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Aminalon quantitative determination in drug dosage forms by spectrophotometric method

K. P. Portna [1*], S. O. Vasyuk [1]

1. Zaporizhzhya State Medical University, Ukraine Analitical Chemistry Department. [Email: Kate-portnaya@ukr.net]
2. Zaporizhzhya State Medical University, Ukraine Analitical Chemistry Department. [Email: vasyuk1@mail.ru]

Author for correspondence: K. P. Portna, Email: Kate-portnaya@ukr.net; Tel: (067)732-29-28

A new spectrophotometric method for the quantitative determination of aminalon in pharmaceutical formulations has been developed. This method is based on the measurement of aqueous aminalon solutions absorption at 470 nm. The proposed method is actual according to the validation requirements of Ukrainian Pharmacopeia. According to the experimental data, the technique can be correctly reproduced and it is suitable for using in the laboratories of the State Inspection for Quality Control of Medicines and QCD of the chemicopharmaceutical enterprises.

Keyword: aminalon, quantitative determination, spectrophotometric method, drug dosage forms.

1. Introduction

Gamma-aminobutyric acid (Aminalon) is a biogenic amine, contained in the central nervous system and participate in neurally mediated and metabolic processes of the brain. Aminalon is the main mediator, involved in the central inhibitory processes as a result of interaction with specific GABAergic receptors. Under the influence of the drug brain metabolic processes are restored: energy processes are activated, improves glucose utilization, increased respiratory activity of the tissues, improves blood circulation. Gamma-aminobutyric acid provides the dynamics normalization of neural processes. Increases thinking productivity, improves memory, has a mild psychostimulant action, a positive effect on the recovery of movement and speech after a disorder of cerebral circulation. Has an anticonvulsant activity.

Based on the fact, that aminalon drugs have fairly high demand in the pharmaceutical Ukrainian market, there is no doubt in the supplying desirability of worthy quality control of these drugs.

For the modern pharmaceutical analysis actual problem is the development of accurate, expressways and available methods of active substances quantitative determination in drug dosage forms.

According to the literature data, the classic reagents for quantitative primary aliphatic amines determination, mainly, amino acids, are ninhydrin, alloxan, indandione derivatives-1, 3 [1, 2].

On the interaction basis with 1, 3-dimethyl-alloxan are developed methods for aminalon quantitative determination in substances and drug dosage forms recipes [1].

Described luminescent methods analysis for primary aliphatic amine determination [3, 4]. So, known method, based on the catalyzed activity of

Os (8+) on the chemiluminescence, which occurs in the interaction of 1, 10-phenathroline and H_2O_2 and decreases in the presence of primary amino acids.

Khuhawar M.Y. and co-authors developed method of aminalon quantitative determination by method of liquid chromatography with usage 2-hydroxynaphthaldehyde as reagent [5].

Some of the proposed methods are complex in cases inaccessible reagents are used. So, the desirability of developing new, simple and valid methods for the aminalon quantitative determination is no doubt.

The aim is to study the optimal reaction conditions between aminalon and the sodium salt of 1, 2-naphthoquinone-4-sulfonic acid and the development of valid, sensitive, and simple in implementation method of aminalon quantitative determination in drug dosage forms.

2. Research Materials and Methods

For the experiment, following were used: aminalon substance; drugs – «Aminalon» pills 0,25 g γ - aminobutyric acid (PJSC «Vitamins», Ukraine) and capsules – «Aminalon-KV» 0.25 g γ - aminobutyric acid (PJSC «Kiev vitamin factory», Ukraine) series 120312 and 60412 respectively.

As the reagent and solvent the sodium salt 1, 2-naphthoquinone-4-sulfonic acid c.p. qualification, 0, 05 M NaOH liquor, purified water were used.

Analytical equipment: spectrophotometer Specord 200, electronic scales ABT-120-5DM, water-bath Memmert WNB 7-45, A class volumetric apparatus.

2.1 General technology of aminalon quantitative determination

An aliquot part of aminalon liquor (0, 70-1, 30 mg) was placed in a measuring bottle with 25,00 ml volume, treated with 1,00 ml of a 1% liquor of the sodium salt of 1, 2-naphthoquinone-4-sulfonic acid, add 1,00 ml 0,05 M NaOH liquor, mixing. The resulting reaction mix was heated for 5 min in a water-bath at 65 °C, cooled and adjusted with purified water to the line. Optical density was measured at compensation solution background, not containing the test substance, at 470 nm. The definition with 1, 00 ml aminalon standard liquor was parallel conducted. Standard aminalon liquor (0, 1%) was prepared by the sample weight resolving in purified water. Reagent liquor (1%) was prepared by dissolving the sample weight in purified water.

2.2 Aminalon definition in drug dosage forms

By aminalon quantitative determination exact sample weight of the chopped tablet (0, 0358-0, 0666 g) or capsula (0, 0167-0, 0310 g) weight was placed in a measuring bottle with 25, 00 ml volume and adjusted to the mark of purified water. Obtained liquor was filtered, discarding the first portion of the filtrate and subsequent 1, 00 ml was selected and analyzed by the general technology of quantitative aminalon determination. Content calculation of active substance in one tablet or capsula, was carried by standard method with the standard formulas [6].

