

SHORT COMMUNICATION

L-PROLINE ANALOGUES OF ANTHRAQUINONE-2-CARBOXYLIC ACID: CYTOTOXIC ACTIVITY IN BREAST CANCER MCF-7 CELLS AND INHIBITORY ACTIVITY AGAINST TOPOISOMERASE I AND II

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A series of proline analogues of anthraquinone-2-carboxylic acid (**1–3**) were synthesized and evaluated for cytotoxic activity in the cultured breast cancer MCF-7 cells. The concentrations of **1**, **2** and **3** needed to inhibit [³H]thymidine incorporation into DNA by 50% (IC₅₀) were found to be 107 ± 6 nM, 185 ± 5 nM and 87 ± 6 nM, respectively. To test whether cytotoxic properties were related to topoisomerase action, the most potent compounds **1** and **3** were evaluated in a cell-free system. Compound **3**, which contains a basic substituent at C terminus of the amino acid such as (dimethylamino)propyl inhibited the catalytic activity of both topoisomerases I and II at a concentration of 30 and 60 nM, respectively. However, compound **1** containing an electrostatically neutral moiety, such as methyl ester did not inhibit topoisomerase I or topoisomerase II. In summary, compound **3** is a promising lead compound for a further structural variation in the design of new antitumour drugs.

Key words: breast cancer MCF-7, cytotoxicity, DNA topoisomerase, proline analogues of anthraquinone-2-carboxylic acid

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