken when using high doses of the above-mentioned vitamins, especially when they are used together, which is very often observed during the COVID-19 treatment. Even though side effects are registered in clinical practice, no data from animal experiments were found regarding the safety of the simultaneous use of high doses of vitamins C and D. This emphasizes the necessity of corresponding experiments.

**Aim.** The study of rats' urine microscopy under the conditions of oral administration of high doses of vitamins C and D for determination of the type of crystalline calculus.

**Materials and methods.** The studies were carried out on 60 male rats, divided into 6 equal groups (controls and experimental groups of vitamin C 200 mg/kg + vitamin D 1000 IU/kg with/without calcium 2500 mg/kg). After 14 days of oral administration, 24-hour urine samples were collected in metabolic cages, urine pH was analyzed by pH meter pH-150MI, urine microscopy was performed without staining by microscope «Granum L3003» in optical magnification 250x and 400x, The type of salt that formed the crystal was determined by the form; if necessary, microchemical reactions were used.

**Results and discussion.** Separate administration of active substances did not lead to changes in microscopic view of rats' urine, crystals corresponded to neutral and slightly alkaline urine, but rats, which were administrated vitamin C, have a little decreased urine pH. Under the combined administration of vitamins C and D or vitamin D and calcium combination, it was observed the significant increasing of crystals in urine, which were represented mainly by amorphous phosphates and calcium oxalate. Also it caused significant changes in urine pH. It should be noted that the increase in the number of crystals did not correlate with calcium intake, but was caused precisely by high doses of vitamin C and D.

**Conclusions.** High-dose use of vitamins C and D for a long time obviously leads to a decrease in the pH of urine and an increase in the intake of calcium in the primary urine. This, in turn, causes an increased formation of insoluble calcium salts, which are not absorbed. Thus, combination therapy with these drugs has a high risk of provoking the development of urolithiasis.

## SYNTHESIS AND PHYSICO-CHEMICAL PROPERTIES OF ESTERS OF 2- (4-R-5- (5-BROMOTHIOPHEN-2-YL)-4H-1,2,4-TRIAZOL-3-YLTHIO) ACETIC ACIDS

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**Introduction.** Modern medicines must have certain characteristics, one of which is low toxicity and high efficacy. Thus, in recent decades, the attention of scientists has been attracted by