3. Results and Discussion

On the results of the analytical reactions various factors are influenced, so the objective selection of the optimal conditions of quantitative spectral analysis can be performed only after preliminary studies. When choosing a solvent, were taken into account, first of all the solubility of the analyte, the reagent and the maximum values of the optical densities of the liquors. It was experimentally set, that the reagent reacts with aminalon in an aquatic sphere forming a colored compound with a maximum absorption at 470 nm. The effect of the quantitative added reagent on the optical density is shown in Fig. 1. Besides, it was set that the creation of alkaline condition, followed by heating the reaction mixture increases the optical density value. Optimal amount of 0, 05 M NaOH liquor (Fig. 1), time (Fig. 2) and heating temperature (Fig. 2) were established experimentally, according to the maximum optical density.

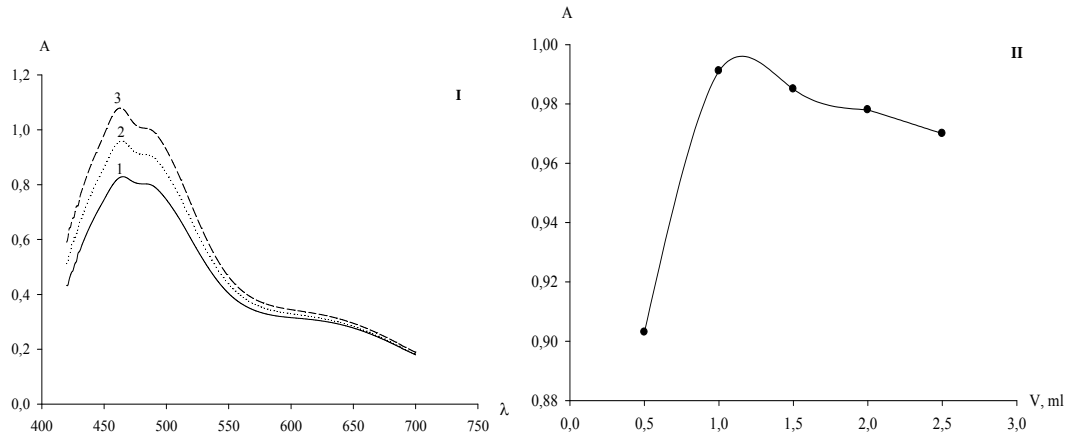

Fig 1: I-optical density depending on the quantity of 1% sodium salt liquor of 1, 2-naphthoquinone-4-sulfonic acid (1–0, 50 ml of reagent, 2 – 2, 00 ml, 3–1, 00 ml); II–on the quantity 0, 05 M NaOH liquor.

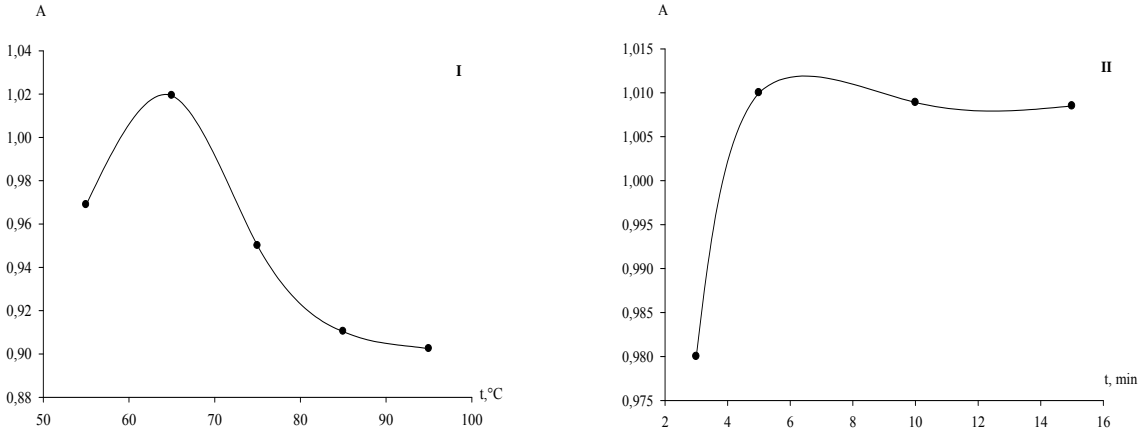

Fig 2: I-optical density depending of the reaction mixture heating temperature; II-on the heating time at 95 °C.

So, the coloring intensity of the reaction products of the sodium salt of 1, 2-naphthoquinone-4-sulfonic acid with aminalon depends on the volume, of 0, 05 M NaOH liquor, on the temperature and heating time.

In optimal conditions, Beer's law subjugation within concentrations 2, 80-5, 20 mg/100 ml. Defined minimum calculated by common method [6], is 1, 59 mcg/ml.

