TITLE: CREAM CONTAINING *Trichilia catigua* EXTRACTS FOR TREATMENT OF HERPES SIMPLEX VIRUS TYPE 1

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ABSTRACT

Herpes simplex virus type 1 (HSV-1) is an infectious agent with neuroepithelial tropism and latent infection in peripheral neurons with reactivation periods. Herpetic encephalitis is a serious consequence, especially for immunocompromised patients. Acyclovir is a specific drug discovered in the 70s. However, the chronic treatment induces selection of resistant strains. Natural products like *Trichilia catigua* are potential sources of compounds with antiviral activity. The present study evaluated the antiviral activity of a new cream formulation containing *Trichilia catigua* extracts, against HSV-1 AR29 strain, resistant to acyclovir. Previously sixteen extracts from *T. catigua* (EB1 to EB16) were evaluated by colorimetric assay (MTT) to determine concentrations capable of reducing cell viability (Vero ATCC CCL81) and viral inhibition by 50%: CC50 and IC50, respectively. The selectivity index (SI) was calculated by the ratio CC50/IC50. Viral suspensions (10^{-2}) were initially incubated for 1h with different extracts concentrations (0.35 to 50 µg/mL), followed by Vero cell inoculation and evaluation for 72h (virucidal effect). The EBs that showed strong inhibition *in vitro* were used to develop new topicals formulations (BR102021006486-2). For the *in vivo* assay, BALB/c mice, inoculated with HSV-1, were treated with the formulations 4 h post-infection, 3 times a day, for 9 days. The sore score was classificated from 0 to 5, according to the severity. ANOVA and Tukey tests were used for data normalization and analysis. The extracts with the highest IS *in vitro* were EB12 (885.7), 13 (491.4) and 16 (481.9) being used for the development of three new cream formulations and evaluated for *in vivo* activity. Cream containing EB12, 13 or 16 had average sore scores of 1.4, 1.8 and 2.0, respectively and were significantly smaller compared to the infected and untreated groups (3.5). Of note, there are bibliographic reports of the antiviral activity of *T. catigua* on HSV-1 and poliovirus *in vitro*. However, the *in vivo* anti-HSV activity of three creams developed from *T. catigua* was first demonstrated. It is suggested that *T. catigua* extracts may represent an alternative for the treatment of resistant strains of HSV-1.

Keywords: *Trichilia catigua*, Antiherpetic cream, Acyclovir resistant HSV-1

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