Journal of Organic and Pharmaceutical Chemistry

Review article

OPEN ACCESS
Freely available online on
http://ophcj.nuph.edu.ua

UDC 577.15:5615.2:547.2333.4

M. Ye. Blazheyevskiy[1], E. Bulska[2], A. M. Tupys[2], O. V. Kovalska[1]

[1] National University of Pharmacy of the Ministry of Health of Ukraine,
53, Pushkinska str., Kharkiv, 61002, Ukraine
[2] Biological and Chemical Research Centre, Faculty of Chemistry, University of Warsaw,
101, Zwirki i Wigury, Warsaw, 02-089, Poland

Titrimetric Methods for Determining Cationic Surfactants

Abstract

Aim. To generalize and systematize information on titrimetric methods for determining quaternary ammonium compounds (QACs).

Results and discussion. The review summarizes and systematizes information on the properties of surfactants, provides their classification, shows the main ways of use in the national economy, and their role in pharmacy and medicine. Currently known titrimetric methods for determining cationic surfactants, in particular quaternary ammonium compounds, which are widely used in medicine and pharmacy, are described and summarized.

Conclusions. As a result of the study, the main directions of developing methods for determining QACs by titrimetry methods have been summarized; the disadvantages and advantages of each of the methods described have been shown. In the future, it can be the basis for developing new and more effective methods of analysis.

Keywords: surfactants; quaternary ammonium compounds; titrimetric methods of analysis

М. Є. Блажеєвський[1], Є. Бульська[2], А. М. Тупис[2], О. В. Ковальська[2]

[1] Національний фармацевтичний університет Міністерства охорони здоров'я України,
вул. Пушкінська, 53, м. Харків, 61002, Україна
[2] Варшавський Університет, Центр біологічно-хімічних наук,
вул. Звіркі Вігурі, 101, м. Варшава, 02089, Польща

Титриметричні методи визначення катіонних поверхнево-активних речовин

Анотація

Мета. Узагальнити та систематизувати інформацію про титриметричні методи визначення четвертинних амонійних сполук (ЧАС).

Результати та їх обговорення. В огляді узагальнено й систематизовано інформацію про властивості поверхнево-активних речовин, наведено їх класифікацію, окреслено основні шляхи використання в народному господарстві та їх роль у фармації і медицині. Описано й узагальнено відомі нині титриметричні методи визначення катіонних поверхнево-активних речовин, зокрема ЧАС, що їх широко застосовують у медицині та фармації.

Висновки. У результаті проведеного дослідження окреслено основні напрями опрацювання методик визначення четвертинних амонійних сполук методами титриметрії, розглянуто недоліки й переваги кожного з описаних методів, що в подальшому може стати основою для опрацювання нових, більш ефективних способів проведення аналізу.

Ключові слова: поверхнево-активні речовини; четвертинні амонієві сполуки; титриметричні методи аналізу

Citation: Blazheyevskiy, M. Ye.; Bulska, E.; Tupys, A. M.; Kovalska, O. V. Titrimetric methods for determining cationic surfactants. *Journal of Organic and Pharmaceutical Chemistry* **2022**, *20* (3), 12–24.
https://doi.org/10.24959/ophcj.22.258547
Received: *28 June 2022*; **Revised:** *20 September 2022*; **Accepted:** *22 September 2022*

Funding: The work is a part of the research of the National University of Pharmacy on the topic "Organic synthesis and analysis of biologically active compounds, drug development based on synthetic substances" (the state registration No. 01144000943; the research period 2019–2024).
Conflict of interests: The authors have no conflict of interests to declare.

ISSN 2308-8303 (Print) / 2518-1548 (Online)

Introduction

Surfactants (a contraction of surface-active agent, devised in 1950) have found application in almost every branch of chemical industry. They play an important role as cleaning, wetting, dispersing, emulsifying, foaming and anti-foaming agents in many products, including detergents, fabric softeners, motor oils, emulsions, soaps, paints, adhesives, inks, anti-fogs, ski waxes, snowboard wax, deinking of recycled papers, in flotation, washing and enzymatic processes, and as laxatives [1]. Personal care products, such as cosmetics, shampoos, shower gels, hair conditioners, and toothpastes, also contain them. Alkali surfactant polymers act to displace dirt and debris using detergents when washing wounds [2] and *via* the application of medicinal lotions and sprays to the surface of the skin and mucous membranes [3]. Therefore, many efforts are being made to understand the physical and analytical chemistry of surface-active agents.

The main property of surfactants that determines how they are used is to reduce the surface tension (or interfacial tension) between two liquids, between a gas and a liquid, or between a liquid and a solid [4]. From the structural point of view surfactants are amphiphilic molecules consisting of a non-polar hydrophobic "water-avoiding" group (the tail), usually a straight or branched hydrocarbon or fluorocarbon chain containing 8–18 carbon atoms attached to a polar or ionic hydrophilic "water-seeking" group (the head) [5]. The water-insoluble hydrophobic group may extend out of the bulk water phase, into the air or into the oil phase, while the water-soluble head group remains in the water phase.

Most commonly, surfactants are classified according to the polar head group into four classes, i.e., non-ionic, cationic, anionic, and zwitterionic/amphoteric surfactants [6]. A non-ionic surfactant has no charged groups in its head. The head of an ionic surfactant carries a full positive, or a full negative charge. If the charge is negative, the surfactant is called anionic; if the charge is positive, it is called cationic. In case a surfactant contains the head with two oppositely charged groups, it is termed zwitterionic (Figure 1).

We would like to note right away that this review will focus specifically on the analytical aspects of cationic surfactants (CS), and the main reason is their high impact on the chemical industry and involvement in almost all spheres of human life. CS first became important more than 70 years ago when their unique bactericidal properties were reported [7, 8]. To quote Anna Gillis: "In the industry they are considered the ultimate workhorses. They decolorize sugar, kill bacteria growing in waterbeds, and help to pull the last driblets of oil from drilling wells. They serve as ingredients in products ranging from underarm deodorants to fiberglass for sail boats. Mostly, they're used to keep the laundry soft. These jacks-of-all-trades are quaternary ammonium compounds, or quats." [9]. CS have the capacity of self-assembling [8], being widely used in biotechnology [11, 12]. They play an important role in biotechnological applications, determining the huge potential of cationic amphiphilic agents as drug carriers in pharmacy and biomedicine [13]. Occurrence of positively charged fragments in an amphiphilic scaffold is responsible for their attractiveness in nanotechnological applications as antimicrobial and bioimaging agents [14, 15],

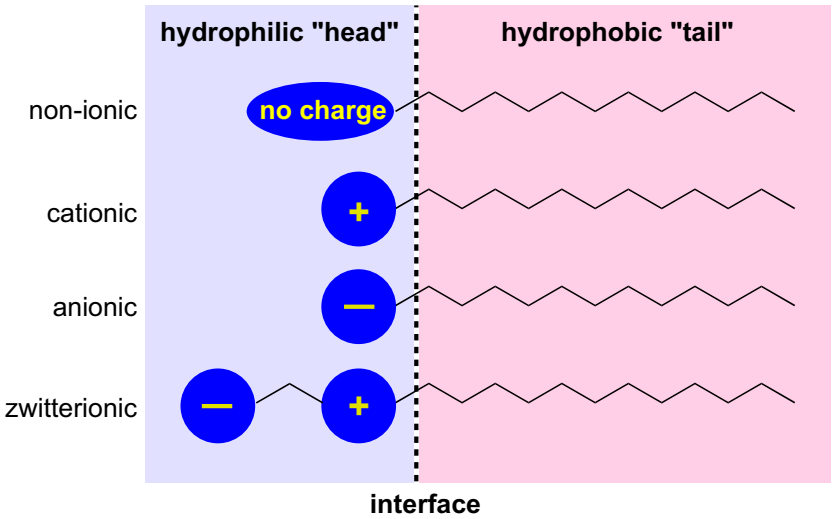


Figure 1. Classes of surfactants

corrosion inhibitors [16], supramolecular catalysts [17], stabilizers of nanoparticles and nanocarriers [18, 19], and especially as drug and gene nanocarriers [20]. Cationic head groups of surfactants provide their high affnity toward biopolyanions, such as DNA [21, 22], cell membranes, and intracellular organelles, such as mitochondrion, thereby initiating the development of a promising area of therapy, the so-called mitochondrion medicine [23, 24]. A series of works focusing on the application of CS in drug delivery have been recently reviewed [25, 26], with the emphasis given to their use for gene therapy [27, 28], as a template for the synthesis of mesoporous materials [29], as well as to their biocidal action against bacteria and fungi [30, 31].

