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The influence of the non ionic surfactant solutions on the protolytic properties of aliphatic amines

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The decrease of pK_a^{app}-value of aliphatic amines in the water-micellar solutions of the non-ionic surfactant was shown. The phenomenon is explained by the progress of the solubilization processes and the change of the substrate microsurroundings polarity from the water high-polar to the less polar one in the micelles. The absolute pK-shift of the amines under the effect of the non-ionic surfactant OP-7 in experimental conditions reaches 3 units for dodecylamine. The differentiating influence of the non-ionic surfactant micellar solutions on the protolytic properties of aliphatic amines depending on the carbon atoms number in the hydrocarbon chain was established. At that, the regulations of the pK_a^{app}-value change are different for the hydrophilic, moderately hydrophobic and high hydrophobic amines. The predominant influence of the substrate concentration on the protolytic properties of amines in comparison with the non-ionic surfactant concentration was shown. The procedures for amines determination in their mixtures and thiamine hydrochloride determination in "Vitamin B_1" ampoule preparations by pH-metric titration were suggested.

Keywords: *pK · amines · non-ionic surfactants · protolytic properties*

Surfactants influence on the whole complex of chemical properties of substrates in the water solutions owing to the solubilization [1–3]. At that the protolytic properties change is the characteristic and peculiar indicator for the estimation of such modification for acidic or basic substrates. There are many data concerning the influence of the self-assembled systems on the protolytic properties of reagents in the micellar solutions. These data are practically significant in analytical and biological chemistry, pharmaceutics etc. Generally, reagents of acidic nature are the traditional objects for study of surfactants influence on the protolytic properties of the substrates [1]. Thus the protolytic properties of fatty acids solubilized in different types of micelles, cationic, anionic and nonionic, have been investigated experimentally and theoretically [4]. The experimentally observed apparent pK_a value (pK_a^{app}) changes from 7,6 to 4,9 when solubilizing lauric acid in sodium dodecylsulphate (SDS) and cationic micelles, respectively. For the nonionic micelle it is found to be approximately 6,6 [4]. Also the dissociation equilibria of substituted benzoic acids in cationic and anionic micellar systems, investigated by potentiometric titration, show pK shifts of less than 1.0 in cationic and 0.5–3 in anionic micelles [5]. Stepwise dissociation and tautomerism of 2,4,5,7-tetranitrofluorescein were studied by using vis-spectroscopy in cetyltrimethylammonium chloride micellar solutions and compared with pK_a values in dimethylsulfoxide and aqueous acetone [6]. The variations of the acidity constants in the presence of sodium dodecylsulphate were used to estimate the binding constants of a series of methyl-substituted phenols with the SDS micelles [7]. The acidity constants of halophenols, sulphonamides, sulfophthaleinic indicators and benzimidazole have been also determined in the different types of self-assembled micellar media [8–12].

From another hand there are not much data concerning protolytic properties of organic bases in the water-micellar solutions. The pK_a^{app}-values of some amines (Am) in the solutions of ionic and non-ionic surfactants are cited in [13].

Generally, the pK value shift in the self-assembled media is determined by two main factors – solubilization and ionic association processes [1]. Solubilization changes the substrates' microsurroundings polarity from the water high-polar to the less polar one in the micelles. Solubilization ability in the micellar systems depends on the substrate hydrophobicity. With this, the solubilization efficacy increases with the increase of general hydrophobicity of the substrate. So the maximal pK shift is observed for high-hydrophobic substrates. Solubilization factor is predominant for non-ionic surfactant solutions [1–3]. From another hand, changes of dissociation constants of acidic reagents are caused by the formation of ionic associates with cationic surfactants [1–3]. For basic reagents, the formation of ionic associates with

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anionic surfactants is typical. The influence of ionic association on the protolytic properties is the predominant factor for ionic surfactant solutions and their mixtures with non-ionic surfactants.

