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Amino-β-cyclodextrin Complex Assisted Ionization for Labile Sesamins and their Ion-mobility Separation in ESI Q-TOF MS

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Abstract: Sesamin, one of the lignans in sesame seed, was a labile compound in MS and it was reported that the protonated molecule of sesamin decomposed easily in ES ionization process and it cannot be detected (G. Yan, et al., *Rapid Commun Mass Spectrom.* 2007, *21*, 3613-3620). To protect labile compounds, an amino-cyclodextrin (NCyD) was added to the sample to promote the host-guest interaction complex in ESI-MS. As a result, sesamin was ionized as the NCyD-sesamin-NCyD (1:2) complex without undesired decomposition, suggesting that the amino-CyDs assist the ionization of the labile molecules capped with CyDs by host-guest interaction and these compounds were ionized without their decomposition, those are like amino-CyD complex-assisted ionization. The amino-CyD complexes of sesamin and sesamolin were also analyzed by their ion-mobility MS.

Keywords: cyclodextrin, host-guest interaction, ionization assist

Introduction

Sesamin is a lignan from sesame seed, and many bioactivities of sesamin for human health were reported.[1-3] Their analytical methods using mass spectrometry (MS) are useful, but G. Yan reported that sesamin decomposed in electrospray ionization (ESI) ion-trap MS and that the protonated molecule of sesamin $[M + H]^+$ was not detected but the dehydrated molecule $[M - H_2O + H]^+$ or dehydrogenated molecule $[M - H_2 + H]^+$ were clearly detected,[4,5] although the fragmentation from those in-source ion were useful.

Matrices in matrix-assisted laser desorption/ionization (MALDI) are labile and decompose under the laser irradiation. Yamaguchi reported that the matrix-cyclodextrin complex used as a matrix and the cyclodextrin complex suppress the in-source decomposition of the matrix under the laser irradiation.[6]

Here, we thought that the labile compound of sesamin in the ionization is protected by the sesamin-cyclodextrin complex. A conventional cyclodextrin consists of α-D-glucopyranoses, and its ionization efficiency as the protonated molecule $[M + H]^+$ was expected to be lower than that of the compound having amino group ($-NH_2$).[7] So, we used amino-β-cyclodextrin instead of conventional cyclodextrin, which has the amino group and high ionization efficiency.

Recently, ion-mobility MS was applied to the separation of organic compounds, lipids, carbohydrates, peptides, and proteins. We reported that ion-mobility MS was a powerful tool for distinguishing among the sugar chain isomers such as the branching isomers and glycosidic linkage isomers.[8,9] The self-association property of the molecules was clearly revealed by ion-mobility MS technique for the different linkage sugar chains such as cello-oligosaccharides (β1-4 linkage), laminari-oligosaccharides (β1-3), malto-oligosaccharides (α1-4 linkage), isomalto-oligosaccharides (α1-6 linkage). We are interested in the intermolecular binding complexes with ion-mobility MS, and in this study, we analyzed the complex between cyclodextrin and lignans such as sesamin, episesamin, and sesamolin.

Experimental section

Mass Spectrometry

Positive ion electrospray time-of-flight mass spectrometry was carried out by using a Waters Synapt G2-S quadrupole time-of-flight mass spectrometer (Waters Inc., Milford, USA) equipped with travelling-wave ion mobility spectrometry. For the detection of amino-β-cyclodexitrin (NβCyD) complexes with lignans, each sample (1 mM) was prepared in

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acetonitrile/0.1% aqueous formic acid (1:1, v/v) and mixed at the molar ratio of NβCyD/lignans (2/1), which was directly infused into the ion source at 180 μL/h of flow rate. Optimum positive-ion electrospray conditions included the following: capillary voltage, 1.5 kV; sampling cone voltage, 20 V; ion source temperature, 80°C; desolvation temperature, 280°C; cone gas flow rate, 0 L/h; desolvation gas flow rate, 500 L/h. The optimized ion mobility separation parameters at an IMS gas flow rate of 90 mL/min (N_2) included a wave velocity of 1000 m/s and a ramping wave height from 10 V to 40 V. Data were acquired by using MassLynx software Ver. 4.1 (Waters Inc., Milford, USA) and processed by using Driftscope Ver. 2.1 software (Waters Inc, Milford, USA).

Material

Solvents used in mass spectrometry were HPLC grade (NACALAI TESQUE, INC. Kyoto, Japan) and H_2O used was purified by using ultrapure water preparing systems (Adventure A and Elix-UV3, Millipore, Darmstadt, Germany). 3A-Amino-3A-deoxy-(2A*S*, 3A*S*)-β-cyclodextrin ($C_{42}H_{71}NO_{34}$; the calculated exact mass is 1133.3857) hydrate (amino-βCyD or NCyD, Tokyokasei, Co. Tokyo, Japan) was used. Sesamin ($C_{20}H_{18}O_6$; the calculated exact mass is 354.1103) and sasamolin ($C_{20}H_{18}O_7$; the calculated exact mass is 370.1053) (ChromaDex Inc., Irvine, USA) was used without further purification. Reagents used in derivatization and purification of sesamin analogue were all special grade.

