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Developing New Instrumental Approaches for Biological Warfare Detection: Exploring AP-MALDI/MS and AP-MALDI/FAIMS/MS

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Introduction

The most widely used method for detection, identification and overall analysis of biological agents has been MALDI/MS. Even though MALDI can distinguish between spores at the species level and gives reproducible biomarkers for characterization of some species, the biggest disadvantage is still the chemical background interference associated with the real sample. AP-MALDI however, has been shown to yield less analyte fragmentation. This research focuses on examining AP-MALDI as an alternative to vacuum MALDI, in addition to further increasing the selectivity of the method by incorporating FAIMS (high-field asymmetric-waveform ion mobility spectrometry). The added selectivity offered by the addition of FAIMS may prove useful in reducing the number of false positives obtained from biological agent analysis.

Instrumentation

Initial experiments were performed on a Finnigan MAT LaserMAT MALDI-TOF instrument. The spectra obtained were used for comparison with the spectra obtained from the AP-MALDI experiments. Standard solutions of various compounds known to be amenable to MALDI were used to test the efficiency of the ion transmission with the AP-MALDI ion source (Mass Tech, Burtonsville, MD). The source was easily interfaced with a Thermo Finnigan (San Jose, CA) LCQ quadrupole ion trap mass spectrometer. The design of this source also allows for easy interfacing of a side-to-side FAIMS cell for conducting future AP-MALDI/FAIMS/MS experiments and examining ion transmission efficiency and limits of detection of the source.

Matrix effects

Various matrices were examined on the LaserMat MALDI-TOF instrument to determine the most suitable matrix for the group of peptides chosen as model compounds. A 1µL aliquot of a 300 ppm (283 µM) standard solution of the nonapeptide, bradykinin, was spotted onto a sample plate, overlaid with 1 µL of a 50mM standard preparation of sinapinic acid (SA) in 70% ACN/0.1% TFA and allowed to air dry. This procedure was repeated two more times using instead 2,5-dihydroxybenzoic acid (DHB) and α-cyano-4-hydroxycinnamic acid (CHCA) as the matrices. A fourth sample plate was spotted using α-cyano-4-hydroxycinnamic acid (CHCA) in 70% acetone/0.1% TFA. The plates were then analyzed and the data shown below in figures 1-4.

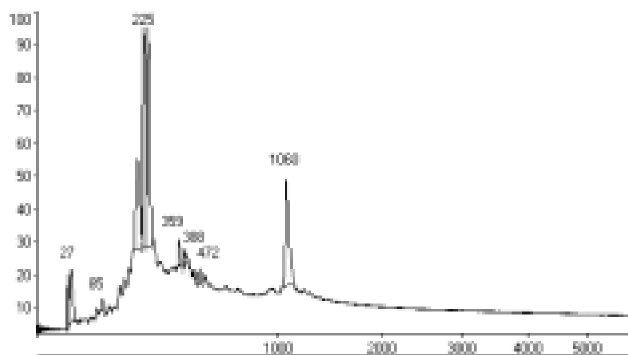

Figure 1. Bradykinin (m/z 1060) in ***SA*** in 70% ACN/0.1% TFA (283 pmoles/spot).

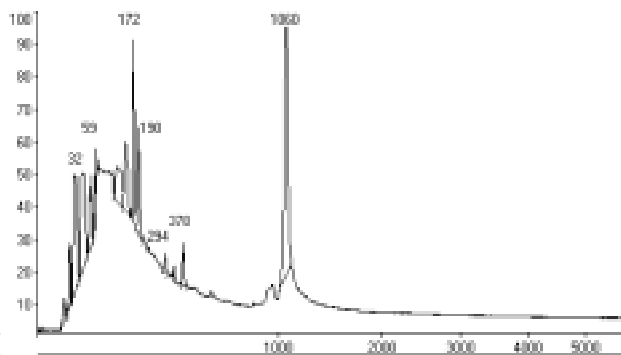

Figure 3. Bradykinin (m/z 1060) in ***CHCA in 70% ACN/0.1%TFA*** (283 pmoles/spot)

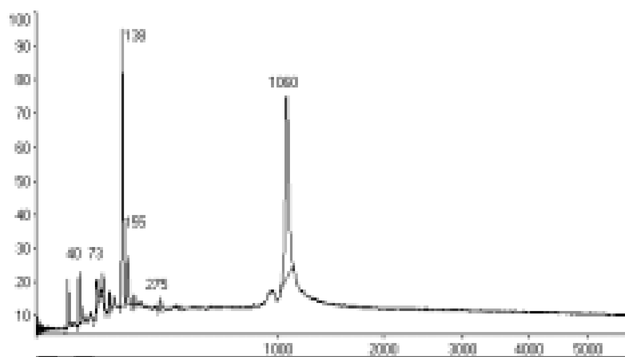

Figure 2. Bradykinin (m/z 1060) in ***DHB*** in 70% ACN/0.1% TFA (283 pmoles/spot

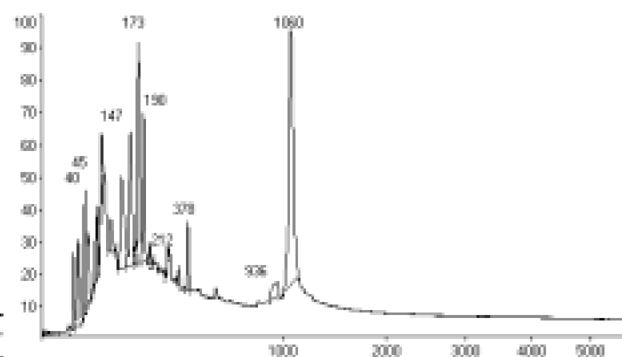

Figure 4. Bradykinin (m/z 1060) in ***CHCA in 70% acetone/0.1% TFA*** (283 pmoles/spot)

The results of the experiment above show the effect of different matrices on the ionization of the bradykinin. CHCA dissolved in 70% acetone/0.1% TFA was chosen as the matrix of choice. A comparison of figures 3 and 4 shows that the matrix ions are slightly reduced when using the acetone/TFA solvent compared to the acetonitrile/TFA solvent. The absolute intensity of the bradykinin peak, however, seems to remain the same. Even though the matrix ions for DHB, shown in figure 2, are much less reduced than for CHCA, in figures 3 and 4, the bradykinin ion signal is lower compared to the ion signal of bradykinin in figures 3 and 4.