



## Simultaneous Determination of Tolbutamide and Hydroxytolbutamide in Rat Plasma After Acute Hydrogen Sulfide Poisoning by Liquid Chromatography-Mass Spectrometry

Meiling ZHANG<sup>1</sup>, Xiaole CHEN<sup>2</sup>, Guoxin HU<sup>1</sup>, Jianchun PAN<sup>1,3</sup> & Xianqin WANG<sup>1\*</sup>

<sup>1</sup> School of Pharmacy of Wenzhou Medical University, Wenzhou 325035, China

<sup>2</sup> Department of pharmacy of Wenzhou City People's Hospital, Wenzhou 325000, China

<sup>3</sup> Shanghai Key Laboratory of Forensic Medicine  
(Institute of Forensic Science, Ministry of Justice), Shanghai 200063, China

**SUMMARY.** Hydrogen sulfide (H<sub>2</sub>S) is a natural decaying product of organic matter, which is highly toxic as a result of environmental and industrial exposure. A sensitive and selective liquid chromatography-mass spectrometry (LC-MS) method for determination of tolbutamide and its metabolite hydroxytolbutamide in rat plasma was developed and validated. We take the method of acetonitrile precipitation to extract the analytes and internal standard carbamazepine from plasma. The chromatographic separation was performed on a Zorbax SB-C18 column (150 × 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 tolbutamide and its metabolite hydroxytolbutamide. Calibration curves were linear in the concentration ranges of 20-5000 ng/mL for tolbutamide and 5-500 ng/mL for hydroxytolbutamide, with a lower limit of quantification (LLOQ) of 20 ng/mL for tolbutamide and 5 ng/mL for hydroxytolbutamide. This developed method was successfully used for determination of tolbutamide and its metabolite hydroxytolbutamide in rat plasma after acute hydrogen sulfide poisoning for pharmacokinetic study. The main pharmacokinetic parameters of tolbutamide and its metabolite hydroxytolbutamide had no significantly different between acute hydrogen sulfide poisoning and control rats. The findings of this study suggest that acute hydrogen sulfide poisoning have no effect on the activity of CYP2C9 enzyme.

**KEY WORDS:** Acute hydrogen sulfide poisoning, Hydroxytolbutamide, LC-MS, Plasma, Tolbutamide.

\* Author to whom correspondence should be addressed. E-mail: lankywang@foxmail.com