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## Diclofenac with metformin can slow hamster fibrosarcoma development

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Diclofenac and metformin separately exhibit limited anticancer potential. We examined whether combining these two drugs in doses equivalent to human doses would synergize their anticancer activity on fibrosarcoma inoculated to hamsters. BHK-21/C13 cell culture was subcutaneously inoculated to Syrian golden hamsters of both sexes (~ 70 g), which were randomly allocated to control and experimental groups (6 animals per group). The hamsters were treated in control group 1 with physiological saline, in group 2 with diclofenac 120 mg/kg, in group 3 with metformin 1000 mg/kg, in group 4 with combination of diclofenac 60 mg/kg and metformin 500 mg/kg, via a gastric probe daily after cancer cell inoculation. The animals were sacrificed 18 days post tumor cells inoculation. Tumor growth kinetics, biophysical, pathological, histological and immunohistochemical characteristics of excised tumors and hamster organs and biochemical blood and hematological tests were compared among the groups. Only the co-treatment with diclofenac and metformin simultaneously significantly ( $P < 0.05$ ) inhibited tumor growth. The pathohistological and immunohistochemical evaluation confirmed these biophysical findings. Neither single diclofenac, nor single metformin treatments, regardless of doubling doses used in the combined treatment, exhibited significant anticancer effect in comparison to control. Metformin exhibited significant synergistic inhibitory effect with diclofenac on all parameters of tumor growth, without toxicity and influence on biochemical blood and hematological tests.

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