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# Synthesis and Evaluation of Thymoquinone Analogues as Anti-Ovarian Cancer Agents †

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Thymoquinone (TQ), 2-isopropyl-5-methyl-1,4-benzoquinone, a natural product isolated from *Nigella sativa* L., has previously been demonstrated to exhibit antiproliferative activity in vitro against a range of cancers, including ovarian, prostate, colon, breast, pancreatic cancers, leukaemia, and osteosarcoma [1–3]. Recently, TQ has been shown to block substrate recognition by the Polo-Box domain of Polo-like-kinase 1 (Plk1), a mitotic regulator that when overexpressed causes cancer [4]. We describe here the synthesis of a series of analogues of TQ that explore the potential for nitrogen-substitution to this scaffold, or reduction to a hydroquinone scaffold, in increasing the potency of its antiproliferative activity against ovarian cancer cell lines. In addition, alkyl or halogen-substituted analogues of TQ were commercially sourced and tested in parallel. Several TQ analogues with improved potency against ovarian cancer cells were found, although this increase was moderate. Key aspects of the structure activity relationship that could be further explored are highlighted [5]. In particular, a synthetic aminothymoquinone obtained via substitution of the CH of the isopropyl group in TQ by a single nitrogen atom showed significant improvement of water solubility, and synergism with two clinically used ovarian cancer drugs, carboplatin and paclitaxel.

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