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**High voltage nano-electrospray ionization Mass Spectrometry for aqueous solution**

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**N**ano electrospray (nESI) has widely been used in the field of chemistry, biology, medicine, pharmaceutical industry, clinical assessment and forensic science. nESI can be done without corona discharge if the sample is prepared in organic solvent. The corona discharge is typically observed in negative ion mode at nESI emitter tip under high aqueous solvent conditions, resulting in low ion intensity. The corona discharge can be quenched using a 10 G $\Omega$  resistor between a pulled glass capillary and high voltage power supply. In order to elucidate the scenario of the adduct of Na<sup>+</sup> and enhanced

the signal intensity of peptides and proteins, a high-voltage is applied to nanocapillary and compared with conventional nESI in this study. Different proteins and peptides could be selected and assessed using Bruker-HCT ion trap mass spectrometer. The performance of high voltage-nESI could be superior to low voltage or conventional nESI in terms of ion intensity and the effect of Na<sup>+</sup> adduct for the analysis of biomolecule in aqueous solution.

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