THE EFFECT OF NOVEL SULFONAMIDE DERIVATIVES ON HUMAN PROSTATE AND TRIPLE-NEGATIVE BREAST CANCER CELL LINE VIABILITY UNDER NORMOXIA AND HYPOXIA

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Prostate cancer makes up 13,5% of diagnosed cancer wordwide, marking it as the fourth most widespread and the second most commonly diagnosed cancer in men [1]. Triple-negative breast cancer accounts for 10–15% of all new breast cancer cases, as it is an aggressive subtype with unfavorable prognosis [2]. Sulfonamide derivatives are potential anticancer agents with the ability to inhibit carbonic anhydrase IX, that are more expressed in cancer cells[3]. Research for new effective substances creates progress in the treatment of cancer. Our research aimed to evaluate the anticancer activity of sulfonamide derivatives synthesized at Kaunas University of Technology (Lithuania) on human prostate and triple-negative breast cancer cell line viability.

In our study, we investigated the activity of 23 sulfonamide derivatives bearing substituted aromatic and different heterocyclic moieties on prostate cancer cell line PC3 and triple-negative breast cancer cell line MDA-MB231. The effect on cell viability was determined by the MTT assay at 20 μM of compounds after 72 hours of incubation. The comparative compounds with significant cell viability-reducing capabilities were chosen for further studies, and the EC50 values were established.

Compounds 1, 4a, 4b, 4c, 7a, 7b and 12 reduced the viability of all cell lines by up to appr. 20-25%. These compounds were selected for the determination of EC50 values. The greatest difference in normoxia and hypoxia conditions were to MDA-MB231 cell line, as in hypoxia, viability was reduced by up to appr 70-90%. Compounds 1 and 4c are selective to the MDA-MB231 cell line, but compound 1 was more active under normoxia, while 4c was more active under hypoxia. Also, compounds 4b, 7a and 7b are only selective to MDA-MB231 cell line in hypoxia, although 7b had similar EC50 values in normoxia for both cell lines. Compounds 4a and 12 are more selective to the PC3 cell line in normoxia, but under hypoxia they become selective to the MDA-MB231 cell line.

In conclusion, compounds 1, 4a, 4b, 4c, 7a, 7b and 12 showed a significant reduction of cell viability by MTT assay. Compound 1, 7a and 7b are more effective in normoxia, while 4a, 4b, 4c and 12 reduce the viability higher in hypoxia. Especially effective in hypoxia are compounds 4a and 12 in the MDA-MB231 cell line.

[1] M. N. E. Almeeri, M. Awies, and C. Constantinou, “Prostate Cancer, Pathophysiology and Recent Developments in Management: A Narrative review,” Current Oncology Reports, vol. 26, no. 11, pp. 1511–1519, Oct. 2024, doi: 10.1007/s11912-024-01614-6.
[2] A. M. Karim et al., “Triple-negative breast cancer: epidemiology, molecular mechanisms, and modern vaccine-based treatment strategies,” Biochemical Pharmacology, vol. 212, p. 115545, Apr. 2023, doi: 10.1016/j.bcp.2023.115545.
[3] Y. Wan, G. Fang, H. Chen, X. Deng, and Z. Tang, “Sulfonamide derivatives as potential anti-cancer agents and their SARs elucidation,” European Journal of Medicinal Chemistry, vol. 226, p. 113837, Sep. 2021, doi: 10.1016/j.ejmech.2021.113837.