The positive charge within CS is almost invariably centered around one or more nitrogen atoms. Although corresponding analogs containing sulfur, phosphorus, or arsenic have been found, they are considerably more expensive than their nitrogenous counterparts. Hence, they have not found a practical application. Some the most common substances of this class are given in Figure 2.

The charge of CS may be either permanent or only exist in certain pH value ranges. Quaternary ammonium compounds (QACs) retain their cationic character at any pH. Primary, secondary, and tertiary amines can be positively charged, depending on the ambient pH value. A typical fatty primary amine has a pK_b value of approximately 3.4. Although the simple equilibrium between the free base (RNH_2) and its conjugate acid (RNH_3^+) is complicated by adsorption of both species from the solution and by the micelle formation, as a rough guide the concentration of the cationic form is equal to that of the free base at a pH value of 10.6 and greater than it at lower values. Fatty amines are therefore justifiably included as CS in their own right in addition to being intermediates in the synthesis of QACs [32].

The most important property of CS from an environmental perspective is that they are

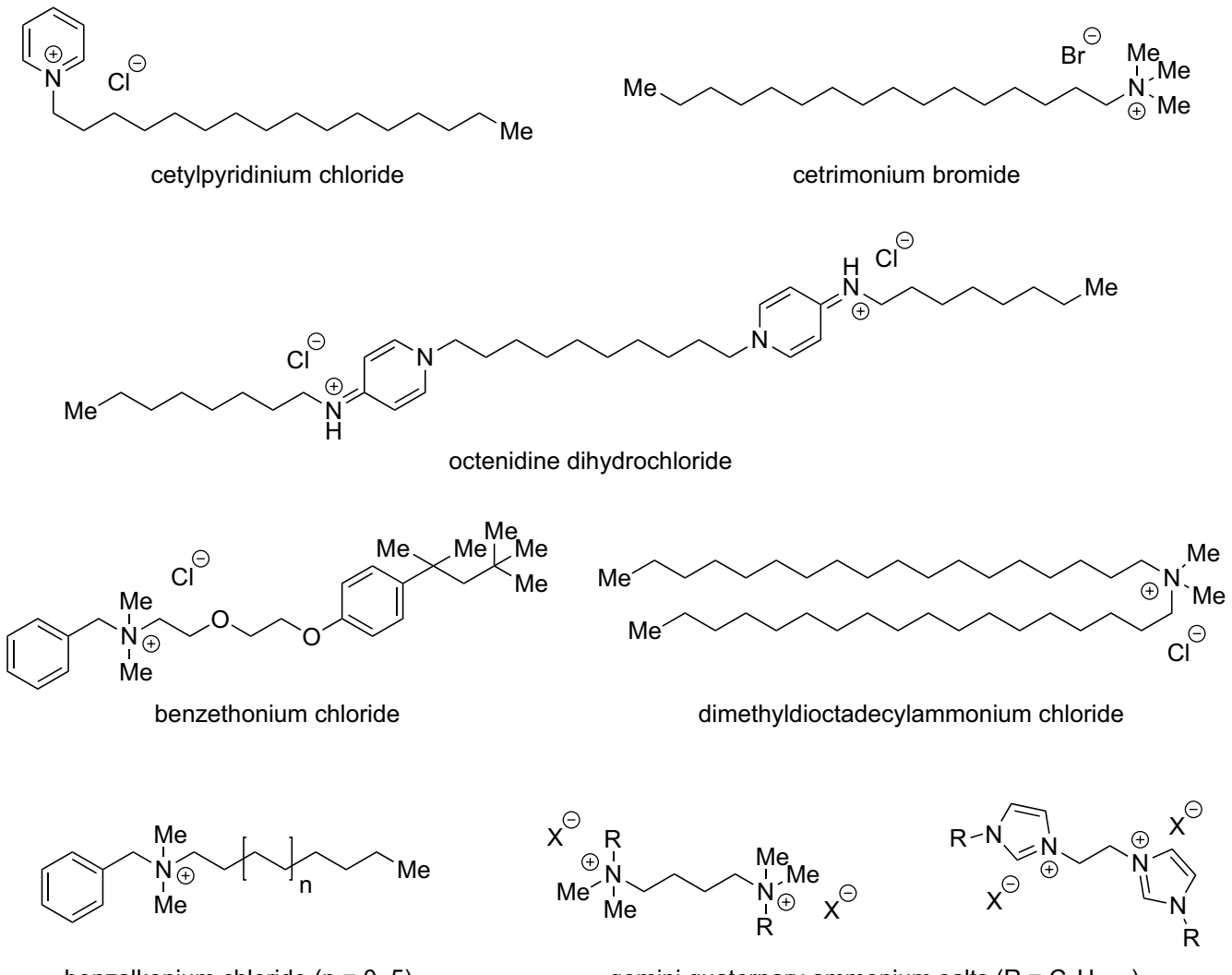


Figure 2. Examples of cationic surfactants

ISSN 2308-8303 (Print) / 2518-1548 (Online)

Table 1. The surfactant market in personal care by type in US$, Bn

	US$ billion					CAGR[a], %
	2015	2016	2018	2021	2024	
Anionics	0.48	0.49	0.52	0.57	0.61	2.7
Nonionics	1.99	2.11	2.31	2.62	2.97	4.7
Cationics	1.76	1.90	2.19	2.68	3.28	7.4
Amphoterics	1.46	1.58	1.82	2.25	2.77	7.7
Others	0.44	0.42	0.44	0.54	0.64	4.7
Total	6.13	6.49	7.29	8.65	10.27	5.9

Note: [a] CAGR (compound annual growth rate) is a business and investing specific term for the geometric progression ratio that provides a constant rate of return over the time period

strongly sorbed by a wide variety of materials, such as natural sediments and soils. Numerous studies indicate that CS are also rapidly and strongly sorbed by many other materials of environmental relevance [33, 34]. A related property of CS is that they form 1:1 complexes with anionic materials, especially anionic surfactants. The complexes are relatively hydrophobic, but largely ionic in character [35]. This leads to the fact that CS may not be detected by some analytical methods, causing a failure to demonstrate their presence in environmental samples or confusion of complexation with degradation in fate studies.

Consumption of CS was estimated to be 190,000 and 150,000 tons in 1987 in the United States and Western Europe, respectively [36] and since then it has been increasing. It is likely that most or at least a large portion of this was sewered. The available data suggest that CS are ubiquitous environmental contaminants, at least in populated areas. Table 1 demonstrates utilization of various groups of surfactants in personal care. It reveals that CS are among the most used ones, and it is confirmed by growth rates and estimated value for 2024.

Considering the huge spread of CS, their toxicity remains a serious problem that hinders their widespread practical use and raises many environmental safety concerns. Thus, the toxicity of QACs, which are antibacterial and antifungal, varies. Dialkyldimethylammonium chlorides used as fabric softeners have a low LD_{50} (5 g kg^{-1}) and are essentially non-toxic, while the disinfectant alkylbenzyldimethylammonium chloride has LD_{50} of 0.35 g kg^{-1}. Prolonged exposure to CS can irritate and damage the skin since they disrupt the lipid membrane that protects the skin and other cells. Many CS are not only potent germicides, but also acutely toxic in the milligram per liter range and lower to aquatic organisms, including algae, fish, mollusks, barnacles, rotifers, starfish, shrimp, and others [37–40]. CS have been shown to elicit acute toxic effects in aquatic organisms by disrupting gill membranes, thus interfering with O_2 exchange [41]. Benzalkonium bromide acts as an inhibitory uncoupler in mitochondria. CS are possibly toxic to higher plants [42].

