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Benzo[*f*]indole-4,9-dione derivatives: synthesis and evaluation as potent antitumor agents to suppress the growth of triple-negative breast cancer

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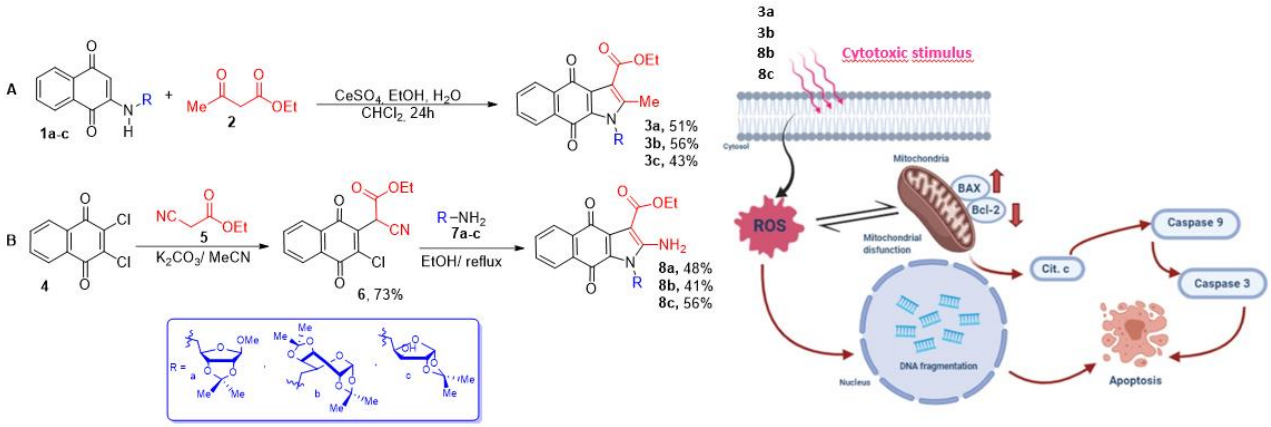
ABSTRACT

This work describes the synthesis and evaluation of the antitumor activity against triple-negative breast cancer (TNBC) of two classes of benzo[*f*]indole-4,9-dione glycoconjugates **3a-c** and **8a-c**. The first route utilizes cerium(IV)-mediated oxidative free radical cyclization involving 1,4-amino-naphthoquinones and ethyl acetoacetate (Scheme 1A). The second consists of the nucleophilic substitution of 2,3-dichloro-naphthoquinone by the ethyl cyanoacetate (Scheme 1b), followed by the replacement of the second chlorine atom by the aminocarbohydrates.

Glycoconjugated quinones **3a-c/8a-c** have been tested for TNBC and four derivatives can induce apoptotic cell death by increasing reactive oxygen species (ROS), causing DNA damage and inducing cell cycle arrest in the G2/M phase. Furthermore, we showed that the four benzo[*f*]indole-4,9-dione derivatives can induce caspase cleavage, thereby activating the intrinsic apoptosis pathway. These results suggest that compounds are potent cytotoxic agents and offer new possibilities for the development of a series of compounds for the treatment of TNBC and other cancers.



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