OPTIMIZATION OF THE WAYS OF FUROSEMIDE IDENTIFICATION

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Introduction. The search of new cost-effective methods of analysis of medicinal substances is being carried out at the Pharmaceutical Chemistry Department of National University of Pharmacy. Furosemide (4-chloro-2-[(furan-2-ylmethyl)amino]-5-sulphamoylbenzoic acid) is a drug that possesses diuretic properties. Furosemide is included in the European Pharmacopoeia (EP), the Britain Pharmacopoeia, and the State Pharmacopoeia of Ukraine. There are different methods of identification of furosemide. The EP suggests usage of both instrumental and non-instrumental methods of dentification of this substance. They include infrared absorption spectrophotometry, ultraviolet (UV) and visible spectrophotometry. Non-instrumental method is the identification of a primary aromatic amino group after hydrolysis using naphthylethylendiamine to obtain an azo dye.

Aim. The target of our work is the optimization of identification for a widely used pharmaceutical substance furosemide to discover and find the most suitable and appropriate methods of identification of furosemide based on its structure and properties.

Materials and methods. We used the analytical balance Axis ANG-200 and the measuring glass wear of class A. For the spectrophotometric investigations we used spectrophotometer Evolution 60S; the methods of chemical identification.

The object of our investigation being the pharmaceutical active ingredient furosemide was checked for the possibility of other ways of the identification alternative for the mentioned above.

We have checked that furosemide in the reaction for a primary aromatic amino group (diazotization by sodium nitrite in the presence of hydrochloric acid and next diazotization) gives a characteristic red colour when alkaline solution of β-naphthol is used to obtain an azo-dye. This possibility of this reagent usage was proved instead of naphthylethylene diamine dihydrochloride suggested by the EP when a violet-red colour develops.

The ability of aromatic carboxylic acids to form coloured products with the salts of heavy metals is used in pharmaceutical analysis. It was observed that furosemide forms the coloured precipitates with such reagents and we consider the aromatic carboxylic group to form the salt. At first we obtained the sodium salt of furosemide: 0.1 g of furosemide were shaken with 3 ml of 0.1 M sodium hydroxide solution during 1-2 min and then filtered. Then the salt of a heavy metal was added.

We obtain a light-green precipitate with copper sulphate solution, the pink precipitates with the salts of cobalt (II) (chloride and nitrate were used), and a brown-red precipitate with ferric chloride solution.

We have checked the spectral characteristics of furosemide in different solvents. The solution suggested by EP for this determination is a solution of sodium hydroxide, because the substance is practically insoluble in water but dissolves in dilute solutions of alkali hydroxides. Taking into consideration the fact that furosemide is sparingly soluble in ethanol 96% we have checked the UV characteristics in this solvent. Furosemide has functional groups of acidic character along with the groups of basic character so we checked its UV characteristics also in 0.1M hydrochloric acid solution.

Test solutions. A) 50 mg of furosemide were dissolved in a 4 g/l solution of sodium hydroxide and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with a 4 g/l solution of sodium hydroxide. B) 50 mg of furosemide were dissolved in ethanol 96 per cent and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with ethanol 96 per cent. C) 50 mg of furosemide were dissolved in 0.1M hydrochloric acid solution and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with 0.1M hydrochloric acid solution.

The spectra were obtained in the spectral range 200-400 nm. The obtained spectra have three defined absorption maxima: A) at 228, 270, and 333 nm, B) at 235, 283, and 335 nm; C) at 231, 273, and 336 nm. The ratios of the values of absorbance in the second and the first maximum were calculated and are A) 0.56; B) 0.55; C) 0.61.The absorbance ratio for the determination in sodium hydroxide solution corresponds to EP.

The results of absorbance measurement in the range of concentrations of analyzed substance where they submit the combined *Beer-Lambert-Bouguer* law were used to calculate the specific absorbance. The average value of specific absorbance $A_{1cm}^{1\,per\ cent}$ was determined.

Results and conclusion. The obtained results suggest the alternative ways of furosemide identification and give the possibility to identify furosemide reliably. The described variants of identification can be used depending on the presence of resource base of certain laboratory.

The results of validation studies show that the specific absorbance was calculated with good accuracy and can be used for the quantification of furosemide by the method of specific absorbance.