

Simultaneous Determination of Polar Destruction Products of Nerve Agents by HPLC-MS/MS with Preliminary Derivatization

Vokuev, M.F.*, Baygildiev, T.M., Braun, A.V., Rodin, I.A., Rybalchenko, I.V.

Lomonosov Moscow State University, Chemistry Department, Moscow, Russia

Nowadays a serious problem of the modern world is the possibility of using chemical weapons (CW) during armed conflicts or terrorist attacks. The most dangerous component of CW are nerve agents, which are derivatives of organophosphate acids (sarin (GB), soman (GD), cyclosarin (GF), VX, VR). Nerve agents irreversibly bind to the enzyme acetylcholinesterase, which is responsible for the inactivation of acetylcholine, which leads to blocking the transmission of nerve impulses.

Markers of nerve agents are stable alkylphosphonic acids (APAs) and alkyl methylphosphonic acids (AMPAs), which are formed as a result of nerve agents' hydrolysis and are present in samples for a long time. According to their content in the environment or in biological materials, it can be concluded that CW were used. Therefore, the development of modern analytical methods for the detection and determination of nerve agents destruction products is an important task of analytical chemistry.

The purpose of this study was to create a reliable, highly sensitive method for the simultaneous determination of APAs (methyl, ethyl, propyl) and AMPAs (ethyl, isopropyl, isobutyl, pinacolyl) using liquid chromatography and tandem mass spectrometry.

For the determination of APAs and AMPAs, derivatization was used, since these compounds are polar and have a low molecular weight, which makes their detection at a low level difficult by the method of reversed-phase HPLC-MS/MS. For the derivatization of acids p-methoxyphenacyl bromide (PMPB) was proposed as a reagent. Products by one OH-group are formed in the case of AMPAs as a result of the reaction. Products both by one and two OH-groups are formed in the case of APAs. Sensitive MS detection was performed in the multiple reaction monitoring mode. In the registration mode of negatively charged ions, AMPAs derivatization products are not formed, in contrast to APAs by one OH-group. However, in the registration mode of positively charged ions it is possible to detect products of APAs and AMPAs by one and two groups, as a result, it is possible to determine all analytes in one run.

The conditions of chromatographic separation in the reversed-phase chromatography mode were selected. It was shown that the derivatization reaction proceeds only in the presence of bases, such as K_2CO_3 or Et_3N . Derivatization reaction conditions were optimized. It was established that the presence of water in the reaction mixture greatly reduces the yield of the reaction with AMPAs. The achieved detection limit of phosphonic acids was at the level of 0.1 ng mL^{-1} .

This work was supported by the Russian Foundation for Basic Research (Grant No. 18-33-20068 mol_a_ved).