The distinctive feature of the surfactant based self-assembled media is their differentiating influence on the protolytic properties of substrates [2]. Traditionally the differentiating effect is the unequal pK-value change of the protolytes at the substitution from one solvent to another. As a result, acids and bases, which have similar protolytic properties in a standard solvent, become different in another one. In most cases, water is a standard medium [14]. The differentiating influence of micellar and emulsion systems on the protolytic properties of carboxylic acids was partly studied in [15,16]. This differentiating influence is based on the different solubilization ability of substrates depending on their hydrophobicity.

As mentioned above, the influence of micellar media on the protolytic properties of organic bases is studied to a smaller extent and the literature data concerning this problem is poor and not systematized. At the same time, organic amines are the classical analytical reagents [17]. They are widely used in liquid–liquid extraction for preconcentrating and determination of acids, bulky organic and inorganic anions and for the separation of metals [17]. The biologically active derivatives of amines are used in pharmaceutical practice. The hydrophobicity of aliphatic amines is determined by the hydrocarbon chain length. So they are convenient objects for the investigation of the differentiating influence of micellar media on the protolytic properties of basic substrates.

The aim of the work was to investigate the protolytic properties of amines in non-ionic surfactant (NS) micellar media and the tracing of the differentiating effect of self-assembled media on the protolytic properties of basic substrates.

Experimental

Measurements of pK_a^{app} of amines in micellar solutions

$$R-NH_3 \Leftrightarrow R-NH_2 + H^+$$

$$K_a = \frac{[R-NH_2]\cdot[H^+]}{[R-NH^+_3]}$$

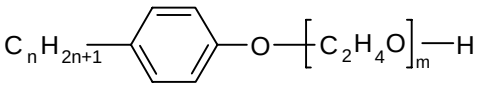
The apparent pK_a value (pK_a^{app}) is the most convenient parameter for the description of the substrate protolytic properties in the surfactant solutions [1]. The difference between pK_a-value of the amine in the water and pK_a^{app} in the micellar solution is the pK shift ($\Delta pK = pK_a - pK_a^{app}$).

For the pK_a^{app}-value measurements water-micellar solutions of amines were titrated using pH-meter. On the basis of titration data the pK_a^{app} of amines have been calculated using the "Hyperquad" program.

Acidity of the solutions during titration was controlled with pH-meter pH 340 using the glass lithium electrode ESL 43 07.

Reagents

Polyoxyethylated alkylphenol OP-7 (Zavod tonkogo organicheskogo sinteza "Barva", Ivano-Frankovsk, Ukraine; purity > 98%) was used throughout the work. The OP 7 initial solutions were prepared by dissolving the exact mass of the substance in distilled water.



OP-7, n = 8–10, m = 6–9

Primary aliphatic amines (Merck) of a general formula $C_nH_{2n+1}NH_2$ were used in the work. These amines were the commercial samples of 99,0% (for n=5–12) and 99,5% (n=4) purity. The long-chain amines were additionally purified by the boiling with the backflow condenser at the presence of solid KOH during 3 hours; then amines were distilled at a normal pressure on a Vigre column.

Solutions of the amines were prepared by dissolving of the weighed portions in the non-ionic surfactant solutions. The amines content in the solutions was controlled by pH-metric titration with HCl.

Results and discussion

Protolytic properties of aliphatic amines in non-ionic surfactant solutions

The hydrocarbon chain length of aliphatic amines has a little influence on the pK_a-value in the water solutions. Thus, the pK_a-value of methylamine is 10.62 for water and 10.67 units for ethylamine. The pK_a-values for amines with $n \geq 4$ are close to 10.64 units [18].

It was established, that in the non-ionic surfactant solutions the pK_a-values of amines change in compare with water solutions. As a result of solubilization processes in the micellar solutions, the pK_a^{app}-value of amines decreases (Fig. 1a).

The weakening of the substrates protolytic properties in organic solvents is traditionally explained by the decrease of polarity of the media [14].

