Full Paper _____ *Thematic Section:* Physicochemical Research.
Reference Object Identifier – ROI: jbc-01/18-56-11-38 *Subsection:* Analytical Chemistry.
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/18-56-11-38
Submitted on October 26, 2018.

Comparative analysis of meldonium by TLC in water-organic, aqueous micellar and cyclodextrin mobile phases

© **Elena G. Sumina**,[1]*+ **Varsenia Z. Uglanova**,[2] **Olga N. Sorokina**,[3] and **Anna O. Ustyugova**[1]
[1] *Department of Analytical Chemistry and Chemical Ecology*
[2] *Department of Petrochemistry and Technological Safety. N.G. Chernyshevsky Saratov National Research State University. Astrakhanskaya St., 83. Saratov, 410012. Russia. Phone:* [1)] *+7 (964) 879-65-27;* [2)] *+7 (919) 833-02-05. E-mail:* [1)] *SuminaEG@yandex.ru,* [2)] *UglanovaVZ@mail.ru*
[3]*Saratov State Medical University named after V.I. Razumovsky under Ministry of Health of the Russian Federation, Bolshaya Kazachia st., 112. Saratov, 410012. Russia. Phone: +7 (908) 555-56-34. E-mail: Sorokina-O-N@yandex.ru*

*Supervising author; +Corresponding author
Keywords: thin-layer chromatography, surfactants, cyclodextrins**,** meldonium**,** medications.

Abstract

Meldonium belongs to the class of quaternary ammonium bases, which are products of the complete alkylation of ammonium salts. Possessing metabolic properties and a wide range of therapeutic action, meldonium is widely used in medicine. At present, modern analytical techniques are used to analyze meldonium in industrial and natural objects. However, most of them are quite expensive and require considerable time. Thin-layer chromatography (TLC), characterized by simplicity, availability of analysis, separation efficiency and cheapness, has gained much less use. In this connection, the purpose of this work was to reveal the analytical capabilities of water-organic, micellar and cyclodextrin mobile phases for meldonium analysis by means of TLC.

Initial meldonium solutions with a concentration of 20 mg/ml were prepared by diluting solutions for injections. Their chromatography was carried out by ascending thin-layer chromatography on plates of various polarities (Sorbfil, Plasmachrom, and RP-18) with a fixed sorbent layer. Aqueous solutions of surfactants (cetyltrimethylammonium bromide [CTAB], cetylpyridinium chloride [CPC], sodium dodecyl sulfate [SDDS], Triton X-100 [TX-100]), of cyclodextrins (β-cyclodextrin (β-CD), 2-hydroxypropyl-β-cyclodextrin (2-HP-β-CD), hydroxypropyl-γ-cyclodextrin (HP-γ-CD)) were used as mobile phases. Chromatographic zones were identified on a Sorbfil video-densitometer (Sorbopolymer, Krasnodar, Russian Federation).

Basic features of the behavior of meldonium were revealed. Based on the calculation of the number of theoretical plates and the height equivalent to a theoretical plate, it is shown that aqueous micellar and cyclodextrin mobile phases allow improving the efficiency of the chromatographic process and the shape of the chromatographic zones of meldonium as compared to water-organic eluents. Optimal chromatographic systems and conditions for their use in the thin-layer chromatography of drugs were selected and substantiated.

References

[1] N. Sjakste, A. Gutcaits, I. Kalvinsh. Mildronate: an antiischemic drug for neurological indications. *CNS Drug Rev*. **2005**. No.11(2). P.151-168.
[2] A.A. Gorbunova, S.Yu. Kireev, I.V. Rashevskaya. Meldony: communication of a structure, structure and properties. *Bulletin of the Penza state university*. **2017**. No.2(17). P.92-99. (russian)
[3] A.L. Vertkin, N.O. Khovasova, V.V. Pshenichnikova, M.A. Alekseev, A.U. Abdullaeva. Meldonium: effective action points. *Kardiovaskulyarny therapy and prevention*. **2013**. No.12(2). P.94-97. (russian)
[4] I.V. Samorodskaya. Meldony: review of results of researches. *JRM*. **2013**. Vol.21. P.1818-1822. (russian)
[5] A.I. Bereznikov, N.G. Philippenko. Application of meldoniy in the treatment of circulatory disorders in the vessels of the retina and optic nerve. *Scientific sheets of the Belgorod state university. Series: Medicine. Pharmacy*. **2012**. Vol.20. No.2-1. P.74-77. (russian)
[6] A.A. Azaryan, A.Z. Temerdashev, E.V. Dmitrieva. Determination of Meldonium in human urine by HPLC with tandem mass spectrometric detection. *J. of Anal. Chem.* **2017**. Vol.72. No.10. P.885-889. (russian)

