



PREDICTION OF $\log P$ BY HPLC OF THE ALKALOID CIMITRYPAZEPINE ISOLATED FROM *Psychotria nemorosa*

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INTRODUCTION

Psychotria nemorosa has been extensively studied by many research groups due to its effect in the Central Nervous System (CNS). Klein-Júnior *et al.* (2020, J Nat. Prod.) isolated and identified 16 indol alkaloids from *P. nemorosa*, including cimitrypazepine, which showed promising results regarding its activity in the inhibition of enzymes involved in the mechanism of neurodegenerative diseases, such as Parkinson's and Alzheimer's Diseases: Butyrylcholinesterase (BChE), Monoamine Oxidase A and B (MAO-A) and (MAO-B). The partition coefficient (P) is an important parameter for the development of drugs, which is the ratio of the equilibrium concentration of a compound in a 1-octanol and water system (OECD, 2022), and give some information of the capacity of the compounds to permeate membranes, such as Blood Brain Barrier (BBB). In this work, cimitrypazepine was isolated from *P. nemorosa* and its logarithmic partition coefficient ($\log P$) was determined for the evaluation of the compound's lipophilicity.

MATERIAL AND METHODS

$\log P$ was determined by High Performance Liquid Chromatography (HPLC) with reverse phase, as described in Test Guideline of OECD n°117 (OECD, 2022). In an LC-10ADvp (Shimadzu) liquid chromatography system, compounds with known $\log P$ were analyzed, including caffeine, benzylic alcohol, benzene,

toluene and naphthalene. Posteriorly, their capacity factors were calculated in logarithmic scale as a function of their retention times (t_r). The correlation between $\log P$ and $\log k$ was determined through linear regression for the estimation of the $\log P$ for cimitrypazepine. A Luna C18(2) 5 μm 100 Å 250x4.6 mm column (Phenomenex) was used for the separation. As mobile phase, it was used 10 mM borate buffer (pH 8.5) and HPLC grade acetonitrile (10:90). The detection of the analytes was carried out with a DAD at the wavelength of 280 nm.

RESULTS

The linear equation $\log P = 1.7025 + 9.5842 \log k$ was obtained through the analysis of the compounds with known k . The determination coefficient r^2 obtained was 0.9009, which indicates a very strong relationship between $\log P$ and $\log k$. In the same chromatographic conditions, the parameters t_r , $\log k$ and $\log P$ of cimitrypazepine were 3.375 min, 0.1670 and 3.3030, respectively. This $\log P$ indicates a good possibility to permeate BBB, in line with the already demonstrated pharmacological activity.

CONCLUSIONS

The linear regression method was successfully employed for the estimation of the $\log P$ of cimitrypazepine.

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