

Details about LC-MS measurement

Analyses were performed by Agilent 1290 Series UHPLC instrument (Agilent, Waldbronn, Germany) coupled to Sciex TripleTOF 5600+ MS (Sciex, Concord, Ontario; Canada) with duospray source and Pal HTC-XS autosampler from CTC (Zwingen, Switzerland). Positive and negative ESI ionization were used in separate LC-MS runs with the following chromatographic separation conditions: Acquity UPLC CSH C18 (130Å, 1.7 µm, 2.1 mm X 100 mm) column was utilized with Acquity UPLC CSH C18 VanGuard pre-column (130Å, 1.7 µm, 2.1 mm X 5 mm) (Waters, Eschborn, Germany). The mobile phase was composed of 10 mM ammonium formate and 0.1 % formic acid dissolved in 60:40 ACN:H₂O (v/v) (A) and 90:10 (v/v) IPA:ACN (B). The gradient profile was as follows: 0.0 min, 15 % B; 2.0 min, 30 % B; 2.5 min, 48 % B; 11.0 min, 82 % B; 11.5 min, 99 % B; 12.0 min, 99 % B; 12.1 min, 15 % B, 15.0 min, 15 % B. Flow rate was equal to 600 µL/min and column was kept at 65 °C. The injection volume was 3 µL for positive mode and 5 µL for negative mode.

MS settings were used as follows: Curtain gas (CUR) 35 psi, nebulizer gas (GS1) 60 psi, drying gas (GS2) 60 psi, ion-spray voltage floating (ISVF) +5500 V in positive and -4500 V in negative mode, source temperature (T) 350°C, collision energy (CE) 45 V, collision energy spread (CES) 15 V, declustering potential (DP) 80 V, mass range m/z 50 – 1250 in ESI (+) and 50 – 1050 in ESI (-), and RF Transmission (RF) m/z 40: 50 % and m/z 120: 50 %.

MS/MS data were obtained by data independent acquisition (DIA) using sequential window acquisition of all theoretical fragment ion mass spectra (SWATH).