International Journal of Criminal Investigation

Volume 2
Issue 4 / 2012
251-257

NICOTINE AND TOBACCO ALKALOIDS: A GC-MS ANALYSIS. PART 2: THE TOBACCO AND SMOKING

Gheorghita ZBANCIOC, Gabi DROCHIOIU, Ionel I. MANGALAGIU[i]

"Al. I. Cuza" University of Iasi, Organic and Biochemistry Department,
Bd. Carol 11, 700506, Iasi, Romania

Abstract

The emphasis of this work was to present a study concerning the main tobacco metabolites, focused in structure identifications by GC-MS. The main fragmentation reactions and the consequences correlation of the principal metabolites resulting from tobacco it is also presented.

Keywords: *metabolites, cotinine, 3-hydroxycotinine, nicotine-1-N-oxide, fragmentation*

Introduction

Smoking has enormous negative health consequences worldwide, being the leading cause for many human diseases, especially cardiovascular and pulmonary diseases. Lung cancer also could not be neglected. Many people are now aware not only for the caused diseases, bat also many are aware for the addiction caused by tobacco products.

Nicotine is the main component in commercial tobacco products, the concentrations range varying from 6 to 18 milligrams per gram (mg/g). When a cigarette is smoked, the amount of nicotine deliver it into the air is around 1.6 mg per cigarette, the danger for non-smoker via passive inhalation being of high risk.

After smoking, tobacco alkaloids are initially absorbed into the pulmonary circulation, than distributes rapidly to brain and heart tissues.

The negative effects of smoking are not only due to the alkaloids but also in equal measure because of their metabolites. The liver represents the primary site of metabolism for nicotine (lung and kidney contribute to the metabolism in a minor manner). Into the liver, the nicotine alkaloids are metabolized to a large numbers of metabolites, the most important of than being: cotinine, 3-hydroxycotinine, norcotinina, nicotine-1-N-oxide, 2-hydroxynicotine, nornicotine, nicotine isomethonium ion, and nicotine glucuronide, Figure 1.

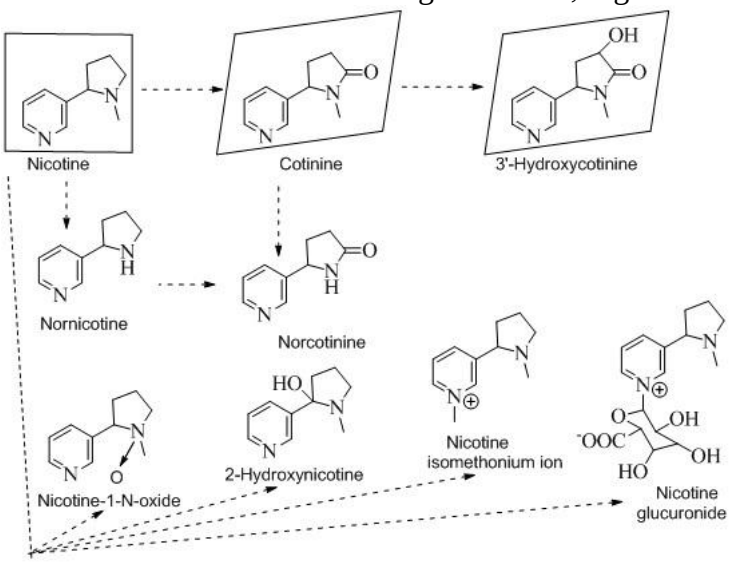


Fig. 1*. The main metabolism pathway for nicotine*

In humans, about 70 to 80% of nicotine is converted to cotinine. On its turn, cotinine is metabolized to 3-hydroxycotinine (trans-3'-hydroxycotinine), this is why in the urine of both active and passive smokers, 3-hydroxycotinine is the predominant nicotine metabolite (around 40% of the total nicotine excretion). In continuation of our concern in the field of forensic chemistry and tobacco alkaloids, we present here a study concerning the fragmentation reactions of the main metabolites resulting from metabolization of the tobacco alkaloids.

