Determination of Metoprolol in Pharmaceutical Preparations by GC-MS Using N-Methyl-N-(Trimethylsilyl)Trifluoroacetamide As Derivatizing Agent

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Metoprolol, a β1-selective receptor antagonist, is used successfully for a broad spectrum of cardiovascular disorders [1-2]. A simple, rapid, precise, accurate and specific gas chromatographic-mass spectrometric (GC–MS) method has been developed and validated for the qualitative and quantitative determination of metoprolol in commercial tablets, using atenolol as internal standard (IS). Metoprolol and IS were determined by GC–MS after derivatization with N-methyl-N-(trimethylsilyl)trifluoroacetamide (MSTFA).

GC–MS analyses in selected ion monitoring (SIM) mode were performed with an Agilent 6890 gas chromatograph interfaced to an Agilent 5973 mass-selective detector (70 eV, electron impact mode) and installed with a capillary column (5% phenyl-95% methylpolysiloxane bonded phase; 30m×0.25mm I.D., 0.25 µm film thickness). The temperatures of injector, interface and ion source were 280, 300 and 230 ºC, respectively. Helium was used as carrier gas at a flow rate of 1.0 ml min⁻¹ with constant flow mode. Samples were introduced in the splitless injection mode and the oven temperature was set initially at 150 ºC (1 min) and programmed to 220 ºC at 20 ºC min⁻¹ and finally to 300 ºC (1 min) at a rate of 10 ºC min⁻¹. The mass chromatograms were generated using 72 m/z ion for metoprolol and IS. All the GC-SIM-MS runs were performed in triplicate.

To determine the linearity of GC-SIM-MS, standard solutions of metoprolol were prepared in acetonitrile. The linear ranges were found to be 12.5-500 ng ml⁻¹. The regression equations obtained by least square regression method were y=0.0124x+0.001 (y and x are mean peak height ratio and concentration, respectively, r =0.9964). The limits of quantitation (LOQ) and detection (LOD) were 10 ng ml⁻¹ and 5 ng ml⁻¹, respectively. Intra- and inter-day precision, expressed as the relative standard deviation (RSD) was less than 3.83 %, and accuracy (relative error) was better than 2.53 %. The developed method was applied to the analysis of the pharmaceutical preparations. The percent analytical recovery values were found to be 99.90 % (Beloc ZOK® tablet; 100 mg/tablet) and 100.12 % (Problok® tablet; 100 mg/tablet), respectively.

In this study, a simple, sensitive and reliable GC-SIM-MS method consisting of one-step derivatization procedure were developed and fully validated for the determination of metoprolol in pharmaceutical preparations for the routine quality control analysis.

References