Evaluation of the Inhibitory Activity of Natural Benzophenones on Proteolytic Enzyme

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Papain and Trypsin are model enzymes in the study of cysteine and serine proteases, respectively. The discovery of specific inhibitors for these protease families can provide useful tools to understand several diseases in which these proteases are involved. In the present study, polyprenylated benzophenones extracted from a *Garcinia* gender plant were evaluated as possible candidates to inhibit the above proteases. The activity of the enzymes was determined fluorimetrically (λ_{ex}=380 nm and λ_{em}=460 nm) by hydrolysis of the substrate Z-Phe Arg-MCA. Papain (7.8 nM) was incubated in 50 mM sodium phosphate buffer; pH 6.8 containing 1.0 mM EDTA. Trypsin (56.1 nM) was incubated in 50 mM Tris-HCl buffer; pH 8.0 containing 10 mM $CaCl_2$. Increasing concentrations of the benzophenones studied were added as inhibitors (5 min; 25^oC) to both enzyme. After incubation, the substrate (3.1 mM) was added and the spectrofluorimetric readings were performed. The results showed that the benzophenones M_{11}, M_6, and M_3 were able to inhibit 50% of papain enzimatic activity at concentrations (IC_{50}) 2±0.1, 20±2, and 132±5 µM, and trypsinolytic activity 9±0.3, 20±2, and 104±9 µM, respectively. These results demonstrated a correlation between inhibitory capacity and number of prenyl groups present in the structure of the benzophenones evaluated. Our data point out to the set of these phytocompounds, especially M_{11}, as potential compounds to be used in the treatment of pathologies in which these protease families are involved.
Supported by CNPq and UNIFAL-MG