Taking into account the abovementioned issues concerning enormous spread and toxicity of CS, numerous analytical methods have been developed aiming at controlling their content in various environmental objects and products of different purposes. Many of the older methods are colorimetric, in which CS react with anionic dyes; the surfactant-dye complexes are extracted into an organic solvent, and the absorbance of the solution is measured spectrophotometrically [43]. However, these methods are generally unsuitable for monitoring levels of cationics in sewage or environmental samples or for laboratory studies, in which anionic surfactants are also present, since the affinity of CS for anionic surfactants is often greater than their affinity for the dyes. Here we are going to give a brief overview of classical and new titrimetric analytical methods designed to quantify CS.

■ Results and discussion

Currently, various methods are used for the quantitative and qualitative analysis of CS in analytical chemistry, including pharmaceutical chemistry. They are titrimetry, spectrophotometry, capillary electrophoresis, chromatography, and electrochemical methods.

Direct, reverse and two-phase titration of CS

In particular, to control the composition of a CS substance and the quality of the final products at cosmetic enterprises, the following methods are used: two-phase titration [44], spectrophotometry [45] and chromatography [46]. These methods are fast, simple and allow determining the class of CS. The main disadvantages of these methods, with the exception of chromatography, are as follows: the accuracy of CS determination

depends on the presence of impurities, these methods are not selective in relation to individual representatives of CS, do not allow homologous identification, i.e. with the help of these methods it is impossible to determine the content of an individual CS in the mixture. At the same time, most often only individual identification allows to assess the scope of application, toxicity and biodegradation of CS if they are released into the environment [47].

Titrimetric methods were the first ones widely used for the CS analysis, and they still remain quite common today [48, 49]. Titration is an effective and economical method of measuring the surfactant concentration. High speed and low cost make this method particularly advantageous and suitable for use, even in field conditions.

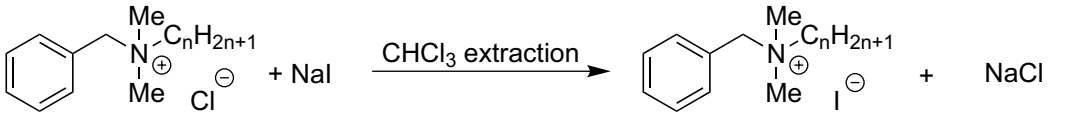
The pharmacopoeial method of analysis of QACs using an example of benzalkonium chloride as a QAC is based on the exchange reaction. A known excess of iodide is added to the sample solution, and the quaternary ammonium iodide is removed when shaking with chloroform. The excess of iodide is titrated by the iodate method. When the chloroform extraction is made from a slightly alkaline solution only quaternary ammonium compounds are measured; if it is made from a slightly acid solution, non-quaternary cationic amine impurities are also included. The difference between assay results obtained from acid and alkaline extractions represents the non-quaternary amine content (Figure 3) [50, 51].

However, the titration of QACs can be performed simpler in an aqueous solution with application of sodium dodecyl sulphate as a titrant and methyl orange or bromophenol blue as an indicator. Cetylpyridinium tetrachlorozincate is recommended as a standard to determine the titrant concentration [52].

Halogen-containing salts of QACs can be titrated in the medium of a non-aqueous solvent – glacial acetic acid, and halogen anions bound to a quaternary nitrogen atom are determined. Such methods are suitable for the analysis of pure samples that do not contain other salts, and other anions. At the same time, the choice of the titrant depends on the halide ion present in the salt (Figure 4) [53].

A more specific analysis of CS is the two-phase titration with an anionic surfactant. A number of indicator dyes, in particular bromophenol blue, methylene blue, which are often used during the analysis of anionic surfactants AS, are also suitable for the titration of cationic ones. [54]. According to Hartley and Runicle [55, 56], bromophenol blue should be used as an indicator for CS. Under these titration conditions, after adding an excess drop of the titrant, the aqueous phase of the solution becomes blue.

The method of the analysis according to *Epton* [57] (with methylene blue as an indicator) is still widely used (Figure 5). In this titration, CS is precipitated by an anionic surfactant in a biphasic mixture of water and chloroform. The ion pair formed must be extracted into chloroform with vigorous shaking. The endpoint is the point at which a purple color of the aqueous phase of the solution becomes colorless. The disadvantages



$$5I^-_{excess} + IO_3^- + 6H^+ \rightleftharpoons 3I_2 + 3H_2O$$

$$3I_2 + 2S_2O_3^{2-} \rightleftharpoons 2I^- + 2S_4O_6^{2-}$$

Figure 3. The scheme of the pharmacopoeial method of analysis of quaternary ammonium compounds

$$2\,B^+Cl^- + Hg(CH_3COO)_2 \rightleftharpoons HgCl_2 + 2\,B*CH_3COOH$$

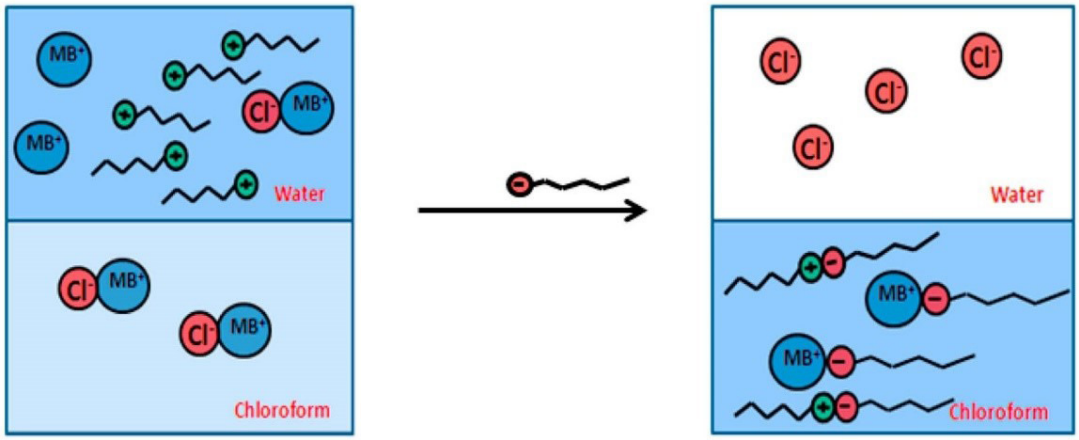
$$B*CH_3COOH \rightleftharpoons BH^+ + CH_3COO^-$$

$$CH_3COO^- + HClO_4 \rightleftharpoons CH_3COOH + ClO_4^-$$

Note: 'B' represents the quaternary ammonium part

Figure 4. The determination of QACs

ISSN 2308-8303 (Print) / 2518-1548 (Online)



Note: MB^+ – methylene blue

Figure 5. The titration of cationic quaternary ammonium compounds by *Epton*

of this complex method are: the use of chloroform which is a relatively toxic solvent; a long waiting period for the phase distribution; inaccurate visual recognition of the endpoint.

Simultaneously, *Preston* [58] used the change in the surface tension as an indicator to record the endpoint of the titration. However, none of the methods for determining the endpoint of the titration is completely satisfactory. In the first case, the color change is not clear (sharp), and in the other one, the change in the surface tension is affected by the presence of inorganic salts.

Since the scope of application of methods for the quantitative determination of QACs is quite wide, the interest is quite high. Therefore, the method of the two-phase titration with methylene blue for determining the concentration of various cationic surface-active substances in water with a high salt content (22% of dissolved solids) is also presented in the literature. The endpoint of the titration was determined by decolorization, while the blue color completely changed from the aqueous phase to the chloroform phase. Light absorption at the characteristic wavelength of methylene blue was measured using a spectrophotometer. When the absorbance fell below a threshold value of 0.04, the aqueous phase was considered colorless, indicating that the endpoint of the titration had been reached. Using this improved technique, the total error of the titration of CS, such as dodecyltrimethylammonium bromide, in deionized water and high salinity water was 1.27% and 1.32% with detection limits (LOD and LOQ) of 0.149 and 0.215 mM, respectively [59].

