Application of the Method of Thermodesorption Surface Ionization Spectroscopy in The Analysis of Psychotropic Substances

D. A. Zulfikarieva, Z. U. Usmanalieva, Z. A. Yuldashev
Tashkent Pharmaceutical Institute

ANNOTATION
Methods for the determination and identification of droperidol and cyclodol by thermodesorption surface ionization spectroscopy have been developed. At the same time, it was found that alcoholic solutions of droperidol have absorption maxima at ~365 ± 5 ° C, cyclodol at ~90 ± 5 °The developed method is recommended for rapid analysis of droperidol and cyclodol in biological fluids in cases of acute poisoning.

Keywords: thermodesorption surface ionization spectroscopy, droperidol, cyclodol, biofluids.

In the practice of chemical and toxicological analysis, cases of poisoning with psychotropic substances have become more frequent. The most frequent poisoning occurs with neuroleptic substances. These include droperidol and cyclodol. Droperidol is a fast, strong, but short-acting neuroleptic. It has an anti-shock and antiemetic effect, has strong cataleptic activity. Suppresses aggression, manic states, hallucinations and delusions. It is used for anesthesia and pre-anesthesia preparation. Droperidol reduces mental and motor activity, which is manifested by the suppression of active behavior and the development of emotional indifference to external stimuli, with a sharp inhibition of motor activity up to catalepsy ("mineralization"). Droperidol has an antipsychotic effect, primarily anti—hallucinatory. With a single administration, droperidol causes tranquilization, while the patient looks peaceful, but later complaints of unpleasant sensations of mental restlessness and agitation may arise. This effect is avoided by co-administration of droperidol with opioids or benzodiazepines. Droperidol narrows the vessels of the brain, which causes a decrease in cerebral blood flow and intracranial pressure [1]. Cyclodol has a cholinolytic effect, it is used in medicine for the treatment of Parkinsonism. For the treatment of chronic alcoholism, cyclodol is used with stagerazine. Cyclodol is metabolized in the body, metabolites are excreted in the urine. With cyclodol poisoning, four stages of poisoning are observed: euphoria, temporary loss of consciousness, hallucinations, exit from hallucination. Substance abusers take cyclodol mainly to induce the first (euphoria) and third (hallucination) stages. With hallucinations caused by cyclodol, acute pleasant sensations are observed, as if a person is flying. [2]. In cases of acute poisoning with these drugs, there is a need for an emergency analysis of the biological fluids of poisoned people. The method of thermodesorption surface ionization spectroscopy (TDPIS) is a sensitive method that can be used in emergency cases of poisoning [3,4]. Detection of psychotropic substances is carried out by chemical and physico-chemical methods. However, to date, the method of analysis of neuroleptic drugs by the TDPIS method has not been developed. Taking into account this fact, we set ourselves the task of developing a methodology for the analysis of droperidol and cyclodol by the TDPE method in biological fluids.

The Department of Toxicological Chemistry is conducting research within the framework of the practical project AL-4721035120 - "Creation of ultrafast innovative expertise in forensic medical examination in acute and chronic poisoning with potent psychotropic substances" for 2022-2023.

Purpose of the work – development of analytical conditions for the thermodesorption spectroscopic method of surface ionization (TDSI), which is one of the methods of rapid analysis for the determination of potent psychotropic substances, and its application in forensic chemical practice.

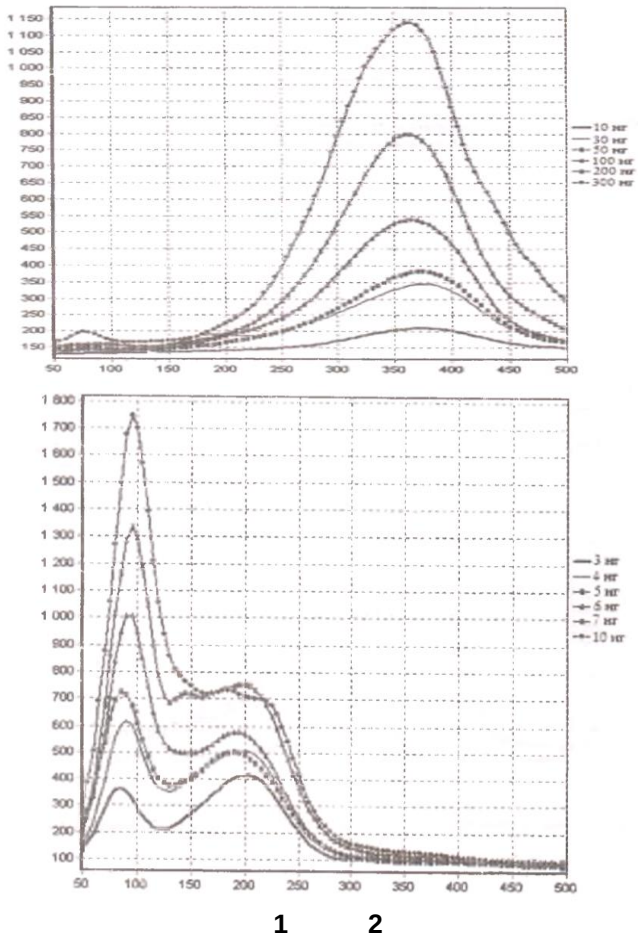
Research methods: To detect droperidol and cyclodol by the TDPIS method, the following analysis conditions were selected:

