Synthesis of two new series of 7-aminocarbohydrate-isoquinoline-5,8-dione derivatives

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INTRODUCTION

Several natural compounds containing quinone and carbohydrate moieties possess significant antibiotic and antitumor activities. In this context, the synthesis of carbohydrate-quinone conjugates is currently an important field of pharmacy and chemistry. Herein, we report the synthesis and in vitro antitumor activity evaluation of two homologous series of sugar-based quinones 1a–c and 2a–c (Scheme).

RESULTS AND DISCUSSION

Isoquinolinequinone (5), prepared in 80% yield by the method of Valderrama and coworkers, was submitted to addition reaction with different aminocarbohydrates 6a–c under ultrasound irradiation, giving the corresponding new 7-substituted amino-isoquinoline-5,8-quinone derivatives 1a–c, in good yields.

Scheme 1: Synthesis of naphtoquinones 1 and 2.

Although the possibility of the nucleophilic attack of amine derivatives 6a–c on the carbonyl carbon atom C-6 or C-7 of 5, only aminouquinone compounds 1a–c were isolated, resulting of the nucleophilic addition to the more electrphilic carbonyl group (C-7). The reaction of 1a–c with N-bromosuccinimide (NBS) led to the corresponding brominated compounds 2a–c in good yields.

The compounds 1a–c and 2a–c were purified by silica gel column chromatography and their structures were determined on the basis of NMR spectroscopy (one- and two-dimensional techniques: 1H, 13C-APT, COSY-1H x 1H and HSQC). The in vitro anticancer activity of the new quinones 1a–c and 2a–c were assessed against HL-60, HCT-116, SF-295 and OVCAR-8 human cancer cell lines.

Among these quinone derivatives, only the brominated compound 1a showed potential activity (IC50 below 2.0 µg/mL) against leukemia and colon cell lines.

CONCLUSION

In summary, two new series of quinone derivatives 1a–c and 2a–c have been synthesized and were evaluated for anticancer activity against human cancer cell lines. Only, the brominated compound 1a showed significant anticancer activity against leukemia and colon cell lines (IC50 values below 2 µg/mL).

We can speculate that the anticancer activity of 1a can be related to the chemical structure (e.g., conformation and intermolecular interactions) of the furanose ring and to the lipophilic characteristic of the halogen atom attached at position C-6 of quinone moiety.

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