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## Development of methods for identification of cetylpyridinium hexafluorosilicate

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### ABSTRACT

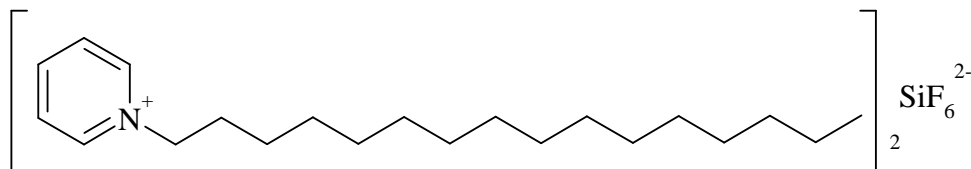
The methods for identification of Cetylpyridinium hexafluorosilicate – a potential caries preventive and antibacterial agent have been developed. To identify Cetylpyridinium hexafluorosilicate according to the requirements of the State Pharmacopoeia of Ukraine (SPhU) it has been suggested to use IR- and UV spectroscopy and chemical reactions.

**Key words:** pharmaceutical analysis, identification, Cetylpyridinium hexafluorosilicate, thermogravimetric analysis, microbiological purity.

### INTRODUCTION

It is known that hexafluorosilicates of amino acids can be used as potential caries preventive and hyposensitive agents that have some advantages compared with traditional remedies of fluoride therapy in caries. The search for new caries preventive agents, which include a fluoride component in the form of  $\text{SiF}_6^{2-}$  anion combined with a cation that reveals the antibacterial activity, is conducted. These cations include Chlorhexidine, Cetylpyridine, etc. [1,2]. Cetylpyridinium hexafluorosilicate has been synthesized in the Odessa National Medical University, it has shown caries preventive and antibacterial properties in the experiment [3]. To introduce a medicinal product into production it is necessary to conduct standardization of the active ingredient in the substance.

The aim of this work is to develop methods for identification of 1-hexadecylpyridine hexafluorosilicate (Cetylpyridinium hexafluorosilicate) for their further use in the methods of the quality control for this substance.



By its chemical properties Cetylpyridinium hexafluorosilicate can be referred to quaternary ammonium salts, the residue of the heteroaromatic pyridine ring is in the basis of their structure. For identification of Cetylpyridinium hexafluorosilicate according to the requirements of the SPhU a set of physical (determination of the melting point), chemical and physicochemical (IR, UV spectroscopy) methods of analysis was used. Experiments were carried out according to the requirements of the SPhU regarding substances [4,5].

## MATERIALS AND METHODS

To conduct the research a chromatographically pure sample of Cetylpyridinium hexafluorosilicate (the content of impurities is less than 0.5%) was used. The measuring glassware of class A, reagents meeting the requirements of the SPhU, "AXIS" analytical balance, an "Evolution 60s" spectrophotometer, Q-1000 derivatograph, "Seven Easy" pH meter by "Mettler Toledo" company (USA) were used in the work. The IR-spectrum of the substance was recorded on a "TENSOR 27" device in KBr tablets with the concentration of the substance of 1%.

## RESULTS AND DISCUSSION

By its physical properties Cetylpyridinium hexafluorosilicate is a white or white with a slightly yellowish tint powder, and it has a soapy feel. It is soluble in water and alcohol. The aqueous solution foams abundantly when shaking. The reaction medium is slightly acid to methyl orange. The melting point is from 148°C to 152°C.

For identification of the substance its spectral characteristics were studied. Thus, the absorption spectrum of 0.005% aqueous solution of the substance in the range from 220 nm to 280 nm is characterized by the maximum at the wavelength of 259 nm and two shoulders at the wavelengths of 254 nm and 265 nm, which is caused by the presence of the molecule of the pyridine ring (Fig 1) [6].

