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

Wanderson A. da Silva[a], Angela Cristina P. B. dos Santos[a], Vitor F. Ferreira[a], Raquel C. Montenegro [b], Vinícius R. Campos[a], Maria C. B. V. de Souza [a] and Anna C. Cunha[a]*

[a] *Universidade Federal Fluminense, Departamento de Química Orgânica, Programa de Pós-Graduação em Química, Outeiro de São João Batista, 24020-141 Niterói, RJ, Brasil*

[b] *Universidade Federal do Pará, Instituto de Ciências Biológicas, Belém, PA, Brasil.*

**corresponding author. Tel.: +55 21 26292364; Fax: +55 21 26292135; e-mail: annac@vm.uff.br*

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INTRODUCTION

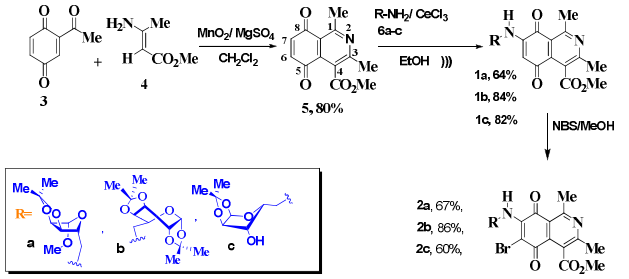
Several natural compounds containing quinone and carbohydrate moieties possess significant antibiotic and antitumor activities[1].

In this context, the synthesis of carbohydrate-quinone conjugates is currently an important field of pharmacy and chemistry[2].

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[3], 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.



Scheme1: Synthesis of naphthoquinones **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 aminoquinone compounds **1a-c** were isolated**,** resulting of the nucleophilic addition to the more electrophilic 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: ^{1}H, ^{13}C-APT, COSY-^{1}H x ^{1}H 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 cells lines.

Among these quinone derivatives, only the brominated compound **1a** showed potential activity (IC_{50} below 2.0 $\mu g/mL^{-1}$) against leukemia and colon cells 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 four human cancer cell lines. Only, the brominated compound **1a** showed significant anticancer activity against leukemia and colon cell lines (IC_{50} values below 2 $\mu g/mL^{-1}$).

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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