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Fazliddin Jalılov Sodiqovich
Department of Standardization and Quality Management of Medicines, Faculty of Industrial Pharmacy, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan

Lola Pulatova Tairxanovna
Department of "Classification and certification of goods", Customs Institute of the State Customs Committee of the Republic of Uzbekistan, Tashkent, Uzbekistan

Feruza Jalılova Sodiqovna
Department of Pharmacology and Clinical Pharmacology, Department of Dentistry, Bukhara State Medical Institute, Bukhara, Uzbekistan

Oydina Sharipova Zarifovna
Department of Pharmacology and Clinical Pharmacology, Department of Dentistry, Bukhara State Medical Institute, Bukhara, Uzbekistan

Shoxista Meliboyeva Sharofiddin qizi
Department of Pharmacology and Clinical Pharmacology, Department of Dentistry, Bukhara State Medical Institute, Bukhara, Uzbekistan

Corresponding Author:
Fazliddin Jalılov Sodiqovich
Department of Standardization and Quality Management of Medicines, Faculty of Industrial Pharmacy, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan

Analysis of sertraline from biological fluids by thermal desorption surface-ionizing spectroscopy

Fazliddin Jalılov Sodiqovich, Lola Pulatova Tairxanovna, Feruza Jalılova Sodiqovna, Oydina Sharipova Zarifovna and Shoxista Meliboyeva Sharofiddin qizi

Abstract
The procedures for determination and identification of sertraline by the method of thermodesorption surface-ionizing spectroscopy have been developed. It was established that alcoholic solutions of sertraline had maximum absorption at ~131±15 °C and ~190±15 °C. The linear-dynamic range is in the interval of 50-300μg/mL of substance concentration in the sample. Sensitivity of the method is 0,5μg/mL. The developed method is recommended for analysis of sertraline in biological liquids.

Keywords: thermo desorption surface-ionization spectroscopy, sertraline, biological fluids

Introduction
Sertraline, (Altruline; Serad; Zoloft; Asentra; Serlift; Stimuloton) is the medicine. White or almost white crystalline powder. Sertraline is the antidepressant. Despite the widespread use of sertraline in medical practice the cases of the manifestation of their toxic effects are not excluded (in overdose and individual hypersensitivity), as evidenced by cases of acute and chronic poisoning with these drugs described in the literature [1, 2, 3, 8]. Sertraline is associated with the increased suicide risk in different age groups: in youth, adolescents and adults. In connection with this the study of sertraline in the biopharmaceutical and chemical and toxicological regard is the crucial task. The purpose of this study is to develop the analytical procedure for sertraline by thermo desorption surface-ionizing spectroscopy (TDSIS) method and the application in the study of biological liquids.

Experimental part
For the study the method of thermo desorption surface-ionization spectroscopy was used. The essence of the method lies in the temperature-programmed regime of evaporation of molecules of required substances in the extracts from biological samples with their subsequent entry the surface ionization detector, the signals of which are recorded in the form of thermo desorbtion spectra. These thermo desorption spectra are quite specific for certain test substances. The basis for registration is the principle of operation of surface-ionization detector. In the diode detector as the anode there is thermo emitter, and as the cathode – there is the collector of positive ions. While passing through the diode of the analyzed mixture, the molecules entering the surface of the emitter can be desorbed in the form of ions that are delivered to the collector by the electric field for registration [9].
In the detector, due to its high selectivity for the ionization potential the molecules of organic solvents (alcohols, ketones, aldehydes, esters, hydrocarbons, etc.) and simple gases are practically not ionized by surface ionization. The detector allows to register only the molecules of nitrogen bases, the derivatives of which are many narcotics, alkaloids and other synthetic nitrogen compounds [4, 5, 7].
The authenticity of the substances is established according to the effective temperature of desorption using standard samples of the studied drugs. For the detection of sertraline by the method thermo desorption surface-ionization spectroscopy (TDSIS) the analysis was performed under the following conditions: the emitter – oxidized molybdenum, having iridium in its composition; emitter voltage – 405 V; emitter temperature – 390-420 °C; temperature of evaporation – 20-505 °C; air flow – 50 l/hour, (the voltage of the compressor is 12 V); volume of the test sample taken for analysis - 1.0 μl; analysis time – 3 minutes; recording of the spectra is performed directly by using computer program.

To conduct the study the standard solutions of sertraline were prepared. Accurately weighed quantity of 0,01 sertraline is dissolved in 95% ethyl alcohol in 10ml flask. Solution is diluted with 95% ethyl alcohol to the mark. From this solution working standard solution (100 µg/ml) was prepared and from which 1 µl of solution was taken by micro syringe and injected into cylindrical cavity of evaporative tape of PII-N-S "Iskovich-1" apparatus, and thermodesorption surface-ionization spectra were received. At the temperature of ~131±15°C and ~190±15 °C the appearance of peaks was observed typical for sertraline (Figure 1.).