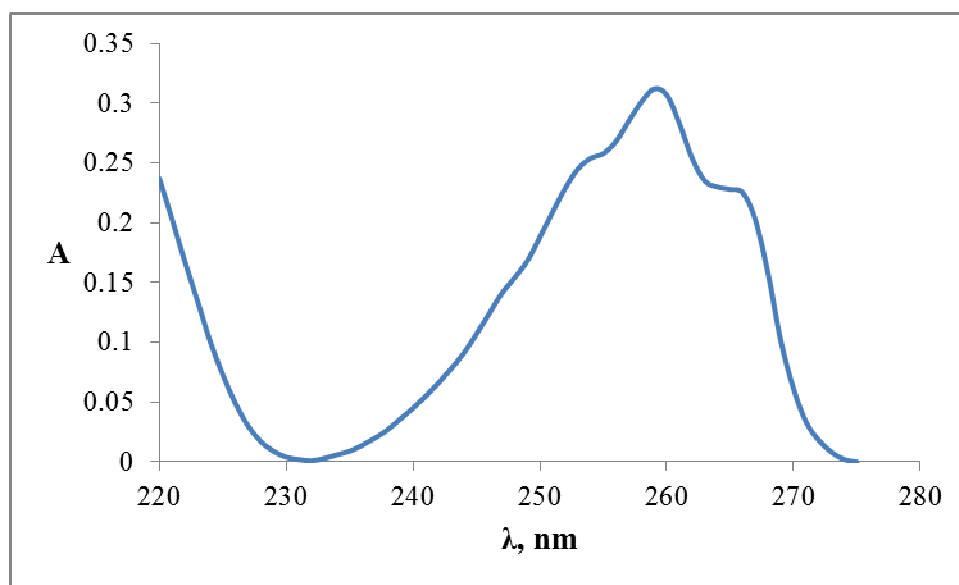


Fig. 1 The UV absorption spectrum of 0.005% aqueous solution of Cetylpyridinium hexafluorosilicate

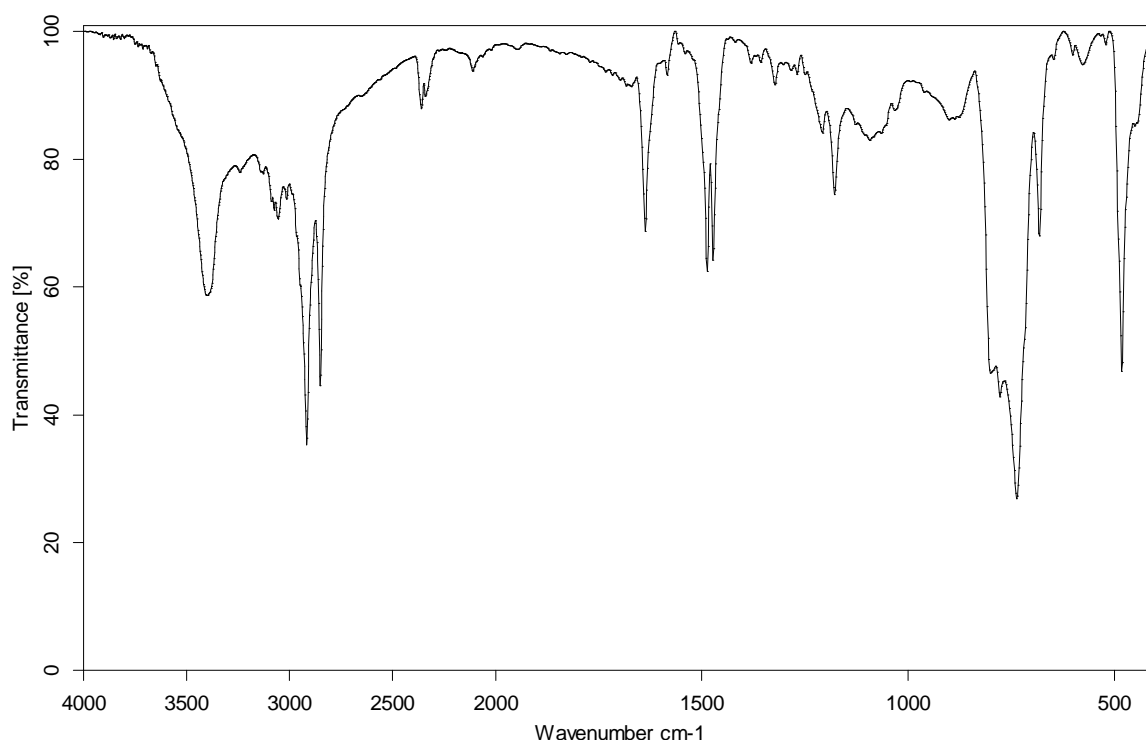
To increase the specificity of identification it is advisable to find the specific absorption rate at maximum. To do this, the aqueous solutions of the test substance of various concentrations were prepared, and their optical density was found. It was determined that the specific rate of absorption with the maximum at the wavelength of 259 nm was from 62 to 70 (Table 1).