In the micellar solutions the decrease of polarity of the substrates microsurroundings results due to the solubilization. At that, the state of acid-base equilibriums in the micellar solutions is conditioned by the different efficacy of solubilization of different substrate forms. It is logical that the best solubilization is characteristic for

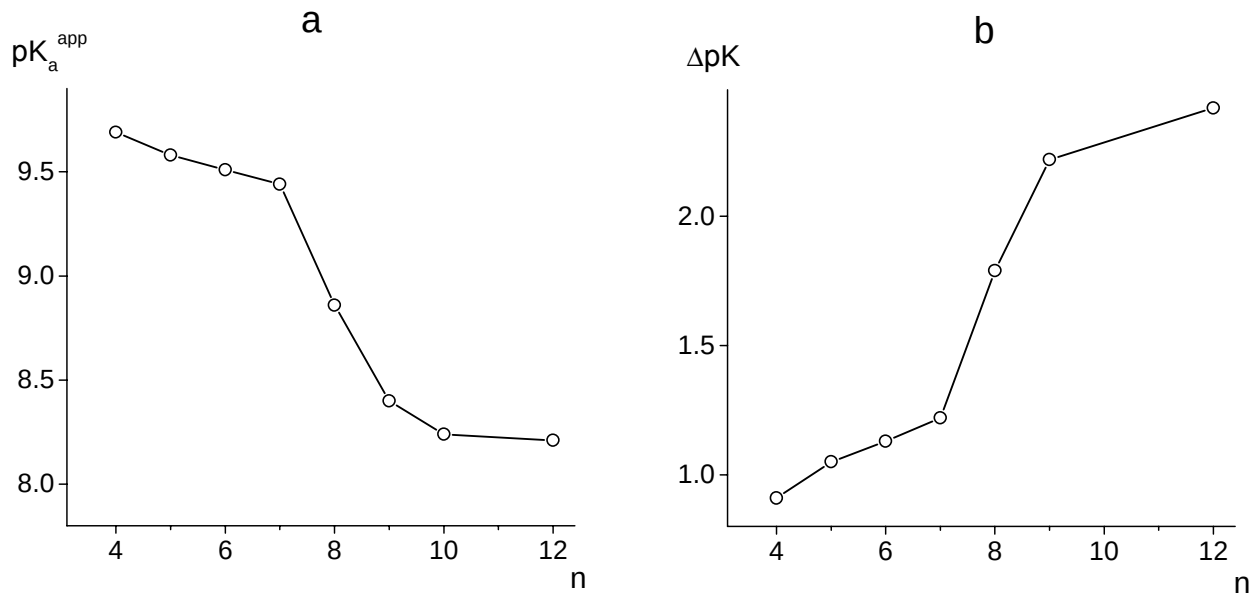
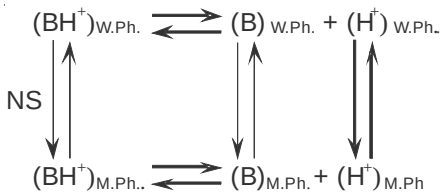


Fig. 1. The dependence of pK$_a^{app}$ (*a*) and ΔpK-values (*b*) of aliphatic amines in the non-ionic surfactant solution via the carbon atoms number in the hydrocarbon chain of amines. C_{Am}=0.01M, C_{NS} = 2% (w/v).

the electroneutral hydrophobic molecular forms of amines. From another hand, the increase of the amines hydrophilicity (protonation of aminogroup) decreases the effectiveness of their solubilization. So, the processes in the micellar solutions could be presented as following:



The differentiating influence of the non-ionic surfactant media on the pK$_a^{app}$ value of aliphatic amines

In contrast to the water solutions, the pK$_a^{app}$-value of amines in the micellar solutions of the non-ionic surfactant gradually decreases with the increase of the hydrocarbon chain length. With that, the dependence ΔpK= f(n) for investigated amines is characterized by three linear sections with different slopes (Fig.1b). At that, the slope (tgα) for every part of the line is the increment of a methylene group of amines into the ΔpK-value. Such character of this dependence allows sorting of the studied amines on three groups. The first group includes soluble in water hydrophilic amines with n= 4–7. The tgα-value for this group of amines is 0.10±0.01 units. The smallness of ΔpK-value for hydrophilic amines is explained by the weakness of solubilization in the system. So, the primary localization of these substrates in the micellar solutions is the water phase.

