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Determination of Metroprolol in Rat Plasma after Acute Hydrogen Sulfide Poisoning by Liquid chromatography–mass Spectrometry

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***SUMMARY*. A sensitive and selective liquid chromatography-mass spectrometry (LC-MS) method for determination of metroprolol in rat plasma was developed and validated. After addition of carbamazepine as internal standard (IS), protein precipitation by acetonitrile was used as sample preparation. The chromatographic separation was performed on a Zorbax SB-C18 column (150 x 2.1 mm, 5 μm), using acetonitrile-0.1 % formic acid as the mobile phase with gradient elution, delivered at a flow rate of 0.4 mL/min. Electrospray ionization (ESI) source was applied and operated in positive ion mode, and selected ion monitoring (SIM) mode used to quantify metroprolol. Calibration curves were linear in the concentration ranges of 5-2000 ng/mL for metroprolol, with a lower limit of quantification (LLOQ) of 5 ng/mL. Intra- and inter-day precision were less than 12 % and the accuracy ranged from -6.3 % to 4.9 %. The validated method was used to study the pharmacokinetic profile of metroprolol in rat plasma after acute hydrogen sulfide poisoning on I.V. metroprolol sodium for intravenous administration. The main pharmacokinetic parameters of metroprolol was significantly different in hydrogen sulfide exposured rats. The $t_{1/2}$ and AUC(0-∞) of metroprolol increased significantly and CLz decreased markedly after acute hydrogen sulfide poisoning. The findings of this study suggest that acute hydrogen sulfide poisoning tended to inhibit CYP2D6.**

KEY WORDS: CYP 2D6, LC-MS, Hydrogen sulfide poisoning, Metroprolol, Plasma.

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