

The structural studies of the selected organic compounds with the use of ion mobility technique coupled to mass spectrometry

Author: Anna Troć

Supervisor: Witold Danikiewicz

The aim of this Ph.D. dissertation is to explore the application of the ion mobility technique coupled to mass spectrometry (IM-MS) to the separation and structural studies of the selected groups of organic compounds. The flavonoids (catechins as stereoisomers and constitutional isomers of flavonoids) and β -lactams were chosen as model compounds due to their rich stereo- and regiochemistry. Additionally, the IM-MS was used to study the three-dimensional structures of noncovalent complexes of folic acid with α -, β - and γ -cyclodextrins and noncovalent aggregates of calixalenes.

The catechin isomers were successfully separated by complexation with selected *D*- and *L*-amino acids and copper ions. The clusters having the form of $[2M + D\text{-amino acid} + \text{Cu}^{2+} - 3\text{H}]^-$ (M stands for (-)-epicatechin or (+)-catechin) showed improvement in stereodifferentiation between two epimeric catechins. Among various examined *D*- and *L*-amino acids only *D*-alanine, *D*-leucine and *D*-proline led to the improvement of the separation of epimeric catechins. The peak-to-peak resolution (R_{p-p}) was greater or equal to 0.60. The catechin enantiomers were separated as complexes with copper ions and *D*-leucine ($R_{p-p} = 0.44$) and *L*-proline ($R_{p-p} = 0.40$).

The IM-MS was also used to study the constitutional isomers of flavonoids, such as apigenin, baicalein, chrisin, daidzein, kaempferol, and luteolin. The separation was observed for $[M+\text{Na}]^+$ ions of chrisin and daidzein ($R_{p-p} = 0.74$) and apigenin and baicalein ($R_{p-p} = 0.47$) using N_2 as ion mobility drift gas. The improvement of separation efficiency of chrisin and daidzein as well as apigenin and baicalein was obtained by using carbon dioxide as a drift gas. In this case the peak-to-peak resolutions were 1.23 and 0.98, respectively. The application of potassium cation induced significant increase of the peak-to-peak resolution (R_{p-p}) values for all examined flavonoids. The best R_{p-p} was determined to be 3.22 for $[M+\text{K}]^+$ clusters of the mixture of chrysin and daidzein.

The ion mobility spectrometry and theoretical calculations were used to separate and structural description of diastereoisomeric β -lactams. The best separation of isomers of β -lactams was observed for $[M+\text{Na}]^+$ and $[M+\text{Li}]^+$ ions. Other factors such as travelling wave height (WH), wave velocity (WV), source and desolvation temperatures, the use of drift gases

with varying masses and polarizabilities had little or no impact on separation efficacy. The theoretical cross section values obtained from extensive molecular dynamics (MD) and DFT calculations for obtained structures were in good agreement with those established experimentally. The interactions of metal ions with the aromatic rings of benzyloxy groups played a crucial role in differentiation of β -lactams.

The combination of ion mobility mass spectrometry studies and theoretical calculations was applied to detailed structural description of noncovalent complexes of folic acid (FA) and native cyclodextrins (α -CD, β -CD and γ -CD). Two different types of complexes were suggested, depending on the size of the cavity of cyclodextrin. The structure of FA/ α -CD represented the exclusion complex. The inclusion complex was characteristic for the noncovalent associates folic acid with β -CD and γ -CD.

In the last part of this Ph.D thesis, the use of IM-MS in combination with theoretical calculations for studying structural behaviour of calixsalens and their dimeric associates has been described. Depending on the modes of interaction, dimers of calixalenes can be formed as capsule or “host-guest” complexes. The results were in good agreement with data obtained by X-ray structural analysis.