



LC-MS Method Development for Simultaneous Determination of Trans-3'-hydroxycotinine and Three Mercapturic Acids in Urine

L. V. Lopukhov¹ · A. V. Laikov¹ · V. A. Romanova¹ · D. Z. Gatina¹ · V. L. Lopukhov¹ · S. R. Abdulkhakov¹ · T. A. Zaitseva² · S. N. Medvedeva² · E. V. Gnuchikh² · I. I. Salafutdinov¹ · T. V. Grigoryeva¹

Published online: 18 May 2018

© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract

The negative impact of tobacco smoke on the human body is due to a wide range of harmful substances including volatile organic compounds (VOCs). Some VOCs of tobacco smoke metabolize in human organism into mercapturic acids (MAs). The determination of the amount of MAs in readily available biological fluids, for example in urine, allows to assess the level of exposure of these VOCs in a particular person. It is useful to assess the impact of individual VOCs on the body together with the assessment of the intake of nicotine. The intake of nicotine can be determined by the content of its metabolites in the urine, in particular by the content of trans-3'-hydroxycotinine (tH-Cot). A joint assessment of the concentrations of trans-3'-hydroxycotinine and MAs in urine allows obtaining selective information about effects of different VOCs and nicotine on the smoker's body. We have developed a liquid chromatography–mass spectrometry (LC-MS) method for simultaneous quantifying of tH-Cot and three MAs: N-Acetyl-S-(3-hydroxypropyl)cysteine (HPMA), N-Acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HMPMA), N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CEMA). We used this method to quantify the levels of MAs and tH-Cot in the urine of a group of 15 smokers just before and 5 days after smoking cessation. For all studied compounds, we have found statistically significant changes in concentration on the fifth day of smoking cessation. The method developed can be used to jointly assess the levels of exposure to nicotine and VOCs in the study of various tobacco products.

Keywords Mercapturic acids · Nicotine · Tobacco · LC-MS

1 Introduction

Volatile organic compounds (VOCs) of tobacco smoke are an important factor in its impact on the body. Estimation of the amounts of individual VOCs received by the body of a smoker is necessary in the study of the exposure and biological effects of various tobacco products and measures to reduce the harmful effects of smoking. When assessing the biological effects of smoking, as a proxy measure, it is convenient to do this by

determining the amount of VOC metabolites in the urine. This approach combines non-invasiveness, reliability, and relative simplicity. In particular, to assess the impact of smoking associated with certain VOCs, it is convenient to use the content of their metabolites—mercapturic acids (MAs) in urine. It is useful to evaluate MA content simultaneously with the nicotine metabolite content evaluation to have data on both VOCs and nicotine exposure.

Mercapturic acids are formed from VOCs contained in tobacco smoke entering the body. Table 1 lists precursor substances for certain mercapturic acids [1, 2].

It can be seen from the table that the precursors of HPMA and HMPMA are unsaturated aldehydes (acrolein and crotonaldehyde), which are highly reactive. Acrolein and crotonaldehyde are toxic and carcinogenic and have a strong irritant effect [3–5], so they can be attributed to the important factors of smoking harmfulness.

According to the literature, concentrations of HPMA, CEMA [1], and HMPMA [2] differ significantly among smokers and non-smokers.

✉ L. V. Lopukhov
leonidlopuhov@rambler.ru

¹ Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan, Russian Federation

² Federal State Budget Scientific Institution All-Russian Scientific Research Institute of Tobacco, Makhorka and Tobacco Products, Krasnodar, Russian Federation