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New potent P-glycoprotein modulators with the cucurbitane scaffold and their synergistic interaction with doxorubicin on resistant cancer cells.
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Abstract
The novel cucurbitacins, balsaminagenin A and B (1-2) and balsaminoside A (3) and the know cucurbitacin karavelagenin C (4), together with five new mono or diacylated derivatives (5-9) of karavelagenin C were evaluated for multidrug resistance reversing activity on human MDR1 gene transfected mouse lymphoma cells. Compounds 2-6 exhibited a strong activity compared with that of the positive control, verapamil. Structure-activity relationships are discussed. Moreover, in the checkerboard model of combination chemotherapy, the interaction between doxorubicin and compounds 2-5 synergistically enhanced the effect of the anticancer drug. Compounds 1-4 were isolated from the aerial parts of Momordica balsamina L. The structures of the compounds were established on the basis of spectroscopic methods including 2D NMR experiments (COSY, HMQC, HMBC and NOESY).
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