emitter – oxidized molybdenum, containing iridium; emitter voltage – 405 V; emitter temperature – 200-300 ° C; evaporation temperature - 20-505 ° C; air flow – 50 l/hour (compressor voltage 12 V);

the volume of the test sample taken for analysis is 0.1 ml; the analysis time is 3 minutes; the spectra are recorded directly using a computer program.

Solutions of standard samples of droperidol and cyclodol were prepared for the research. Thermodesorption surface-ionization spectra of droperidol and cyclodol were obtained using these solutions. The appearance of linear spectra of droperidol at ~365 ±5°C and cyclodol at ~90 ±5°C was observed. Thermal desorption spectra of these substances were used to determine droperidol and cyclodol isolated from biological fluids.

Then a number of solutions of droperidol and cyclodol, of various concentrations, were prepared. The thermal desorption spectra of the substances under study and the current values corresponding to these spectra are shown in Fig. 1 and in Tables 1 and 2.



1 2

Fig.1.Spectra of droperidol (1) and cyclodol (2)

Table 1

Dependence of the current strength of TP And on the content of droperidol in solution

№	Droperidol content	Current strength I, A
1	10 нг	205
2	30 нг	370
3	50 нг	535
4	100 нг	725
5	200 нг	925
6	300 нг	1145

Table 2

Dependence of the current strength of the TPI on the content of cyclodol in the solution

№	Cyclodol content	Current strength I, A
1	3 нг	325
2	4 нг	530
3	5 нг	765
4	6 нг	1000
5	7 нг	1265
6	10 нг	1555

The detection limit of droperidol was 10 ng, cyclodol 3 ng. Based on the data obtained, calibration graphs of the dependence of the TP current strength and the spectra of droperidol and cyclodol on their concentration in solution were constructed (Fig. 2).

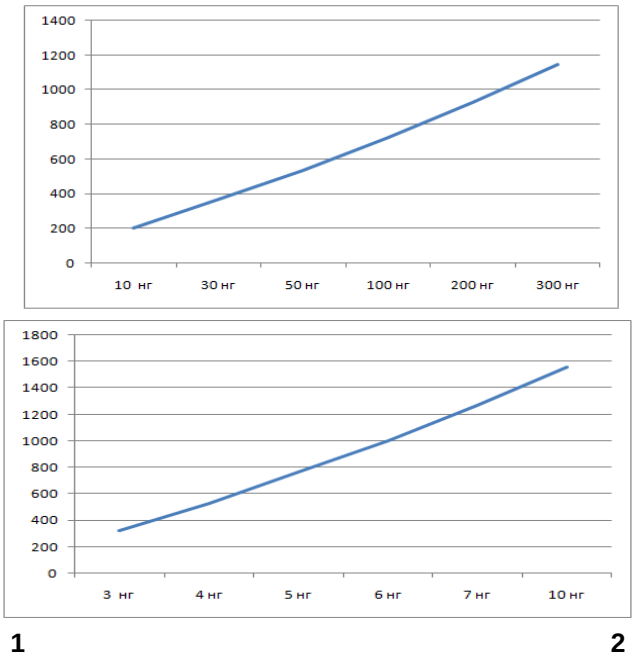


Fig. 2. Calibration graph for quantitative determination of droperidol (1) and cyclodol (2)

At the next stage of the research, the developed methodology was tested in the analysis of droperidol and cyclodol isolated from biofluids (blood and urine).

Isolation of droperidol from blood and urine.

A 10% sodium hydroxide solution was added to the model blood samples with a volume of 5 ml, urine (25 ml) to a pH value of 10 (according to the universal indicator), the resulting mixture was heated in a boiling water bath with an air refrigerator for 30 minutes. After cooling, the resulting mixture was extracted using a separating funnel three times with 20 ml ethyl acetate for 5 minutes on a mixing device. The obtained extracts were filtered through a filter with anhydrous sodium sulfate, evaporated in a current of warm air to a dry residue.

The dry residue of extraction from the blood was dissolved in 8 ml of alcohol. The dry residue of extraction from urine was dissolved in 12 ml of alcohol. 1 µl of the resulting solution was injected into the cylindrical cavity of the vapor-forming tape of the PPI-N-S Iskovich-1 apparatus and thermodesorption surface-ionization spectra were obtained. At a temperature range of 200-210 °C observed the appearance of a peak characteristic of droperidol.

