DETERMINATION OF METOPROLOL ENANTIOMERS IN HUMAN PLASMA AND SALIVA SAMPLES UTILIZING MICROEXTRACTION BY PACKED SORBENT AND LIQUID CHROMATOGRAPHY–TANDEM MASS SPECTROMETRY

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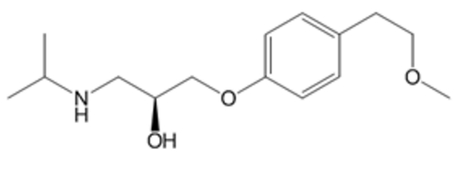
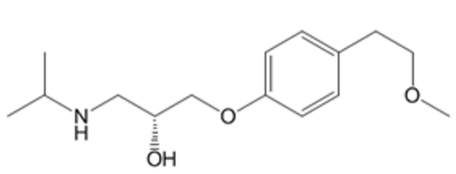
introduction

Metoprolol is a chiral b-blocker drug that is used for treatment of hypertension, arrhythmia and heart failure.

The S-enantiomer is the one responsible for the pharmacological action. However the drug is commercially available as racemate.

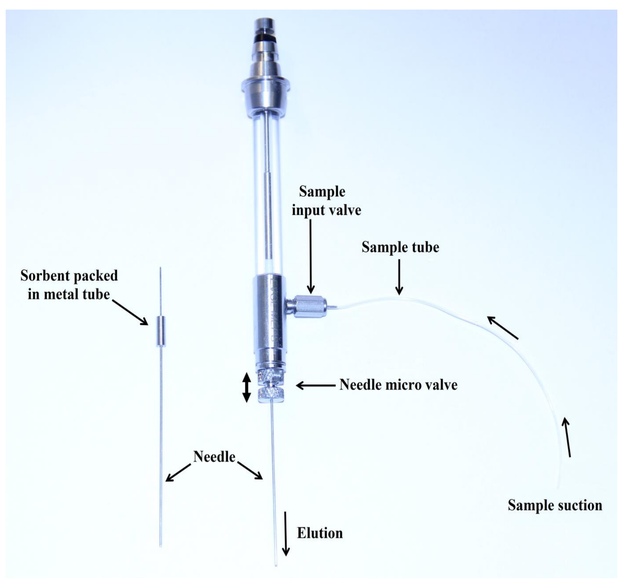


(S)-metorpolol



(R)-metoprolol

We developed a method for enantioselective determination of metoprolol enantiomers in human plasma and saliva using LC-MS/MS after the extraction of the analyte utilizing micro-extraction by packed sorbent (MEPS) syringes (Fig. 2)

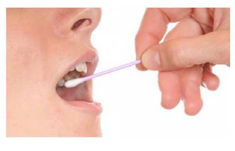


MEPS syringe

Methods

- **Chiral separation using Cellulose-SB column.**
- **MEPS: using automated syringe device eVol for sample loading, washing and elution.**

Saliva



Extraction

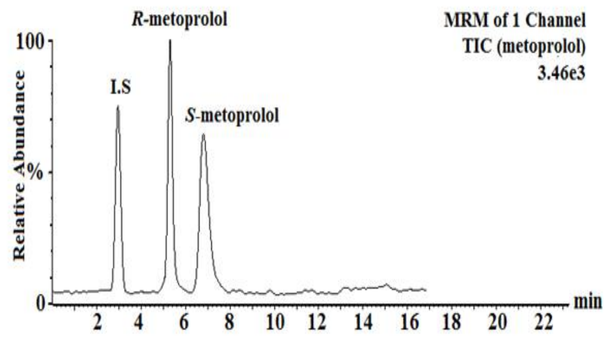
eVol MEPS device

Blood

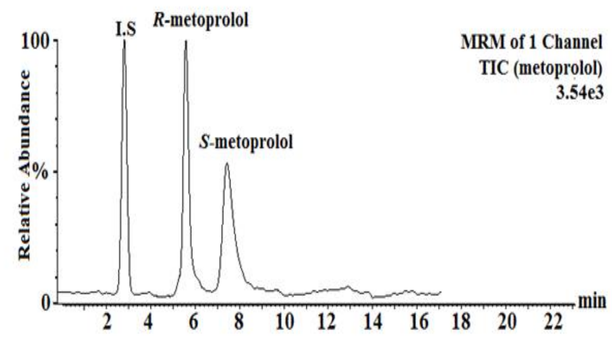
Results & Discussion

Metoprolol enantiomers were separated into two well resolved peaks after extraction from spiked plasma and saliva samples.

A post column solvent assisted ionization using 0.5 % formic acid in isopropanol was applied to enhance metoprolol ionization signal in positive mode monitoring (+ES)



Spiked Plasma sample



Spiked saliva sample

The linearity range was 2.5 – 500 ng mL^{-1} for both *R*-metoprolol and *S*-metoprolol in plasma and saliva. The limits of detection and quantitation for both enantiomers were 0.5 and 1.5 ng mL^{-1} respectively, in both matrices (plasma and saliva). The intra- and inter-day precisions were RSD % < 5 % for replicate analysis of quality control samples and the accuracy of determinations varied from 96 % to 99 %.

The method can aid in the therapeutic drug monitoring in clinical laboratories.

Conclusion

The utilization of MEPS for bioanalysis of enantiomers provides efficient tool for sample purification and pre-concentration. The detection and quantitation of metoprolol enantiomers in saliva and plasma samples was attained successfully and the method could be applied for monitoring of the drug enantiomers in both fluids.

References:

- **Abdel-Rehim M Recent advances in microextraction by packed sorbent for bioanalysis. Journal of Chromatography A 2010; 1217 (16): 2569-2580. DOI: 10.1016/j.chroma.2009.09.053.**
- **Ali I, Al-Othman ZA, Hussain A, Saleem K and Aboul-Enein HY Chiral separation of β-adrenergic blockers in human plasma by SPE-HPLC. Chromatographia 2011; 73 (3-4): 251-256. DOI: 10.1007/s10337-010-1891-4.**