Ramipril is an Angiotensin-Converting Enzyme (ACE) inhibitor and ramiprilat is well known of ramipril as active metabolite. It is, therefore, used for hypertension, congestive cardiac failure and β-blocker in order to reduce the risk of heart attack [1, 2].

Proper clean-up of plasma samples for Bioequivalence Studies is prerequisite and particularly important in order to reach the sensitivity at where metabolites can be detected at required level of concentration more easily.

Initial studies shows that the use of liquid Liquid Extraction (LLE) technique for the clean-up of plasma sample gave a better recovery rate and reproducibility over the Solid Phase Extraction (SPE) technique.

In this study, simultaneous determination of ramipril and ramiprilat in human plasma by using Liquid Chromatography Mass Spectrometry LC-MS/MS technique was compared employing SPE, Co-Sense and LLE for the clean-up purposes at sample preparation stage.

Linear range of calibration curve of ramipril was ranged from 0.6 to 100.0 ng/mL. The Lower Limit of Quantitation (LLOQ) is defined as the lowest concentration on the calibration curve, it was validated using an LLOQ sample for which an acceptable accuracy within ±20% and a precision (RSD) below 20% were obtained[1].

The average extraction recovery of ramipril for LLOQ (0.6 ng/mL), low (1.8 ng/mL), middle (10.0 ng/mL) and high (100.0 ng/mL) concentration levels were obtained as % 110.7, % 106.8, % 115.1 and 108.5 respectively by using LLE extraction technique.

The stability of stock solution of ramipril was assessed during 24 hours and 5 days separately. It was found that no significant change was observed within the concentration of ramipril for imposed time intervals. It also presents a good stability at the end of the three cycle of freeze-thaw stability study.

KEYWORDS: ramipril, ramiprilat, liquid-liquid extraction, solid phase extraction, Co-Sense

REFERENCES