Results and discussions

In Figures 2-4 are presented the mass spectra of the main metabolites resulting from metabolization of the tobacco alkaloids.

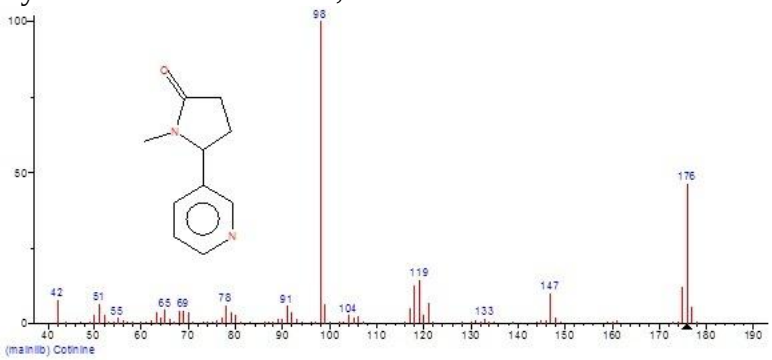
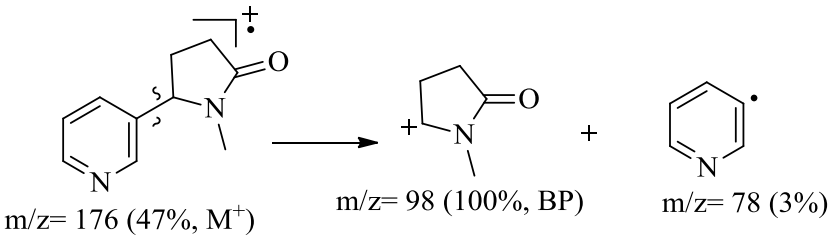
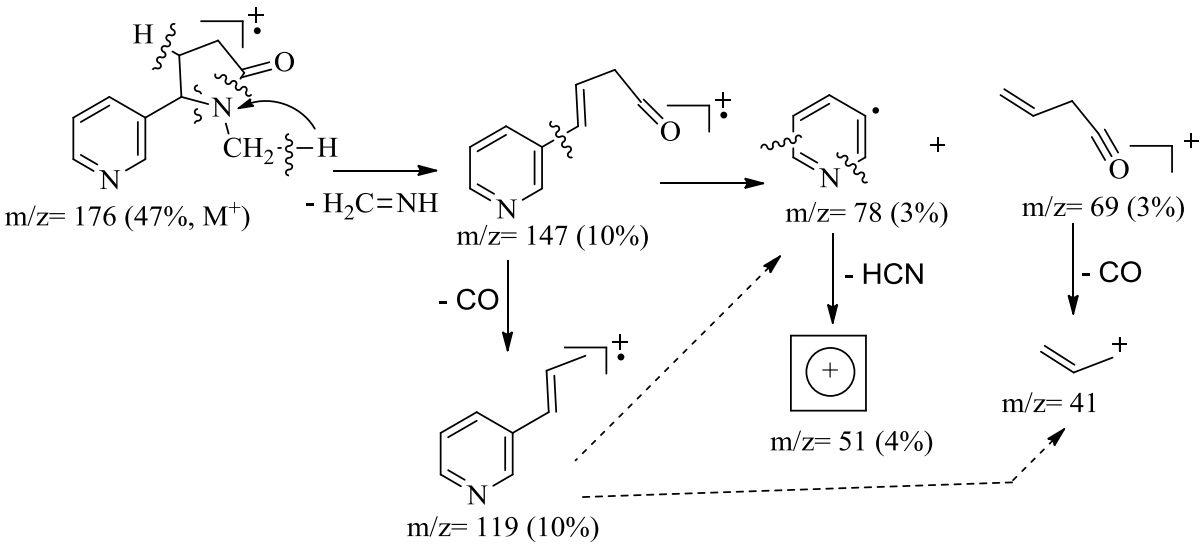


