Original Article

Determination of Mebudipine in Human Plasma by Liquid Chromatography–tandem Mass Spectrometry

Arezoo Asgari, Farzad Kobarfard, Fariborz Keyhanfar, Shohreh Mohebbi and Maryam Noubarani

Abstract

In previous studies, mebudipine, a dihydropyridine calcium channel blocker, showed a considerable potential to be used in cardiovascular diseases. The aim of the current study was to develop a valid method using reversed-phase high performance liquid chromatography coupled with electrospray ionization mass spectrometry to assay mebudipine in the human plasma. Separation was achieved on a Zorbax Eclipse® C18 analytical column using a mobile phase consisted of methanol/water (90:10, v/v). The flow rate was 0.6 mL/min and carbamazepine was used as an internal standard (IS). This method involved the use of $[M + Na]^+$ ions of mebudipine and IS at $m/z$ 411 and 259, respectively with the selected ion monitoring (SIM) mode. There were no interfering peaks from endogenous components in blank plasma chromatograms. Standard curves were linear ($r^2 > 0.99$) between 5 to 100 ng/mL. The mean extraction efficiency was about 84% and the limit of quantification for mebudipine was 5 ng/mL in plasma. The coefficient of variation and error at all of the intra-day and inter-day assessments were less than 11%. The results indicated that this method is a fast, accurate, sensitive, selective and reliable method for the determination of mebudipine in the human plasma. The assay method has been successfully used to estimate plasma concentration of mebudipine after the oral administration of 2.5 mg tablet in healthy adults.

Keywords: Mebudipine; Liquid chromatography-mass spectrometry; Human plasma.

Introduction

Mebudipine [(±)-t-butyl, methyl-1, 4-dihydro-2, 6-dimethyl-4 -(3-nitrophenyl)-3,5-pyridinedicarboxylate] is a dihydropyridine derivative with a calcium channel blocking property (Figure 1) that was first synthesized by Mahmoudian et al. in 1997 (1). Calcium channel blocking property of mebudipine was confirmed in early studies (1,2). Also mebudipine antagonizes the contractile response of K+-depolarized guinea-pig common bile duct to calcium (3). Mebudipine is as potent as amlodipine in inhibition of peak Ca$^{2+}$ currents in differentiated PC12 cells (4).

Mebudipine is a vasoselective and potent blood pressure lowering compound (5). Due