Preparation of episesamin

Episesamin was chemically prepared from sesamin. To a solution of HCl (5-10%, v/v) in 50 mL methanol, 50 mg of sesamin was added and heated at 90°C for 19 h. Obtained reaction mixture was subjected twice to a preparative thin layer chromatography (PLC silica gel 60 F_{254}, 2 mm, Merck, Germany) with the eluent of hexane-ethyl acetate (7/3, v/v) at Rf 0.46. Finally episesamin was purified with a chiral column CHIRALPAK IB (id 20 × 250 mm) (Dicel Chemical Industries, LTD., Osaka, Japan), and it was identified by ^1H and ^{13}C NMR spectroscopy.

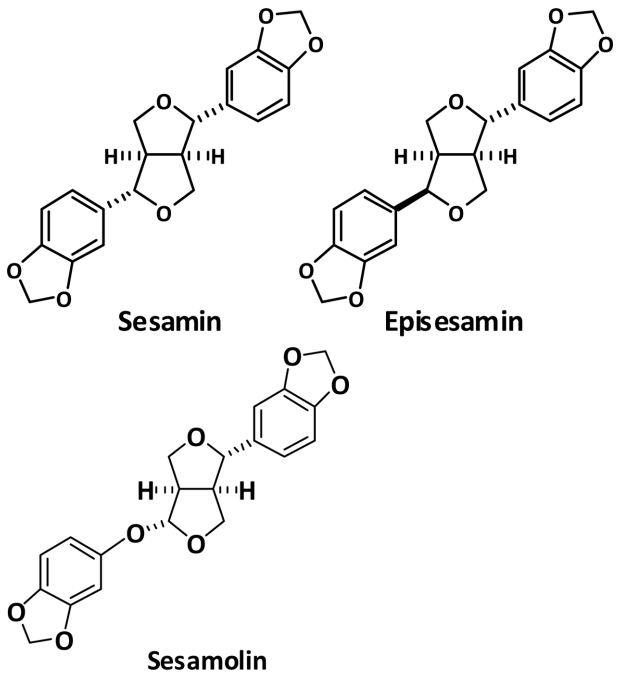

Figure 1. Structure of sesamin, episesamin, and sesamolin.

Results and discussion

Detection of NβCyD-sesamin-NβCyD complex

NβCyD and sesamin were dissolved and mixed in the water/acetonitrile as described in Experimental section. The mixture was analyzed with (+) ESI Q-TOF MS. The mono isotope peak at *m/z* 1311.492 was detected predominantly and the isotope pattern showed the doubly charged ion $[M + 2H]^{2+}$. The peak was corresponded to the sesamin-2NβCyD (1:2) complex as shown in Figure 2. The abundance of the sesamin-NβCyD (1:1) complex at *m/z* 1488.559 with single charge was very low. Sesamin has two 3,4-methylenedioxyphenyl groups at both the ends and high hydrophobicity. Cyclodextrins have hydrophobic pore indie of the molecules like a molecular bucket. The termini of the methylenedioxyphenyl groups at sesamin were capped with two NβCyDs, and the NβCyD-sesamin-NβCyD complex was formed. NβCyD was ionized as a protonated molecule at *m/z* 1134.426 $[M + H]^+$.(Figure 2) The sesamin-2NβCyD complex was ionized at the NβCyD part, but sesamin itself was not ionized as a protonated molecule. Therefore, the dehydroation ($-H_2O$) and the dehydrogenation ($-H_2$) at sesamin did not proceeded in the complex.

Ion-mobility MS of sesamin/episesamin-2NβCyD complexes

The sesamin-2NβCyD and episesamin-2NβCyD complexes were analyzed by ion-mobility MS. The ion-mobility peak of the sesamin-2NβCyD complex was

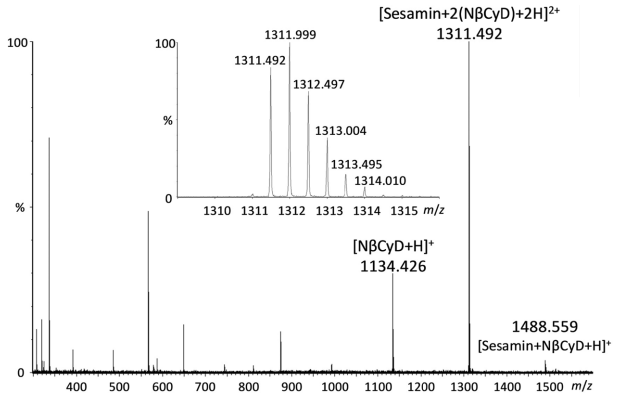

Figure 2. The mass spectrum of the sesamin and amino-cyclodextrin mixture in positive-mode ESI Q-TOF mass spectrometry.

detected predominantly at 131 bins as shown in Figure 3. The low abundance and broad peak was observed at 188 bins, which suggested that the peak from the sesamin-NβCyD (1:1) complex. Unfortunately, the NβCyD complexes of sesamin and episesamin were not separated by their ion-mobility MS.

