

Fragmentation in MALDI-TOF-TOF: fragile peptides and peptides with D-residues.

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Tandem mass spectrometry is now a routine tool in proteomic studies allowing a better protein identification. MALDI due to its natural coupling with Time-Of-Flight MS offers specific properties: the time-of-flight or velocity selection of the precursor, collision with gas at high energy (~keV) and analysis of fragments in a second time-of-flight analyser.

In this talk, we will focus on the MALDI-TOF-TOF fragmentation through three different examples studied at our laboratory. These examples could have some applications in proteomic.

A first example deals with the stability of protonated peptides produced in MALDI. Some peptides were found particularly fragile when others are less fragile and even strongly stable. These fragile peptides behave a proline residue and no basic residue. The results show that peptide ions (protonated molecules and fragments) could be formed in the first steps of ablation, highlighting the role of the charge distribution during the crystallization process. In peptide mass fingerprint, very fragile peptides (proline rich) obtained by enzymatic digestion not including trypsin and forming only fragments ions are not correctly interpreted using databases.

The second example will describe the ability of MALDI-TOF-TOF to detect a residue of D-configuration in a peptide using metastable decomposition¹. The isomerization L/D is now considered as a specific translational modification and it is observed in many peptides extracted from living organisms. Such studies were generally performed using ESI when they can be also addressed with MALDI-TOF-TOF. Quantification in a mixture of two isomers is possible if only the isomers have the same affinity for proton and cation. If the fragmentation of protonated peptide can be used to detect a D residue, the fragmentation of Na or K cationized peptide cannot.

The last example deals with the fragmentation of Na cationized oligopeptides composed of homochiral and heterochiral peptides (Val or Leu). These peptides were produced by polymerisation of activated quasi-racemic monomers (one of the enantiomer being deuterated) in crystal or solution and initiated with non chiral molecule or enantiopure methy ester of α -aminoacids. These studies in collaboration with M. Lahav, Weizmann Institute, aim to explore the non enzymatically routes on the origin of the homochirality of peptides². In contrast to protonated molecules, Na cationized molecules are prone to be insensitive to the residue conformation allowing to show that diastereoisomeric oligopeptides are formed by blocks of residues with the same handedness. This result and others suggest that β -sheets templates play an important role for producing homochiral peptides.

References:

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