

molecular form  $HR^+$  appears ( $\lambda_{max}$  at 232 and 319 nm), in the strong acid medium ( $pH < 1.7$ ) the final product of transformations such as protonated form  $H_2R^{2+}$  ( $\lambda_{max}$  at 277 nm) is presented in the solutions.

**Conclusions.** The constant of equilibrium  $HR^+/H_2R^{2+}$  is determined by two methods. The value of  $pK_a$  is 2.31 in water, and 2.46, 2.63, 2.40 in the mixtures (1:1) of water with isopropanol, acetonitrile and ethanol respectively.

## IODOMETRIC DETERMINATION OF CYSTAMINE DIHYDROCHLORIDE IN TABLETS USING POTASSIUM HYDROGENPEROXOMONOSULPHATE

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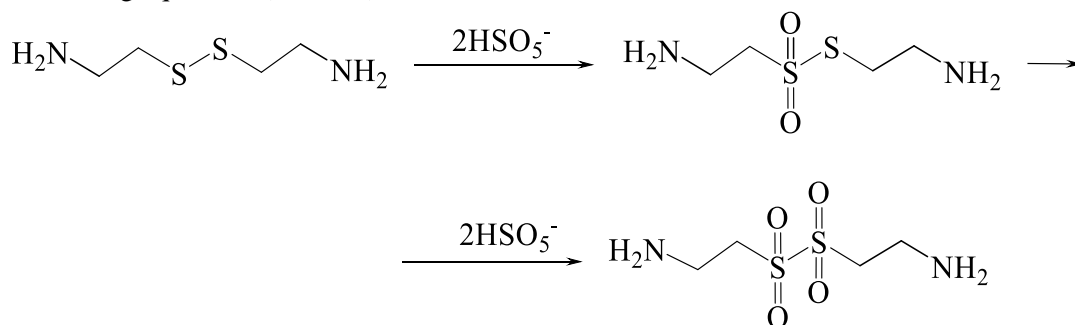
**Introduction.** Cystamine dihydrochloride (cystamine hydrochloride RS-1) is an emergency radioprotection from the group of sulfur-containing drugs. Increases the body's resistance to ionizing radiation. The action is based on the ability to reduce the number of radicals, ionized and excited molecules formed in the tissues during irradiation, as well as the ability of the drug to interact with certain enzymes and to impart resistance to ionizing radiation. Contained in the first-aid kit (AI-2) - two plastic pencil boxes for 6 tablets (0.2 grams) of cystamine dihydrochloride in each. Cystamine dihydrochloride was determined coulometrically with electrogenerated bromine. Potentiometric titration of this compound after its reduction using silver nitrate as titrant and sulfide-selective indicator electrode was also elaborated. Cystamine dihydrochloride in pure form, tablets and biological media have been determined by a number of methods including separation by thin-layer chromatography. The analytical methods used for its determination in substance included alkalimetric titration in non-aqueous medium, direct spectrophotometry or based on the reaction of cystamine with *p*-nitrophenyl-diazonium to form a red-colored diazoamino compound and subsequent photometric analysis, and also using HPLC method with coulometric detection. Like all other disulfides, Cystamine is interesting substrate for oxidation reactions as it may undergo either electrophilic or nucleophilic oxidation. The mode of oxidation is controlled largely by the pH of the reaction mixture, whereas solvent effects are minimal. Thus, stepwise oxidation of Cystamine dihydrochloride with *m*-Chlorperbenzoic acid first gives 2-amonoethyl 2-amonoethanethiolsulfinate dihydrochloride and then the corresponding thiolsulfonate. In acidic or neutral solution, the oxidation follows the same mechanism as that described for the oxidation of sulfide to sulfoxide. In basic solution, however, a nucleophilic attack of the peroxy anion takes place at the sulfur atom. However, no kinetic studies have been carried out to probe the analytical aspects of the oxidation of Cystamine dihydrochloride with potassium hydrogen peroxomonosulfate in aqueous buffer solutions.

**Aim.** The main purpose of our work was to study the possibility of application of potassium hydrogenperoxomonosulphate ( $KHSO_5$ ) as reagent in the oxidimetric determination of Cystamine dihydrochloride.

