Ionic liquid tags as a tool for investigating drugs at the single-cell level

Ksenia S. Egorova[1]*, Fedor A. Kucherov*[1]*, Alexandra V. Posvyatenko*[1,2]*, Dmitry B. Eremin*[1]*, and Valentine P. Ananikov*[1]

[1]*N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prospect 47, Moscow, 119991 Russia*
[2]*Institute of Gene Biology, Russian Academy of Sciences, Vavilova str. 34/5, Moscow, 119334 Russia*
egorova-ks@ioc.ac.ru

High heterogeneity of cellular populations, especially malignant tumors, has attracted a significant attention to the studies on biological activity of drugs at the level of individual cells. Still, successful identification of chemical substances and products of their transformations requires overcoming two limitations: insufficient signal intensity and masking of target signals due to overlapping with signals of other substances present in the living cell. We propose alleviating these issues by employing ionic liquid tags. Ionic liquids with their huge fine-tuning potential have recently been suggested as important players in various pharmaceutical fields (1-3). We demonstrated that the conjugation of the antineoplastic drug mitoxantrone with four imidazolium tags did not lead to significant disturbance of cytotoxic activity of the drug. At the same time, sensitivity of electrospray ionization mass spectrometry (ESI-MS) to the mitoxantrone conjugate was by an order of magnitude higher than that to the original mitoxantrone dihydrochloride. The observed ESI-MS signals were shifted to a 'clearer' lower-mass region of the spectrum, which allowed investigating the drug at the level of individual cells. The synthesized mitoxantrone conjugate was oil at physiological temperatures and demonstrated high aqueous solubility (Figure 1). This research was supported by the Russian Science Foundation (grant 18-13-00116).
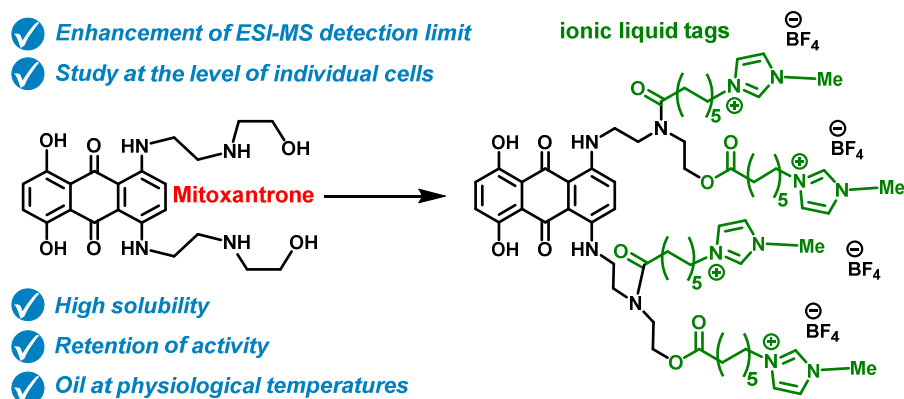

Figure 1. Ionic liquid mitoxantrone conjugate demonstrates high water solubility and biological activity, together with the improved ESI-MS detection limit that allows studying the drug behavior at the level of individual cells.

1. Egorova KS, Gordeev EG and Ananikov VP. *Chem. Rev.* 2017, 117(10): 7132–7189.
2. Egorova KS, Seitkalieva MM, Posvyatenko AV, Khrustalev VN and Ananikov VP. *ACS Med. Chem. Lett.* 2015, 6(11): 1099-1104.
3. Kucherov FA, Egorova KS, Posvyatenko AV, Eremin DB and Ananikov VP. *Anal. Chem.* 2017, 89(24): 13374-13381.