Fig. 2. *Cotinine mass spectra*

Analysing the data furnished by mass spectra of cotinine (Figure 2) reveals the following:
- the molecular ion, M^+, appears at m/z=176 with a great intensity of 47%, characteristic for cyclic amides; the M+1 peak (m/z=177,14%) and M-1 peak (m/z =175,7%) are significant being characteristic for cyclic amides;
- the base peak (BP) appears at m/z=98(100%) and could be explained through a fragmentation on the bond level between the two nitrogen heterocycles; the same fragmentation explains the peak at m/z=78(3%);

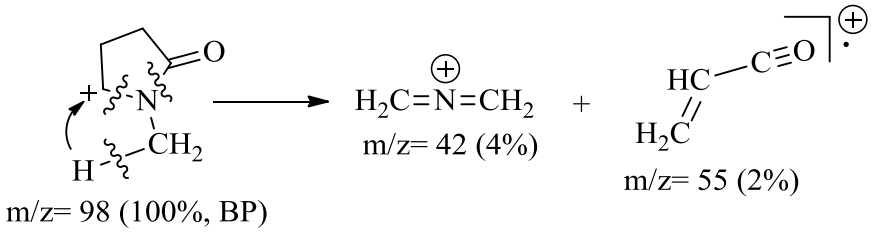


- a complex fragmentation on the pyrrolidinone ring (α-type fragmentation on the level of cyclic tertiary amido group followed by transfer of protons and electrons) explain the peak from m/z=147(10%). Additional fragmentation of the fragment from m/z=147(α-fragmentation to the double bond and pyridinyl cycle) is generating the peaks from 78(3%) and 69(3%); subsequent fragmentation of the pyridinyl fragment from m/z=78(α□□and β- fragmentation to the nitrogen atom, followed by transfer of protons and electrons) is generating the peaks from 51(4%). Another fragmentation of the fragment from m/z= 69(α□□fragmentation to the CO group, followed by transfer of a proton and electrons) is generating the peaks from 41;



Another fragmentation of the fragment from m/z=147(α- fragmentation to the double bond and pyridinyl cycle) is generating the peaks from 119(10%); subsequent fragmentations of this fragment from m/z=119 could generate the fragments from 78 and 41;

- the peaks from m/z=55(2%) and m/z=42(4%), are characteristic peaks for the fragmentation of cyclic amides; the most likely fragmentation reaction which explain the above peaks are complex fragmentation of pyrrolidinone ring (α□□and β- fragmentation to the nitrogen atom, followed by transfer of protons and electrons).



The mass spectra of 3-hydroxycotinine is presented in Figure 3.

