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ОТДЕЛ КАНЦЕРОГЕНЕЗА И ОНКОГЕРОНТОЛОГИИ

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Influence of Potassium Osmate preparation on the growth of transplantable Ehrlich tumor in mice

(report)

1. Introduction

The present study is devoted to studying the effect of platinum drugs on the growth of transplanted solid Ehrlich tumor and the survival of mice after intraperitoneal injection of the drug. Strain of Ehrlich's tumor for many years used for preliminary screening of compounds with potential anticancer activity (Experimental evaluation of anticancer drugs in the USSR and the USA. Ed. ZP Sofin, AB Syrkin (USSR), A. Goldin, A. Klein (USA). M. Medicine, 1979, 296 pp.) intraperitoneal method of administration was selected for the experiment due to the fact that he is the most effective method of delivering the drug to the target (tumor cells) at the lowest required amount of compound administered.

2. Materials and methods

2.1 Drugs

Were used the following substances:

- water for injection (control, Ellar, Russia),
- Cisplatin (Ebewe, Austria),
- platinum compound (provided by customer).

2.2 Animals

The study used male mice outbred lines SHR own wiring Cancer Research Institute.

The animals were kept in plastic cages with steel bars such as T2, and received water and food briquetted full-PC-120 (produced by "Laboratorkorm", Moscow) ad libitum.

2.3 Strain of tumor

We used a strain of transplantable Ehrlich tumor in mice. Strain is maintained in the form of FDI and Oncology ascites carcinoma, which represents a suspension of tumor cells transplanted intraperitoneally. To obtain a solid tumor this suspension was injected into mice subcutaneously.

2.4 Experimental Procedure

tumor transplanted subcutaneously into the right side in the amount of 0,2 ml of 10% suspension of cells used for the maintenance of the strain of Ehrlich ascites carcinoma (107 cells / mouse).

Platinum compound and water for injection (control group) were administered starting 48 h after inoculation tumors in different modes intraperitoneally.

regularly measured the length and width of the tumor nodules. Tumor volume was calculated by the formula:

$$V = (a * b^2)/2,$$

where **a** - bigger and **b** - a smaller linear size of the tumor site.

The effectiveness of treatment was evaluated by inhibition of tumor growth. Percentage growth inhibition was calculated by the formula:

$$(V_k-V_o)/V_k*100\%,$$

where V_k - the average tumor volume in the control group, and V_o - average volume of tumors in the experimental group.

Recorded the timing of animal deaths to assess the survival and calculate the average life expectancy of mice after tumor transplantation. As a criterion for the effectiveness of therapy used increased life span of animals (percentage), which is defined by the formula:

$$U =(L_o/L_k - 1)*100\%,$$

where **U** - the increase in life expectancy in%,
L_o - life expectancy in the experimental group,
L_k - the average life expectancy in the control group

In the experience had been taken following groups of animals (Table 1):

Table 1

Groups of animals in the experiment

group	essence	number of mice
1, control	water for injection, 0.25 ml/mouse once intraperitoneally with	12
2, cisplatin	cisplatin, 125 mg/mouse at 0 25 ml/mouse intraperitoneally once	8
3, the preparation of platinum	platinum compound, 250 mg/mouse in 0.25 ml/mouse once intraperitoneally	10
4, the preparation of platinum	platinum compound, 500 mg/mouse in 0.25 ml/mouse once intraperitoneally	9
5, the preparation of platinum	platinum compound, 250 mg/mouse in 0.25 ml/mouse 3 times a week, 12 times intraperitoneally with	10
6, the preparation of platinum	platinum compound, 500 mg/mouse in 0.25 ml/mouse 3 times a week 12 times intraperitoneally	10

2.5 Statistical analysis of results

The results obtained in the experiments were subjected to statistical analysis to establish the reliability of the differences found. Differences were considered significant at $p < 0.05$.
Results and discussion

3. Animals tolerated the introduction of platinum compound.

The results of studies of the effect of the drug on the growth of Ehrlich solid tumor are presented in Table. 2.

Table 2:

Effect of platinum compound build-up of Ehrlich tumor.

