

# **1*H*-Cyclopenta[b]benzofuran Lignans from *Aglaia* Species Inhibit Cell Proliferation and Alter Cell Cycle Distribution in Human Monocytic Leukemia Cell Lines**

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Thirteen naturally occurring 1*H*-cyclopenta[b]benzofuran lignans of the rocaglamide type as well as one naturally occurring aglain congener all of them isolated from three *Aglaia* species (*Aglaia duperreana*, *A. oligophylla* and *A. spectabilis*) collected in Vietnam were studied for their antiproliferative effects using the human monocytic leukemia cell lines MONO-MAC-1 and MONO-MAC-6. Only rocaglamide type compounds showed significant inhibition of [<sup>3</sup>H]-thymidine incorporation and the most active compound didesmethylrocaglamide inhibited cell growth in a similar concentration range as the well-known anticancer drug vinblastine sulfate. Detailed structure-activity analysis indicated that the OH-group at C-8b which is a common structural feature of most naturally occurring rocaglamide compounds is essential for the described antiproliferative activity since replacement of this group by methylation led to a complete loss of the inhibitory activity for the resulting derivative. Rocaglamide derivatives rapidly inhibited DNA as well as protein biosynthesis of MONO-MAC-6 cells at concentrations well below those of actinomycin D or cycloheximide which were used as positive controls in the respective experiments. Didesmethylrocaglamide was furthermore able to induce growth arrest of MONO-MAC-1 cells in the G<sub>2</sub>/M and probably G<sub>0</sub>/G<sub>1</sub>-phase of the cell cycle with no morphological indication of cellular damage. Our data suggests that 1*H*-cyclopenta[b]benzofuran lignans of the rocaglamide type act primarily by a cytostatic mechanism.