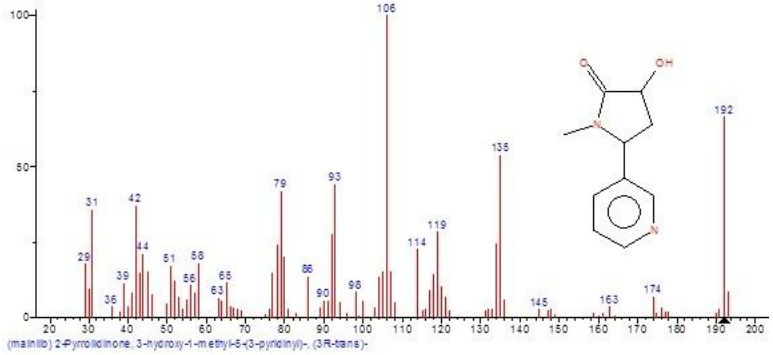


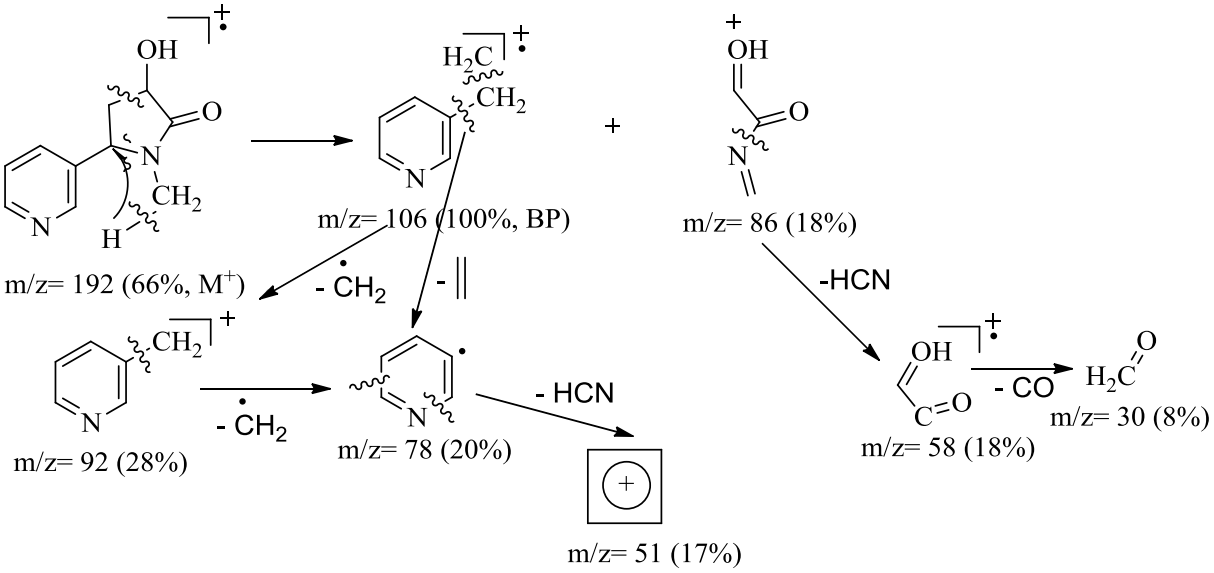
Fig. 3. *3-Hydroxycotinine mass spectra*

In the 3-hydroxycotinine case the main fragmentation reactions are the following:

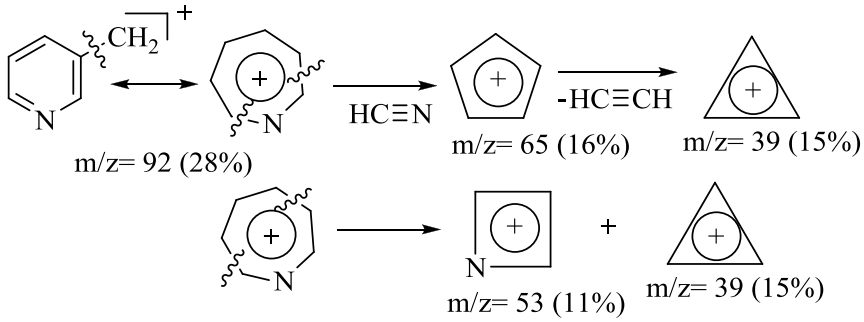
- the molecular ion, M^+, appears at m/z=192 with a great intensity of 66%, characteristic for cyclic amides; the M+1 peak (m/z=193, 5%) is present, being characteristic for cyclic amides;

- the base peak (BP) appears at m/z=106 (100%) and could be explained through a complex fragmentation on the 3-hydroxy-