Research results. The results of the conducted studies have shown that in the analysis of droperidol isolated from biofluid, the TDPE method is suitable for both detection and quantitative determination of the substance under study. The quantitative content of droperidol extracted from model samples was calculated using a calibration graph. The obtained results are statistically processed and presented in Table 3.

Table 3

Results of quantitative analysis of droperidol isolated from biofluids

Amount of droperidol		Statistical processing of results
нг	%	
blood		
29,03 29,45 29,93 31,38 35,20	58,06 58,90 59,86 62,76 70,40	f=4; T (95%, 4)=2,78; $X_{ўр}$=61,99; S^2=6,3032; S=2,513;S_x=1,112; ΔX=6,979; $\Delta X_{ўр}$=1,959 E=12,88%; ε=5,76%
urine		
40,05 40,48 42,41 40,96 35,23	80,10 80,96 84,82 81,92 79,46	f=4; T (95%, 4)=2,78; $X_{ўр}$=81,45; S^2=4,8070; S=2,1924;S_x=0,9851; ΔX=6,0951; $\Delta X_{ўр}$=2,7258 E=7,48%;ε=3,34%

Isolation of cyclodol from blood and urine.

10 ml of the test blood was taken into a flask (100 ml), 30 ml of a solution of 0.02 n H2SO4 and 20% solution of H2SO4 drops to pH = 2 were added and left for 2 hours (post. stirring). Then they were centrifuged. The centrifuge was separated, the volume was adjusted from 0.02n H2SO4 to 100 ml. NaOH solution was added to 50 ml of the mixture to pH 7.5 and extracted 3 times 10 ml with chloroform. The obtained extracts were filtered through a filter with anhydrous sodium sulfate, evaporated in a current of warm air to a dry residue.

The dry residue of extraction from the blood was dissolved in 8 ml of alcohol. The dry residue of extraction from urine was dissolved in 12 ml of alcohol. 1 µl of the resulting solution was injected into the cylindrical cavity of the vapor-forming tape of the PPI-N-S Iskovich-1 apparatus and thermodesorption surface-ionization spectra were obtained. At a temperature range of 200-210 °C observed the appearance of a peak characteristic of cyclodol.

Research results. The results of the conducted studies have shown that in the analysis of cyclodol isolated from biofluid, the TDPE method is suitable for both detection and quantitative determination of the substance under study. The quantitative content of cyclodol extracted from model samples was calculated using a calibration graph. The obtained results are statistically processed and presented in Table 4.

Table 4

Results of quantitative analysis of cyclodol isolated from biofluids

The amount of cyclodol		Statistical processing of results
мг	%	

0,474 0,485 0,467 0,491 0,459	47,41 48,56 46,75 49,18 45,94	X_{cp}=47,56 S^2=1,823 S=1,350 S_x=0,603 ΔX=3,753 X_{cp}=1,678 E=7,89% E_{cp}=3,53%
urine		
0,647 0,675 0,624 0,631 0,659	64,74 67,56 62,75 49,18 45,94	X_{cp}=64,72 S^2=4,282 S=2,069 S_x=0,925 ΔX=5,752 X_{cp}=2,572 E=8,88% E_{cp}=3,975%

CONCLUSION

A method for detecting neuroleptic drugs included in the list of psychotropic substances, droperidol and cyclodol, by thermodesorption surface-ionization spectroscopy has been developed. The possibility of using this method in the detection and quantitative analysis of droperidol and cyclodol isolated from biofluids is shown. At the same time, droperidol is isolated from blood and urine in the amount of 61.99% and 81.45%; cyclodol is isolated in the amount of 47.56% and 64.72%, respectively. It is proposed to use the TDPIS method for express analyses of biological fluids in cases of poisoning with psychotropic substances.

REFERENCES

[1] Davydov A.T., Krupitsky E.M., Remizov L.M. Features of clinical use of typical antipsychotic drugs in psychiatric and narcological practice // Reviews on clinical pharmacology and drug therapy. - 2007. — Vol. 5, No. 1.

[2] Velikanova L.P., Mesnyankin A.P., Kaverina O.V., Bisaliev R.V., Chernova M.A. Selected issues of narcology: textbook / Edited by L.P. Velikanova. — Astrakhan, 2005. — 365 p.

[3] On the analysis of opiates in blood, urine and in cadaveric materials by thermodesorption surface-ionization spectroscopy /Giyasov Z.A., Shakhitov M.M. et al.;– Tashkent, 2003. – 12 p.

[4] Zulfikarieva D.A., Yuldashev Z.A. Application of the method of thermal-security surface-ionization spectroscopy in analysis of alkaloids of conium maculatum / World journal of pharmacy and pharmaceutical sciences. Vol.8, Issue 6. Indiya, 2019. pp.48-53.

[5] Usmanalieva Z.U., Abdugaffarov M. The development of analytical conditions of levamizole by thermodesorption surface ionization spectroscopy /Asian Journal of Research in Social Sciences and Humanities. – 2021. - V.11, N 11. – P. 295-298.