Abstract

Mass spectrometry (MS) is one of the most powerful analytical tools which has been extensively used for bio-molecule analysis. It plays an important role in a wide-field, such as diagnosis, pharmaceutical research, and environment monitoring. Despite many advantages, the MS system is bulky and expensive which only can be operated inside a laboratory. Therefore, a miniaturized MS system is desired to meet the needs of on-site detection. Although there are several kinds of portable MS system have been reported, they are only capable with the small molecular weight samples. Hence, the aim of this study is to develop a miniaturized MS system which could be used to analysis a broad mass range of bio-molecules.

Recently, an on-chip pulse-heating desorption/ionization (PHDI) source has been developed for protein analysis in the positive ion detection mode. Without the need of laser or high voltage, the PHDI method shows the ability of protein ionization with matrix by only applying thermal energy. In the early stage of study, not only singly charged ion signal and multiply charged ion signals, but also many fragmentation ion signals were observed, resulting difficulties in explaining the mass spectra and identifying the ion signal.

To obtain a clear mass spectrum with less backgrounds and fragmentations, the performance of the MS system has been improved from mainly two ways. Firstly, the thickness and uniformity of the sample film was found to affect the generation of fragmentation ion signals. In order to reduce the thickness of sample film, the oxygen plasma treatment process was introduced to increase the wettability of the chip surface. The thickness of sample film was reduced to 20 nm. Secondly, the alignment of ion source and inlet of mass filter was found to affect the signal shift. To solve this problems, a chip-holder was designed to fix the chip position. Then a calibration method for the on-chip ion source mass spectrometry was established. As a result, a clear mass spectrum was able to be obtained with very less fragmentations and backgrounds under optimized conditions.

The negative ion detection mode was introduced to understand the ion formation mechanism. The initial date was obtained with the simple organic sample. By comparing the mass spectra in both positive and negative ion detection modes, we found that the positively charged and negatively charged ion signals are generated at same time under the same conditions. The ionization of protein mixed with matrix samples were investigated under different level of supplied thermal energy with both positive and negative ion detection modes. With a low thermal energy supplied, only desorption process was occurred. With a proper thermal energy supplied, the sample could be desorbed and ionized. Then, the singly charged ion signal could be observed with very less fragmentation. When increase the supplied energy, the fragmentation ion signals are observed due to decomposition and fragmentation.

In this study, a matrix-free ionization process is introduced to the on-chip PHDI source to avoid the matrix effects and simplify the sample preparation process. A wide range of bio-molecules have been tested by this MS system, including amino acids, carbohydrates, peptide, and proteins to prove this concept. As a results, the PHDI source shows excellent capability for matrix-free biomolecular ionization.

In conclusion, a miniaturized MS system has been developed with an on-chip PHDI source which is capable with a broad range of bio-molecules, including amino acids, carbohydrates, peptide, and proteins. Under the optimized conditions, a clear and reproducible mass spectrum is able to be obtained for all these samples with only singly charged ion signal and very less fragmentations and backgrounds. A matrix-free ionization process is established with this on-chip PHDI MS system. It is believed that this work offers a new technique for bio-molecule analysis which overcomes the limitations of the conventional MS system.

Keywords: Miniaturized mass spectrometry; on-chip ion source; pulse-heating ionization; matrix-free ionization; bio-molecule analysis.