Structure Activity Relationships of Antiproliferative Rocaglamide Derivatives from *Aglaia* Species (Meliaceae)

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Eleven rocaglamide derivatives (cyclopentatetrahydrobenzofurans) and one structurally related aglain congener all isolated from different *Aglaia* species (Meliaceae) were tested for growth inhibiting properties using the human cancer cell lines MONO-MAC-6 and MEL-JUSO. Proliferation of both cell lines was efficiently inhibited in a dose and compound dependent manner. Applying a MTT-Assay, the IC_{50} of the most active compound didesmethylrocaglamide **(1)** was observed at 0.002 and 0.006 μg/ml (0.004 and 0.013 μM) depending on the cell line investigated. Bulky aminoacyl substituents at C-2, acetylation of the OH substituent at C-1 or insertion of a OH or OMe substituent at C-3' of the rocaglamide skeleton all diminished the activity of the compounds investigated. The aglain derivative **12** was inactive up to a concentration of 3 μg/ml (4.6 μM). This loss of activity is assumed to be mainly due to the presence of a pyran ring in the aglains vs. a furan ring as found in rocaglamide derivatives. Rocaglamide derivatives may act primarily by inhibition of cell proliferation as evidenced by the absence of a significant cytotoxic effect in long-term cultures of MONO-MAC-6 cells treated with high doses of didesmethylrocaglamide.

Our data suggest that rocaglamide derivatives could exert a potential role in the treatment of malignant diseases and are worth to be investigated in further studies of experimental medicine and pharmacology.

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