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PHARMACOKINETIC STUDY OF GOVANIADINE IN MALE RATS

Lucas Maciel Mauriz Marques[a], Daniel Roberto Callejon[a], Larissa Garcia Pinto[a], Norberto Peporine Lopes[a]

Faculdade de Ciências Farmacêuticas, Universidade de São Paulo, Ribeirão Preto, Brazil; lucasmauriz@yahoo.com.br

Abstract:
Govaniadine (GOV) is an active compound from *Corydalis govaniana* wall which was identified as a new category of dopamine receptor ligand, an anti-malarial and an antileishmanial agent[1,2]. Considering its therapeutic potential, a preclinical screening stage development is necessary in order to obtain its main pharmacokinetic parameters[3]. Therefore, the aim of the current study was to assess the pharmacokinetic of GOV in rat plasma after intravenous administration of a dose of 1 $mg.kg^{-1}$. For this reason, a sensitive and selective UHPLC–ESI–MS/MS method was developed and validated[4]. Prior to analyses, the plasma samples were extracted with simple liquid–liquid extraction method employing ethyl acetate as organic solvent. Chromatographic separation was performed on a C18 ACQUITY BEH column (Ethylene Bridged Hybrid), with a gradient elution consisting of acetonitrile and water containing 0.1% (v/v) formic acid at a flow rate of 0.3 $mL.min^{-1}$. Detection was performed on a triple quadrupole tandem mass spectrometer via electrospray ionization (ESI) in the multiple reaction monitoring (MRM) mode. Mianserine was employed as internal standard (IS). The method exhibited a linear range of 2.3 – 2863.6 $ng.mL^{-1}$, with the following calibration curve: y= 0,00749x + 0,0040 (r > 0,99). The lower limit of quantification was verified to be 2.3 $ng.mL^{-1}$. The precision and accuracy were assessed for both within-day and between-day determinations; neither relative standard deviations (RSD%) nor relative errors (RER) exceeded a value of 15%. The mean absolute recovery was 90 %, with an RSD value below 4 %. This validated method was successfully applied to a pharmacokinetic study. Plasma samples were obtained by veinure punction (i.v.) in nine different instants over a time interval of 5- 180 min. From plasma concentration versus time profiles following i.v. administration was possible to identificate a two compartment model from which afforded the calculation of the main pharmacokinetics parameters: distribution half-time of 6,4 ± 0,4 min, an elimination half-time of 47,9 ± 5,3 min, area under plasma concentration versus time curve (AUC) of 28521,02 ± 2989,93 ng.min mL^{-1} and a clearance of 32,60 ± 4,96 mL/min.kg. To the best of our knowledge, this is the first report on the pharmacokinetics of govaniadine *in vivo*. The results would be helpful to provide some references to clinical application of this alkaloid.

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