від 0,25 мкг/мл – 1,25 мкг/мл, коефіцієнт кореляції для гіпоксантину складає 0,99997, для гуанозину – 0,99997.

Прецизійність та правильність визначення проводили на 9 модельних розчинах (плацебо та стандартний розчин субстанції рибоксину), кількісний вміст основної речовини у яких визначено відносно стандартного розчину ФСЗ ДФУ рибоксину. Розраховані критерії статичної та практичної невизначеності (критерії правильності) відповідають критеріям прийнятності. Відносний довірчий інтервал Z для визначення супутніх домішок склав для гіпоксантину Z=1,47%, для гуанозину Z=0,83%. Отримані результати не перевищували повну невизначеність результатів $\Delta_{AS}$% (критерій прицезійності).

Оцінку робастності проводили на стадії розробки методики шляхом встановлення стабільності розчинів у часі, впливу температури, а також вплив швидкості рухомої фази. Встановлено, що розчини зостаються стабільними протягом 12 годин, вплив температури та швидкість рухомої фази не впливають на придатність хроматографічної системи.

**Висновки.** Всі валідаційні параметри відповідають необхідним критеріям прийнятності. Методика вважається валідованою та може бути використана для визначення супутніх домішок рибоксину у готовій лікарській формі – таблетки рибоксину 200 мг.

## ANALYTICAL CONTROL OF CELANDINE ALKALOIDS AMOUNT

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The total amount of alkaloids content in acid broth and purity of alkaloids, which have been isolated by electrolysis, were carried out using amperometric titration.

Amperometric titration of alkaloids organic cations Kat+ by solutions 12-molybdophosphatic heteropoly acid $H_3PMo_{12}O_{40}$ (MPA) is based on the reaction of deposition:

$$3Kat^{+} + PMo_{12}O_{40}^{3-} = (Kat)_3 PMo_{12}O_{40}$$

Celandine alkaloids contain in their structures five membered heterocycle with nitrogen atom, which has distinct proton acceptor abilities. While interaction of alkaloids with heteropoly acids, slightly soluble in water sediments with ion-associative nature of communication are formed, the stoichiometric ratio heteropolyanion (HPA) MPA – organic cation (OC) of alkaloids amount HPA:OK is equal 1:3.

During voltammetric study of the electrochemical behavior of organic cations Kat+ of alkaloids it was found that with cathode polarization in the range from +0.5 V to -0.5 V they are non-electroactive chemical compound. In the same conditions heteropolyanion of 12- molybdophosphatic acid when 0.1 M sodium sulphate solution used as a background electrolyte gives a clear wave of two atoms of molybdenum electroreduction:

$$PMo^{VI}_{12}O_{40}^{3-} + 2e = PMo^{V}_{2}Mo^{VI}_{10}O_{40}^{5-}$$

On the basis that between the substance, which is being determined and the titrant reaction with the formation of slightly soluble compound takes place, and titrant is electroactive substance, amperometric titration of alkaloids organic cations Kat+ from aqueous solution MPA with indication of the equivalence point on the strength of diffusion current of heteropolyanion electroreduction is possible.

During amperometric titration after adding a separate portion of the reagent amperage was noted, at a voltage that corresponds to the sustaining diffusion current. For these data amperometric titration curves in coordinates were built, amperage – the volume of titrant and the equivalence point was graphically found.

Thus, the amperometric titration of aqueous solutions of alkaloids amount by aqueous solution HPC with indication of the equivalence point in strength of the diffusion current by electroreduction HPA is possible. When performing titration system is imposed by voltage which is chosen according to the results of the analysis of current-voltage curves reduction HPA.

Amperometric titration was performed as follows: from broth 10 ml aliquot was taken and placed in an electrochemical cell of 100 ml, 1 ml of background electrolyte (0.01 M sodium sulphate $Na_2SO_4$) was added. In cell system electrodes system (reference electrode – saturated silver-silver chloride half-cell, working electrode – graphite) then applying voltage +0.01V and in 60-90s with value of "zero" current was fixed. Titrated with $10^{-2}$ M solution of 12-molybdophosphatic heteropoly acid (MPA) $H_3PMo_{12}O_{40}$ is made by portions of 0.5ml. Value fixation of sustaining current force – is made within 10s after each addition of titrant. Amperometric titration is completed after a sharp increase in sustaining current. Volume of titrant that was used for titration is determined graphically by curve of amperometric titration.

Amperometric titration showed that the method of acid brothing allows to remove from 1.5 to 2.0% alkaloids in the form of salts, depending on the degree of herbal material reduction.

For the gravimetric determination of celandine alkaloids amount was used the reaction:

$$3Kat^{+} + PMo_{12}O_{40}^{3-} = (Kat)_3 PMo_{12}O_{40}$$

between organic cations of studied alkaloids and heteropolyanion $PMo_{12}O_{40}^{3-}$, which leads to the formation of slightly soluble stable compounds of general formula $(Kat)_3PMo_{12}O_{40}$, which are the optimal deposition and weight forms.

Stoichiometric relationship of organic cation: heteropolyanion = 3:1. Gravimetry was performed as follows: to 30ml of filtrate obtained by acid brothing on water bath an excess of 10ml $10^{-2}$ M solution of MPA was added. The formed deposition has been equilibrating for two hours, then was filtrated through pre-weighed filter "blue ribbon." The deposition was flushed out three times with distilled water, dried in a drying oven at a temperature of 70-80□C. The mass of isolated alkaloids $m_{alk}$ was calculated by the formula:

$$m_{alk} = m \cdot F$$

where,

m – mass of weight form;

F – gravimetrical factor of recalculation.

Gravity confirmed the amperometric titration data, i.e. by method of acid brothing to 2.0% alkaloids can be isolated, depending on the conditions of the isolation process.

The developed methods of gravimetric and amperometric determination of the celandine alkaloids amount using heteropolyanion (HPA) of Kehhin's structure as analytical reagents were adapted to real objects of analysis:

A) Quantification of the alkaloids amount in aqueous-alcoholic extracts of celandine by gravimetric method.

B) Dependence study of % alkaloid content of the celandine vegetation period by amperometric titration.

## ISOLATION OF AMOUNTS OF CELANDINE ALKALOIDS BASES (CHELIDONIUM MAJUS L.) BY ELEKTROLYSIS

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The aim of this paper is to develop a universal complex technology of isolation the amount of alkaloids from herbal raw material of celandine as acid extracts and further electrocrystallization of amounts of alkaloids basis with purity grade not less than 98% by electrolysis.

Defined goal is achieved through integrated technology, which consists of two stages: