Probing the Structural Variations of a Metal-Complexed Model Peptide Using Post-Ion Mobility/Collision-Induced Dissociation Mass Spectrometry

Stephanie Fontenot, Mahsan Miladi, and Touradj Solouki
Department of Chemistry and Biochemistry, Baylor University, Waco, TX

Introduction

Metal Ion binding-induced conformational changes can significantly alter proteins' /peptides' functions [1]. Studying the interactions of proteins/peptides with metal ions can provide insight to chemical reactions involved in binding sites and hence, serve as the basis for designing active drugs [2]. In this study, we have utilized electrospray ionization ion mobility-mass spectrometry (ESI IM-MS) and Post-IM/collision induced dissociation (Post-IM/CID) to investigate the interactions of metals with a model peptide containing proline (P) and glycine (G), designated as Z-PG, where, "Z" is $C_6H_6CH_2COOH$. The glycine residue in the selected model dipeptide lacks a side chain and is conformationally least restricted [3], allowing formation of different metal-dependent complexes. The selected metal ions including Na^+, K^+, and Ca^{+2} can be used to interrogate the effect of metal ion size and charge on the conformations of the Z-PG dipeptide.

Experimental Parameters

Sample Preparation

The Z-PG dipeptide and all other chemicals were purchased from Sigma-Aldrich (Sigma, Saint Louis, MO, USA) and used without further purification. A micromolar concentration of Z-PG in spray solvent of methanol:water:aceticacid (49.95:49.95:0.10) was used for ESI IM-MS experiments.

Instrumentation

The IM-MS data were acquired using a Waters Synapt G2-S HDMS (Waters Inc., Manchester, UK) system (Figure 1) operated in the positive-ESI mode. The ESI source voltage was set at ~2 kV and samples were infused at a flow rate of 0.3 μL/min.

Ion Mobility-Mass Spectrometry (IM-MS)

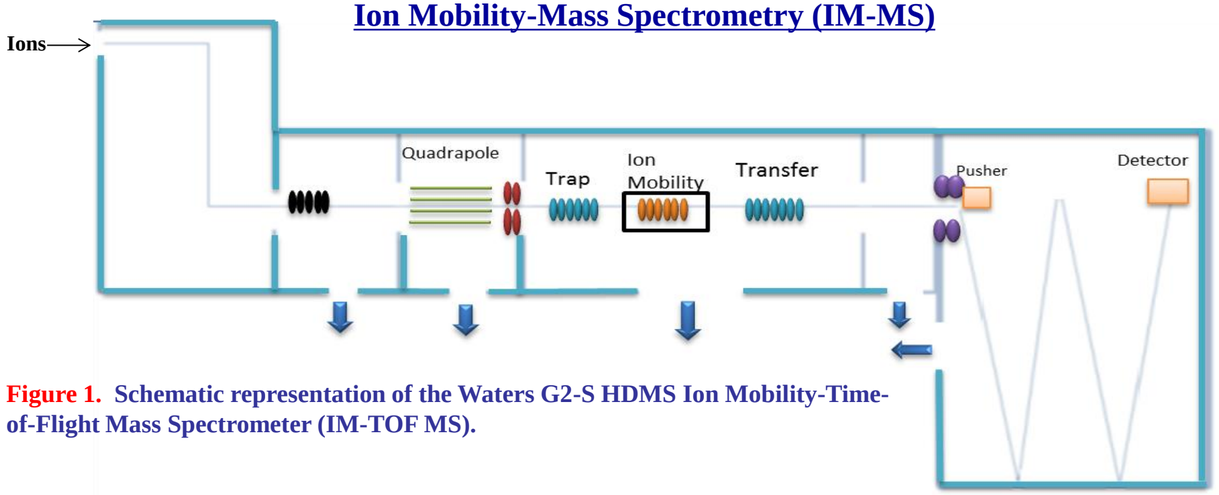

Figure 1. Schematic representation of the Waters G2-S HDMS Ion Mobility-Time-of-Flight Mass Spectrometer (IM-TOF MS).

Results

Post-IM/CID MS Profiles of $[Z\text{-}PG + H]^+$, $[Z\text{-}PG + Na]^+$, and $[Z\text{-}PG + Ca - H]^+$:

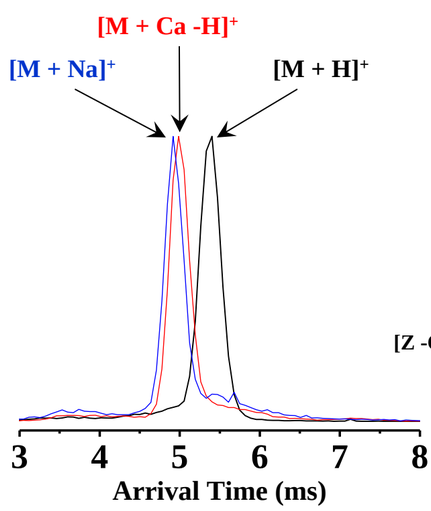

Figure 3. Ion mobility profiles of $[Z\text{-}PG + H]^+$, $[Z\text{-}PG + Na]^+$, and $[Z\text{-}PG + Ca - H]^+$.

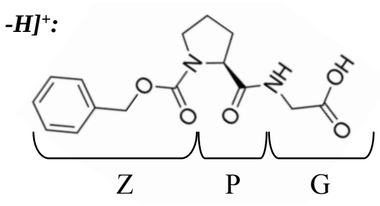

Figure 2. Chemical Structure of Z-PG Dipeptide.

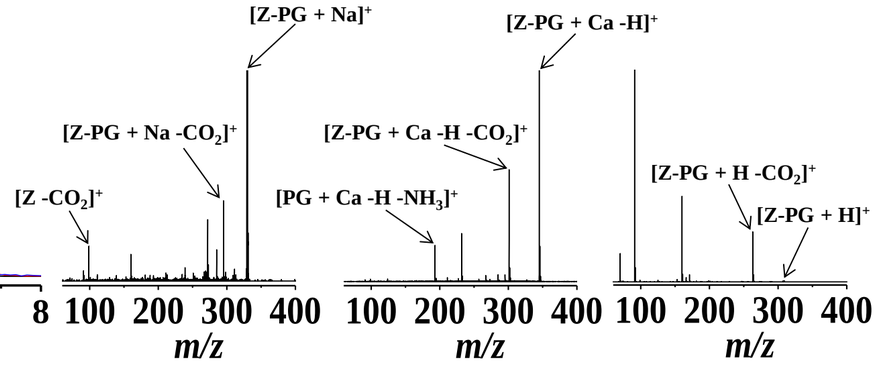

Figure 4. CID mass spectra of $[Z\text{-}PG + H]^+$, $[Z\text{-}PG + Na]^+$, and $[Z\text{-}PG + Ca - H]^+$. The CID of each of the *m/z*-isolated species was performed in the transfer cell (after the mobility separation) by setting a potential difference of 25 V between the IM and transfer cell (please refer to Figure 2 for pictorial representation of the Waters G2 instrument).

Conclusions

• The Post-IM/CID MS results of protonated and metal-complexed species of Z-PG suggest that $[Z\text{-}PG + Na]^+$ and $[Z\text{-}PG + Ca - H]^+$ are easier to dissociate and have higher relative structural stabilities than $[Z\text{-}PG + H]^+$.

• The observed IM arrival time distributions suggest the presence of more compact gas-phase structures for $[Z\text{-}PG + Na]^+$ and $[Z\text{-}PG + Ca - H]^+$ as compared to $[Z\text{-}PG + H]^+$.

References

[1] Solouki, T.; Fort, R. C., Jr.; Alomary, A.; Fattahi, A., *J. Am. Soc. Mass Spectrom.* 2001, 12, 1272-1285.

[2] Hoaglund, C. S.; Valentine, S. J.; Sporleder, C. R.; Reilly, J. P.; Clemmer, D. E., *Anal. Chem.* 1992, 70, 2236-2242.

[3] Ramachandran, G. N.; Ramakrishnan, C.; Sasisekhara, V., *J. Mol. Biol.* 1963, 7, 95-99.

Acknowledgements

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