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Determination of asymmetric and symmetric dimethylarginine in serum from patients with chronic kidney disease: UPLC-MS/MS versus ELISA

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Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide (NO) synthesis, and its structural isomer symmetric dimethylarginine (SDMA) are uremic toxins accumulating in chronic kidney disease (CKD) patients. The objective of this study was to develop and validate a robust UPLC-MS/MS method for the simultaneous determination of ADMA and SDMA in human serum. Chromatographic separation after butylester derivatization was achieved on an Acquity UPLC BEH C18 column, followed by tandem mass spectrometric detection in positive mode. Isotopically labeled ADMA (d_7-ADMA) was used as internal standard. Accuracy was below 12.35%. Within- and between-day precision ranged from 1.93 to 3.48% and from 5.25 to 10.93%, respectively. The applicability of the method was evaluated by the analysis of serum samples from 10 healthy controls and 77 CKD patients on hemodialysis. Both ADMA (0.84 ± 0.19 µM vs. 0.52 ± 0.07 µM) and SDMA concentrations (2.06 ± 0.82 µM vs. 0.59 ± 0.13 µM) were significantly ($p<0.001$) elevated in CKD patients compared to healthy controls. In addition, a commercially available ELISA assay was utilized to determine ADMA (0.97 ± 0.23 µM vs. 0.49 ± 0.06 µM) and SDMA (2.09 ± 0.59 µM vs. 0.62 ± 0.09 µM) concentrations in the serum samples. Correlation between these methods was modest for both ADMA ($r=0.78$, $p<0.0001$) and SDMA ($r=0.72$, $p<0.0001$).