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Violacein enhances the cytotoxic effect of commonly used chemotherapeutics on rhabdomyosarcoma cells

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Background: Investigation of natural compounds showing specific toxicity to tumor cells aims to improve the efficacy of available therapies. Our previous research demonstrated the cytotoxic activity of the bacterial pigment violacein against rhabdomyosarcoma (RMS) cell lines. RMS is the most common soft tissue malignancy in children. In this study, we evaluated the cytotoxicity of violacein on RMS cells in combination with conventional chemotherapeutics doxorubicin, irinotecan, and vinflunine. **Material and Methods:** Toxicity of doxorubicin, irinotecan, and vinflunine was assessed on three cell lines representing different RMS subtypes (SJRH30, RD, and HS-729). IC25 concentrations for each of them, causing a 25% reduction in cell viability, were calculated using the results of MTT viability tests. Cells were then treated with the IC25 concentrations of doxorubicin, irinotecan, or vinflunine in combination with violacein at its IC25 concentration. The effects of the combined treatments were evaluated by MTT assays. The coefficients of drug interaction were calculated using Foucquier and Guedj method, indicating synergy, additivity, or antagonism. **Results:** Sensitivity to chemotherapeutic agents varied among RMS cell lines. The SJRH30 was most sensitive to irinotecan and vinflunine but most resistant to doxorubicin. RD was most sensitive to doxorubicin but highly resistant to vinflunine. HS-729 exhibited the highest resistance to irinotecan. When violacein was combined with doxorubicin, irinotecan, or vinflunine, we observed either additive or synergistic effects, depending on the cell line. The combination of violacein and doxorubicin showed the highest degree of synergy, particularly in RD cells. **Conclusions:** Combining violacein with commonly used chemotherapeutic agents has the potential to enhance RMS treatment efficacy. The next steps would be to understand underlying mechanisms and evaluate safety and effectiveness in preclinical and clinical settings.
Keywords: antineoplastic agents, cytotoxicity, doxorubicin, rhabdomyosarcoma, violacein

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Anticancer effects of non-toxic repurposed drugs on hamster fibrosarcoma – fast applicable in oncology

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Background: Some drugs developed for other illnesses might be repurposed for cancer treatment, to kill cancer cells by hitting previously recognized or unrecognized molecular target or unknown target. This study investigated such drugs, with proven *in vitro* anticancer effects, *in vivo* on fibrosarcoma in hamsters. **Material and Methods:** Anticancer efficacy of selected repurposed drugs: mebendazole, metformin, diclofenac, 2-Deoxy-D-glucose, deoxycholic acid, caffeine, itraconazole, nitroglycerin, disulfiram and selected two-component combinations were tested on fibrosarcoma experimentally induced by BHK21/C13 cells in Syrian golden hamsters. Tumor biophysical characteristics, histology and immunohistochemistry were assessed. Blood samples were collected for hematological and biochemical analyses and the main organs were toxicologically analyzed. **Results:** This study showed that two-drug combinations: metformin with 2-Deoxy-D-glucose, metformin with deoxycholic acid, metformin with caffeine, metformin with itraconazole, metformin with nitroglycerin and metformin with disulfiram can significantly ($P < 0.05$) suppress fibrosarcoma in hamsters with doses equivalent to achievable oncological human doses, without toxicity and influence on biochemical and hematological tests. **Conclusion:** All efficacious repurposed drug combinations recorded in our study on hamster