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ANTIOXIDANT TS-13 as a MODULATOR of the ACTION of ANTITUMOR CYTOSTATICS in MICE WITH P388 LYMPHOYTIC LEUKAEMIA

Currently, there is an active search for substances that can reduce the toxicity and enhance the effectiveness of the chemotherapeutic action of antitumor drugs. These substances include antioxidants that affect the course of redox reactions in cells. Special attention is also paid to the study of nitric oxide donors as potential modifiers of the action of antitumor cytostatics.

The aim of the work was to further study the interaction of the sulfur-containing phenolic antioxidant TS-13 with the antitumor cytostatics-adriamycin (ADR) and cisplatin (CPT) in combination with the nitric oxide donor NaNO2.

The work was performed at the Institute of problems of chemical physics of the Russian Academy of Sciences. Antitumor activity was studied in mice of the BDF1 hybrid line, which were transplanted with p388 lymphocytic leukemia cells, after which the animals were divided into groups. Each group received drugs in different combinations and dosages. The criterion for the effectiveness of treatment was an increase in average life expectancy and the index of increase in average life expectancy.

Table 1. Effect of TS-13 antioxidant and its combination with cytostatics adriamycin (ADR), cisplatin (cPt) and nitric oxide donor NaNO2 on the life span of mice with lymphocytic leukemia P388

Drug	Dose, mg / kg	The mode of administration, day	Number of animals in the experience	The number of animals that survived by 60 days.	ALE, day	ILS, %
control			6	0	10,2	0
TS-13	30	1-7	6	0	10,0	0
ADR	1,0	1, 6	6	0	22,8*	124,0
ADR+TS-13	1,0+30	1,6+1-7	6	0	22,2*	118,0
ADR+$NaNO_2$	1,0+40	1,6+1-7	6	0	19,2*^	90,2
ADR+ TS-13+$NaNO_2$	1,0+ 30+40	1,6+ 1-7+1-7	6	1	20*^	100
cPt	0,6	1-7	6	0	31,2*	206,0
cPt+TS-13	0,6+30	1-7+1-7	6	0	49,7*^	387,0
cPt+$NaNO_2$	0,6+40	1-7+1-7	6	3	36,5*^	265
cPt+ TS-13+$NaNO_2$	0,6+ 30+40	1-7+ 1-7+1-7	6	3	39,8*^	298

According to the data obtained, the antioxidant TS-13 in the studied doses, with monotherapy, does not show antileukemic activity.

Adriamycin (ADR) with monotherapy in a dose has an antitumor effect, because the average life expectancy of mice increases by about 2 times, compared to the control. Combined administration of adriamycin (ADR) with the antioxidant TS-13 increases the toxic effect of adriamycin. The life span of animals is decreasing.

Fig. 1-2. Average life expectancy and the index of increasing the average life expectancy of mice with monotherapy with cytostatics adriamycin (ADR) and its combination with the antioxidant TS-13 and the nitric oxide donor NaNO2

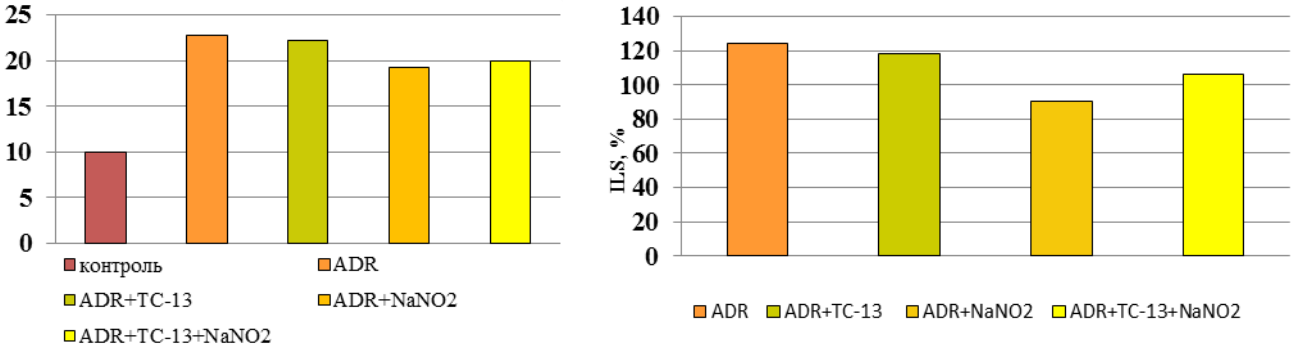
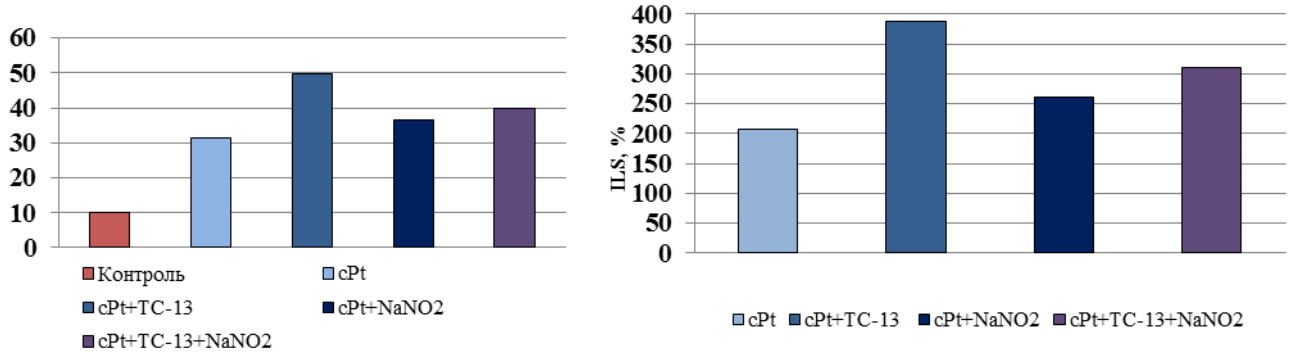


Fig. 3-4.Average life expectancy and index of increase in average life expectancy of mice with cytostatic cisplatin (cPt) monotherapy and its combination with the TS-13 antioxidant and the nitric oxide donor NaNO2



Combinations of cPt with the studied doses of TS-13 increased the life expectancy of animals compared to CPT monotherapy. Thus, the TS-13 antioxidant increases the antitumor activity of this cytostatic and reduces its toxicity.

The combination of ADR with TC-13 and NaNO2 increased the toxicity of ADR by 12%. The use of a dual chemosensitizer with a CPT cytostatic increased its cytoprotective function by 28%.

Conclusions

1. Thus, it was revealed that the antioxidant TS-13 with the cytostatic drug cisplatin enhances its activity, reducing toxicity.

2. In combination with the cytostatic adriamycin, TS-13 increased its toxicity, reducing the lifespan of mice. Apparently, in combination with adriamycin, TS-13 manifests itself as a prooxidant.

The work was carried out under the supervision of candidate of biology, senior researcher T. N. Bogatyrenko (IPCP RAS), candidate of biology, docent M. O. Barinova (IvSU).