J. Cross gave the general rules for the titration of CS by an anionic one. It is valid if:

- one surfactant's alkyl chain should be at least C_{12};
- the titration standards are sufficiently pure and belong to the same class of compounds as the compound being determined;
- nonionic surfactants are absent in the sample analyzed.

The accuracy of the method of non-aqueous titration of CS by an anionic titrant depends on the choice of the titrant and the indicator [60, 61]. When developing titration methods the requirements specified above must be met. It is also necessary to take into account that titration is based on the preservation of surfactants of their ionic character, and therefore, the pH is crucial. All common CS can be titrated at pH 3 using methyl orange as an indicator. At pH 10, only CS belonging to quaternary ammonium salts (QACs) can be determined, at the same time, impurities of non-quaternary amines are insufficiently ionized and do not interfere with titration. At pH 13, only some of the compounds can be identified, including the most common products, such as alkyltrimethyl- and dialkyldimethylammonium and benzyltrialkylammonium salts. Bromophenol blue is a suitable indicator for titrations at pH 10 and 13.

A stepwise titrimetric method for the simultaneous determination of QACs (R_4N^+) and aromatic amines (R_3N) has been developed. The technique is based on the extraction of the ionic associates of R_4N^+ and R_3NH^+ formed with a titrant. Sodium tetrakis(4-fluorophenyl)borate or sodium tetraphenylborate was used as a titrant, and potassium tetrabromophenolphthalein ethyl ether (TBPhE) was used as an indicator. The ionic associate formed between R_4N^+ and TBPhE had a blue color in 1,2-dichloroethane, while the ionic associate formed between R_3NH^+ and TBPhE had a red-violet color. Sample solutions, containing quaternary ammonium and/or amine compounds

were titrated with sodium tetrakis(4-fluorophenyl)borate or sodium tetraphenylborate. When one excessive drop of the titrant was added, the color of the organic phase changed from blue or red-violet to yellow at the endpoint of the titration. On the other hand, in the mixture of R_4N^+ and R_3N the color changed from blue to red-violet in the first endpoint. Therefore, quaternary ammonium compounds and aromatic amines in pharmaceutical preparations can be simultaneously successfully determined by the titration method proposed [62].

Titrimetric methods with the potentiometric determination of the endpoint

Today, a number of titrimetric methods with the potentiometric determination of the endpoint are quite common in the literature. At the same time, to control the endpoint of the titration commercially available perchlorate, nitrate and calcium electrodes can be used. This eliminates the need to manufacture a special liquid membrane or other electrodes, which were most often used until now for the potentiometric titration of surface-active substances. The reverse titration of CS with the standard solution of sodium dodecyl sulfate is usually performed [63]. It is important to note that when the concentration of CS is very low, its adsorption by glassware is significant. Therefore, one should use plastic dishes or glass dishes pre-washed with the sample.

In his work *J. T. Bentglini* compared the methods of determining the quantitative content of QAC derivatives with the visual control of the endpoint and the potentiometric one. To determine the endpoint, standard sodium lauryl sulfate was chosen as a titrant, and a nitrate-ion-selective or surface-active electrode was used. A comparison of the results of these two methods showed that the automatic potentiometric method is more accurate, simpler, faster and, in general, more suitable for use in production laboratories than the biphasic titration method [64].

The potentiometric two-phase titration is also used by the German Institute for Standardization, particularly in the DIN EN 14480 standard. The procedure is as follows: a surfactant solution is introduced into a flask for titration, a two-phase mixture of water and methyl isobutyl ketone/ethanol (1:1) and an emulsifier are added. The resulting emulsion is titrated with intensive stirring. The endpoint of the titration is determined potentiometrically using electrodes sensitive to cationic surface-active surfactants. The method described in this standard has the following advantages compared to the classical *Epton's* titration: the use of safe solvents, expressivity, increased accuracy due to the computerized determination of the endpoint of the titration. The advantage of the method described in the German standard is also its wide range of applications due to the possibility of determining the content of surface-active substances in cosmetic and household products (hair conditioner, bath oil, washing powder), as well as in technical products (industrial cleaning products).

The International Organization for Standardization (ISO) offers separate procedures for the determination of cations with high and low molecular masses. Compounds with a low molecular mass (less than 500), such as alkyltrimethylammonium salts, are dissolved and titrated using 0.005 M sodium dodecyl sulfate (SDS) solution as a titrant (pH adjusted to 2.5 using 1.0 M hydrochloric acid solution). In this method, surfactrode Refill electrodes, the reference electrode Ag/AgCl/3M KCl are used [65]. Compounds with a high molecular mass (more than 500), such as dialkyldimethylammonium fabric softeners, have poor solubility in water and are therefore first extracted from the test sample with isopropanol, then diluted with water, and then titrated with an anionic surfactant. The ISO procedure recommends sodium dodecyl sulfate of high purity for titration. It should be noted that the generally accepted titrant according to GOST standards for the two-phase titration of cations is a tetraphenylborate ion [66]. The titration endpoint can be monitored using fluoroborate ion-selective indicator electrodes and a double jump titration reference electrode [67].

Guang-yu Yuan and co-authors prepared a cationic surface-active ion-selective electrode and described its performance. The electrode had a lower detection limit of about 10^{-6} mol L^{-1}. The concentrations of three CS – cetyltrimetrylammonium bromide (CTAB), dodecyldimethylbenzylammonium chloride (DDMBAC), octadecyltrimethylammonium chloride (OTMAC) were determined by the method of the potentiometric titration using the solution of sodium tetraphenylborate as a titrant. The titration results were satisfactory. Relative errors in potentiometric titration were 2.12%, 3.45% and 4.21%, respectively [68].

Therefore, in view of the above, the biphasic and potentiometric titration are the two main techniques widely used and described in the literature. The biphasic titration is a relatively simple process that requires only minor equipment preparation, but it has a number of disadvantages: it is difficult to determine the titration

ISSN 2308-8303 (Print) / 2518-1548 (Online)

endpoint, laborious, health hazard due to the use of harmful organic solvents, etc. The potentiometric titration has been proven to overcome most of these problems.

Compared to the classical (*Epton*) titration the direct potentiometric titration of CS using surfactants resistant to organic solvents can be easily automated. Even complex matrices, such as fats and oils in bath oils and hair conditioners or strong oxidants in laundry detergents and industrial cleaners, do not interfere with the titration of ionic surfactants, experiments were carried out with CTAB, CPC, benzalkonium chloride (BAC) and didecyldimethylammonium chloride (DDAC). The results obtained show excellent agreement with the *Epton* titration results. Regardless of the substance, the relative standard deviation (RSD) of the triplicate determination was less than 2.1% [69].

Ion-selective electrodes for the determination of quaternary ammonium compounds

A new sensitive potentiometric electrode of a surface-active substance based on highly lipophilic 1,3-didodecyl-2-methylimidazolium and the antagonist ion – tetraphenylborate was developed. This sensor was used as a sensitive material and incorporated into a plasticized PVC membrane**.** The electrode gave a fast Nernst response for the CS studied: cetylpyridinium chloride (CPC), hexadecyltrimethylammonium bromide, and (diisobutylphenoxyethoxyethyl)dimethylbenzylammonium chloride (hiamine) with slopes of 59.8, 58.6, and 56.8 mV decade^{-1}, t = 25 °C, respectively. The electrode served as an endpoint detector during the potentiometric titration of the ion pair of a surfactant using sodium tetraphenylborate as a titrant. Several technical grade CS and several commercial disinfectants were also titrated, and the results were compared to those obtained using the standard two-phase titration method. The electrode showed satisfactory analytical performance in the pH range of 2–11 and excellent selectivity towards CPC compared to all organic and inorganic cations tested [70].

