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Development and validation of a spectrophotometric method for the analysis of low concentrations of paracetamol in serum

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Paracetamol, has a possibility of causing hepatotoxicity if the recommended dosage (15mg/kg body weight every 6 hours) is exceeded. There is a need for analyzing lower concentrations of serum paracetamol using a less expensive and validated bio-analytical method when over dose of paracetamol use is suspected or for pharmacokinetic studies. The spectrophotometric method established by Glynn and Kendal using nitration of paracetamol followed by absorbance measurement at 430 nm, is validated only for higher concentrations of paracetamol usually observed in acute paracetamol poisoning ranging from 25-400 mg/dm^3. In this study, the method was extended to a range of 10-100 mg/dm^3 which includes serum paracetamol concentrations at therapeutic doses (5-25mg/dm^3). The modified method was validated according to the guidelines on validation of bio-analytical methods introduced by European Medicines Agency. Nine calibration standards were used to develop a calibration curve and the correlation coefficient (R^2) was >0.99. Four quality control standards (QC) (10, 30, 50, 75 mg/dm^3- in five replicates) were analysed to determine accuracy and precision. A percentage bias within ±15% of the nominal value was determined as acceptable accuracy. This method demonstrated accuracy within 8% coefficient of variation (CV) of the five replicates within ±15% was considered as acceptable precision. Precision of <±7% was observed. Stability after one week, bench-top stability and freeze-thaw stability were observed. Accepted percentage bias from the nominal concentration of the QCs to determine stability was ±15%, samples demonstrated a percentage bias within ±8%. All the criteria required for validation of a bio-analytical method including selectivity, carry-over, linearity, accuracy and precision (within-run and between-run), dilution integrity and stability were fulfilled, and the method was validated for the analysis of serum concentrations of paracetamol.

Keywords: Paracetamol, validation, spectrophotometry

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