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Quantitative Determination of Clozapine in Rat Plasma by Liquid Chromatography Mass Spectrometry and its Application

Yong WANG [1], Jiangang WANG [1], Xiaoyan XIA [1],
Rong WANG [1], Shuai CHEN [1], Zhili WANG [2] & Xiangjun QIU [1]*

[1] *Medical College of Henan University of Science and Technology, Luoyang 471003, China.*
[2] *Henan Eye Institute & Henan Provincial Eye Hospital, Zhengzhou 450052, China.*

***SUMMARY*. A sensitive and selective liquid chromatography mass spectrometry (LC–MS) method for determination of clozapine in rat plasma was developed. After addition of metoprolol as internal standard (IS), protein precipitation by acetonitrile was used as sample preparation. Chromatographic separation was achieved on a Zorbax SB-C18 (2.1 mm × 150 mm, 5 μm) column with acetonitrile-0.1% formic acid as mobile phase with gradient elution. Electrospray ionization (ESI) source was applied and operated in positive ion mode; selective ion monitoring (SIM) mode was used to quantification using target fragment ions *m/z* 327for clozapine and *m/z* 268 for the IS. Calibration plots were linear over the range of 5-1000 ng/mL for clozapine in plasma. Lower limit of quantification (LLOQ) for clozapine was 5 ng/mL. Mean recovery of clozapine from plasma was in the range 78.9-90.5%. CV of intra-day and inter-day precision were both less than 7%. This method is sensitive and selective enough to be used in pharmacokinetic research for determination of clozapine in rat plasma.**

KEY WORDS: Clozapine, LC-MS, Pharmacokinetics, Rat plasma.

* Author to whom correspondence should be addressed. *E-mail:* luoyangxiangjun@163.com

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