SYNTHESIS AND DEVELOPMENT OF QUALITY CONTROL METHODS OF 3-METHYLAMINOSUCCINOYLAMIDO-N-(3',4'-DIMETHYLPHENYL) ANTHRANILIC ACID

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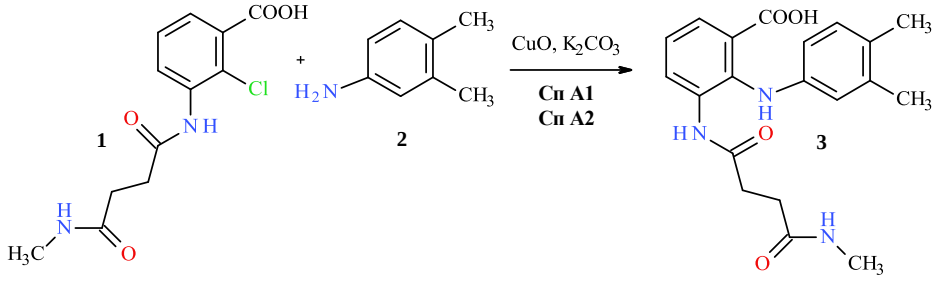
Introduction. In recent years, the most pressing health problems around the world are the quality, efficacy and safety of medicines. This is due to the presence on the pharmaceutical market of a large number of trademarks of medicinal preparations, an increase in the number of new medical supplies, penetration into the sphere of civilian sales of counterfeit medicines. Therefore, one of the most important stages for the introduction of a new medicinal product or substance into pharmaceutical practice is the development of quality control methods.

Aim. Synthesis and development of methods for quality control of promising 3-methylaminosuccinoylamido-N-(3',4'-dimethylphenyl)anthranilic acid substance, which has high anti-inflammatory, analgesic, diuretic and antifungal effects.

Materials and methods. The subject of the study was a patented promising 3-methylaminosuccinoylamido-N-(3',4'-dimethylphenyl)anthranilic acid substance. The required reagents for resynthesis of the substance were obtained and purified using standard techniques. Chromatography was performed on "Silufol UV-254" plates. Manifestation of chromatograms was carried out in UV light. The temperature melting points were determined using the Kofler block. UV spectrum was taken on a "Thermo Fisher Scientific EVOLUTION 60S" device in ethanol within the wavelength range 190-1100 nm. IR spectra were taken on a Spectrophotometer «SpecordM-80» in tablets of potassium bromide (concentration 1%). ^{1}H NMR spectra were recorded on a Varian Mercury 200 MHz device, solvent - DMSO-d6, tetramethylsilane (TMS) was used as an internal standard. Chemical shifts were shown on the scale δ (ppm). Quantitative determination: the precise mass of the test substance (0.1 – 0.18 g) was dissolved in 20 ml of solvent and titrated potentiometrically with a released from carbonates 0.1 M aqueous solution of sodium hydroxide on an ionizer I-160 using an indicator glass (EPS 45-07) and chlorine-silver (EVL-LML) electrodes.

Results and discussions. 3-methylaminosuccinoylamido-N-(3',4'-dimethylphenyl)anthranilic acid ***3*** was resynthesized by the interaction of methylamide of 3-carboxy-2-chlorosuccinanilic acid ***1*** with 3,4-dimethylaniline ***2*** in environment of DMFA (method A1) and in the solid phase (method A2) in the presence of copper catalyst (CuO) and potassium carbonate (Scheme 1).

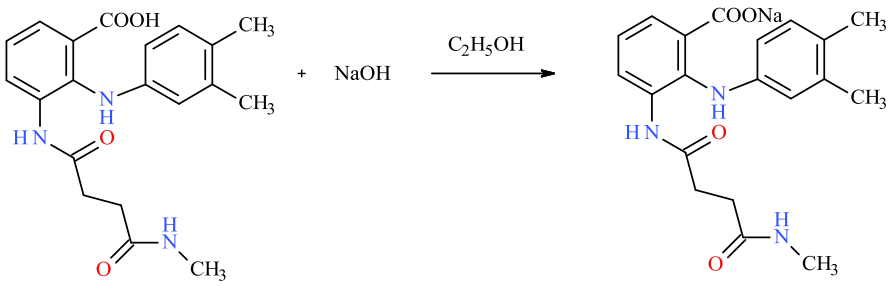
Scheme 1



The purity test, namely the determination of the accompanying impurities, was carried out using thin-layer chromatography. IR, UV, and ^{1}H NMR spectroscopies were used for identification and qualitative reactions were performed for the corresponding functional groups according to the SPhU.

The method of alkalimetry in the ethanol environment with the potentiometric fixation of the final titration point (s=1) was selected for the quantitative determination of a promising substance, due to the fact that this substance has a blue-green color, that complicates its determination by the indicator method (scheme 2).

Scheme 2



The calculation of the substance quantitative content, %, was carried out according to the formula:

$$X, assay = \frac{V titrant \cdot K \cdot T \cdot 100}{m}$$

Conclusions. The synthesis was performed and the methodology for quality control of promising substance of 3-methylaminosuccinoylamido-N-(3',4'-dimethylphenyl)anthranilic acid, which has high anti-inflammatory, analgesic, diuretic and antifungal effects, was developed. The statistical processing of the obtained results was carried out.

ELECTROCHEMICAL METHOD FOR DETERMINATION OF CYCLAMATE USING 12-MOLYBDOPHOSPHORIC ACID

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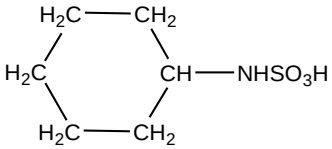
Introduction. Cyclamate – low-calorie sweetener is sweeter than sucrose 30 times. Used in food and beverages and the manufacture of diabetic products. Unlike other sweeteners it can be used in the manufacture of food products, requiring additional heat treatment due to resistance to light, temperature and acidity. The structural formula of sweetener cyclamate (cyclohexylamine - N - sulfonic acid) is as follows:



There are many methods for quantitative determination of cyclamate: colorimetry using pikryl chloride, chromatographic, spectrophotometric with the formation of N,N-dychlorcyclohexylamine, indirect spectrophotometric determination of cyclamate by its degradation products capillary isotachophoresis and others. Chromatographic methods of analysis based on the separation of cyclamate mixture of sweeteners and food additives, followed by determination of individual components using a UV detector and spectrophotometric determination sweetener based on his previous destruction to N,N-dychlorcyclohexylamine. Then carry out specific reactions resulting product with various reagents – resulting in formation of colored complexes that determine photometrically. However, existing methods are complex performance multistage sample preparation and toxic reagents used in the analysis.

Aim. The development of alternative methods for the quantitative determination of cyclamate in substance and industrial production is relevant analytical problem. Newly analytical methods shall have a sufficiently metrological parameters and allow cyclamate determine the presence of auxiliary components without their prior separation.

Materials and methods. Plastifying PVC membrane for ICE synthesized by a known method. As the previously used electrode-active component (EAC) soluble in water ($2 \cdot 10^{-6}$ g/l) and soluble in