DEVELOPMENT OF EXTRACTION-SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATIVE DETERMINATION OF THE ANTIDEPRESSANT MELIPRAMINE WITH METHYL ORANGE

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Introduction. Antidepressant poisonings occupy a leading position among the psychotropic drug intoxications all over the world. Melipramine (10,11-Dihydro-N,N-dimethyl-5H-dibenz[b,f]azepine-5-propanamine hydrochloride) is a tricyclic antidepressant. Cases of acute and lethal poisoning by melipramine has been registered. Postmortem fluid and tissue distribution of melipramine were within the range for various cases: blood 0.8–13 mg/L, liver 75 μg/g, urine 0.8–12.7 mg/L. The main trend of bioanalytical method development for melipramine determination is the prevalence of column chromatography with mass spectrometric detection. However, these analytical methods are not always available for a toxicological laboratory.

Aim. To develop simple and sensitive method for melipramine quantitative determination using extraction-spectrophotometry in the visible region of the spectrum with the methyl orange, suitable for the chemical-toxicological analysis.

Materials and methods. Standard solution (SS) of the drug containing 100 μg/mL of the melipramine-base was prepared. Absorbance of colored solutions was measured at 540±2 nm; 10 mm light pathway cuvette was used.

Results and discussion. To determine the optimal conditions of extraction-spectrophotometric method of the melipramine determination it has been previously found that methyl orange, an acidic azo dye (0.05% aqueous solution) formed the ionic associate with the drug in the medium of the acetate buffer of pH 4.6 which was extracted with chloroform. The colour of ionic associate solution (yellow) was low-intensive, so to enhance the sensitivity of the method the ionic associates formed was destroyed by addition of 1% sulphuric acid solution in absolute ethanol to the resulting chloroform layer. Thus, the colored red solution with a significantly higher absorption was obtained. The absorption values were processed by linear regression method. The equation of the regression line was the following: $y=(0.0057\pm5\cdot10\text{-}5)x+(0.018\pm0.005);\cdot(r=0.999)$; LOD and LOQ values were, respectively, 1.5 μg and 4.6 μg in the sample. The linearity of the calibration curve was within the range of melipramine concentrations from 5.00 to 150 μg in the sample.

Conclusions. Thus, the extraction-spectrophotometric method developed satisfied the requirements of the chemical-toxicological analysis with respect to the sensitivity and can be used in toxicological study of the biological samples for presence of melipramine.

STUDY OF THE CHEMICAL INTERACTION OF REBAMIPIDE WITH MEDICINES IN THE TREATMENT OF HYPERACIDITY STATES

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Introduction. The onset of peptic ulcer disease is facilitated by many factors from genetic to bad habits and taking medications (NSAIDs, hormones, and others). However, the vast majority

are associated with acid aggression and Helicobacter pylori infection. In this regard, pharmacotherapy is carried out in a complex manner. One of the basic drugs, according to the protocols for the treatment of hyperacid conditions of diseases of the gastrointestinal tract, are gastrocytoprotectors, which include the drug rebamipide, which help to restore the integrity of the mucous-epithelial barrier in combination with antacids and astringents, depending on the cause of the hyperacid state.

Aim. Due to the high demand for this drug in the treatment of diseases of the gastrointestinal tract, rebamipide was chosen as an object of research to study the chemical interaction with preparations of bismuth, aluminium and magnesium, which are included in the protocols for the treatment of hyperacid conditions.

Materials and methods. The studies were carried out on the preparations "Mucogen" (rebamipide 100 mg), "De-nol" (colloidal bismuth subcitrate, 120 mg), "Maalox" (aluminum hydroxide 400 mg, magnesium hydroxide 400 mg).

Results and discussion. The leading pharmacopoeias of the world do not include monographs on the finished medicinal product rebamipide. In turn, the modern world makes high demands on the quality of medical care and pharmaceutical care, especially the rational prescription of complex therapy. Therefore, the study of chemical interactions is the key to quality treatment. Therefore, a preliminary method was developed for the quantitative determination of rebamipide by absorption spectrophotometry in the ultraviolet region of the spectrum, by the standard method. A 0.1 M solution of hydrochloric acid was chosen as the test medium, since the drug, in accordance with the instructions for use, exerts its effect in the stomach and chemical interaction with other drugs is possible in the gastrointestinal tract.

The presence of the absorption maximum of rebamipide in the absorption spectrum in a 0.1 M solution of hydrochloric acid at a wavelength of 327 nm was determined experimentally.

The proposed method was used to carry out the pharmacologo-technological test "Dissolution" using other drugs in the dissolution medium of 0.1 M hydrochloric acid solution. A test was carried out with the addition of rebamipide, rebamipide with a medicine of bismuth and rebamipide with a medicine of the combination of aluminum and magnesium into the cells. The test was carried out for 90 minutes.

Conclusions. As a result of the determination, the absorption spectra of the drug rebamipide and the combination with other drugs did not differ, which indicates that the active components do not enter chemical interaction and can be recognized regardless of the time of administration of another ones.

DEVELOPMENT AND VALIDATION OF THE HPLC-METHOD OF QUANTITATIVE DETERMINATION OF DINITRATE ISOSORBIDE IN MATRIX GRANULES

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Introduction. Prolonged forms of isosorbide dinitrate have high antianginal efficacy and lower incidence of side effects compared to conventional tablets. The most reliable prolonged formulations in biopharmaceutical behavior are oral dosage forms containing active substances divided into many individual particles (granules).