Cardiovascular diseases contribute largely to the portion of non communicable diseases and remain a high burden for the population causing more than 17 million deaths worldwide each year. Angiotensin converting enzyme inhibitors (ACEIs) are used for the treatment of cardiovascular diseases. The therapeutic effectiveness of these preventive agents is closely related to medication adherence by patients. Additionally, the increased availability of these drugs has led to the increased events of intoxication either intentionally or unintentionally (1,2). Qualitative screening of these agents using liquid chromatography-tandem mass spectrometry represents a reliable technique for monitoring medication adherence as well as intoxication.

Methods

Fit-for-purpose validation was performed for limit of detection (LOD), recovery and matrix effect. Further the accuracy and precision was also conducted for the semi-quantitation following EMA, FDA and ICH guidelines(3,4,5).

Results

Following results were obtained from the semi-quantitative validation for linearity, accuracy and precision along with recovery and matrix effect.

Concentration

Conclusion:
The screening method was successfully developed and partially validated qualitatively for monitoring of medication adherence and intoxication of 10 ACEIs in 50 µL residual blood samples.

References


More information

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Figure 1: Mean (n=3) calibration curve for all analyte with linearity of 0.78-100 ng/mL. Area ratio: Analyte peak area/ internal standard peak area. Concentration ratio: Analyte concentration/ internal standard concentration. Least square weighted regression was applied. Weightings: 1/x².

Figure 2: Intra-day accuracy in terms of relative error (%) at three quality control levels: n=3, LOD-Lower limit of quantification (0.13 ng/mL), MOC-Middle quality control (25 ng/mL), HQC-High quality control (100 ng/mL). Black dotted line represents acceptance limit for LOD (20%), and blue represents for MOC and HQC (15%) for relative error.

Figure 3: Intra-day precision in terms of coefficient of variation (%) at three quality control levels: n=3, LOD-Lower limit of quantification (0.13 ng/mL), MOC-Middle quality control (25 ng/mL), HQC-High quality control (100 ng/mL). Black dotted line represents acceptance limit for LOD (20%), and blue dotted line represents acceptance limit for MOC and HQC (15%) for variation.

Figure 4: Effect of different conditioning, washing and elution solution on absolute recovery of all analyte and internal standard enalaprilat (25 ng/mL). Black-Water and methanol: acetone (60-40) for washing and 2% formic acid in methanol for conditioning and elution. Light grey: Water methanol: acetone (60-40) and acetone (60%) and methanol for conditioning and elution. Dark grey: Water, methanol: acetone (60-40) and acetone (60%) for washing and 2% formic acid in methanol for conditioning and elution.

Figure 5: Effect of different conditioning, washing and elution solution on absolute matrix effect of all analyte and internal standard enalaprilat (25 ng/mL). Black-Water and methanol: acetone (60-40) for washing and 2% formic acid in methanol for conditioning and elution. Light grey: Water methanol: acetone (60-40) and acetone (60%) and methanol for conditioning and elution. Dark grey: Water, methanol: acetone (60-40) and acetone (60%) for washing and 2% formic acid in methanol for conditioning and elution.

The objective was to develop a qualitative screening method for commonly prescribed angiotensin converting enzyme inhibitors using residual blood volume 50 µL to avoid additional sampling stress both in paediatrics and adults.

Objectives

The objective was to develop a qualitative screening method for commonly prescribed angiotensin converting enzyme inhibitors using residual blood volume 50 µL to avoid additional sampling stress both in paediatrics and adults.