Potentiometric electrodes with plasticized polymer membranes based on organic ion exchangers for the study of cationic and ethoxylated nonionic surface-active substances (CS and EONS) have been proposed. The titration was performed in one step. The anionic titrant (TPB) reacted first with CS:

$$CS^+ + TPB^- \rightarrow CS^+TPB^- \quad (1)$$

$$Ba^{2+} + xEONS \rightarrow [Ba(EONS)x]^{2+} \quad (2)$$

More simply, the above equation can be written as follows:

$$Ba^{2+} + xL \rightarrow Ba(L^{2+})_x \quad (3)$$

where L = EONS.

$$Ba(L^{2+})_x + 2TPB - BaL_x(TPB)_2 \quad (4)$$

The difference of 3–4 pK_s units between the solubility product values of both of the TPB ion associates (Eqs. (1) and (4)) caused the appearance of two distinct inflexions at the titration curve. The first inflexion related to the surfactant that formed with less soluble TPB ion-pair complex (with a lower solubility product value). It was CS. It was shown that ion associates (Eqs. (2) and (4)) were stable up to 60–70 °C, K_S varied in the range from 2×10^{-8} to 5×10^{-10} M. The main electrochemical parameters were also determined. They were the linearity ranges of the electrode function (5×10^{-5} (5×10^{-6})–1×10^{-2} (1×10^{-3}) M) and the slopes of the electrode functions (47–59 mV decade^{-1}), response time (60–90 s), drift potential (2–3 mV in a day), shelf life (3–4 months), limits of detection of tetramethylammonium salts (1×10^{-5}–4×10^{-7} M) [71].

M. Gerhard presented a new type of an ion-selective electrode for determining the content of cetylpyridinium chloride. This new electrode includes screen-printed modified and unmodified ion-selective electrodes for determining cetylpyridinium chloride. Electrodes with screen printing (SPE) show a stable response close to Nernst in the range of concentrations of 1×10^{-2}–1×10^{-6} M cetylpyridinium chloride, at 25 °C in the interval of pH 2–8 with a slope of 60.66 ± 1.10 mV decade^{-1}. The lower detection limit is 8×10^{-7} M, the response time 3 s and the satisfactory shelf life – 6 months. The produced electrodes can also be successfully used in the potentiometric titration of cetylpyridinium chloride using NaTPB. Analytical characteristics of SPE were compared with those for carbon paste electrodes and polyvinyl chloride electrodes (PVC). It was shown that the method could be applied for pharmaceutical preparations with the reproducibility of 99.60% and RSD – 0.53%. The studies used analytical and technical grade cetylpyridinium chloride, as well as various water samples that were successfully titrated, and the results were consistent with those obtained with a commercial electrode and the standard two-phase titration method. The sensitivity of the method proposed was compared

to the official method, and the possibility of field measurements was proven [72].

M. Gerhard with colleagues also investigated the effectiveness of printed carbon ink in the production of simple screen-printed carbon paste electrodes (SPCPE). Such electrodes are used for the potentiometric determination of cetyltrimethylammonium bromidein various pharmaceutical preparations and water samples. Their efficiency is compared to the indicators of electrodes with a carbon paste, an electrode with coating, a graphite and polyvinyl chloride electrode. SPCPE were successfully used for the potentiometric titration of CTAB in model solutions, the potential jump was 1050 mV. The successful application of the method for the analysis of pharmaceutical preparations with a percentage of reproducibility was proven to be 99.20 % and RSD = 0.45%. The electrodes had an almost the Nernst cationic slope – 58.70 ± 1.3 and 56.32 ± 2.4 mV, the method allowed to reach the lower detection limit – 6.8×10^{-7} and 5.80×10^{-7} M, reproducibility – 0.14 and 3.25%, and the reaction time – 3 s; it demonstrated a sufficient shelf life – 6 and 2 month for SPCPE [73, 74].

In order to characterize micellar aggregates of imidazolium-based ionic liquids, a new potentiometric method was developed: a PVC-sensor based on neutral ion-pair complexes of dodecylmethylimidazolium bromide – sodium dodecyl sulfate (C_{12}MeIm(+)DS(-)). The electrode had a linear response in the concentration range of 7.9×10^{-5}–9.8×10^{-3} M with the Nernst inclination of 92.94 mM decade^{-1}, the response time – 5 s and the critical concentration of micelle formation (CCM) – 10.09 mM for C_{12}MeImBr. The performance of the electrode in studying the critical micellar concentration of C_{12}MeImBr in the presence of promazine and promethazine hydrochlorides and three triblock copolymers (P123, L64 and F68) was proven to be satisfactory compared to conductivity measurements. Thus, the electrode makes it possible to implement a simple, clear and relatively fast method for the characterization of micellar aggregates C_{12}MeImBr, supplementing existing conventional techniques [75].

The ISE-electrode was made for determining 1-ethoxycarbonyl) pentadecyltrimethylammonium bromide (Seponex). It was based on using septonex-tetraphenylborate as an electroactive agent and *o*-nitrophenyloctyl ether (o-NPOE) as a plasticizer. The electrode exhibited the response similar to the Nernst one – 59.33 ± 0.85 mV, in the interval of pH from 2 to 9 with a lower detection limit of 9×10^{-7} M, the response time of approximately 5 s, and the storage period of 6 months. The method was used to determine Septonex in pharmaceutical preparations. The percentage of reproducibility of the results was 99.88% with RSD = 1.24%. The electrode was successfully applied in determining Septonex in laboratory-

Table 2. Examples of ion-selective electrodes for potentiometric titration of cationic surfactants

	Composition of an electrode	Titrant	Nernst response, mV decade^{-1}	Cationic surfactants	pH	Ref	LOD or range of linearity
1.	Cationic surfactants	sodium tetraphenylborate	–	DDMBAC, CTAB, OTMAC	3	[68]	10^{-6} mol L^{-1}
2.	1,3-didodecyl-2-methylimidazolium + sodium tetraphenylborate	sodium tetraphenylborate	59.8, 58.6, and 56.8	CPC, CTAB, diisobutyl-phenoxyethoxyethyl) dimethylbenzylammonium chloride (hiamine)	2–11	[70]	–
3.	1,3-didecyl-2-methylimidazolium + tetraphenylborate ion	sodium tetraphenylborate	2–3 mV day^{-1}	CS and EONS	3–10	[71]	1×10^{-5} – 4×10^{-7} M
4.	SPE modified ion-selective electrodes	–	60.66 ± 1.10	CPC	2–8	[72]	LOD = 8×10^{-7} M, 1×10^{-2} to 1×10^{-6} M
5.	SPCPE	–	58.70 ± 1.3	CTAB		[73]	LOD 6.8×10^{-7} M
6.	Dodecyltrimethylammonium + tetraphenylborate + dioctylsebacate DTA+TPB + DOS	–	55.95 ± 0.58	DTAB	3	[74]	LOD = 6.8×10^{-6} mol L^{-1}
7.	C_{12}MeIm $^{+}$-ISE	–	92.94	C_{12}MeImBr	–	[75]	7.9×10^{-5} – 9.8×10^{-3} M
8.	Septonex–tetraphenylborate + -nitrophenyloctylether (*o*-NPOE)	–	59.33 ± 0.85	(Ethoxycarbonyl)penta-decyltrimethylammonium bromide (septonex)	2–9	[76]	LOD = 9×10^{-7} M

ISSN 2308-8303 (Print) / 2518-1548 (Online)

prepared samples by the direct potentiometric method using the calibration curve or the standard application method. The potentiometric titration of Septonex with sodium tetraphenylborate and phosphotungstic acid as a titrant was monitored with the modified screen-printed electrode as an endpoint indicator electrode. Selectivity coefficients for Septonex relative to a number of potential interfering substances were determined. The sensor was highly selective for Septonex over a large number of compounds. Selectivity coefficient data for some common ions showed negligible interference; however, cetyltrimethylammonium bromide and iodide ions interfered significantly. The analytical usefulness of the electrode proposed was evaluated by its application when determining Septonex in laboratory-prepared pharmaceutical samples with satisfactory results. The results obtained with the fabricated sensor are comparable with those obtained by the British Pharmacopeia [76].

As can be seen from the material described, the issue of developing ion-selective electrodes for determining QACs occupies a favorable position in modern analytical chemistry (Table 2).

