**Sampling Matters:**

**Direct Sampling Ionization MS of Complex Mixtures**

Sangwon Cha, Ph.D.

Department of Chemistry, Hankuk University of Foreign Studies, Yongin, Gyeongi 449-791, Korea

**Abstract**

A typical mass spectrometry (MS)-based, complex mixture analysis usually involves intensive chemical extraction and chromatographic separation steps. However, direct sample analysis with minimal sample preparation is sometimes desirable in order to achieve high-throughput screening or to minimize sample denaturation. In this presentation, various MS methodologies for direct complex mixture analysis will be discussed. The first part of presentation will focus on matrix-assisted laser desorption/ionization (MALDI) MS as a metabolite fingerprinting platform. MALDI MS is an intriguing technique for metabolite fingerprinting due to its speed, salt tolerance, and ability of analyzing crude samples. However, conventional MALDI MS faces great challenges in detecting small metabolites due to high matrix background ions in the *m/z* region <500 and ion suppression effects. In order to partially overcome these issues, we developed several alternative MALDI MS strategies. One strategy is so called “matrix engineering”, in which target analyte signals are selectively enhanced with low chemical background by altering LDI environment with nanomaterials. The other strategy is the modifications of the conventional MALDI matrices in order to gain more softness in ionization of labile molecules or to obtain clean chemical background signals in low *m/z* region.

The second part of presentation will focus on ambient ionization MS methods as direct sample analysis platforms. Among various ambient ionization techniques, nanospray desorption ionization (nano-DESI) and paper spray ionization (PSI) will be mainly discussed. Nano-DESI utilizes a steady-state micro-liquid junction formed between two capillaries for extracting analytes and therefore this method allows us to sample analytes with high spatial resolution and also has a potential of depth-profiling. Here, we will demonstrate various applications of nano-DESI MS including *in situ* document ink analysis and plant metabolite analysis. PSI usually employs a planar, triangular-shape paper tip as a sampling base as well as an electrospray tip. One of the unique advantages of PSI MS is that a paper base itself can serve as a filter or a chromatographic medium and therefore *in situ* sample clean up or analyte separation can occur during PSI process. Case studies of lipid fingerprinting will be demonstrated in order to explain this unique advantage. In addition, we will introduce the new format of PSI MS for the rapid raw solid material analysis, named as paper cone spray ionization (PCSI) MS.