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BOOK OF ABSTRACTS

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Benzothienoquinazolinones as new inhibitor of Topoisomerases and Tubulin

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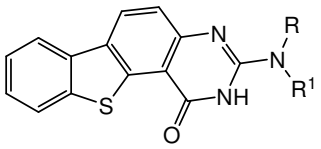
Ellipticine is a naturally occurring alkaloid with a carbazole backbone, well known for their antitumor activities, exerted through DNA intercalation, high DNA binding affinity and inhibition of the topoisomerases [1]. However, because of onset of some side effects the therapeutic application of Ellipticine and its derivatives used in clinic therapy, still remain limited [2]. Accordingly, with the aim to reduce side effects and improving their biologic activities, the search for new Ellipticine analogues is always demanded.

This work is focused on the creation of new library of benzothienoquinazolinones (**4-9**), analogues of Ellipticine, in which both the carbazole moiety and the pyridine ring were replaced by a dibenzothiophene- and a pyrimidine moiety, respectively. The synthesis of these 3-(alkyl(dialkyl)amino)benzothieno[2,3-f]quinazolin-1(2H)-ones) was realized in a simple one-pot reaction using 3-aminodibenzothiophene as a starting material (Figure 1).

These have shown an interesting anti-proliferative activity on two breast cancer cell lines, MCF-7 and MDA-MB-231. Molecular docking of these compounds was performed on the crystallographic enzyme structures of Tubulin, Topoisomerase I and II. The simulation results showed that the compounds investigated bind the enzymes with a relatively high affinity, at least in the low micromolar range. Other *in vitro* assays are in progress to confirm the *in silico* results.



4-9

Figure 1: Benzothienoquinazolinones.

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[2] Caruso A.; Iacopetta D.; Puoci F.; Cappello A. R.; Saturnino C.; Sinicropi M. S., *Mini Review in Medicinal Chemistry* **2016**, 6 (8), 630-43.