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SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM FOR NOSE-TO-BRAIN TRANSPORT OF MYRSINOIC ACID FOR ANTIDEPRESSIVE-LIKE ACTIVITY

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INTRODUCTION

Nose-to-brain transport has been proposed as a strategy to increase the bioavailability of drugs for the treatment of central nervous system (CNS) disorders. *Rapanea ferruginea* has been demonstrated *in vivo* antidepressant activity of the ethanolic extract of the bark and its isolated compounds, myrsinoic acids A (MAA) and B (MAB). Nanocarrier platforms, such as self-emulsifying systems (SEDDS) increases solubility and permeability. The present work aimed to develop SEDDS containing AMA isolated from *R. ferruginea* barks and to evaluate the antidepressant potential *in silico* and *in vivo*.

MATERIAL AND METHODS

From the ethanolic extract of the bark of *R. ferruginea* (SISGen A7106C7), the compounds MAA and MAB and the mixture of MAB:MAA were isolated, which were characterized by HPLC, NMR of H^1 and C^{13}, TGA, DSC. *In silico* and *in vivo* antidepressant-like activity was also evaluated by TST (005/19p1). The development of the SEDDS started with the pseudoternary phase diagram being characterized by visual appearance, internal phase size, polydispersity index, zeta potential, emulsification time, transmittance, physical stability, rheological behavior, evaluation of mucoadhesive strength, and *in vitro* release of the MAA. The SEDDS were administered IN and evaluated under TST.

RESULTS

MAA was obtained with content of 94%, and MAB with content > 99%. The MAA at 10 mg/kg showed better antidepressant-like activity *in vivo*. The SEDDS was obtained by emulsifying in the nanoemulsion form, transparent with bluish reflection, and physically stable. Before dilution in water, it showed mucoadhesive, fluid, and sustained release properties of MAA *in vitro* study following zero-order kinetics. SEDDS showed the same antidepressant-like activity as the emulsion orally administered. *In silico* studies suggest the inhibition of the enzyme monoamine oxidase A as a mechanism of antidepressant activity of mysinoic acids. Predictive safety studies did not detect toxicity.

CONCLUSIONS

The present work obtain SEDDS with adequate physical and physicochemical characteristics, representing a potential vehicle for IN of MAA isolated from *R. ferruginea*, to be used as an antidepressant phytomedicine.

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