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Improved method of quantitative determination of 5-methyl-6-nitro-7-oxo-1,2,4-triazolo[1,5-*a*]pyrimidinide l-argininy monohydrate – active substance of drug "Triazid" in the plasma of the human blood by UPLS method

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Abstract

An important problem of the present time is the creation of effective antiviral drugs. In this aspect it is necessary to note the recently created as a result of joint investigations of the Postovsky Institute of Organic Synthesis (UrB RAS), Ural Federal University, the Research Institute of Influenza of the Ministry of Health of the Russian Federation and PJSC "Otisipharm", the drug "Trizid" with promising characteristics. The first phase of clinical trials of this drug has been carried out. Methods for its quantitative determination in substance and in biological fluids by the HPLC method have been developed. In this article an improved method for the quantitative determination of "Triazide" in human blood plasma by the method of UPLC with UV detection is proposed. In case of using this analytical method economy of solvents and also reduce the time required for analysis can be achieved. The analytical area of the procedure is from 0.03 to 20.00 μg/ml according to the content of "Triazide" in blood plasma.

To achieve the best chromatographic characteristics, a ZORBAX Rapid Resolution High Definition (RRHD) SB-C18 column (Agilent Technologies, USA) has been used. Sample preparation was carried out by precipitating plasma proteins with a solution of hydrochloric acid, followed by extraction with ethylacetate. Various buffer solutions (0.01 M ammonium acetate in 0.04% ammonium hydroxide (pH = 9); 0.01 M ammonium acetate in 0.01% acetic acid; 0.01 M ammonium acetate in various ratios with acetonitrile and methanol) have been tested as mobile phase. The best results have been achieved when using a mixture of 0.05 M ammonium acetate and acetonitrile as the eluent.

The possibility of applying the developed method for the implementation of pharmacokinetic studies and therapeutic drug monitoring of the "Triazid" have been shown by the results of the validation according to GF XIII (this procedure has been carried out for the following parameters: linearity, accuracy, specificity, convergence and intralaboratory precision; in all cases, the data have been corresponded to established norms).

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