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CHARGE TRANSFER DISSOCIATION MASS SPECTROMETRY (CTD-MS) FOR THE STRUCTURAL CHARACTERIZATION OF OLIGOSACCHARIDES



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Charge transfer dissociation mass spectrometry (CTD-MS)¹ is a radical-driven fragmentation technique that provides useful structural characterization of biological molecules, and it works especially well for complex carbohydrates. CTD evolved from keV cation-cation reactions conducted by the groups of Zubarev² and Schlathöler.^{3,4} As a high-energy tandem mass spectrometry tool, CTD performs most similarly to extreme ultraviolet photodissociation (XUVPD). However, unlike XUVPD, CTD is applicable to bench-top mass spectrometers, and CTD is effective on precursors of all charge states except -1.

In our home-built apparatus, we employ a saddle-field fast ion source above a pre-drilled 3D ion trap to enable pulses of kiloelectronvolt reagent gas cations to enter the ion trap and activate the isolated precursor ions. Kinetic energies in the range of 3-10 keV help overcome the coulombic barrier between the reactants and provide practical fragmentation efficiencies well above 5%. One major downside to CTD is that the value of the low mass cut-off (LMCO) of the ion trap during CTD influences the background signal of CTD spectra. With LMCO values below m/z 250, we often see unwanted side reactions of the CTD beam with residual gases and vacuum pump oil.⁵ The presentation will discuss our latest applications of CTD to biological materials (**Figure 1**), including: 1) the production of cross-ring cleavages and the preservation of

labile modifications, such as sulfate groups in the analysis of oligosaccharides;⁶⁻⁸ 2) the cleavage of disulfide linkages in the analysis of proteins;⁹ 3) the generation of side chain losses in the analysis of peptides, which can be helpful in the differentiation of isomeric peptides;⁵ 4) the localization of double bond positions in phospholipids;¹⁰ and 5) the differentiation of β -1,4- and β -1,3-linkage isomers in native oligosaccharides.¹¹ Several of these applications employ CTD in combination with UHPLC for the analysis of complex mixtures. We also demonstrate that the nature of the CTD reagent gas has an insignificant influence on the fragmentation efficiencies or pathways,¹² which supports the electron stopping mechanism of activation proposed by Schlathölter's group.^{3,4}

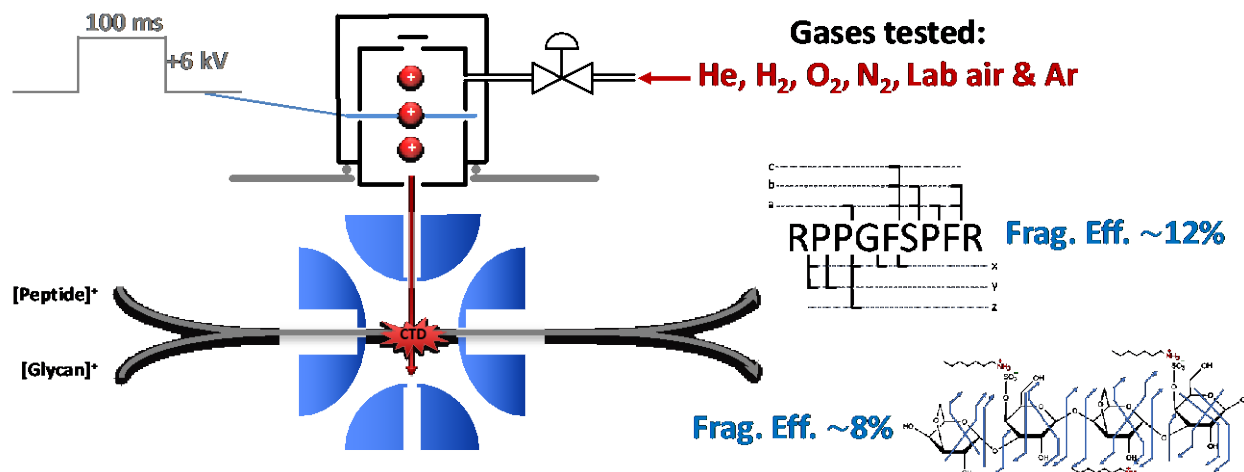


Figure 1: KeV ion activation provides structurally informative products ions for a variety of biological ions on a timeframe that is compatible with UHPLC separations of complex mixtures.

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