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## Metformin synergized anticancer effect of other repurposed drugs in hamster fibrosarcoma

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The tumor growth rate positively correlates with glucose levels. The Warburg effect promotes the glucose uptake of cancer cells. The cancer glucose starvation is an effective way for suppressing tumor growth. Reduction of blood glucose can inhibit the proliferation of cancer cells. In addition, the combination of glucose inhibitors could be a promising direction for cancer therapy. Anticancer efficacy of the glucose lowering antidiabetic drug, metformin, in combination with 2-deoxy-*D*-glucose, deoxycholic acid, caffeine, itraconazole, nitroglycerin and disulfiram was 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. The Combination Index (CI) analysis was used to determine synergistic (CI < 1), additive (CI = 1) or antagonistic (CI > 1) metformin interaction with other investigated drugs. Two-drug combinations with metformin showed significant synergistic (CI < 1) antitumor effects on hamster fibrosarcoma compared to control, regarding all tested tumor parameters (P < 0.05) without toxicity. Combinations of metformin with other repurposed drugs might be an effective and safe approach in novel nontoxic adjuvant anticancer treatment.

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