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DEVELOPMENT OF A POTENTIAL HEPATOPROTECTIVE QUINOLONE QUANTIFICATION PROCEDURE

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Abstract: the procedure for the quantification of a potential drug substance of hepatoprotective action, 3-propyl-1H-2-oxo-4-hydroxyquinoline, was developed. A procedure for alkalimetric titration of the active pharmaceutical ingredient in dimethylformamide medium is suggested. The validation characteristics of the developed procedure have been studied, which showed the accuracy and precision of the procedure and allow using the method in the standardization process of a potential hepatoprotective agent.

Key words: quinolones, alkalimetric titration, quantification, hepatoprotective

Introduction: liver pathologies are often found among the world's population. Certain negative factors contribute to this phenomenon: an increase in infectious, medicinal, toxic, and autoimmune effects. A potential hepatoprotective medicat based on the structure of propyl-1H-2-oxo-4-hydroxyquinoline quinoline was synthesized at the National University of Pharmacy. Among the stages of introducing any new drug, an important place is given to questions of its standardization; therefore, the development of quality control methods for a potential drug is an urgent task.

Purpose of the study: the aim of the work is to develop a methodic for the quantitative determination of 3-propyl-1H-2-oxo-4-hydroxyquinoline.

Materials and methods: for the experiment, we used a sample of the studied substance of chromatographic purity obtained by triple crystallization.

3-Propyl-1H-2-oxo-4-hydroxyquinoline (Fig. 1) is a white crystalline powder, odorless, practically insoluble in water, sparingly soluble in ethanol, soluble in dimethylformamide.

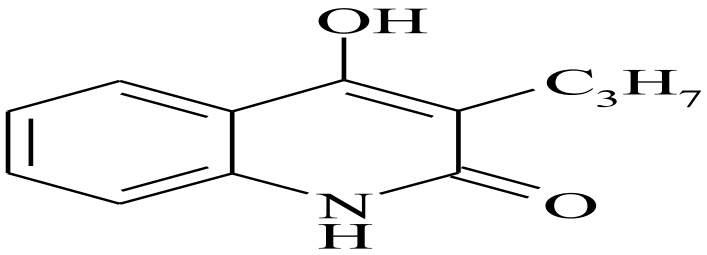

Fig. 1. 3-Propyl-1H-2-oxo-4-hydroxyquinoline

We used the analytical balance Axis ANG-200 and the measuring glass wear of class A [1-3]. The statistical studies were carried out by the common procedure.

The appliance for potentiometric titration was prepared in accordance with the State Pharmacopoeia of Ukraine [4] and the instructions for the ionomer И-160М (indicator electrode is a glass electrode; reference electrode is a silver chloride electrode saturated with potassium chloride). Before the determination, the indicator electrode was soaked for 24 hours in dimethylformamide. The reagents used correspond to the requirements of the State Pharmacopoeia of Ukraine [4].

Results and discussion: an **e**nol hydroxyl is contained in the structure of the molecule in position 4 of the quinoline cycle, due to which 3-propyl-1H-2-oxo-4-hydroxyquinoline (I) exhibits weak acid properties. It seemed advisable to use alkalimetric titration as a possible method of quantitative determination. The quinolone studied is practically insoluble in water, and the acid properties of hydroxyl are weakly expressed that is why we chose alkalimetry in non-aqueous medium. We used dimethylformamide as a non-aqueous solvent because the acidic properties of the analyte are significantly enhanced in this solvent [5]. 0.1 M sodium hydroxide ethanolic solution was used as a titrant. The titration endpoint was fixed by the potentiometric method, which is more sensitive and accurate than the usage of indicator [6]. The determination of the end-point was carried out in two ways:

- by building an integral titration curve or graph of the dependence of the system potential on the titrant volume (Fig. 1);

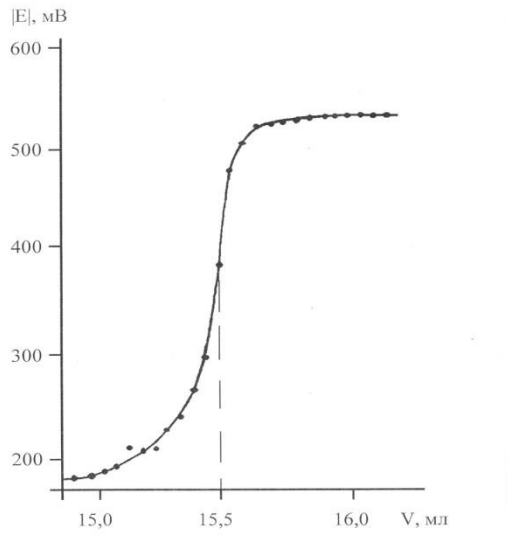

Fig. 1. Graph of the dependence of the potential on the volume of NaOH solution (integral curve)

- by building a differential titration curve or graph of the dependence of the system potential on the change in titrant volume (Fig. 2).