Table 1 The results of determining the optical density of standard solutions

No.	Concentration of solutions, %	Optical density	Specific absorption rate	Metrological characteristics
1	0.001	0.071	71	$\bar{x} = 66$ $S^2 = 22.14$ $S = 4.71$ $S_{\bar{x}} = 1.21$ $\Delta x = 10.09$ $\Delta \bar{x} = 2.61$ $\varepsilon = 15.29\%$ $\bar{\varepsilon} = 3.95\%$
2	0.002	0.133	66	
3	0.003	0.203	68	
4	0.004	0.266	66	
5	0.005	0.340	68	
6	0.006	0.409	68	
7	0.007	0.458	65	
8	0.008	0.517	65	
9	0.009	0.583	65	
10	0.010	0.654	65	
11	0.011	0.720	65	
12	0.012	0.786	65	
13	0.013	0.846	65	
14	0.014	0.912	65	
15	0.015	0.970	65	

In the IR-spectrum of the compound studied in KBr tablets in the frequency range from 4000 to 400  $\text{cm}^{-1}$  the characteristic bands of vibrations were observed. The maximum at 3401  $\text{cm}^{-1}$  ( $\nu$  O–H) indicates the presence of impurity of humidity in the sample. At 3087–3066  $\text{cm}^{-1}$  a series of weak bands corresponding to valence fluctuations = CH of aromatic hydrocarbons was observed. At 2915  $\text{cm}^{-1}$  and 2850  $\text{cm}^{-1}$  the intense absorption bands corresponding to valence fluctuations –C–H in –CH<sub>3</sub>– and –CH<sub>2</sub>– groups were observed. An intense absorption band at 1637  $\text{cm}^{-1}$  was the valence fluctuations –C = C– of the heteroaromatic cycle. Two integrated absorption bands at 1487  $\text{cm}^{-1}$  and 1473  $\text{cm}^{-1}$  corresponded to valence fluctuations of the –C = C– and –C = N– bonds of the pyridine ring and deformation fluctuations of –C–H in –CH<sub>2</sub>– and CH<sub>3</sub> of the cetyl fragment of the molecule. The bands at 795  $\text{cm}^{-1}$  and 778  $\text{cm}^{-1}$  can be attributed to deformation vibrations = C–H of monosubstituted derivatives of heteroaromatic compounds. The intense peaks at 736  $\text{cm}^{-1}$  and 482  $\text{cm}^{-1}$  corresponded to valence fluctuations of the SiF bond and deformation fluctuations of SiF<sub>2</sub> in the structure of SiF<sub>6</sub><sup>2-</sup> (Fig. 2) [7].

It is proposed to introduce such an item as “the infrared absorption spectrum for Cetylpyridinium hexafluorosilicate obtained in the discs of potassium bromide must meet the spectrum of the standard sample of Cetylpyridinium hexafluorosilicate to the methods of quality control.



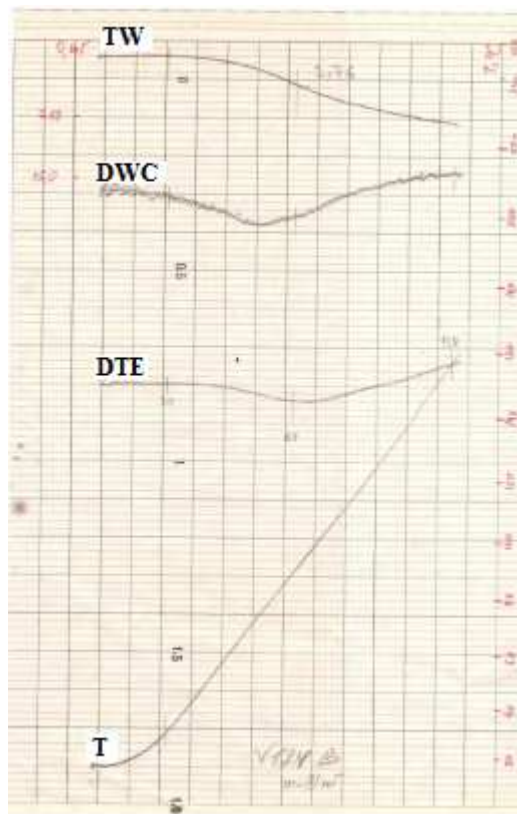
**Fig. 2** The IR spectrum of Cetylpyridinium hexafluorosilicate in tablets of potassium bromide

