Therapeutic Drug Monitoring of Human Blood Samples by Using Nanosheet-Assisted LDI-TOF

Sunho Joh[1], Jaekak Yoo[1,2], Jin Gyeong Son[1], Hyun Kyong Shon[1], Hee-Kyung Na[1], Jeong Hee Moon[3], Mun Seok Jeong[2], Seung Mi Lee[1], Sang-Guk Lee[4], Tae Geol Lee[1*]

(1) Korea Research Institute of Standards and Science, Daejeon 34113, Korea
(2) Hanyang University, Seoul 04763, Korea
(3) Korea Research Institute of Bioscience and Biotechnology, Daejeon 34141, Korea
(4) Yonsei University College of Medicine, Seoul 03722, Korea

Therapeutic drug monitoring (TDM) demands rapid, sensitive, and clinically adaptable analytical platforms. Here, we present a nanosheet-assisted laser desorption/ionization time-of-flight mass spectrometry (LDI-TOF MS) strategy that enables direct, matrix-free detection of therapeutic drugs in human blood.

We first demonstrated that nanostructured inorganic surfaces can replace conventional organic matrices, enabling efficient ionization of small-molecule drugs with significantly reduced background interference and simplified sample preparation [1]. This work established the feasibility of nanomaterial-assisted LDI for bioanalytical applications.

Building on this foundation, we identified tellurium-containing transition metal dichalcogenide nanosheets ($MoTe_2$, WTe_2) as highly effective ionization platforms, achieving markedly enhanced sensitivity and multiplexed detection of antiepileptic drugs in human serum [2]. The method showed strong agreement with clinical gold standards (immunoassay and LC–MS/MS), demonstrating its translational potential for real patient samples.

To uncover the mechanistic origin of this enhancement, we elucidated interfacial charge-transfer dynamics using integrated experimental and theoretical approaches [3]. We revealed that photoinduced hydroxyl radicals, proton-coupled charge transfer, and surface electronic structure synergistically govern ionization efficiency. In particular, surface charge localization and conduction-band energetics were identified as key descriptors that drive Coulombic repulsion and facilitate efficient analyte desorption.

In summary, nanosheet-assisted LDI-TOF MS transforms TDM by eliminating conventional matrix limitations while achieving high sensitivity, rapid analysis, and clinical compatibility. By linking nanoscale electronic structure to macroscopic analytical performance, this approach provides a generalizable design framework for next-generation bioanalytical platforms and enables a practical pathway toward point-of-care diagnostics and precision medicine.

[1] S. Joh et al., ACS Nano 15(6), 2021, 10141-10152.
[2] S. Joh et al., ACS Nano 18(27), 2024, 17681-17693.
[3] J. Yoo et al., ACS Applied Materials & Interfaces, 18(11), 2026, 17105-17115.