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# *In silico* modeling and *in vitro* studies in search for new anticancer agents among anthra[1,2-*d*][1,2,3]triazine-4,7,12(3*H*)-triones

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**Background and aim.** 9,10-Anthraquinone derivatives are considered as anticancer agents due to their structural versatility and ability to target multiple pathways involved in the cancer cell survival and proliferation. The aim of our work was to identify novel anticancer compounds among anthra[1,2-*d*][1,2,3]triazine-4,7,12(3*H*)-triones 22–38 obtained by us earlier [1] using *in silico* methods and experimental *in vitro* study. **Methods.** *In silico* prediction of anticancer activity and $GI_{50}$ values was carried out using *pdCSM-cancer* platform [2]. Experimental *in vitro* study against NCI-60 human cancer cell lines was conducted in The National Cancer Institute (USA) within the Developmental Therapeutics Program by the SRB method. Molecular docking was performed using the software package *Schrödinger Suite* [3]. **Results.** The results of anticancer bioactivity prediction of anthratriazinones 22–38 against 9 tumor types showed a probable action against mainly breast cancer (*MDA-MB-468, MCF-7*), leukemia (*CCRF-CEM*, *HL-60TB, P388-ADR, P388, SR*), melanoma (*MDA-MB-435, MALME-3M*), prostate (*PC-3*), non-small cell lung (*NCI-H522, A-549*), ovarian (*NCI-ADR-RES*) and renal (*SN12K1*) cancer cell lines. The predicted $GI_{50}$% values for the listed cell lines were in the range of 5.025–5.826 −log10(molar). Three compounds 22, 23 and 31 among the investigated 22–38, showed good results *in vitro*. For derivative 22, a cytostatic effect was found against the *EKVX* non-small cell lung cancer and *UO-31* renal cancer cell lines. Anthratriazinone 31 showed selective activity against *MOLT-4* leukemia and *OVCAR-4* ovarian cancer cell lines. Compound 23 showed the broad spectrum of selective cytotoxicity against the following cell lines: *HL-60(TB)* leukemia, *SF-539* CNS cancer, *MALME-3M*, *MDA-MB-435*, *SK-MEL-5* melanoma and *MCF7* breast cancer, *MDA-MB-468*. Anthratriazinone 23 was tested at five concentrations against 60 cancer cell lines. It was established that compound 23 is the most promising for further in-depth studies on melanoma cell lines *MALME-3M, MDA-MB-435, SK-MEL-5* (inhibition level of –97 — 100%). Molecular docking showed a high affinity to serine threonine protein kinase MEK-1 as a possible mechanism of antitumor action of 23 to melanoma-related target protein. **Conclusions.** The results of the *pdCSM-cancer* prediction for anthra[1,2-*d*][1,2,3]triazine-4,7,12(3*H*)-triones derivatives were confirmed in the experiments. A promising anthratriazinone derivative was proposed for in-depth studies against melanoma as a potential MEK-1 inhibitor.

**Keywords:** anthra[1,2-*d*][1,2,3]triazine-4,7,12(3*H*)-triones, *in silico* study, anticancer agents, melanoma, molecular docking.

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