**Materials and methods.** As oxidant was used potassium hydrogenperoxomonosulphate,  $KHSO_5$ , commonly known as potassium monopersulfate, which is present as a component of a triple salt with the formula  $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$  potassium hydrogen peroxymonosulfate sulfate (5:3:2:2), [CAS 70693-62-8], extra pure, 4.7% active oxygen (Acros Organics). Kinetic studies were carried out in buffer solutions under second-order conditions with potassium hydrogenperoxomonosulphate ( $KHSO_5$ ) in the temperature 293 K and over pH range 3.3 to 6.8. The reaction was followed by estimating the unreacted potassium hydrogenperoxomonosulphate as a function of time by using the iodometric method. From the titre values, plots of  $1/c$  vs time were made and from the slope of such plots, the second order rate constants,  $k_{obs}$  ( $L \cdot mol^{-1} \cdot min^{-1}$ ) were obtained.  $c$  - current molar concentration of  $KHSO_5$  (for time  $t$ , min), mol/L.

**Results and discussion.** It was found that one mole of Cystamine dihydrochloride react with four moles of  $KHSO_5$ . The optimum for the Cystamine dihydrochloride determination was pH 5,8 (time of quantitative interaction is 2 min). The observed rate constant  $k_{obs}$  is reasonably constant over the first half of oxidation corresponding to the conversion of Cystamine to the corresponding disulfoxide Cystamine  $NH_2(CH_2)_2S(=O)S(=O)(CH_2)_2NH_2$  or S-dioxocystamine  $NH_2(CH_2)_2S(=O)_2S(CH_2)_2NH_2$ , but later the

reaction slows down, implying that the later stages of formation of the corresponding of disulfone (or tetraoxo) Cystamine  $\text{NH}_2(\text{CH}_2)_2\text{S}(=\text{O})_2\text{S}(=\text{O})_2(\text{CH}_2)_2\text{NH}_2$  by means hydrogenperoxomonosulphate anions are slower or more complex. A suitable mechanism scheme based on these observations is proposed and given in the following equations (**Scheme**):



With this proposed method, 2,0-10 mg of Cystamine dihydrochloride can be accurately and precisely analyzed ( $\text{RSD} < 1.6\%$ ,  $|\bar{x} - \mu| \leq \frac{tS}{\sqrt{n}}$ ). The advantages of the applied analytical techniques in the determination of Cystamine dihydrochloride acid in tablets «Cystamine 0.2 g» has been presented. The recovery was  $102.45 \pm 1.50\%$ .

**Conclusions.** The possibility of application of  $\text{KHSO}_5$  as reagent in the oxidimetric determination of Cystamine dihydrochloride was shown. Statistical analysis of the results obtained by the proposed and the official methods reveals no significant differences between them in accuracy and precision as concluded from Student's t test and the variance ratio.

## THE CHROMATOGRAPHIC DETECTION OF LAMOTRIGINE IN BIOLOGICAL SAMPLES

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**Introduction.** Epilepsy is one of the most common and dangerous neurological disorder all over the world. According to data of the International League against Epilepsy (ILAE) annually 50-70 cases per 100,000 populations are registered in the most developed countries of the world. Anticonvulsants are a diverse group of pharmacological agents used in the treatment of epileptic seizures. Lamotrigine (phenyltriazine derivative) is one of the most common. However, the websites of FDA and patientsville.com cases of lamotrigine lethal poisoning mainly due to suicidal overdoses registered in over 30 countries.

**Aim.** The aim of the work was to develop the conditions for detection of lamotrigine in biological samples by TLC.

**Materials and methods.** The study was performed on Merck silica gel 60 F<sub>254</sub> chromatographic plates (Germany) with the size of 10×10 cm. Before samples eluting the chromatographic plates were previously washed with methanol and activated in oven at 110-120°C for half an hour.

The following systems of solvents were used as mobile phases: butanol-glacial acetic acid-water (30:5:15); ethyl acetate-methanol-25% ammonium solution (17:2:1); chloroform-butanol-25% ammonium solution (70:40:5); chloroform-methanol (9:1); methanol-25% ammonium solution (100:1.5); butanol-glacial acetic acid-water (15:5:30); methanol-butanol (60:40); chloroform-ethanol (20:1); ethyl acetate-chloroform-water (9:3:2.5).

**Chromatographic method.** Standard chromatographic chamber was previously saturated with eluent vapor's for 30 min. 2 ml of lamotrigine chloroform extracts, obtained from the liver tissues were evaporated to the minimal volume of 0.05 ml. Five  $\mu\text{L}$  of lamotrigine extracts were applied at the starting line of the previously activated chromatographic plate with a glass capillary. Five  $\mu\text{L}$  of test solutions of