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Antiviral effect of compounds derived from the seeds of *Mammea americana* and *Tabernaemontana cymosa* on Dengue and Chikungunya virus infections

Cecilia Gómez-Calderón[1,2,3], Carol Mesa-Castro[1,4], Sara Robledo[4], Sergio Gómez[2], Santiago Bolivar-Avila[5], Fredyc Diaz-Castillo[5] and Marlen Martínez-Gutierrez[1*]

Abstract

Background: The transmission of Dengue virus (DENV) and Chikungunya virus (CHIKV) has increased worldwide, due in part to the lack of a specific antiviral treatment. For this reason, the search for compounds with antiviral potential, either as licensed drugs or in natural products, is a research priority. The objective of this study was to identify some of the compounds that are present in *Mammea americana* (*M. americana*) and *Tabernaemontana cymosa (T. cymosa)* plants and, subsequently, to evaluate their cytotoxicity in VERO cells and their potential antiviral effects on DENV and CHIKV infections in those same cells.

Methods: Dry ethanolic extracts of *M. americana* and *T. cymosa* seeds were subjected to open column chromatographic fractionation, leading to the identification of four compounds: two coumarins, derived from *M. americana*; and lupeol acetate and voacangine derived from *T. cymosa*.. The cytotoxicity of each compound was subsequently assessed by the MTT method (at concentrations from 400 to 6.25 μg/mL). Pre- and post-treatment antiviral assays were performed at non-toxic concentrations; the resulting DENV inhibition was evaluated by Real-Time PCR, and the CHIKV inhibition was tested by the plating method. The results were analyzed by means of statistical analysis.

Results: The compounds showed low toxicity at concentrations ≤ 200 μg/mL. The compounds coumarin A and coumarin B, which are derived from the *M. americana* plant, significantly inhibited infection with both viruses during the implementation of the two experimental strategies employed here (post-treatment with inhibition percentages greater than 50%, $p < 0.01$; and pre-treatment with percentages of inhibition greater than 40%, $p < 0.01$). However, the lupeol acetate and voacangine compounds, which were derived from the *T. cymosa* plant, only significantly inhibited the DENV infection during the post-treatment strategy (at inhibition percentages greater than 70%, $p < 0.01$).

Conclusion: In vitro, the coumarins are capable of inhibiting infection by DENV and CHIKV (with inhibition percentages above 50% in different experimental strategies), which could indicate that these two compounds are potential antivirals for treating Dengue and Chikungunya fever. Additionally, lupeol acetate and voacangine efficiently inhibit infection with DENV, also turning them into promising antivirals for Dengue fever.

Keywords: Dengue Virus, Chikungunya Virus, Antiviral, *Mammea americana*, *Tabernaemontana cymosa*

* Correspondence: marlen.martinezg@campusucc.edu.co
[1]Grupo de Investigación en Ciencias Animales-GRICA, Universidad Cooperativa de Colombia, Calle 30A # 33-51, Bucaramanga, Colombia
Full list of author information is available at the end of the article