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SAKURANETIN AS A PROMISING PROTOTYPE IN DRUG DEVELOPMENT - PHARMACOKINETICS AND in vivo *ANTI-*Schistosoma mansoni *ACTIVITY*

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Sakuranetin (SAK), a flavanone found in several plant families, exhibits various biological activities, including antimutagenic, anticancer, antiviral, anti-inflammatory, antidiabetic, and antiparasitic.[1] As part of our ongoing research on discovering new antischistosomal prototypes based on natural products[2], SAK underwent *in silico* and *in vitro* pharmacokinetic experiments and was then tested for *Schistosoma mansoni* using an *in vivo* model. To conduct this study, the aerial parts of *Baccharis lateralis* (Asteraceae) were defatted with hexane and then extracted with MeOH. The MeOH extract was partitioned into hexane (0.5 g) and CH_2Cl_2 (10.7 g). Part of the CH_2Cl_2 phase (10.0 g) was chromatographed over SiO_2 (eluent hexane:EtOAc in different proportions) to produce 12 groups (A–L). Group B (977 mg) was then chromatographed over Sephadex LH-20 using the following eluents: hexane:CH_2Cl_2 (1:4), CH_2Cl_2:acetone (3:2 and 1:4), and pure acetone. This process yielded 12 additional groups (B1–B12). As evidenced by NMR and MS analysis, group B8 (618 mg) contained pure SAK. *In silico* pharmacological analyses were performed using the SwissADME tool, which indicated no violations of drug-likeness or PAINS and high absorption by the GI tract. Thus, it was considered similar to orally administered drugs. Next, we validated an analytical method for the extraction and detection of SAK in rat plasma, following the recommendations of ANVISA and the FDA, for concentrations up to 50 ng/mL. We also performed a Plasma Protein Binding experiment, finding that only 8.3% of the drug was unbound. Liver microsomal vesicles were used to calculate the metabolic rate: 40% of the drug was metabolized within 120 minutes. Considering that the *in silico* and *in vitro* pharmacokinetic parameters indicated favorable drug-like properties, the *in vivo* anti-*S. mansoni* activity was assessed in mice infected subcutaneously and treated with a single oral dose of 400 mg/kg of SAK or PZQ (the standard drug), compared to untreated mice as the control group. After euthanizing the mice, the parasites were sexed and counted, and quantitative oograms and the Kato-Katz technique were used to assess the worm burden reduction (WBR) and egg burden reduction (EBR), respectively. As results, SAK achieved total WBR and EBR of 84 ± 6% and 96 ± 5%, respectively, compared to the standard drug, which achieved reductions of 88 ± 2% and 87 ± 2%. Based on these results, SAK is a promising candidate for the development of new oral schistosomiasis drugs.

References: [1]Stompor et al., 2020. *Nutrients* 12(2), 513; [2]Souza et al., 2024. *Phytomedicine* 135, 156045.
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