Design and analysis of Pharmacokinetic, Pharmacodynamics and Toxicological properties of Canabidiol analogs using *in silico* Tools

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Cannabidiol (CBD), a non-psychoactive phytocannabinoid from *Cannabis Sativa*, have received increasing attention in recent years because of their potential therapeutic benefits, including neuroprotective, antiepileptic, anxiolytic, antipsychotic, anti-cancer and anti-inflammatory properties. Therefore, the CBD scaffold has become an interesting option for medicinal chemists in the development of new drug candidates. In this scenario, the aim of this study was the design, quantitative analysis of physicochemical properties, pharmacodynamics and pharmacokinetic of CBD analogues. The 16 analogs proposed were designed using the PubChem Sketcher V. 2.4® software. Then, CBD analogs were subjected to different in silico tools: Molinspiration®; SwissADME®; SwissTargetPrediction® and OSIRIS Property Explorer®. The physical-chemical data obtained showed that only analogs 4, 5, 7 and 8 did not violate Lipinski's rule. Pharmacokinetic data showed that compounds 10 and 11 had low oral absorption and that structures 5, 10-13 and 16 were not permeable to the blood-brain barrier. Structures 4-9 and 11 did not inhibit the CYP3A4 isoform and structures 1-3, 5-7, 10, 11 and 13-16 did not inhibit CYP2D6. The data also show that only molecules 9, 11 and 16 have a selective profile for interactions with CB1/CB2 receptors. *In silico* toxicity data showed that compounds 10, 11 and 14 are at risk of toxic event in humans. The screening of CBD analogs carried out in this study shows that compounds 9 and 16 would have a better profile as drug candidates to be tested later *in vitro* and *in vivo* models. It follows that the computational methods employed in this study allowed the elucidation of pharmacokinetic properties, pharmacodynamics and toxicological analogs of cannabidiol. Additionally, we found that compounds in the screening performed 9 and 16 were as shown most promising for further preclinical testing.

Keywords: Cannabidiol, *In silico* tools, *Cannabis Sativa*, ADMET.

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