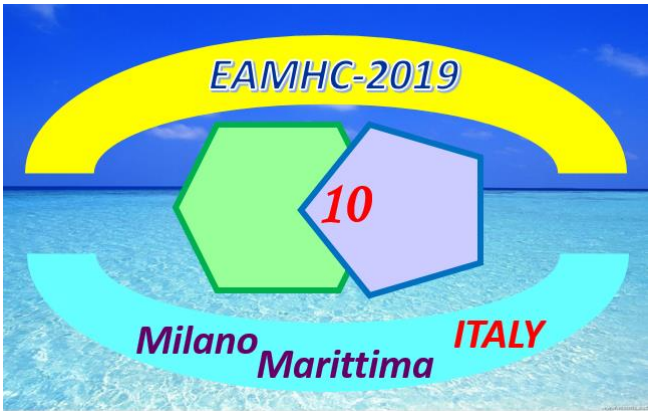

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PP-8

Diamine derivatives and dithiourea analogues: new multi-target tools against cancer

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Tumorigenesis is a complex process involving different signaling pathways. Thus, in some cases a single-target therapy has exhibited side effects, lack of efficacy and drug resistance. For these reasons, multi-target therapy is considered highly attractive for cancer fighting and the research of new molecules able to act with a synergistic mechanism could represent a good strategy [1]. With this aim, we designed and synthesized a new library of diamine derivatives and dithiourea analogues, structurally related to a known antitumor compound, namely NCS 109555 (Fig. 1). Our compounds showed a good antitumor activity against a large panel of cancer cell lines (breast, colon and uterine cancer cells), without any cytotoxicity on non-tumoral cells. Moreover, they are also able to induce programmed cell death, acting on different important steps of apoptotic cascade. Docking studies highlighted that some of them were able to inhibit crucial players in many cellular events (cell division and replication, cell movement, mitosis, etc): tubulin and topoisomerases I and II. The prediction for the first one target was already confirmed by *in vitro* tubulin polymerization inhibition assay, while the *in vitro* evaluation of both topoisomerases isoforms inhibition is in progress.

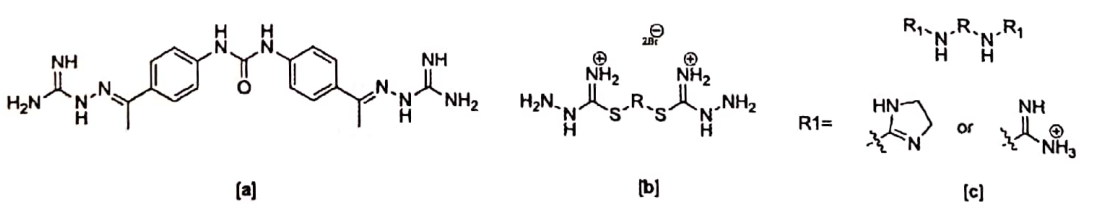

Figure 1. *Structure of 4,4'-diacetyldiphenylurea-bis(guanylhydrazone) (NCS 109555) [a], dithiourea analogues [b] and diamine derivatives [c].*

References

[1] Lu, J. J.; Pan, W.; Hu, Y. J.; Wang, Y. T. *Plos One* **2012**, 7, e40262.