**Determination of Tuberostemonin in Rat Plasma by UPLC-MS/MS and its Application to Pharmacokinetic Study**

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**SUMMARY.** Tuberostemonine was elucidated as the major components of Radix Stemona. In this work, a sensitive and selective UPLC-MS/MS method for determination of tuberostemonin in rat plasma was developed and validated. After addition of hupehenine as an internal standard (IS), liquid-liquid extraction by ethyl acetate was used as sample preparation. Chromatographic separation was achieved on a UPLC BEH C18 column (2.1 ×100 mm, 1.7 μm) with 0.1% formic acid and acetonitrile as the mobile phase with gradient elution. An electrospray ionization source was applied and operated in positive ion mode; multiple reaction monitoring (MRM) mode was used for quantification using target fragment ions m/z 376.2→55.1 for tuberostemonin, and m/z 416.3→98.0 for IS. Calibration plots were linear throughout the range 2-1000 ng/mL for tuberostemonin in rat plasma. Mean recoveries of tuberostemonin in rat plasma ranged from 90.3% to 97.5%. RSD of intra-day and inter-day precision were both < 8%. The accuracy of the method was between 95.1% and 107.5%. The method was successfully applied to pharmacokinetic study of tuberostemonin after either oral or intravenous administration. The bioavailability of tuberostemonin was reported as 77.9%.

**KEYWORDS:** tuberostemonin, UPLC-MS/MS, pharmacokinetics, bioavailability, rat

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