DEVELOPMENT OF THE ISOLATION PROCEDURE FOR KETOTIFEN USING SULPHURIC ACID

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Ketotifen fumarate is the medicine with antihistamine action, however, it should be noted that the medicine can show expressed sedative action, strengthen the action of hypnotic and antipsychotic agents, and alcohol. The cases of poisonings by the medicine are known, however the methods of its chemical and toxicological analysis are developed not enough.

To develop the ketotifen isolation procedure from biomatrices.

10 g of the model mixture of biological material with ketotifen were placed into the beaker and coated with 20 ml of 0.01 mole/dm^3 sulphuric acid solution, following which the mixture was acidified with 20% sulphuric acid solution to pH = 2 and kept for 2 hours while continuously shaking. The mixture was centrifuged (during 10 min. under 5000 revolutions per minute) and the centrifugate was collected into the clean beaker. Infusion of biological material with new portions of water acidified with sulphuric acid was carried out twice for 1 hour more. The «acid» water extracts were joined, placed into the separating funnel and extracted with chloroform by portions of 10 ml three times. The obtained extracts («acid» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 1). The «acid» water extract were alkalified by ammonia solution to pH = 11 and extracted with chloroform by portions of 10 ml three times. The obtained extracts («alkaline» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 2).

The extracts 1 and 2 were used for identification of ketotifen by the methods of thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC). Their quantitative determination we carried out by the methods of HPLC, ionometry, UV-spectrophotometry and extraction photometry.

We could not find ketotifen in the extract 1 and identified it in the extract 2. The developed procedure allowed to isolate about 60% of ketotifen from the biological matrices – all medicine was present in the extract from the alkaline medium, that correspond to the theoretical information about ketotifen ionisation constant.