The second group consist of amines of the intermediate hydrophobicity with n=7–9. The tgα-value of the ΔpK= f(n) dependence for n=7–9 increases four times and reaches 0.50±0.04 units. The increase of hydrophobicity of these amines increases the effectiveness of their solubilization. Amines of this group are distributed between the water and the micelles.

The highly hydrophobic amines with n=9–12 are referred to the third group. The pK-shift for these substrates is maximal. At that, the tgα value for this group of amines is the lowest and takes a value of 0.07 units. Amines of the third group localize mostly in the less polar micelles of the non-ionic surfactant. The further increase of the carbon chain length has a little influence on the interphase distribution of substrates. So, the ΔpK-value takes on a maximal constant value.

The revealed differentiating influence of the non-ionic surfactant solutions on the protolytic properties of amines is in accordance with the literature data. Analogical tendencies were obtained in the earlier investigations of the micellar and emulsion media influence on the protonodonor properties of aliphatic carboxylic acids [15].

The influence of the non-ionic surfactant concentration on the pK$_a^{app}$-value of aliphatic amines

Hexyl- and oktylamine were used for the study of the influence of the non-ionic surfactant and substrate concentrations on the pK$_a^{app}$-value.

The decrease of amines pK$_a^{app}$–value with the increase of NS concentration in the solution was shown. This can be explained by the increase of the portion of solubi-

lized amine (Fig. 2). Such tendency of the pK_a^{app}-value change with an increase of the NS concentration was observed in the systems with the different substrate concentration (Fig. 2, curves 1–3). However, at C_{NS}=3% the dependence $pK_a^{app}=f(C_{NS})$ changes its character. The obtained pK_a^{app}-values of hexylamine somewhat increase in the NS concentration interval 3–4%. This can be explained by the structural reorganization of micelles and the corresponding change of the hydration of the micelles. Such reorganization in the micellar solutions appears at the use of the non-ionic surfactant OP 7 in other methods too.

It was shown, that with the substrate concentration decrease the pK_a^{app}-value of hexylamine also decreases in the whole OP-7 concentration range (Fig. 2). At that, the pK-shift is maximal at the minimal hexylamine content. This corresponds to the conditions when the surfactant : substrate ratio is maximal.

Analogously to hexylamin, the pK_a^{app}-value of oktylamine decreases with the increase of the non-ionic surfactant concentration in the system. The pattern of the $pK_a^{app}=f(C_{NS})$ dependences change with the variation of oktylamine content is just the same as for the less hydrophobic hexylamin.

The influence of substrate concentration on the pK_a^{app}-value of aliphatic amines

It was established that the increase of hexylamine concentration from 0.005 M to 0.02 M leads to the pK_a^{app}-value augment by 1.1 units (Fig. 3). This effect can be explained by the change of the substrate localization. When the amine content is small, it is located in the less polar micelles mainly. With that, the amino group is isolated from the water and the pK_a^{app}-value is minimal. With the hexylamine concentration increase, and the system solubilization capacity exceed, the possible location of the substrate is the more polar and hydrated polyoxyethylized micellar surface. As a result, the pK_a^{app} value increases.

Noteworthy the dependences $pK_a^{app}=f(C_{Am})$ are linear (Fig. 3). On the basis of these dependences the coefficients of the corresponding linear regressions were calculated (Table 1). At that, established coefficient "b" characterizes the "sensitivity" of the pK_a^{app}-value to the substrate concentration change. Interestingly, the maximal value of coefficient "b" for hexylamine is observed at C_{NS}=3%. So, the structural reorganization of micelles at C_{NS}=3% was confirmed once again.

All the marked tendencies and peculiarities of the substrate concentration influence on the pK_a^{app}-value are also similar for oktylamine.