[7] P.N. Sorokoumov, E.I. Savelieva, G.V. Karakashev, V.A. Kopeikin, A.S. Radilov. Determination of meldonium gamma-butyrobetaine and carnitine in blood plasma by high-performance liquid chromatography with mass-selective detection. *Development and registration of medicines*. **2016**. No.1(14). P.176-183. (russian)
[8] Y.-F. Lv, X. Hu, K.-S. Bi. Determination of mildronate in human plasma and urine by liquid chromatography-tandem mass spectrometry. *J. Chromatogr. B*. **2007**. Vol.852. P.35-39.
[9] L.-J. Cai, J. Zhang, W.-X. Peng, R.-H. Zhu, J. Yang, G. Cheng, X.-M. Wang. Determination of Mildronate in Human Plasma and Urine by UPLC-Positive Ion Electrospray Tandem Mass Spectrometry. *Chromatogr.* **2011**. Vol.73. P.659-665.
[10] Y. Peng, J. Yang, Z. Wang, J. Wang, Y. Liu, Z. Luo, A. Wen. Determination of mildronate by LC-MS/MS and its application to a pharmacokinetic study in healthy Chinese volunteers. *J. Chromatogr. B*. **2010**. Vol.878. P.551-556.
[11] A.A. Azaryan, A.Z. Temerdashev, N.V. Kiselyeva. Way of definition a meldonium in urine of the person. *Patent №217.015.F80B*, 29.12.2017. (russian)
[12] M.V. Gavrilin, Yu.V. Mudretsova. Micellar electrokinetic chromatography and mass spectrometry studies of mildronate stability in aqueous solutions. *Pharmaceutical Chemistry Journal*. **2014**. Vol.48. No.2. P.53-56. (russian)
[13] O.L. Mezinceva, G.B. Slepchenko. Use of the modified carboniferous electrodes for definition a meldonium in biological objects. «Analytics of Siberia and Far East». Materials X of the All-Russian scientific conference with the international participation, 12-17 September, Barnaul, 2016. *Barnaul: Publishing house AltGU*. **2016**. P.80-81. (russian)
[14] M.V. Gavrilin, Yu.V. Mudretsova, S.V. Senchenko, S.A. Rozhnova. Development of quantification method for determination of choline alphoscerate and meldonium by capillary electrophoresis. *Questions of biological, medical and pharmaceutical chemistry*. **2012**. Vol.10. No.4. P.12-17. (russian)
[15] L.A. Kartsova, E.G. Strel'Nikova. Determination of endo- and exogenous corticosteroids by cyclodextrin-modified micellar electrokinetic chromatography with the use of on-line preconcentration. *J. of Anal. Chem.* **2007**. Vol.62. No.9. P.965-968. (russian)
[16] S.N. Shtykov, E.G. Sumina, V.Z. Uglanova, O.N. Sorokina. Thin-layer chromatography of some amino acids on silica in aqueous–organic and modified micellar mobile phases. *J. of Anal. Chem.* **2017**. Vol.72. No.8. P.742-750. (russian)
[17] E.G. Sumina, V.Z. Uglanova, O.N. Sorokina, and A.I. Danchuk. Comparative analysis of glycyrrhizic acid by TLC and HPLC modified with surfactants and organic solvents. *Butlerov Communications.* **2015**. Vol.44. No.12. P.94-100. DOI: 10.37952/ROI-jbc-01/15-44-12-94
[18] E.G. Sumina, V.Z. Uglanova, O.N. Sorokina, D.O. Afonina. Analysis of the purity of preparations of corticosteroid hormones by thin-layer chromatography in mobile phases based on cyclodextrins and surfactants. *Izv. Saratov University. New Series. Chemistry. Biology. Ecology*. **2011**. Vol.11. No.2. P.48-53. (russian)
[19] E.G. Sumina, S.N. Shtykov, V.Z. Uglanova, O.N. Sorokina. Liquid chromatography of some steroid hormones in aqueous-organic, micellar, and cyclodextrin mobile phases. *J. Anal. Chem*. **2014**. Vol.69. No.10. P.1105-1113. (russian)
[20] S.B. Savvin, R.K. Chernova, S.N. Shtykov. Surfactants (Analytical reagents). *Moscow: Science*. **1991**. 251p. (russian)
[21] T.J. Ward, D.W. Armstrong. Improved cyclodextrin chiral phases: a comparison and review. *J. Liquid Chromatogr.* **1986**. Vol.9. P.407-423.
[22] D.W. Armstrong. Cyclodextrin as chiral mobile phase additives in TLC. *J. Chromatogr*. **1988**. Vol.452. P.331-345.
[23] E.G. Sumina, V.Z. Uglanova, and O.N. Sorokina. Use of cyclodextrin mobile phases in chin-layer chromatography of fluoresceins. *Butlerov Communications.* **2017**. Vol.50. No.4. P.123-132. DOI: 10.37952/ROI-jbc-01/17-50-4-123
[24] E.G. Sumina, V.Z. Uglanova, T.E. Sorokina, and O.N. Sorokina. Thin-layer chromatography of some benzene derivatives in aqueous and modified by cyclodextrins mobile phases. *Butlerov Communications.* **2016**. Vol.45. No.3. P.51-59. DOI: 10.37952/ROI-jbc-01/16-45-3-51
[25] E.G. Sumina, V.Z. Atayan, S.N. Shtykov. Application of cyclodextrins mobile phases in the thin-layer chromatography of the xantens and chinolins organic reagents of ranks. *Sorb. & chromatogr. processes.* **2008**. Vol.8. No.1. P.83-93. (russian)
[26] F. Geiss. Fundamentals of Thin Layer Chromatography (Planar Chromatography). *Heidelberg–Basel–New York: Dr Alfred Huethig Verlag.* **1987**. (russian)
[27] V.D. Shatz, O.V. Sakhartova. High-performance liquid chromatography. *Riga.* **1988**. 160p.

[28] P.K. Zarzycki, H. Ohta, Y. Saito, K. Jinno. Interaction of native α-cyclodextrin, β-cyclodextrin and γ-cyclodextrin and their hydroxypropyl derivatives with selected organic low molecular mass compounds at elevated and subambient temperature under RP-HPLC conditions. *Anal. Bioanal. Chem.* **2008**. Vol.391. P.2793-2801. (russian)
[29] A.A. Shteinman. Cyclodextrins. *J. All-Russian Chem. Soc.* **1985**. Vol.30. No5. P.514-518. (russian)