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MYRICITRIN ACYLATED DERIVATIVES: ENZYMATIC SYNTHESIS, ADMET PROPERTIES, AND DOCKING STUDIES

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Flavonoids constitute one of the largest classes of secondary metabolites and are notable for their pharmacological properties. However, their applicability is limited due to their hydrophilic nature. The use of lipases for enzymatic acylation of these compounds has resulted in greater stability and solubility. This study aims to perform transesterification reactions using nine vinyl esters with Novozyme®435 followed by the isolation of the products. It also aims to perform their ADMET properties and docking evaluation. Each reaction mixture consisted of 22.5 mg of myricitrin, 4.5 - 11.25 mg of the enzyme (Novozyme® 435 lipase (1531 U/g) (from *Pseudozyma antarctica*) (20-50% relative to the amount of flavonoid), and 1.5 mL of the vinyl ester. Exceptionally, the reaction with vinyl benzoate (40 Ml) was carried out for 288 h and 29.93 mg of enzyme. For propionate and pivalate reactions, isopropanol (0.5 mL) was used as solvent. The ionic liquid $[C_4mim][BF_4]$ was used alternatively. The reactions were monitored by TLC and the kinetics were established through the obtained relative area percentages by UHPLC-DAD The highest conversion percentages to monoesters were reached after 144 h, except for the reaction with vinyl propionate, in which the maximum peak was achieved at 72 h. The products furnished isolated yields of 20.20%, 47.91% and 9.8% for myricitrin benzoate, butyrate, and pivalate, respectively; 27.06%, 47% and 30.2% for myricitrin cinnamate, laurate, and neodecanoate, respectively; and 23.1%, 62.7% and 32.8% for myricitrin decanoate, propionate, and stearate, respectively. The structures of the products were elucidated by NMR and Mass Spectrometry, and their ADMET properties were evaluated using ADMETlab 3.0 and VegaHub softwares. Myricitrin propionate and benzoate showed the highest drug score and drug likeness values, and predicted low toxicity in mammalian cells. Docking studies with the enzyme myeloperoxidase — a target of great biological relevance — are currently in progress, as well as their *in vitro* evaluation. The authors would like to acknowledge CAPES, CNPq, and FAPERJ.

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