The influence of the total concentration conditions in the system on the pK_a^{app} values of amines

One of the primary factors which determines the acid-basic properties of the protolytes in the water-organic solvents is the polarity of the media. With that, the substrate concentration influence on the pK-value is of a smaller importance. On the contrary, in the water-micellar systems studied the pK_a^{app}-values of aliphatic amines depend on their hydrophobicity, substrate and

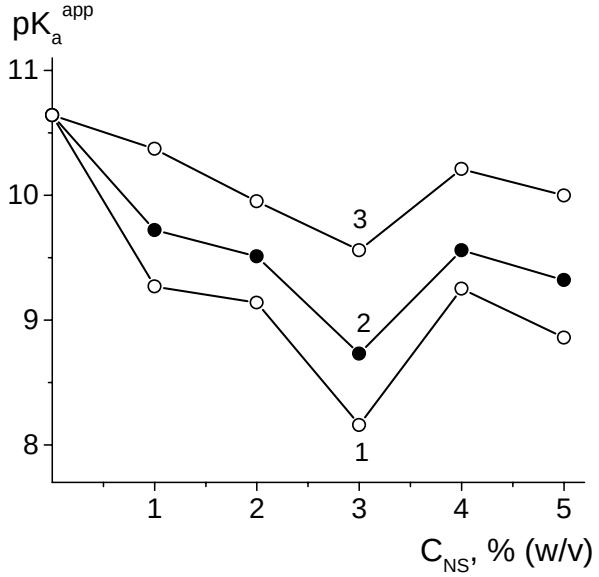


Fig. 2. The dependences of the pK_a^{app}–value of hexylamine via the non-ionic surfactant concentration in the solution. C_{Am}=0,005 M (1); 0,01 M (2); 0,02 M (3)

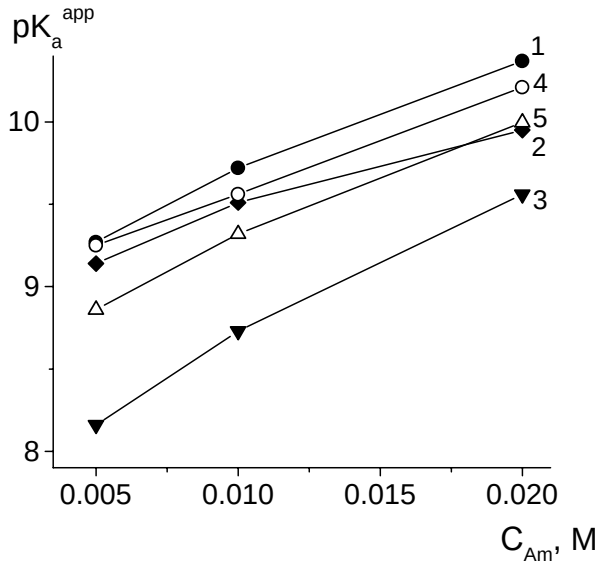


Fig. 3. The dependences of the pK_a^{app}-value of hexylamine via its concentration in the non-ionic surfactant solution. C_{NS} = 1% (1), 2% (2), 3% (3), 4% (4), 5% (5) (w/v)

Table 1. The coefficients of the linear regressions $pK_a^{app} = f(C_{Am})$ for hexylamine and oktylamine at different non-ionic surfactant concentrations

Amine	C_{NS}, %	a; S_a	b; S_b	R
Hexylamine	1.0	8.9; 0.1	72; 6	0.99
	2.0	8.9; 0.1	53; 7	–"–
	3.0	7.8; 0.1	92; 8	–"–
	4.0	9.1; 0.1	53; 11	–"–
	5.0	8.5; 0.1	75; 6	–"–
Oktylamine	1.0	8.8; 0.4	62; 28	0.91
	2.0	8.1; 0.1	68; 10	0.99
	3.0	7.9; 0.2	98; 12	–"–
	4.0	8.2; 0.1	70; 2	–"–
	5.0	7.9; 0.2	47; 13	0.96

non-ionic surfactant concentrations. With that, at a correct comparison of concentration factors it was unexpectedly found that the substrate concentration influence is predominant. This conclusion was obtained when the statistical parameters of the gotten multiple regressions $pK_a^{app} = 1,9 + 68,4 \cdot C_{Am} + 0,2 \cdot C_{NS}$ were compared.

In the discussions of the micellar media influence on the protolytic properties of substrates it is generally accepted that the influence of the solubilizer concentration is dominating. At the same time, the influence of the substrate concentration is of a smaller importance and is often not investigated at all.

