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In vitro permeability of MDPV across Caco-2 cells for assessment of intestinal absorption and enantioselectivity

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Abstract

Background: Synthetic cathinones, such as 3,4-methylenedioxypyrovalerone (MDPV), are widely studied chiral psychoactive substances [1]. Enantioselectivity studies on the toxicokinetic of synthetic cathinones are still scarce [2], namely on their ability to cross the intestinal membrane, which was evaluated only for methylone and pentedrone [3]. To isolate enantiomers for these studies, liquid chromatography (LC) using chiral columns has been the technique of choice [4]. Objective: The aims of this work were the semi-preparative enantioresolution of the enantiomers of MDPV and development and validation of an UHPLC-UV method to further evaluate the potential enantioselectivity in intestinal permeability using the Caco-2 cell line. Methods: A semi-preparative LC method using a polysaccharide-based column was optimized to obtain the enantiomers of MDPV. Caco-2 monolayers were exposed to each enantiomer and samples were collected and quantified by UHPLC-UV. For the validation of the UHPLC-UV method, specificity, linearity, accuracy, precision, limit of detection (LOD) and limit of quantification (LOQ) and samples' stability were evaluated [5]. Results: The enantiomers were successfully separated by the optimized LC method with good resolution (R_s of 1.7) and enantioselectivity (α of 1.4), being collected with high enantiomeric ratios (>95%) and recovery rates (>92%). Regarding the UHPLC-UV, high selectivity and good linearity were obtained ($r^2 > 0.999$). Acceptable accuracy (between 102-109%) and inter-day and intra-day precisions (CV < 15%) low LOD and LOQ values (0.063 μ M and 0.19 μ M, respectively) were also observed. Samples were stable for 6 weeks of storage in different temperatures (room temperature, 4 °C, -20 °C and -80 °C). Conclusions: The enantiomers of MDPV were found to be highly permeable across the Caco-2 monolayer and enantioselectivity was found for the Papp values in the basolateral (BL) to apical (AP) direction.

Keywords: Caco-2 cells; enantioselectivity; liquid chromatography; MDPV; permeability

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