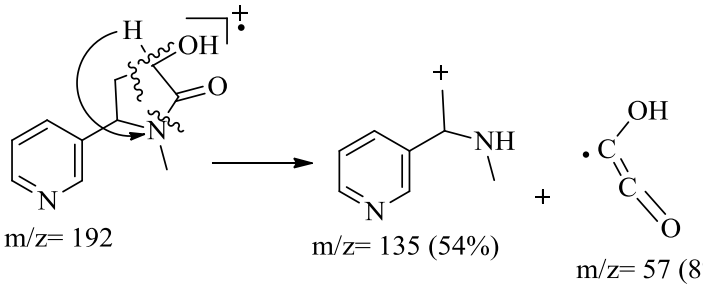
pyrrolidone ring heterocycles; the same fragmentation explains the peak at m/z = 86(18%); α- and β-fragmentation of the lateral chain from BP fragment explain the azatropilium fragments from 92(28%), 78(20%) and the subsequent fragment from 51(17%); α-fragmentation of the fragment from m/z=86, explain the fragments from 58(18%) and the subsequent fragment from 30(8%);



- the azatropiliu fragment from 92, could suffer multiple complex ways of fragmentation (analogous fragmentation with tropiliu cation), generating the peaks from 65(16%), 53(11%), 39(15%);

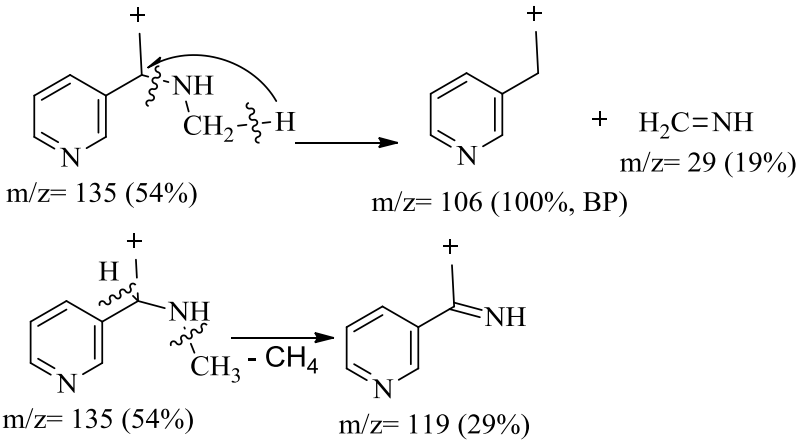


- the peaks from m/z=135(54%) and m/z=57(8%), could be explained through a complex fragmentation on the 3-hydroxy-pyrrolidone ring heterocycles (α- type fragmentation on the level of cyclic tertiary amido group and hydroxyl group, followed by transfer of protons and electrons);



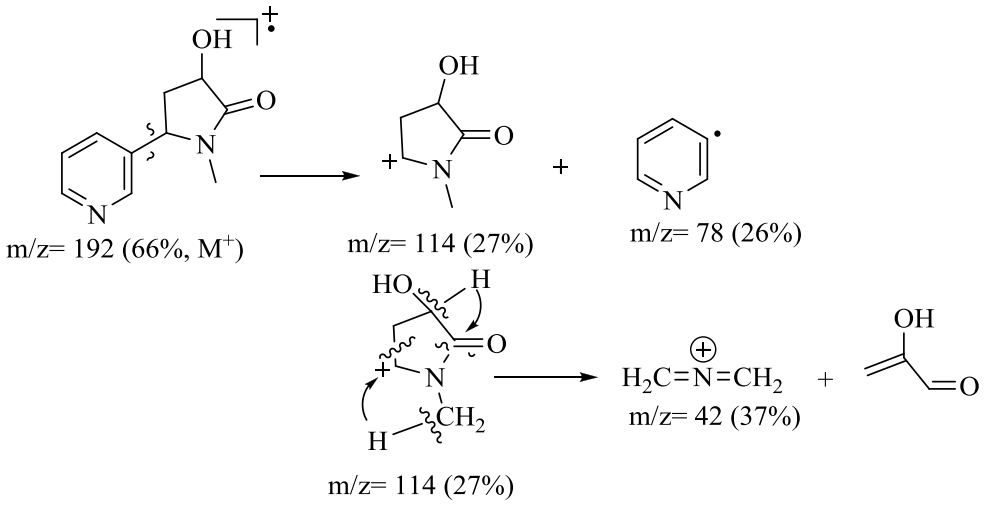
-subsequent α-fragmentation to the secondary amino group accompanied by a proton transfer of the fragment from m/z=135, could explain again apparition of the BP and of the fragment from 29(19%); α-fragmentation to the secondary amino group accompanied by a proton transfer and subsequent elimination

of methane, explain apparition of the fragment from 119(29%).