The data obtained point out the inexpediency of the discussion of solubilization processes within the classical model of the interphase distribution only. The consideration of the specific chemical interactions between the substrates and the NS micelles is also required.

Thus, the decrease of pK_a^{app}-value of aliphatic amines in the water-micellar solutions of the non-ionic surfactant was shown. The phenomenon is explained by the progress of the solubilization processes and the change of the substrate microsurroundings polarity from the water high-polar to the less polar one in the micelles. The differentiating influence of the non-ionic surfactant micellar solutions on the protolytic properties of aliphatic amines depending on the carbon atoms number in the hydrocarbon chain was established. At that, the regulations of the pK_a^{app}-value change are different for the hydrophilic, moderately hydrophobic and highly hydrophobic amines. The correlation of the pK_a^{app}-value changes of amines with the structural reorganization in the micellar solutions was shown. The increase of pK_a^{app}-value for hexyl- and oktylamine with the increase of their concentration was revealed. The predominant influence of the substrate concentration on the protolytic properties of amines in comparison with the non-ionic surfactant concentration was shown.

Determination of aliphatic amines in mixtures in the water solution is impossible because of the closeness of their pK_a-values. The studied differentiating influence of the non-ionic surfactant solutions on the protolytic properties of aliphatic amines gives the opportunity to de-

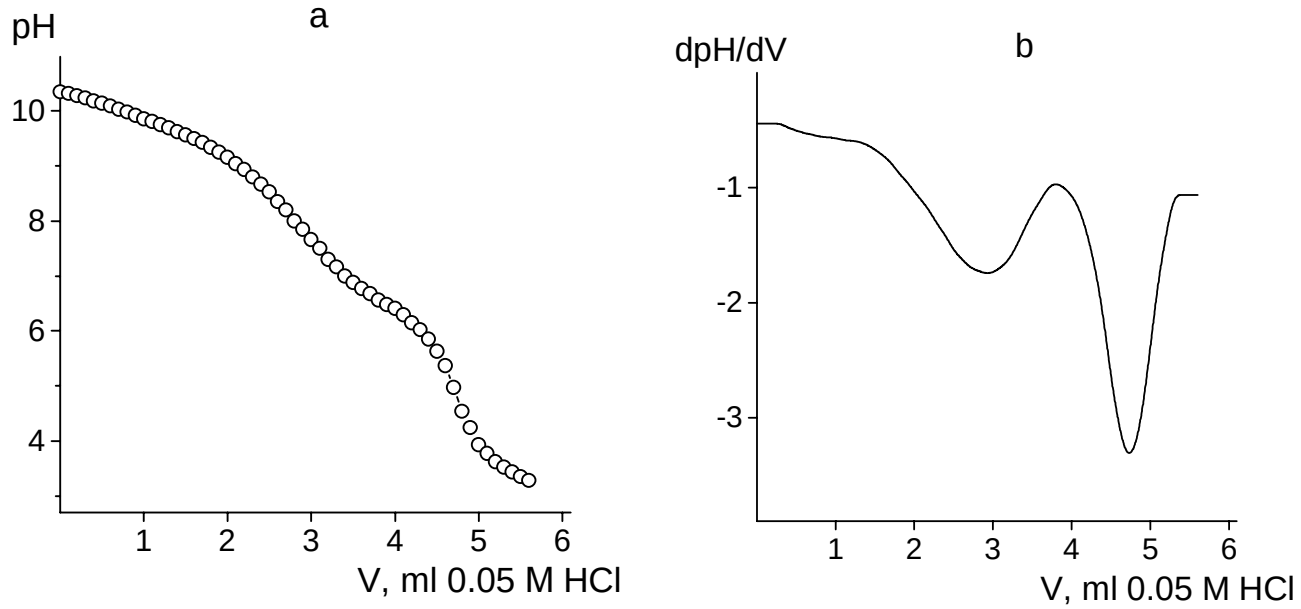


Fig. 4. The curve of pH-metric titration of amylamine and dodecylamine mixture in 2% OP-7 solution (a) and the corresponding differential curve (b). V_0=25 ml; C_{Am}=0.01 M

