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Structural design of triterpenic acid 1,2,4-triazole linked gold nanoparticle bioconjugates, as potential treatment for malignant melanoma.

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Pentacyclic triterpenes are natural occurring compounds with well described pharmacotherapeutic potential but have some pharmacodynamic drawbacks such as low bioavailability [1]. To address this inconvenience, previous studies have attempted various formulations in order to increase their bioavailability and antitumor activity [2,3]. The current study proposes the structural design of a series of new gold nanoparticle (GNP) based bioconjugates in which each component can exert a synergic antiproliferative effect.

In our current work, based on their antiproliferative activity against malignant melanoma, ursolic acid, oleanolic acid and betulinic acid were chosen to be formulated as GNP bioconjugates. In order to bind to the GNP surface, the use of linker molecules is required. For the conceptualization of chemically suitable linkers that are also potentially active in melanoma, we choose the 3-mercapto-4-amino-1,2,4-triazole ring as a starting point template. In this regard, a virtual compound library was constructed (3-mercapto-4-amino-5-R-1,2,4-triazole derivatives) for the purpose of obtaining a selection of potentially active molecules, using molecular docking based virtual screening. The target proteins chosen are key nodes in melanoma active signalling pathways. The 3D structures of the targets were obtained from the RCSB database: EGFR (1XKK), MEK1 (3EQG), AKT1 (4GV1), mTOR (4JT5) and PI3K α (6GVF). After docking the compound library in the mentioned targets, using PyRx, based on the obtained docking scores and binding site pose analysis, five compounds were retained as possible candidates with theoretical antiproliferative potential: 4-amino-5-(4-ethoxyphenyl)-1,2,4-triazole-3-thiol, 2-(4-amino-5-sulfanyl-1,2,4-triazol-3-yl)phenol, 4-amino-5-(4-nitrophenyl)-1,2,4-triazole-3-thiol, 4-amino-5-(2-naphthyl)-1,2,4-triazole-3-thiol, 4-amino-5-(4-quinolyl)-1,2,4-triazole-3-thiol. These molecules will be used as linkers in the synthesis of future pentacyclic triterpene-GNP bioconjugates.

References

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