■ Conclusions

Thus, based on the generalized and systematized information of literary sources, one can conclude that titrimetry is the generally accepted standard method for determining the content of CS. At the same time, it is necessary to note that researchers pay their attention to the prospect of developing new instrumental methods for determining the endpoint of titration since these methods are more accurate, simpler, and faster than visual ones. The combination of titrimetry with instrumental methods expands the possibilities of applying the methods, providing expressivity and increased accuracy in the computerized determination of the endpoint of titration.

■ Acknowledgements

We acknowledge the Biological and Chemical Research Centre, University of Warsaw for the financial support and the opportunity to conduct research created within the project “Nowe Idee – Ukraina” 2022, implemented under the “Inicjatywa Doskonałości – Uczelnia Badawcza” Programme.

■ References

1. Paria, S. Surfactant-enhanced remediation of organic contaminated soil and water. *Adv. Colloid Interface Sci.* **2008,** *138* (1), 24–58. https://doi.org/10.1016/j.cis.2007.11.001.
2. Percival, S. L.; Mayer, D.; Malone, M.; Swanson, T.; Gibson, D.; Schultz, G. Surfactants and their role in wound cleansing and biofilm management. *Journal of wound care* **2017,** *26* (11), 680–690. https://doi.org/10.12968/jowc.2017.26.11.680.
3. Mc Callion, O. N. M.; Taylor, K. M. G.; Thomas, M.; Taylor, A. J. The influence of surface tension on aerosols produced by medical nebulisers. *Int. J. Pharm.* **1996,** *129* (1), 123–136. https://doi.org/10.1016/0378-5173(95)04279-2.
4. Rosen, M. J.; Kunjappu, J. T. *Surfactants and Interfacial Phenomena*, 4th ed.; John Wiley & Sons, 2012. http://dx.doi.org/10.1002/9781118228920.
5. Zhang, W.; Dai, X.; Zhao, Y.; Lu, X.; Gao, P. Comparison of the Different Types of Surfactants for the Effect on Activity and Structure of Soybean Peroxidase. *Langmuir* **2009,** *25* (4), 2363–2368. https://doi.org/10.1021/la803240x.
6. Raeisi, F.; Mousavi, S. M.; Hashemi, S. A.; Malekpour, L.; Bahrani, S.; Lai, C. W.; Chiang, W.-H.; Babapoor, A.; Mazraedoost, S.; Esmaeili, H. Application of biosurfactant as a demulsifying and emulsifying agent in the formulation of petrochemical products. In *Green Sustainable Process for Chemical and Environmental Engineering and Science*; Inamuddin; Adetunji, C. O.; Asiri, A. M., Eds.; Elsevier, 2021; pp 399–422.
7. Domagk, G. Eine neue Klasse von Desinfektionsmitteln. *Dtsch Med Wochenschr* **1935,** *61* (21), 829–832.
8. Domagk, G. Preserving and disinfecting media. US2108765A, Feb. 15, 1938.
9. Gillis, A. Surfactants & detergents news. *Journal of the American Oil Chemists' Society* **1987,** *64* (6), 887–893. https://doi.org/10.1007/BF02641502.
10. Shi, W.; He, S.; Wei, M.; Evans, D. G.; Duan, X. Optical pH Sensor with Rapid Response Based on a Fluorescein-Intercalated Layered Double Hydroxide. *Adv. Funct. Mater.* **2010,** *20* (22), 3856–3863. https://doi.org/10.1002/adfm.201001081.
11. Matile, S.; Vargas Jentzsch, A.; Montenegro, J.; Fin, A. Recent synthetic transport systems. *Chem. Soc. Rev.* **2011,** *40* (5), 2453–2474. https://doi.org/10.1039/C0CS00209G.
12. Busseron, E.; Ruff, Y.; Moulin, E.; Giuseppone, N. Supramolecular self-assemblies as functional nanomaterials. *Nanoscale* **2013,** *5* (16), 7098–7140. https://doi.org/10.1039/C3NR02176A.
13. *Cationic surfactants: analytical and biological evaluation*; Cross, J.; Singer, E. J., Eds.; Surfactant Science Series; Marcel Dekker: New York, 1994; Vol. 53.
14. Paluch, E.; Piecuch, A.; Obłąk, E.; Lamch, Ł.; Wilk, K. A. Antifungal activity of newly synthesized chemodegradable dicephalic-type cationic surfactants. *Colloids and Surfaces B: Biointerfaces* **2018,** *164*, 34–41. https://doi.org/10.1016/j.colsurfb.2018.01.020.
15. Wang, L.; Zhao, Q.; Zhang, Z.; Lu, Z.; Zhao, Y.; Tang, Y. Fluorescent Conjugated Polymer/Quarternary Ammonium Salt Co-assembly Nanoparticles: Applications in Highly Effective Antibacteria and Bioimaging. *ACS Applied Bio Materials* **2018,** *1* (5), 1478–1486. https://doi.org/10.1021/acsabm.8b00422.

