New Method for the Analysis of Pharmaceutical Drugs by MALDI-MS.

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Abstract

The work presented herein aims the development of a new, simple and rapid methodology to directly analyze medicines in diverse pharmaceutical forms by MALDI-MS. Ionic matrices were used in order to minimize matrix interference in the low *m/z* range. Using this method, 14 medicines were analyzed and all their active ingredients were detected.

Introduction

The World Health Organization estimates that up to 10% of the pharmaceutical drugs all over the world may probably be counterfeit.[1] Therefore the development of new, simple and rapid methodologies for the analysis of medicines is of great importance.

Matrix Assisted Laser Desorption/Ionization Mass Spectrometry (MALDI-MS) is a high throughput and easy to use analytical technique. However, organic crystalline matrices are ionized during analysis process, generating ions in the low *m/z* range (< *m/z* 700) which confounds the interpretation of low molecular weight compounds spectra. Ionic matrices arise as a solution for this problem as it produces reduced low *m/z* range interference.[2]

Based on the above description, in this work, ionic matrices were applied to the analysis of pharmaceutical drugs containing low molecular weight active ingredients.

Results and Discussion

Eight ionic matrices were synthesized through the reaction of the matrix α-cyano-4-hidroxycinamic acid (CHCA) with aniline, pyridine, isopropylamine, n-propylamine, n-butylamine, 1-methylimidazole, triethylamine (TEA) and diisopropylamine (DIPA).

The ionic matrices CHCA-TEA and CHCA-DIPA showed the best performance, since only the protonated amine signal was detected, and no CHCA signal was present in their spectra (**Figure 1**). Both of them were applied in medicine analysis.

Sample deposition over the sample plate spots was accomplished taking into account the pharmaceutical form of each medicine. For medicines in solution, 1.0 µL was directly transferred to the sample spot by using a micropipette. Non coated tablets were directly rubbed against the spot surface. Coated tablets were split in order to expose its internal part, which was rubbed on the MALDI plate spot surface. Capsules were opened and the internal material deposited over a spot with a micropipette tip. After medicines sampling, 1,0 µL of matrix solution was deposited above it and the analysis was promptly accomplished.

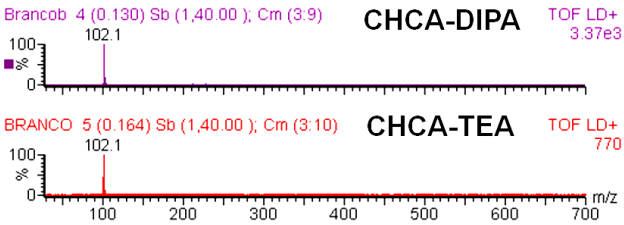

Figure 1. MALDI-TOF-MS spectra of CHCA-DIPA and CHCA-TEA ionic matrices.

This simple and rapid methodology provided the detection of 14 pharmaceutical drugs active compounds, shown in **Table 1**.

Table 1. Ion types of detected active ingredients for each analyzed medicine.

Entry	Active Ingredient	$[M+H]^+$	$[M+Na]^+$	$[M+K]^+$	$M^{+\cdot}$	M^+
1	Metochlopramide	300.1	-	-	-	-
2	Fenoterol	304.1	-	-	-	-
3	Fluoxetine	310.1	-	-	-	-
4	Bromazepam	316.0	-	-	-	-
5	Escitalopram	325.2	-	-	-	-
6	Loperamide	477.2	-	-	-	-
7	Rosuvastatin	482.2	504.2	520.1	-	-
8	Bromopride	344.1	366.1	-	-	-
9	Pantoprazole	384.1	406.1	-	-	-
10	Sildenafil	475.2	497.2	-	-	-
11	Nafazoline	211.1	-	239.1	-	-
12	Dexchlorphenyramine	275.1	-	313.1	-	-
13	Vinpocetine	-	-	-	350.2	-
14	Ipratrópium	-		-	-	332.2

Conclusions

The new methodology described herein is a powerful tool for forensic investigation of pharmaceutical drugs. It is rapid, simple and versatile since it can be applied in different pharmaceutical forms of medicines.

Aknowledgements

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