Ion-mobility MS of NβCyD-sesamolin-NβCyD complex

Sesamolin has one more oxygen atom between methylenedioxyphenyl group and furan ring at the ether part from sesamin (Figure 1). The complex of sesamolin and amino-CyD was analyzed by ion-mobility MS (Figure 4). The complex consisted one sesamolin and two amino-CyD molecules with the doubly charge from the *m/z* 1319.458. Sesamolin has also two hydrophobic 3,4-methylenedioxyphenyl groups at the both termini, and sesamolin was capped with two NβCyDs in the complex as the same manner of the sesamin complex. The ion-mobility of the NβCyD-sesamolin-NβCyD complex (127 bins) was slower than that of the NβCyD-sesamin-NβCyD complex (124 bins), indicating the shape of the NβCyD-sesamolin-NβCyD complex was larger than that of the sesamin-2NβCyD complex. It was suggested that the hydrophobic end groups of sesamin and sesamolin were fitted to the cavity of NβCyD in their host-guest interaction. That result was reasonable because the molecular length of sesamolin was longer than that of sesamin as the added ether part.

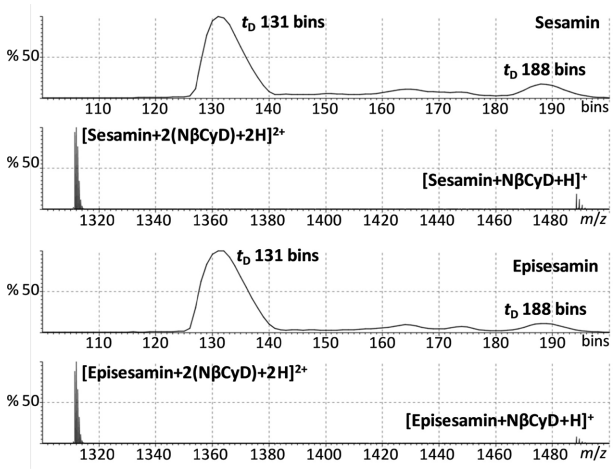

Figure 3. Ion Mobility MS spectra of the complex of NβCyD and sesamin/episesamin measured by positive-ion mode ESI Q-TOF MS.

Conclusion

A labile compound of sesamin was ionized without decomposing of the molecule as the amino-βCyD complex because the ionization efficiency of amino-CyD itself is very high. The results suggested that the amino-CyDs assist the ionization of the labile molecules and low polar compounds without their decomposition by the formation of the amino-CyD complexes with these hydrophobic ligands, those are like amino-CyD complex-assisted ionization. The sesamin-2NβCyD and episesamin-2NβCyD complexes showed almost the same separation in the ion-mobility. The ion-mobility of the sesamolin-2NβCyD complexes was longer than those of the complexes of sesamin-2NβCyD and episesamin-2NβCyD.

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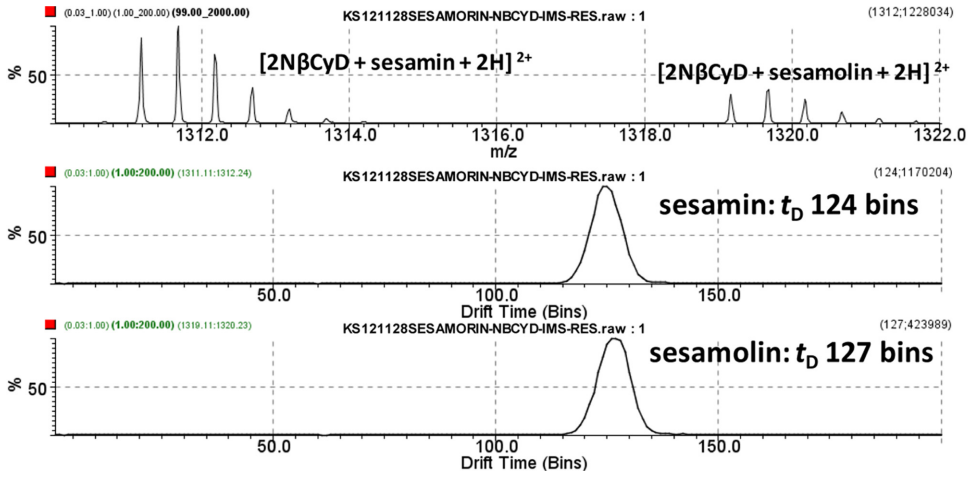

Figure 4. Ion mobility MS spectra of the complex of NβCyD and sesamin/sesamolin measured by positive-ion mode ESI Q-TOF MS.

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