16. Shalabi, K.; Helmy, A. M.; El-Askalany, A. H.; Shahba, M. M. New pyridinium bromide mono-cationic surfactant as corrosion inhibitor for carbon steel during chemical cleaning: Experimental and theoretical studies. *J. Mol. Liq.* **2019,** *293*, 111480. https://doi.org/10.1016/j.molliq.2019.111480.
17. Buurma, N. J. Aggregation and reactivity in aqueous solutions of cationic surfactants and aromatic anions across concentration scales. *Current Opinion in Colloid & Interface Science* **2017,** *32*, 69–75. https://doi.org/10.1016/j.cocis.2017.10.005.
18. Wang, L.; Quan, P.; Chen, S. H.; Bu, W.; Li, Y.-F.; Wu, X.; Wu, J.; Zhang, L.; Zhao, Y.; Jiang, X.; Lin, B.; Zhou, R.; Chen, C. Stability of Ligands on Nanoparticles Regulating the Integrity of Biological Membranes at the Nano–Lipid Interface. *ACS Nano* **2019,** *13* (8), 8680–8693. https://doi.org/10.1021/acsnano.9b00114.
19. Botto, C.; Mauro, N.; Amore, E.; Martorana, E.; Giammona, G.; Bondì, M. L. Surfactant effect on the physicochemical characteristics of cationic solid lipid nanoparticles. *Int. J. Pharm.* **2017,** *516* (1), 334–341. https://doi.org/10.1016/j.ijpharm.2016.11.052.
20. Muzzalupo, R.; Pérez, L.; Pinazo, A.; Tavano, L. Pharmaceutical versatility of cationic niosomes derived from amino acid-based surfactants: Skin penetration behavior and controlled drug release. *Int. J. Pharm.* **2017,** *529* (1), 245–252. https://doi.org/10.1016/j.ijpharm.2017.06.083.
21. López-López, M.; López-Cornejo, P.; Martín, V. I.; Ostos, F. J.; Checa-Rodríguez, C.; Prados-Carvajal, R.; Lebrón, J. A.; Huertas, P.; Moyá, M. L. Importance of hydrophobic interactions in the single-chained cationic surfactant-DNA complexation. *J. Colloid Interface Sci.* **2018,** *521*, 197–205. https://doi.org/10.1016/j.jcis.2018.03.048.
22. Guo, Q.; Zhang, Z.; Song, Y.; Liu, S.; Gao, W.; Qiao, H.; Guo, L.; Wang, J. Investigation on interaction of DNA and several cationic surfactants with different head groups by spectroscopy, gel electrophoresis and viscosity technologies. *Chemosphere* **2017,** *168*, 599–605. https://doi.org/10.1016/j.chemosphere.2016.11.019.
23. Edeas, M.; Weissig, V. Targeting mitochondria: Strategies, innovations and challenges: The future of medicine will come through mitochondria. *Mitochondrion* **2013,** *13* (5), 389–390. https://doi.org/10.1016/j.mito.2013.03.009.
24. Kalyanaraman, B.; Cheng, G.; Hardy, M.; Ouari, O.; Lopez, M.; Joseph, J.; Zielonka, J.; Dwinell, M. B. A review of the basics of mitochondrial bioenergetics, metabolism, and related signaling pathways in cancer cells: Therapeutic targeting of tumor mitochondria with lipophilic cationic compounds. *Redox Biology* **2018,** *14*, 316–327. https://doi.org/10.1016/j.redox.2017.09.020.
25. Zakharova, L. Y.; Pashirova, T. N.; Doktorovova, S.; Fernandes, A. R.; Sanchez-Lopez, E.; Silva, A. M.; Souto, S. B.; Souto, E. B. Cationic Surfactants: Self-Assembly, Structure-Activity Correlation and Their Biological Applications. *International Journal of Molecular Sciences* **2019,** *20* (22), 5534. https://doi.org/10.3390/ijms20225534.
26. Dhawan, V. V.; Nagarsenker, M. S. Catanionic systems in nanotherapeutics – Biophysical aspects and novel trends in drug delivery applications. *J. Controlled Release* **2017,** *266*, 331–345. https://doi.org/10.1016/j.jconrel.2017.09.040.
27. Buck, J.; Grossen, P.; Cullis, P. R.; Huwyler, J.; Witzigmann, D. Lipid-Based DNA Therapeutics: Hallmarks of Non-Viral Gene Delivery. *ACS Nano* **2019,** *13* (4), 3754–3782. https://doi.org/10.1021/acsnano.8b07858.
28. Grijalvo, S.; Puras, G.; Zárate, J.; Sainz-Ramos, M.; Qtaish, N. A. L.; López, T.; Mashal, M.; Attia, N.; Díaz Díaz, D.; Pons, R.; Fernández, E.; Pedraz, J. L.; Eritja, R. Cationic Niosomes as Non-Viral Vehicles for Nucleic Acids: Challenges and Opportunities in Gene Delivery. *Pharmaceutics* **2019,** *11* (2), 50. https://doi.org/10.3390/pharmaceutics11020050.
29. Silva, L. L.; Zapelini, I. W.; Cardoso, D. Catalytic transesterification by hybrid silicas containing CnTA+ surfactants. *Catal. Today* **2020,** *356*, 433–439. https://doi.org/10.1016/j.cattod.2019.07.030.
30. Obłąk, E.; Piecuch, A.; Rewak-Soroczyńska, J.; Paluch, E. Activity of gemini quaternary ammonium salts against microorganisms. *Appl. Microbiol. Biotechnol.* **2019,** *103* (2), 625–632. https://doi.org/10.1007/s00253-018-9523-2.
31. Fait, M. E.; Bakas, L.; Garrote, G. L.; Morcelle, S. R.; Saparrat, M. C. N. Cationic surfactants as antifungal agents. *Appl. Microbiol. Biotechnol.* **2019,** *103* (1), 97–112. https://doi.org/10.1007/s00253-018-9467-6.
32. Rapp, B. E. *Microfluidics: modeling, mechanics, and mathematics*; Elsevier, 2017.
33. Takeda, S.; Usui, S. Adsorption of dodecylammonium ion on quartz in relation to its flotation. *Colloids and Surfaces* **1987,** *23* (1), 15–28. https://doi.org/10.1016/0166-6622(87)80246-9.
34. Schwarz, R.; Heckmann, K.; Strand, J. Adsorption model of pyridinium salts on quartz. *J. Colloid Interface Sci.* **1988,** *124* (1), 50–56. https://doi.org/10.1016/0021-9797(88)90323-2.
35. Scowen, R. V.; Leja, J. Spectrophotometric studies on surfactants. I. Interactions between cationic and anionic surfactants. *Can. J. Chem.* **1967,** *45* (22), 2821–2827. https://doi.org/10.1139/v67-455.
36. Roes, I. J. I.; de Groot, S. In *Surfactants in Our World-Today and Tomorrow*, Proceedings of the 2nd World Surfactants Congress, Paris, May 24–27, 1988.
37. Huber, L. *Munch. Beitr. Abwasser Fisch. Flussbiol.* **1979**, *31*, 203.
38. Lewis, M. A.; Wee, V. T. Aquatic safety assessment for cationic surfactants. *Environ. Toxicol. Chem.* **1983,** *2* (1), 105–118. https://doi.org/10.1002/etc.5620020112.
39. Krzeminski, S. F.; Martin, J. J.; Brackett, C. K. The environmental impact of a quaternary ammonium bactericide. *Household & Personal Products Industry* **1973**, *22*, 24.
40. Lewis, M. A.; Hamm, B. G. Environmental modification of the photosynthetic response of lake plankton to surfactants and significance to a laboratory-field comparison. *Water Res.* **1986,** *20* (12), 1575–1582. https://doi.org/10.1016/0043-1354(86)90123-5.
41. Biesinger, K. E.; Stokes, G. N. Effects of Synthetic Polyelectrolytes on Selected Aquatic Organisms. *Journal (Water Pollution Control Federation)* **1986,** *58* (3), 207–213.
42. Walker, J. R. L.; Evans, S. Effect of quaternary ammonium compounds on some aquatic plants. *Marine Pollution Bulletin* **1978,** *9* (5), 136–137. https://doi.org/10.1016/0025-326X(78)90589-1.
43. Llenado, R. A.; Jamieson, R. A. Surfactants. *Anal. Chem.* **1981,** *53* (5), 174–182. https://doi.org/10.1021/ac00228a012.
44. Gąsiorowska, M.; Wróblewska, E. K. Two-Phase Titration Method for Cationic Surface Active Agents Determination with Use of 5-(3-Bromo-4-hydroxy-5-methoxyphenyl)-7,7-dimethyl-7H-indolo[1,2-a]quinolinium Perchlorate Dye. *Tenside Surfactants Detergents* **2012,** *49* (1), 23–25. https://doi.org/10.3139/113.110160.

ISSN 2308-8303 (Print) / 2518-1548 (Online)

