

THE RESEARCHING OF PHARMACOKINETICS AND POSSIBLE METABOLITES OF POTASSIUM 2-((4-AMINO-5-(MORFOLINOMETYL)-4H-1,2,4-TRIAZOL-IL-3)THIO)ACETATE

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The process of creating new medicines is a complicated and lengthy process, because pharmacological documentation must include a large research array of potential impact of the drug on humans. The studying of the pharmacokinetic parameters and possible metabolites of new drug is the part of this huge process. In our previous studies we have marked the hepatoprotective and antioxidant properties of new derivative of 1,2,4-triazoles - potassium 2-((4-amino-5-(morfolinometyl)-4H-1,2,4-triazol-il-3)thio)acetate (PKR-173). Therefore, the aim of this work is to study the pharmacokinetic parameters and possible metabolites of named substance with intragastric administration to rats.

The study was performed on Wistar rats. During the experiment, the animals had limited access to food and water intake is not restricted. Substance potassium 2-((4-amino-5-(morfolinometyl)-4H-1,2,4-triazol-il-3)thio)acetate was administered orally in isotonic solution, with rigid probe. To assess the pharmacokinetic properties of the compound, next parameters were calculated - the area under the pharmacokinetic curve, total clearance, elimination constant, the total volume of distribution, half-life. Chromatographic separation was performed using an Agilent 1260 Infinity HPLC system. Data collection was performed using the Open LAB CDS. Column ZORBAX RX-SIL (50 × 4,6, 1,8 microns). Introduced volume was 20 ml for metabolite identification and 2 ml for pharmacokinetic studies.

Determination of PKR-173 was carried out for 24 hours and determining preliminary calculated from 24 logarithm base 10 with an interval of 0.5. Thus, based on the data, determine the concentration of potassium 2-((4-amino-5-(morfolinometyl)-4H-1,2,4-triazol-il-3)thio)acetate in the serum was carried out for 0.08 (5 min) 0.25 (15 min), 0.75 (45 min), 2.5, 7.5, 13.5 and 24 hours. The main pharmacokinetic parameters are calculated depending on the concentration of the compound in the plasma of rats on time show no high value half-life ($T_{1/2} = 0.32$ hours). The area under the pharmacokinetic curve of $AUC = 150,8998 \text{ mg} \times \text{h/mL}$.

Subsequently, to determine the possible metabolites of potassium 2-((4-amino-5-(morpholinomethyl)-4H-1,2,4-triazol-yl-3)thio)acetate, chromatographic studies were performed by liquid chromatography of plasma.

Thus, the chromatogram obtained on the 5th minute of introduction of the compound has a peak with a retention time of 2.008 min. A molecular ion with a mass of 288.2 m/z is present in the mass spectrum of this peak. The obtained data indicate the potential metabolites, such as: 4-amino-5-((carboxymethyl)thio)-3-((3-oxomorpholino)methyl)-4H-1,2,4-triazol-1-ium, 4-amino-5-((carboxymethyl)thio)-3-((2-oxomorpholino)methyl)-4H-1,2,4-triazol-1-ium, 4-amino-5-((carboxymethyl)thio)-3-((2-oxomorpholino)methyl)-4H-1,2,4-triazol-1-ium, 4-amino-5-

((carboxymethyl)thio)-3-((3-oxomorpholino)methyl)-4H-1,2,4-triazol-1-ium,
5-((carboxymethyl)thio)-3-(morpholinomethyl)-4-nitroso-4H-1,2,4-triazol-1-ium.

As a result of the study, the pharmacokinetic parameters of potassium 2-((4-amino-5-(morpholinomethyl)-4H-1,2,4-triazol-yl-3)thio)acetate (PKR-173) were studied by intragastric administration to rats. The half-life of this substance ($T_{1/2} = 0.32$ hours) was established and possible metabolites were noted.

CASE OF MIXT INFECTION OF SALMONELLOSIS AND INFESTATION WITH THE LARVAE OF MOSQUITO CULEX IN A 9 YEARS OLD CHILD

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Infestation (from the Latin. *Infestare* – attack) – infection of the human or animal body with parasites (insects, mites and other arthropods). Infestations belong together with hirudinosis and helminth infections to the group of invasive parasitic diseases. The clinical observation presented by us in a 9-year-old child is a mixed infection of gastrointestinal form of salmonellosis (*S. enteritidis* D) in combination with gastrointestinal infestation by the larvae of the present mosquito (*Culex*), which is widespread in Ukraine. A person can become infected with eggs or larvae of mosquitoes by using poor quality water, liquid food, swimming in reservoirs with stagnant water. Child V. was admitted on the first day of the disease in a moderately severe condition with complaints of weakness, anorexia, shortness of breath of mixed character, rare dry cough, presence of puffiness in the face and elements of the urticaria exanthema on the face, trunk and extremities, small inspiratory dyspnea, sneezing, obstruction of nasal breathing, moderate serous discharge from the nose.

Epidemiological history: possible infection with eggs or larvae of mosquitoes occurred as a result of unboiled water or liquid products, on the surface of which female mosquitoes lay their eggs. According to the mother, the family uses water, which is stored in a jar without a lid. Water is replaced as used, but not every day. The child did not swim in the waters. The child fell ill in early May, at that time of year when there was an active mosquito breeding.

Anamnesis of the disease. The child became seriously ill when the above mentioned complaints appeared, the temperature did not rise. On the 2nd day of disease, the child's body temperature rose to 38.7 ° C, multiple vomiting appeared (up to 20 times a day), anorexia, cramping abdominal pain, nausea, watery diarrhea started up to 20 times a day on the 3rd day of the disease, thirst, dry skin, decreased diuresis. At the background of exicosis of 2nd degrees, metabolic ketoacidosis joined (intense smell of acetone in exhaled air, urine, feces, a sharply positive test with sodium nitroprusside in the urine).

Objective status. The condition of the child is of moderate severity. The skin is pale, dry, turgor is reduced. On the skin of the trunk and extremities there are sepa-