Prêmio

2255-2 ANTI-CANDIDAL ACTIVITY AND PROTEASES INHIBITION OF 7-HYDROXYCALAMENENE ISOLATED FROM Croton cajucara

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Resumo

The leaves from *Croton cajucara* Benth. (family Euphorbiaceae), a shrub from the Amazon, have been locally used in folk medicine to treat diabetes, malaria, gastrointestinal and liver disorders. A chemotype of this species was found with an essential oil rich in 7-hydroxycalamenene. 7-hydroxycalamenene is a hydroxylated sesquiterpene found in *Heritiera ornithocephala*, *Eremophila drummondii*, *Heteroscyphus planus*, *Tilia europea*, *Morus alba*, *Ulmus thomasii* and other elm species, and methanolic and dichloromethanic extracts of *Bazzania trilobata*. This substance is reported to have antifungal activity against *Botrytis cinerea*, *Cladosporium cucumerinum*, *Phythophthora infestans*, *Pyricularia oryzae* and *Septoria tritici*. In *Candida* species, proteases that use different catalytic mechanisms and display distinct pH optima presumably could be used to retain maximum flexibility for the pathogen to survive under different environmental conditions, including pH, substrate availability and ionic content. For these reasons, extracellular proteases could be a good target for the development of an antifungal peptidyl drug strategy based on protease inhibitors. During our studies we isolated 7-hydroxycalamenene by silicagel column chromatography. The pure compound (>98%) was tested to inhibit secreted proteases of *C. albicans* (ATCC10231). Minimum inhibitory concentration (MIC) was evaluated according standard method from Clinical and Laboratory Standards Institute (CLSI), and the MIC value obtained was 39.06 µg/mL. To determining a possible target, it was performed assays of proteolytic activity inhibition. Cell-free supernatants of *C. albicans*, grown in RPMI and BHI broths, were incubated with bovine serum albumin (0.1 mg/mL), as proteic substrate, and pHs buffers ranging of 1-12. Extracellular peptidases were able of hydrolizate the proteic substrate on pH 7 in RPMI and pH 6 in BHI. In addition, the results of standards inhibitors showed 100% of inhibition to Pepstatin A and Aprotinin in the RPMI and BHI supernatants, respectively. Their proteolytic inhibitions obtained was 100% with 7-hydroxycalamenene (concentration at MIC value)in both RPMI and BHI supernatants. Together, these results suggesting that 7-hydroxycalamenene showed as a promising aspartic and serine protease inhibitor and as an effective antifungal.