



RESEARCH PAPER

# SIMULTANEOUS DETERMINATION OF AMLODIPINE AND OLMESARTAN IN HUMAN PLASMA BY LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY AND ITS APPLICATION IN PHARMACOKINETIC STUDY

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**The present study describes a sensitive, specific and rapid method based on liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) for the simultaneous determination of amlodipine (AML) and olmesartan (OLM) in human plasma by using amlodipine D4 (IS1) and olmesartan D6 (IS2) as internal standards. Plasma samples were extracted by solid-phase extraction (SPE). The method was validated over parameters like selectivity, matrix effect, sensitivity, specificity, linearity, precision and accuracy, various stabilities in plasma, recovery and reinjection reproducibility. During the validation, inter and intra-batch precision were less than 15% and the accuracy was within 85-115%. Extraction recoveries were 75.30%, 81.41%, 79.19% and 81.72% for AML, OLM, IS1 and IS2 respectively. The method was applied to the pharmacokinetic study of OLM and AML in healthy subjects following a single oral dose of OLM and AML 40 mg/10 mg.**

**Key words:** Tandem mass spectrometry, Amlodipine, Olmesartan, Solid-phase extraction.

## INTRODUCTION

OLM Medoxomil is a pro-drug and is hydrolyzed to OLM during absorption from the gastrointestinal tract (Yanagisawa *et al* 1996; Mire *et al* 2005). OLM is described chemically as the (5-methyl-2-oxo-1,3-dioxol-4-yl) methyl ester of 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[[20-(1H-tetrazol-5-yl)[1,10-biphenyl]-4-yl]methyl]-1H-imidazole-5-carboxylic acid. OLM is an angiotensin II receptor antagonist used for hypertension (Mizuno *et al* 1995). AML Besylate chemically dihydropyridine is a potent calcium channel blocking agent, inhibits the calcium influx through slow channels in peripheral vascular and coronary smooth muscle cells, and thus is useful in hypertension and angina pectoris (Murdoch and Heel, 1991; Haria and

Wagstaff, 1995). AML Besylate is described chemically as the 3-ethyl-0-5-methyl-2-(2-amino ethoxy methyl)-4-(2-chloro phenyl)-6-methyl-1, 4-dihydropyridine-3,5-dicarboxylate. New drugs and their combinations offers better inpatient compliance, than a single drug. Combinations of two or more drugs in the pharmaceutical dosage forms are very much useful in multiple therapies. The US FDA has approved fixed dose combination of AML Besylate and OLM Medoxomil (5 mg /20 mg, 5 mg /40 mg, 10 mg/20 mg and 10 mg/40 mg) for patients with hypertension who do not respond efficiently to monotherapy of either drug (Punzi *et al* 2010; Bramlage *et al* 2010).

HPLC has been remained as a method of choice for determination of drugs alone or in