Among the chemical reactions of identification the typical reaction for quaternary ammonium bases – formation of the ion associate with bromophenol blue dissolving in chloroform and coloring it blue was used [5]. The presence of the residue of fluorosilicate acid was confirmed by the reaction with the solution of ammonium molybdate. The precipitate of a lemon yellow color was formed (in these conditions the initial product of synthesis of cetylpyridine hydrochloride forms a white precipitate) [3]. When adding the solution of ammonium thiocyanate to the aqueous solution of the test compound a pink jelly-like precipitate was formed; a colorless jelly-like precipitate was formed with cetylpyridine chloride in the control experiment.

Based on the scheme of the synthesis of the compound [3] the acidity was identified when determining purity by measuring the pH of the aqueous solution using a “Seven Easy” pH meter by “Mettler Toledo” company (USA). It was found that the pH of 1% aqueous solution was 1.93–1.95. The starting compound for the synthesis was cetylpyridinium chloride [3]; therefore, it was reasonable to identify impurities of chlorides with the content of not more than 0.02% (200 ppm) [4]. It was found that the water content was between 2% and 5% (determined by titration according to Fischer method and using the thermographic analysis).

The thermogravimetric analysis was performed on a Q-1000 derivatograph of the system by F. Paulik, I. Paulik, L. Yefdey with a platinum to platinum/rhodium thermocouple when heating samples in ceramic crucibles from 20 to 300°C in air. The heating rate was 5°C per a min. The tempered aluminum oxide was used as a standard. The weight

of the samples was 50–100 mg. The following curves were recorded: T (temperature change); TW (change in weight); DTE (differentiated curve of changes in thermal effects); DWC (differentiated curve of weight change) (Fig. 3).



**Fig. 3** The thermogram of Cetylpyridinium hexafluorosilicate

The data of thermographic analysis, namely such curves as T, TW, DTE and DWC suggest that at 88°C the substance begins to lose weight, its percentage is 4.64%, and destruction of the compound occurs at approximately 158 °C. Thus, the studies conducted may indicate the thermal stability of the substance under research and the loss of about 5% of water, and it is consistent with the experimental data for determination of water by titration according to Fischer method.

The compound is hexafluorosilicate acid salt. Therefore, according to the method of the SPhU [4] the content of sulfated ash (not more than 0.50%) and ash that is insoluble in hydrochloric acid (not more than 0.20%) has been determined.

Determination of microbiological purity of the substance was carried by the pour plate method and the double layered plate method (Table 2).

**Table 2** The results of the study of Cetylpyridinium hexafluorosilicate by the "microbiological purity" value

Sample	The pour plate method		The double layered plate method	
	The number of CFU/g			
	Aerobic microorganisms (TAMC)	Yeasts and moulds (TYMC)	Aerobic microorganisms (TAMC)	Yeasts and moulds (TYMC)
Cetylpyridinium hexafluorosilicate	to 100	to 100	to 100	to 100

Notes: CFU/g – colony forming units in 1.0 g of the sample.

It has been determined that the total aerobic microbial count (TAMC) does not exceed  $10^3$  CFU/g, the total combined yeasts and moulds count (TYMC) does not exceed  $10^2$  CFU/g, and it corresponds to the requirements of the SPhU for substances for pharmaceutical use [4,5].

**CONCLUSION**

The methods for identification of a new potential medicinal substance – Cetylpyridinium hexafluorosilicate have been developed; they will allow to reliably identify the compound studied.

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