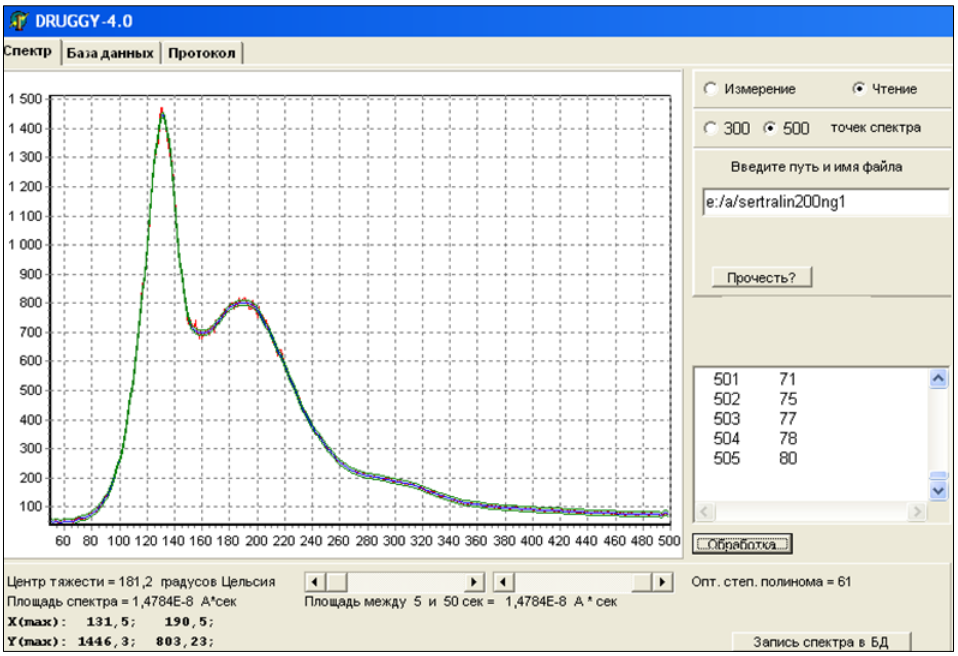

Fig 1: TDSI spectra of sertraline.

The obtained thermo desorption spectra were recorded as the references to the database of the computer. The sensitivity of the method is within 0,5 µg/ml range. Further, we examined the specificity of the conditions of sertraline analysis by TDSIS method. The temperature of the surface-ionization spectrum of sertraline was differ from the above temperatures of the studied antidepressants. The results are shown in table 1.

Table 1: The results of study of specificity of the conditions of sertraline analysis by TDSIS method.

Test substance	Temperature of maximum ionization, ºC
Fluoxamine	~123±10ºC and ~203±10 ºC
Fluoxetine	~96±15ºC and ~212±15 ºC
Paroxetine	~144±15ºC and ~230±15 ºC
Sertraline	~131±15ºC and ~190±15 ºC

Quantitative determination was carried out according to calibration graph drawn up according to the exact concentration of the standard nominal solution. To construct the calibration curve 1 ml of standard alcohol solution in the concentrations of 50, 100, 150, 200, 250, 300 µg/ml, respectively by using micro syringe is injected into the cylindrical cavity of the evaporative tape of PII-N-S "Iskovich-1" apparatus and their average values are obtained (based on the peak of sertraline at ~131±15°C). The results of the analysis are given below in table 2 and on Fig.2.

Table 2: The results of study of the linear dependence of sertraline analysis conditions by TDSIS analysis (sertraline ~131±15oC) n=5)

Solution concentration, µg/ml	Amount of sertraline, ng	The height of TDSI spectra (at current intensity ($Ix10^{-12A}$).
50	50	451
100	100	748
150	150	1082
200	200	1446
250	250	1856
300	300	2130