- the fragmentation reaction on the bond level between the two nitrogen heterocycles explain the peak from m/z=114(27%) and from m/z=78(26%).

Subsequent fragmentation of peak from m/z=114 explain apparition of the fragment from m/z=42(37%).



The mass spectra of nicotine-1-N-oxide is presented in Figure 4.

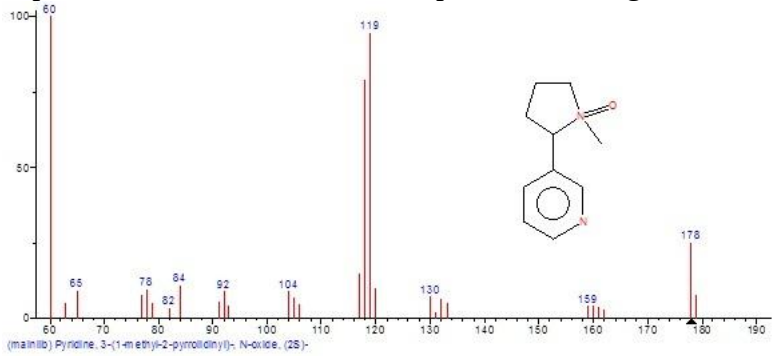
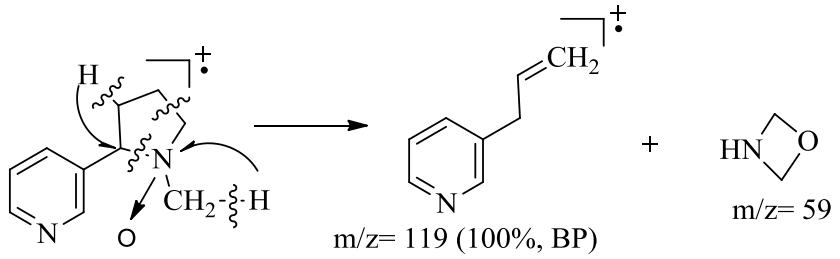
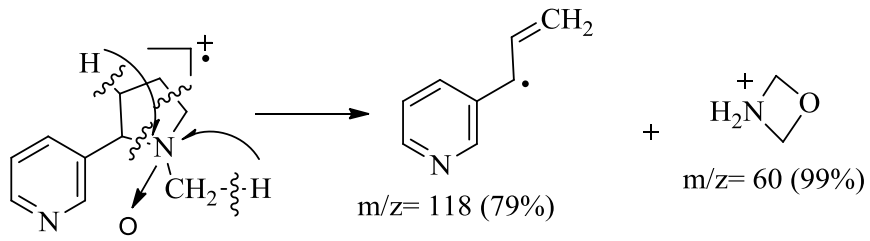


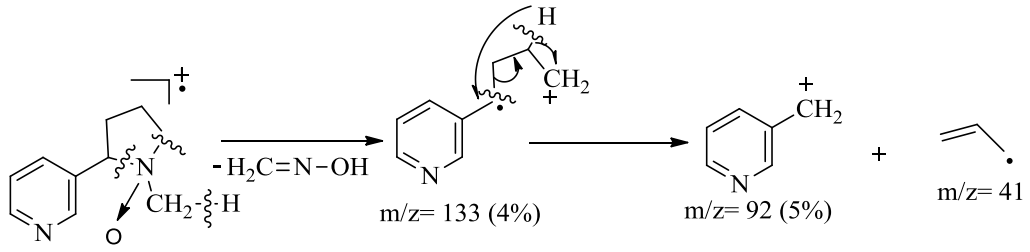
Fig. 4. *Nicotine-1-N-oxide mass spectra*