Experimentally determined aminalon optimal reaction conditions with the sodium salt of 1, 2-naphthoquinone-4-sulfonic acid as the basis for the development of spectrophotometric methods for aminalon quantitative determination in the drug dosage forms.

3.1 Determination of some validation characteristics

State Pharmacopoeia of Ukraine (SPU) establishes the need to hold validation procedures of the techniques, included in analytical normative documents. Such validation basic

features, as linearity, precision, accuracy and robustness for the developed techniques were determined according to a standardized validation method of standard procedures [7].

i. Linearity

The resulting dependence (Fig. 3) describes the linear regression equation y=0,1978x+0,0124, the correlation coefficient *r* and the residual standard deviation *Sr*, calculated by the method of the minimal squares, are respectively 0,9997 and 0,4420.

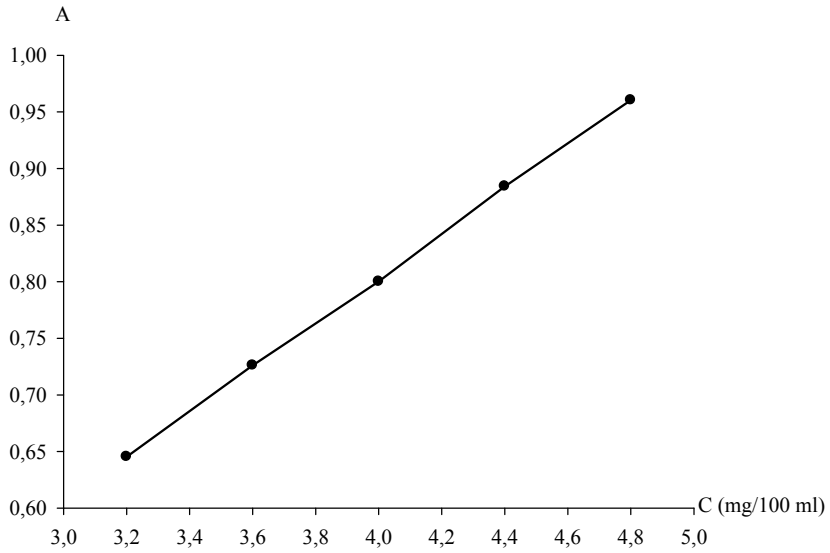

Fig 3: Graph of optical density from the aminalon concentration.

ii. Precision

Precision was determined at convergency level. To this for each of drug dosage forms were conducted on nine determinations covering a range of application techniques (three concentrations/three determinations for each). According to SPU technique is accurate at the convergency level if the relative confidence interval (Δ_x) is not more than the maximum relative uncertainty of the quantitative results determination (%). Based on the data, shown in Table 1, the technique is accurate.

Table 1: Definition of convergency results of the aminalon drug dosage forms quantitative determination.

Drug dosage form	$\overline{X}$ (n=9)	S	RSD%	Δ_x	%
Capsules «Aminalon- KV», 0,25 г (PJSC «Kiev vitamin factory», Ukraine)	0,249	$1{,}20 \cdot 10^{-3}$	0,483	0,898	3,20
«Aminalon» pills , 0,25 г (PJSC «Vitamins», Ukraine)	0,250	$2{,}82 \cdot 10^{-3}$	1,12	2,09	3,20

iii. Accuracy

Accuracy was set for 2 drug dosage forms by the addition method (Table 2). The results of the determinations are correct, if there is no meaningful systematic mistake, i.e. the true value of the determined amount is getting in a setting confidence interval ($\Delta\overline{Z}$).

Table 2: Accuracy definition of aminalon quantitative determination results in drug dosage forms.

Drug dosage form	$\overline{Z}$ (n=9)	RSD%	$\Delta\overline{Z}$	$\overline{Z}-100$
«Aminalon- KV» capsules, 0,25 г (PJSC «Kiev vitamin factory», Ukraine)	99,96	0,376	0,235	0,040
«Aminalon» pills , 0,25 г (PJSC «Vitamins», Ukraine)	99,78	0,488	0,305	0,223

iv. Robustness

Robustness valuation was performed on development techniques stage. It was set, that the tested colored liquors are stable for at least 60 min, fluctuation amounts of the added reagents within ± 10-20% and changing the heating time does not affect the optical density value that allows to obtain reliable analysis results even with small changes in the parameters techniques.

4. Conclusions

It was set that aminalon reacts with the sodium salt of 1, 2-naphthoquinone-4-sulfonic acid in in the aquatic environment presence of 0, 05 M NaOH liquor (1, 00 ml) by heating the reaction mixture at 65 °C (5 min). Studied reaction is highly sensitive, identification limit is 1, 59 mcg/ml.

Developed sensible, the economic technique of aminalon analysis in 2 modern drug dosage forms.

It was proved that the developed technique for quantitative determination, according to validated characteristics as linearity, precision, accuracy and robustness are valid, diggers is simple execution, not toxicity, availability, and may be recommended for drug dosage forms quality control.

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