Group number 1

control - water for injection

daily after transplantation	2	14	17	21	24	28	31	36	41	45	49	52
quantity of animals	12	12	12	12	10	10	9	6	5	4	4	3
average tumor volume value, mm^3	0	1277	2723	4475	5284	6696	6899	9483	11374	10762	14952	12581
error of mean		299	582	831	1087	1422	1278	2707	2844	3448	4936	4216

Group number 2
cisplatin intraperitoneally once

daily after transplantation	2	14	17	21	24	28	31	36	41	45	49	52
quantity of animals	8	8	8	8	8	8	7	5	2	1	1	0
average tumor volume value, mm^3	0	641	1381	2364	3848	6592	6270	9501	5301	4063	7149	
error of mean		205	437	703	967	1728	1530	2807	2651	4062	7148	
p		0,01	0,08	0,07	0,34	0,96	0,76	0,10	0,17	0,31	0,46	
inhibition of tumor growth		50%	49%	47%	27%	2%	9%	0%	53%	62%	52%	

Party number three
platinum compound 250 mcg / mouse once

daily after transplantation	2	14	17	21	24	28	31	36	41	45	49	52
quantity of animals	10	10	10	10	8	7	5	2	0	0	0	0
average tumor volume value, mm^3	0	1200	5658	6392	6402	7896	6387	6310				
error of mean		294	2399	2441	1760	1900	1645	3178				
p		0,86	0,26	0,47	0,60	0,62	0,81	0,48				
inhibition of tumor growth		6%	-108	-43%	-21%	-18%	7%	33%				

Party № 4
platinum compound 500 mcg / mouse once

daily after transplantation	2	14	17	21	24	28	31	36	41	45	49	52
quantity of animals	9	9	9	9	9	8	7	7	7	7	6	5
average tumor volume value, mm^3	0	521	1200	2416	3527	2916	1969	3336	6345	8057	8036	9191
error of mean		197	435	1018	1518	1343	849	1282	2486	2980	3116	4135
p		0,05	0,05	0,13	0,36	0,07	0,01	0,07	0,21	0,57	0,27	0,58
inhibition of tumor growth		59%	56%	46%	33%	56%	71%	65%	44%	25%	46%	27%

Group number 5
platinum compound 250 mcg / mouse 12-fold

daily after transplantation	2	14	17	21	24	28	31	36	41	45	49	52
quantity of animals	10	10	10	10	10	8	8	5	2	1	1	1
average tumor volume value, mm^3	0	846	1729	2710	3305	4990	6131	5950	5627	32	32	0
error of mean		335	491	708	820	1143	1415	2142	5595	31	31	
p		0,35	0,21	0,12	0,16	0,36	0,69	0,33	0,43	0,04	0,04	0,06
inhibition of tumor growth		34%	36%	39%	37%	25%	11%	37%	51%	100%	100%	100%

Group № 6
platinum compound 500 mcg / mouse 12-fold

daily after	2	14	17	21	24	28	31	36	41	45	49	52

transplantation												
quantity of animals	10	10	8	8	8	8	8	7	5	3	3	3
average tumor volume value, mm^3	0	375	605	905	1428	2949	3319	4499	6317	2888	6737	6680
error of mean		137	181	247	385	822	997	1430	2639	1218	2690	2954
p		0,01	0,001	0,001	0,01	0,04	0,04	0,14	0,22	0,08	0,19	0,30
inhibition of tumor growth		71%	78%	80%	73%	56%	52%	53%	44%	73%	55%	47%

It should be noted that Table 2 shows the tumor volume only up to 52 days after inoculation. This is because in the later stages of the experiment due to tumor growth all the mice in the control (group 1) had fallen.

The above data suggest that a single intraperitoneal injection of platinum compound at a dose of 250 micrograms / mouse had no effect on tumor growth.

A single intraperitoneal infusion of platinum in a dose of 500 micrograms / mouse several inhibits tumor growth, although not in all terms of this inhibition was statistically significant. At the same time in this group, one mouse tumor did not catch on, while the second - resorbed before reaching a substantial amount. 12-fold intraperitoneal infusion of platinum at a dose of 250 micrograms / mouse somewhat inhibited tumor growth, although not statistically significant. One mouse in the group, however, the tumor resorbed before reaching a substantial amount, but a week later began to grow again. It should be noted that the spontaneous resorption of transplanted tumors are sometimes observed without the influence of drugs under the influence of transplantation immunity.

12-fold intraperitoneal infusion of platinum in a dose of 500 mcg / mouse significantly inhibited the growth of tumors from 14 th to 31 th day after inoculation. Maximum inhibition of tumor growth was 80%, indicating a fairly high antitumor efficacy of platinum in this mode of administration.

For a more complete and objective analysis of the antitumor effect of it is expedient to study its effect on the growth of spontaneous and induced tumors in animals.

The results of studies of the effect of the preparation of platinum on the average life span of mice with Ehrlich's tumor are presented in Table. 3.

Table 3

Effect of the preparation of platinum on the lifespan of mice with solid Ehrlich tumor.