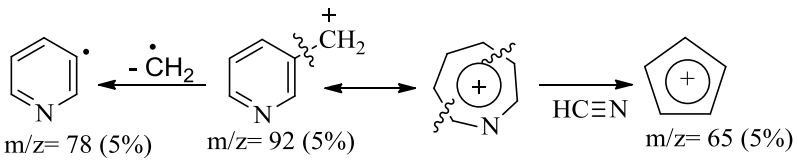
In the nicotine-1-N-oxide case the main fragmentation reactions are the following:
- the molecular ion, M^+, appears at m/z=178 with a great intensity (25%), characteristic for cyclic amines; the M+1 peak (m/z=179, 8%) is significant being characteristic for cyclic amines;
- the base peak (BP) appears at m/z=119(100%) and could be explained through a complex fragmentation on the N-methyl-N-oxide-pyrrolidinyl ring (α□□and β- fragmentation on the level of cyclic amino-oxide group followed by transfer of protons and electrons); a similarly fragmentation explains the main peaks, very intense, from m/z=60(99%) and m/z=118(79%);





- another complex fragmentation on the pyrrolidinyl ring (α-type fragmentation on the level of cyclic amino-oxide group followed by transfer of protons and electrons) explain the peaks from m/z=133 (4%) and its subsequent azatropilium fragment from 92(5%); finally, the fragmentation o azatropilium fragment is generating the peaks from 78(5%) and 65(5%);





Conclusions

In this paper was presented a study concerning the main tobacco metabolites, focused in structure identifications by GC-MS. The main fragmentation reactions and the consequences correlation of the principal metabolites resulting from tobacco it is also presented.

Acknowledgment

Financial support by European Union and Romanian Government through the European Social Fund POS DRU 2007-2013, Contract POSDRU/86/1.2/S/62307 is gratefully acknowledged.

References

1. Benowitz N.L., *Pharmacology of nicotine: addiction and therapeutics*, **Annu. Rev. Pharmacol. Toxicol.**, 36, 597-613, *1996*.
2. Benowitz N.L., Jacob P., III., *Nicotine and cotinine elimination pharmacokinetics in smokers and nonsmokers*, **Clin. Pharmacol. Ther.**, 53, 316-323, *1993*.
3. Haufroid V., Lison D., *Urinary cotinine as a tobacco-smoke exposure index: a minireview*, **Int. Arch. Occup. Environ. Health**, 71, 162-168, *1998*.
4. Jacob P., III., Benowitz N.L., Shulgin A.T., *Recent studies of nicotine metabolism in humans*, **Pharmacol. Biochem. Behav.**, 30, 249-253, *1988*.
5. McLafferty F.W., Turecek F., **Interpretation of Mass Spectra** (4-thy Ed.), University Science Books, Sausalito, California, 1993.
6. Neurath G.B., Dünger M., Orth D., Pein F.G., *trans-3'-Hydroxycotinine as a main metabolite in urine of smokers*, **Int. Arch. Occup. Environ. Health**, 59, 199-201, *1987*.
7. Toumi T., Johnsson T., Reijula K., *Analysis of nicotine, 3-hydroxycotinine, cotinine, and caffeine in urine of passive smokers by HPLC-tandem mass spectrometry*, **Clin. Chem.**, 45, 2164-2172, *1999*.
8. Zbancioc, G., Gradinaru, R., Drochioiu, G., Mangalagiu, I.I., *Nicotine and tobacco alkaloids: A GC-MS approach*, **International Journal of Criminal Investigation**, 2(1), 3-10, *2012*.

[i] Corresponding author: ionelm@uaic.ro, tel +40 +232201343, fax +40+ 232 201313