Table 2. The results of pH-metric determination of amines in their mixture in 2% OP-7 solution (n=4, P=0,95)

Amine	Added, mg	Found, mg
Amylamine	8.0	8.2 ± 0.3
Dodecylamine	26.4	26.6 ± 0.4

termine the content of individual amines in their mixtures. Thus, the curve of pH-metric titration of amyl- and dodecylamine mixture is characterized by two inflections (Fig. 4). And the corresponding differential curve has two clear minimums. The first one corresponds to amylamine content and the second one corresponds to dodecylamine content.

On the basis of data obtained the procedure for amines separate pH metric determination in their mixtures in OP-7 water-micellar solution was proposed.

The procedure. The sample (25–50 mg) of the amylamine and dodecylamine mixture was dissolved in 2% nonionic surfactant OP-7 solution. The titration was performed with standard HCl solution and the equivalent points were determined from the minimums on the differential curve.

The results of pH-metric determination of amines content in their mixture in 2% nonionic surfactant solution are presented in table 2. Acceptable metrological performance was obtained at analysis of amylamine and dodecylamine mixtures at their molar ratio from 1:3 to 3:1. But when the molar ratio of amines reaches 1:5 or 5:1 the reliable determination of substrates is impossible.

The thiamine hydrochloride is widely used in the medical practice. It is the basic substrate of the pharmaceutical preparation "Vitamin B_1". According to the British Pharmacopoeia, thiamine hydrochloride identification is performed chromatographically or by test-methods with dyes [19]. According to the International and Ukrainian Pharmacopeias determination of thiamine hydrochloride is performed by titration with perchloric acid in the glacial acetic acid medium at the presence of mercury acetate [20, 21]. Such hard conditions for thiamine hydrochloride determination by the standard method show the appropriateness of the use of surfactants micellar media for drug analysis.

The procedure for thiamine hydrochloride determination. The content of ampoule with thiamine hydrochloride was dissolved in 25 ml 2% OP-7 solution and the pH-metric titration with 0.010 M KOH aqueous solution was performed. The equivalent point was determined as a maximum of the corresponding differential curve.

The proposed conditions for thiamine hydrochloride

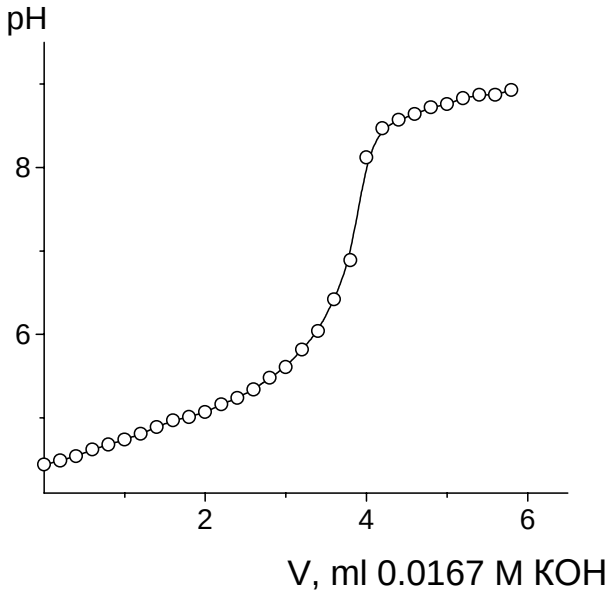


Fig.5. The curve of pH-metric titration of thiamine hydrochloride in 2% OP-7 solution. V_0=25 ml

determination were verified by the "added–measured" method at analysis of model solutions and tested for "Vitamin B_1" ampoule solutions. It was added 25 mg of thiamine hydrochloride; it was found 24.7 ± 0.4 mg (S_r=0.02, n=4, P=0.95). At analysis of "Vitamin B_1 - Darnytsa" ampoule preparation it was found 49.9 ± 0.7 mg (S_r=0.02, n=4, P=0.95) of thiamine hydrochloride (50 mg of the substrate content was declared by the manufacturer).

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