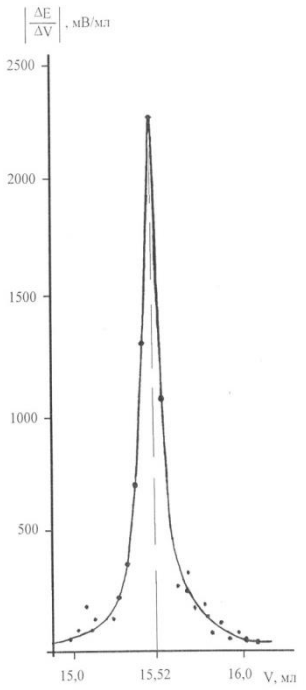

Fig 2. A graph of the dependence of the change in the system potential on the change in the volume of NaOH solution (differential curve)

An experiment using a chromatographically pure sample of 3-propyl-1H-2-oxo-4-hydroxyquinoline (I) showed that the titration jump is clearly determined, and the slope index at the end-point point reaches 2380 mV/ml.

According to the requirements of the European GMP standards [7,8], as well as the European Pharmacopoeia [9] and State Pharmacopoeia of Ukraine [4], the validation of new analytical procedure for quality control of medicinal substances is an obligatory procedure [10]. A series of quantitative measurements of 3-propyl-1H-2-oxo-4-hydroxyquinoline (I) was carried out and the results of them were subjected to statistical analysis to obtain such validation characteristics of the developed technique as accuracy, precision, and linearity [11,12]. Metrological characteristics of the technique obtained are presented in the tab. 1.

Table 1

Metrological characteristics of the method of alkalimetric determination of 3-propyl-1H-2-oxo-4-hydroxyquinoline

μ (100%)	v	$\bar{x}$	s^2	s	P,%	$t(P,v)$	Δx	ε
100.00	5	100.06	0.1154	0.3397	95	2.57	0.87	0.87

Thus, the statistical processing of the data obtained in a series of experiments showed that the suggested alkalimetric quantification provides reliable estimation of the quantitative content of the active substance, 3-propyl-1H-2-oxo-4-hydroxyquinoline. The developed procedure can be used in the preparation of analytical regulatory documentation for a potential medicinal substance.

Conclusions:

1. Based on the study of the physicochemical properties of 3-propyl-1H-2-oxo-4-hydroxyquinoline, the conditions for its alkalimetric titration are developed and the procedure for its quantification is suggested.

2. The validation characteristics of the developed procedure for the quantitative determination of 3-propyl-1H-2-oxo-4-hydroxyquinoline were studied.

4. The suggested procedure for the quantification of the potential substance with hepatoprotective activity, 3-propyl-1H-2-oxo-4-hydroxyquinoline, allows obtaining

the correct and accurate results and can be used for the further standardization of this substance.

REFERENCES:

1. Гризодуб А. И. Стандартизованные процедуры валидации методик контроля качества лекарственных средств. Харьков: Государственное предприятие «Украинский научный фармакопейный центр качества лекарственных средств». 2016. 396 с.
2. Леонтьев Д.А., Гризодуб А. И. Метрологический контроль качества результатов измерений . *Фармаком.* 2007. №2. С. 16–25.
3. Системы качества и надлежащие практики в фармации: учебное пособие /Ю.В. Подпружников и др., под общ. ред. В.П. Черных и Ю.В. Подпружникова. Киев: «СТК ГРУП УКРАЇНА», 2017. 652 с.
4. Державна Фармакопея України: в 3 т. / Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Харків: Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів». 2015. Т. 1. 1128 с.
5. Мчедлов-Петросян Н.О. Дифференцирование силы органических кислот в истинных и организованных растворах. Харьков: Изд-во Харьков. нац. ун-та, 2004. 326 с.
6. Skoog Д.А., West D.M., Holler F.J., Crouch S.R. *Fundamentals of Analytical Chemistry, 9-th ed. Belmont: Brooks/Cole: Cengage Learning. 2014. 958 p.*
7. Good pharmacy practice in Europe / Pharmaceutical Group of the European Union PGEU. London: Community pharmacists.1998. 37 p.
8. Technical Guide for the Elaboration of monographs. 6th Edition. - European Pharmacopoeia, European Directorate for the Quality of Medicines & Health Care. 2011. 72 p.
9. European Pharmacopoeia. 8.0. Vol.1. Strasbourg: European Directorate for the Quality of Medicines, Council of Europe. 2014. 1380 p.

10. Эрмер Й.. Миллер Дж., Валидация методик в фармацевтическом анализе. Москва: 2013. 495 с.

11. Гризодуб А.И., Леонтьев Д.А., Чикалова С.О., Верушкин А.Г. Стандартизованная процедура валидации количественных методик титрования лекарственных средств. *Фармаком*. 2009. № 2. С. 5-29.

12. Алдышева Ж.И., Беляев В.В., В.В. Практические аспекты работ по валидации аналитических методик. *Фармация*. 2008. № 7. С. 9- 12.