45. Biswas, S.; Pal, A. Spectrophotometric determination of cationic surfactants in aqueous media using chrome azurol S as colour forming agent and 1-butanol as extracting solvent. *Talanta* **2020,** *206*, 120238. https://doi.org/10.1016/j.talanta.2019.120238.
46. Schnee, V. P.; Palmer, C. P. Cationic surfactants for micellar electrokinetic chromatography: 1. Characterization of selectivity using the linear solvation energy relationships model. *ELECTROPHORESIS* **2008,** *29* (4), 767–776. https://doi.org/10.1002/elps.200700494.
47. Lange, K. R. *Poverhnostno-aktivnye veshchestva. Sintez, svojstva, analiz, primenenie* [Surfactants: synthesis, properties, analysis, and application, *in Russian*]; Professiya: St. Petersburg: Professiya, 2004.
48. Price, R.; Wan, P. Determination of Quaternary Ammonium Compounds by Potentiometric Titration with an Ionic Surfactant Electrode: Single-Laboratory Validation. *J. AOAC Int.* **2019,** *93* (5), 1542–1552. https://doi.org/10.1093/jaoac/93.5.1542.
49. Mousavi, Z. E.; Butler, F.; Danaher, M. Validation of a Simple Spectrophotometric Method for the Measurement of Quaternary Ammonium Compound Residue Concentrations in Food Production Facility. *Food Analytical Methods* **2013,** *6* (5), 1265–1270. https://doi.org/10.1007/s12161-012-9537-9.
50. *The United States Pharmacopeia USP 24, the national formulary NF19*; United States Pharmacopeial Convention: Rockville, MD, 1999.
51. Brown, E. R. A Specific Method of Assay of Strong Solutions of Benzalkonium Chloride and Other Quaternary Ammonium Germicides. *J. Pharm. Pharmacol.* **2011,** *15* (1), 379–385. https://doi.org/10.1111/j.2042-7158.1963.tb12801.x.
52. Hilp, M.; Zembatova, S. Cetylpyridinium tetrachlorozincate as standard for tenside titration. Analytical methods with 1,3-dibromo-5,5-dimethylhydantoin (DBH) in respect to environmental and economical concern, part 19. *Pharmazie* **2004**, *59* (8), 615–617.
53. Miller, J. H. M. Determination of halide acid salts of organic bases and quaternary ammonium compounds by titration. *J. Pharm. Biomed. Anal.* **1989,** *7* (6), 771–775. https://doi.org/10.1016/0731-7085(89)80123-2.
54. Schmitt, T. M. *Analysis of surfactants*, 2nd ed.; Surfactant Science Series; Marcel Dekker: New York, 2001; Vol. 96.
55. Hartley, G. S. 216. Azo-indicators with a quaternary ammonium group. *Journal of the Chemical Society (Resumed)* **1937,** 1026–1029. https://doi.org/10.1039/JR9370001026.
56. Hartley, G. S.; Runnicles, D. F.; Donnan, F. G. The determination of the size of paraffin-chain salt micelles from diffusion measurements. *Proceedings of the Royal Society of London. Series A. Mathematical and Physical Sciences* **1938,** *168* (934), 420–440. https://doi.org/10.1098/rspa.1938.0181.
57. Epton, S. R. A Rapid Method of Analysis for Certain Surface-Active Agents. *Nature* **1947,** *160* (4075), 795–796. https://doi.org/10.1038/160795b0.
58. Preston, J. M. Tensimetric Analysis of Surface-active Electrolytes. *Journal of the Society of Dyers and Colourists* **1945,** *61* (7), 165–166. https://doi.org/10.1111/j.1478-4408.1945.tb02359.x.
59. Cui, L.; Puerto, M.; López-Salinas, J. L.; Biswal, S. L.; Hirasaki, G. J. Improved Methylene Blue Two-Phase Titration Method for Determining Cationic Surfactant Concentration in High-Salinity Brine. *Anal. Chem.* **2014,** *86* (22), 11055–11061. https://doi.org/10.1021/ac500767m.
60. Cross, J. T. The identification and determination of cationic surface-active agents with sodium tetraphenylboron. *Analyst* **1965,** *90* (1071), 315–324. https://doi.org/10.1039/AN9659000315.
61. *Handbook of Detergents, Part B: Environmental Impact*; Zoller, U., Ed.; Surfactant Science Series; Marcel Dekker: New York, 2004; Vol. 121.
62. Waldhoff, H.; Scherler, D.; Bütfering, L. Analyse von Tensiden. In *Analytiker-Taschenbuch*; Günzler, H.; Bahadir, A. M.; Danzer, K.; Engewald, W.; Fresenius, W.; Galensa, R.; Huber, W.; Linscheid, M.; Schwedt, G.; Tölg, G., Eds.; Springer Berlin Heidelberg: Berlin, 1999; pp 251–289.
63. Sakač, N.; Madunić-Čačić, D; Karnaš, M; Đurin, B; Kovač, I; Jozanović, M. The Influence of Plasticizers on the Response Characteristics of the Surfactant Sensor for Cationic Surfactant Determination in Disinfectants and Antiseptics. *Sensors* **2021**, *21* (10), 3535. https://doi.org/10.3390/s21103535.
64. Battaglini, G. T. Assay of quaternary ammonium antimicrobial compounds by aqueous potentiometric titration. *Journal of Surfactants and Detergents* **2002,** *5* (2), 117–121. https://doi.org/10.1007/s11743-002-0210-4.
65. *Surface active agents – Detergents – Determination of cationic-active matter content – Part 1: High-molecular-mass cationic-active matter*; ISO 2871-1:1988; International Organization for Standardization: Genève, 1988.
66. *Rechovyny poverkhnevo-aktyvni. Zasoby myini. Metod vyznachennia vmistu kation-aktyvnykh rechovyn. Chastyna 2. Kation-aktyvni rechovyny z nyzkoiu molekuliarnoiu masoiu (mizh 200 i 500) (ISO 2871-2:2010, IDT)* [Surface-active substances. Detergents. Method for determining the content of cation-active substances. Part 2. Cation-active substances with a low molecular weight (between 200 and 500) (ISO 2871-2:2010, IDT), *in Ukrainian*]; DSTU ISO 2871-2:2015; State enterprise «Ukrainian scientific research and training center for problems of standardization, certification and quality»: Kyiv, 2015.
67. Selig, W. The potentiometric titration of surfactants and soaps using ion-selective electrodes. *Fresenius' Zeitschrift für analytische Chemie* **1980,** *300* (3), 183–188. https://doi.org/10.1007/BF00488331.
68. Yuan, G.-Y.; Hou, J.-R.; Liu, B.-X.; Luo, Y.-Y. Preparation and Application of Cationic Surfactant Ion-selective Electrode. *Tenside Surfactants Detergents* **2013,** *50* (3), 204–208. https://doi.org/10.3139/113.110250.
69. Jozanović, M.; Sakač, N.; Karnaš, M.; Medvidović-Kosanović, M. Potentiometric Sensors for the Determination of Anionic Surfactants – A Review. *Crit. Rev. Anal. Chem.* **2021,** *51* (2), 115–137. https://doi.org/10.1080/10408347.2019.1684236.
70. Madunić-Čačić, D.; Sak-Bosnar, M.; Galović, O.; Sakač, N.; Matešić-Puač, R. Determination of cationic surfactants in pharmaceutical disinfectants using a new sensitive potentiometric sensor. *Talanta* **2008,** *76* (2), 259–264. https://doi.org/10.1016/j.talanta.2008.02.023.
71. Samardžić, M.; Sak-Bosnar, M.; Madunić-Čačić, D. Simultaneous potentiometric determination of cationic and ethoxylated nonionic surfactants in liquid cleaners and disinfectants. *Talanta* **2011,** *83* (3), 789–794. https://doi.org/10.1016/j.talanta.2010.10.046.
72. Mohamed, G. G.; Ali, T. A.; El-Shahat, M. F.; Al-Sabagh, A. M.; Migahed, M. A.; Khaled, E. Potentiometric determination of cetylpyridinium chloride using a new type of screen-printed ion selective electrodes. *Anal. Chim. Acta* **2010,** *673* (1), 79–87. https://doi.org/10.1016/j.aca.2010.05.016.
73. Mohamed, G. G.; Ali, T. A.; El-Shahat, M. F.; Al-Sabagh, A. M.; Migahed, M. A. New Screen-Printed Ion-Selective Electrodes for Potentiometric Titration of Cetyltrimethylammonium Bromide in Different Civilic Media. *Electroanalysis* **2010,** *22* (21), 2587–2599. https://doi.org/10.1002/elan.201000096.

74. Mohamed, G. G.; Ali, T. A.; El-Shahat, M. F.; Migahed, M. A.; Al-Sabagh, A. M. Novel screen-printed electrode for the determination of dodecyltrimethylammonium bromide in water samples. *Drug testing and analysis* **2012,** *4* (12), 1009–1013. https://doi.org/10.1002/dta.366.
75. Sanan, R.; Mahajan, R. K. Micellar and analytical implications of a new potentiometric PVC sensor based on neutral ion-pair complexes of dodecylmethylimidazolium bromide–sodium dodecylsulfate. *J. Colloid Interface Sci.* **2013,** *394*, 346–352. https://doi.org/10.1016/j.jcis.2012.12.051.
76. Mohamed, G. G.; El-Shahat, M. F.; Al-Sabagh, A. M.; Migahed, M. A.; Ali, T. A. Septonex–tetraphenylborate screen-printed ion selective electrode for the potentiometric determination of Septonex in pharmaceutical preparations. *Analyst* **2011,** *136* (7), 1488–1495. 10.1039/C0AN00662A.

Information about the authors:
Mykola Ye. Blazheyevskiy, D.Sc. in Chemistry, Professor of the General Chemistry Department, National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0002-8032-347X.
Ewa Bulska, Dr. hab., Professor, Biological and Chemical Research Centre, Faculty of Chemistry, University of Warsaw; https://orcid.org/0000-0003-4872-5521.
Andrii M. Tupys, Ph.D. in Chemistry, Biological and Chemical Research Centre, Faculty of Chemistry, University of Warsaw.
Olena V. Koval'ska (*corresponding author*), Ph.D. in Pharmacy, Associate Professor of General Chemistry Department, National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0003-0113-7060;
e-mail for correspondence: lena05021985@ukr.net; tel. +380 97 0710498.

ISSN 2308-8303 (Print) / 2518-1548 (Online)