Ultrasensitive CESI-MS quantification of biomolecules based on chemical derivatization

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Abstract

As a crucial post-translational modification for expressions and functions of proteins, glycosylation has been recognized as a promising biomarker for diagnostics and pathology. Due to its diverse compositions and complicated conformations, mass spectrometer (MS) has been applied as universal tool for glycan analysis but suffers low ionization efficiency and low abundance of analytes. In this work, we have achieved high sensitive equalization and relative quantification of N-glycans on CESI-MS using a novel Rhodamine B-based labeling reagent. Rhodamine B hydrazide (RBH) and deuterated Rhodamine B hydrazide (d_4-RBH) were synthesized with high purity and low cost. Under the optimized labelling and separating conditions, signals of glycans were enhanced by tens to hundreds folds due to the increased hydrophobicity, which would significantly reduce sample usage and identify more glycans. Meanwhile, the relative quantification of N-glycans was achieved since the 4 Da mass shift could effectively distinguish glycans labeled with normal and heavy RBH. This method is facile, economic and reliable, and exhibits great potential for discovery and analysis of glycan biomarkers in clinical diagnosis.