PÔSTER - RESUMO - MATERIAIS E BIOMATERIAIS

SYNERGISTIC MEMBRANE INTERACTIONS OF BIOACTIVE ACETOGENINS MIXTURES STUDIED BY LANGMUIR MONOLAYERS

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Annonaceous Acetogenins (ACGs) are a class of natural products with reported bioactivity against microbial pathogens and tumor cells (1). Two acetylenic ACGs isolated from Porcelia macrocarpa have shown activity against the protozoa Trypanosoma cruzi and Leishmania infantum. Notably, their cytotoxic effects correlate with the degree of unsaturation in their alkyl chains: the more unsaturated compound is biologically active, whereas the more saturated analogues show little or no activity. Furthermore, the mixture of those acetogenins showed increased bioactivity in comparison to their pure forms, highlighting possible synergistic effects between these compounds. Therefore, it is of great importance to study the interactions of these compounds with models of parasitic membranes, gathering insights on their mechanism of action and possible sinergistic effects on membrane binding. This study investigated the interfacial behavior of the mixture of acetogenins (ACGs 1 and 2) alone and with protozoan membrane models based on Langmuir films of DPPE (dipalmitoylphosphatydilethanolamine). Surface pressure-area isotherms, compressional modulus, stability, compression-decompression assays and

Brewster Angle Microscopy were executed with films of pure DPPE and with the acetogenins. The results show that unsaturated acetogenins disrupt and destabilize the lipid monolayers through mechanisms distinct from those of the fully saturated compounds. In addition, the unsaturated molecules form filamentous aggregates at surface pressures up to 25 mN/m, promoting significant molecular rearrangements in mixed films. The mixture of ACGs induced changes on the morphology of the DPPE monolayer in comparison to the pure ACGs. The mixture also induced changes on the pressure-area isotherms, stability and rheology. These data indicates that the mixture of ACGs have a synergistic effect that disrupts the membrane models differently from the pure compounds, which might be related to an enhanced interaction with the protozoa membrane, leading to a higher bioactivity. Together, these findings provide mechanistic insight into how structural features such as chain unsaturation influence acetogenin–membrane interactions, helping to clarify their mode of action at biological membranes.

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References

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