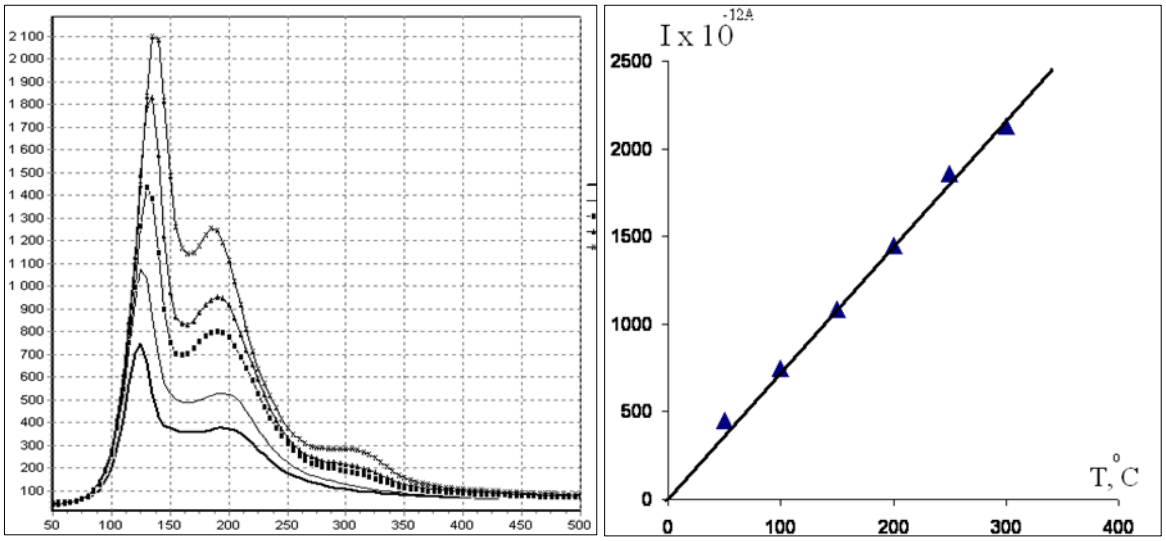

Fig 2: Graph of TDSI sertraline spectra height dependence on the solution concentration.

After quantitative determination of sertraline by TDSIS method metrological calculation was conducted. The results are shown in table 3.

Table 3: The results of study of accuracy and reproducibility of sertraline analysis conditions by TDSIS analysis.

Preparation amount, µg\ml	Obtained amount		Temperature of maximum ionization, °C	Results of metrological calculation	
	ng	%			
150	151,9	101,27	130,5	X_{mean}=100,08	S^2=2,959
150	148,4	98,93	130	S=1,720	S_x=0,769
150	146,8	97,87	129	ΔX=4,783	ΔX_{mean}=2,139
150	153,2	102,13	131	ε=4,779%	E_{mean}=2,137%
150	150,3	100,20	130		

Thus, in the result of the analysis of sertraline TDSIS we have Xmean = 100,08%, the average relative error is Emean = 2,137%.

In the next stage of study the verification of the developed procedure was conducted in the analysis of sertraline extracted from biological fluids (blood and urine).

Extraction of sertraline from blood and urine

2 ml of blood and 5 ml of urine model sample (containing 300 µg of sertraline) are diluted with 10% aqua ammonia to pH = 8,0-9,0 and 5 ml of chloroform. Samples were shaken for 5 minutes and then centrifuged for 5 minutes at 3000 rpm. Chloroform extracts were passed through anhydrous sodium sulphate and evaporated to dryness on a water bath. Dry residue was dissolved in ethyl alcohol and cleaned from ballast substances by TLC method in the system of organic solvents, benzon-chloroform-ethanol (2:1:2). Then sertraline was eluted from the sorbent of chromatography plate with ethyl alcohol and quantitative determination was carried out by TDSIS method. The results are shown in table 4.

Table 4: The results of quantitative determination of sertraline extracted from biological fluids

Amount of sertraline		Statistic processing of results	
µg/ml	%		
blood			
174,42	58,14	X_{mean}=59,57	S^2=2,4971
178,17	59,39	S=1,5802	S_x=0,7067
185,78	61,93	ΔX=4,3931	ΔX_{mean}=1,9646
180,62	60,21	E=7,3746%	E_{mean}=3,2980%
174,55	58,18		
urine			
228,42	76,14	X_{mean}=73,51	S^2=3,0557
218,16	72,72	S=1,7481	S_x=0,7818
221,64	73,88	ΔX=4,8596	ΔX_{mean}=2,1733
214,15	71,38	E=6,6110%	E_{mean}=2,9565%
220,27	73,42		

Thus, at the analysis of the determination of sertraline from dosage forms and physical evidences (blood, urine) we have achieved positive results.

Conclusions

1. The procedure of sertraline detection has been developed by the method of thermo desorption surface-ionization spectroscopy. Here it was established that alcoholic solutions of sertraline at ~131±15 °C and ~190±15 °C have maximum absorption.
2. The indicators such as specificity, accuracy, reproducibility, linear dynamic range and mean result

accuracy have been studied. Linear dynamic range is in the interval of concentration of 50-300 µg/ml in the sample. The sensitivity of the method is 0,5 µg/ml.

3. With the help of calibration curve the quantitative content of sertraline was calculated. It was established that quantitative determination of sertraline by TDSIS method makes up in average Xmean =100,08%, and Emean=2,137%. The possibility of application of this method is shown in quantitative analysis of sertraline isolated from the biological fluids. In this case, from the blood and urine sertraline is isolated in the amount of 59, 57% 73, 51%, respectively.

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