# of group	substances and methods of introducing	life expectancy of animals after tumor transplantation, the days of
1	**control - water for injection, intraperitoneal**	40,2 ± 3,46
2	**cisplatin, 125 mcg / mouse once**	36,4 ± 4,28
3	**platinum compound, 250 mcg / mouse once**	32,6 ± 2,15
4	**platinum compound, 500 mcg / mouse once**	47,0 ± 4,75
5	**platinum compound, 250 mcg / mouse 12 -fold**	36,7 ± 2,61
6	**platinum compound, 500 mcg / mouse 12-fold**	42.0 ± 5.07

Note: in groups 2 and 4 animals in which the tumor has not grown are not included

Thus, a statistically significant increase in life expectancy was not observed in any group of animals.

4. Conclusions

Thus, a 12-fold intraperitoneal infusion of platinum in a dose of 500 mcg / mouse 3 times a week, 12 times as much, and significantly inhibits the growth of solid Ehrlich carcinoma of mice at different times, but has no effect on life expectancy of animals after tumor transplantation.

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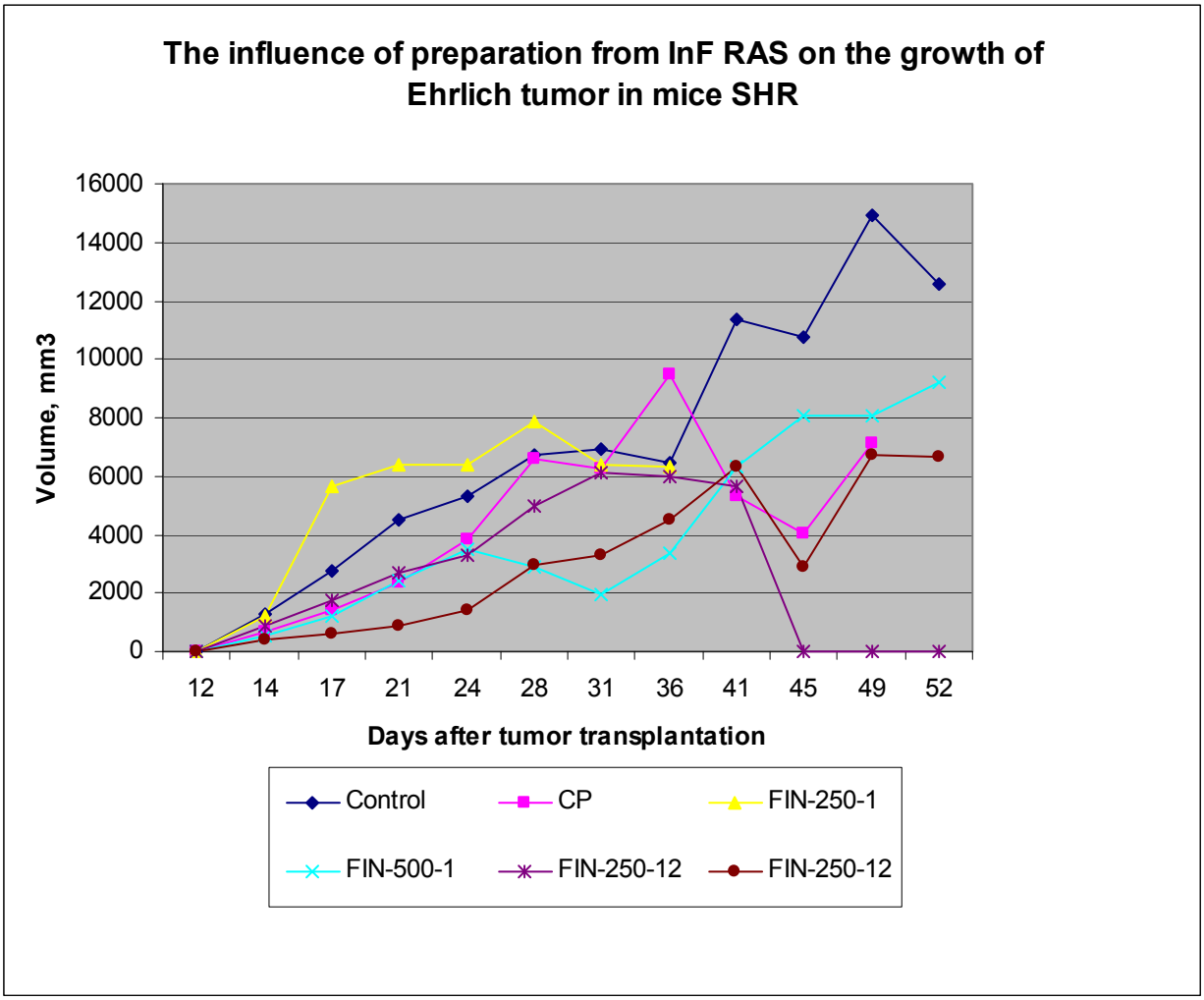
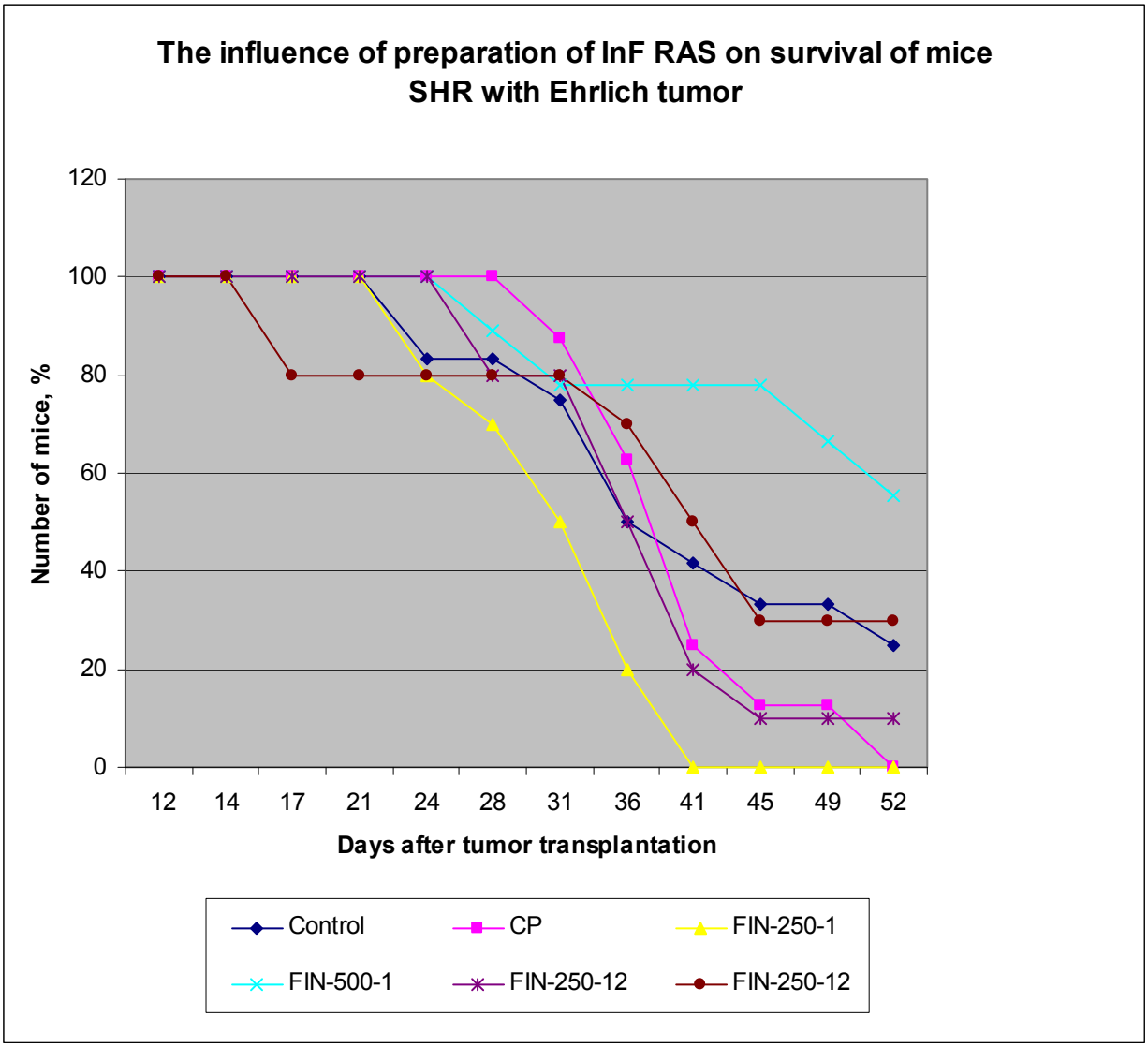
Anisimov V.N.


The influence of preparation from InF RAS on the growth of Ehrlich tumor in mice SHR
Volume, mm3
16000
14000
12000
10000
8000
6000
4000
2000
0
12
14
17
21
24
28
31
36
41
45
49
52
Days after tumor transplantation
Control
CP
FIN-250-1
FIN-500-1
FIN-250-12
FIN-250-12


The influence of preparation of InF RAS on survival of mice SHR with Ehrlich tumor
Number of mice, %
120
100
80
60
40
20
0
12
14
17
21
24
28
31
36
41
45
49
52
Days after tumor transplantation
Control
CP
FIN-250-1
FIN-500-1
FIN-250-12
FIN-250-12