

Fig. 1. Feinbereichsbeugungsdiagramm von einem aus der Nebenkronen der Narzisse isolierten Karotinekriställchen. Siemens Elmiskop I, 60 kV.

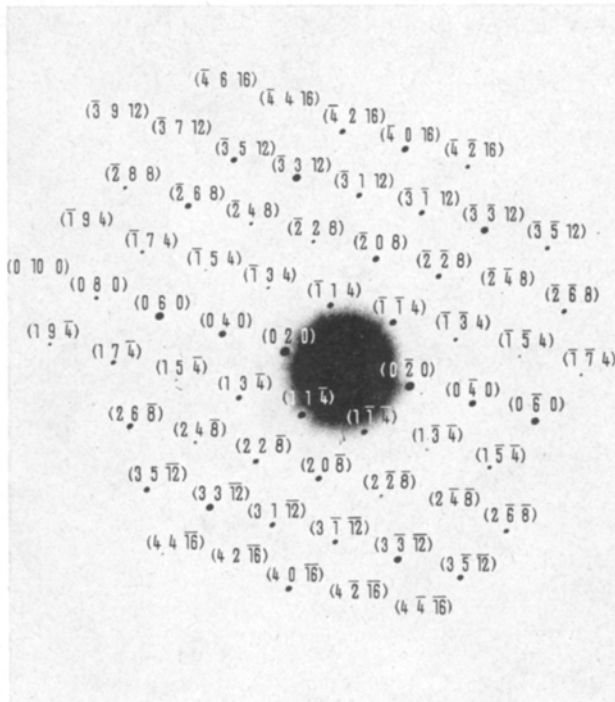


Fig. 2. Indizierung des Feinbereichsbeugungsdiagramms von Figur 1.

beruhen, dass die Bestimmungen nicht mit einem speziellen Diffraktographen ausgeführt wurden, sondern mit dem für allgemeine elektronenmikroskopische Arbeiten ausgerüsteten Elmiskop I. Die gemessenen Winkelwerte stimmen gut mit den berechneten überein (Tabelle III).

Diese Resultate beweisen, dass sich die nativen Kriställchen in der Nebenkronen der Narzisse im strukturellen Aufbau von den synthetischen  $\beta$ -Karotinkriställchen nicht unterscheiden und dass keine hexagonale Struktur<sup>7,8</sup> vorliegt.

**Summary.** Crystals of carotene in plant cells (carrot root, corona of *Narcissus* etc.) have been attributed to the orthorhombic<sup>1,2</sup> or the hexagonal<sup>7,8</sup> system. However, an optical investigation<sup>3</sup> showed that they have a lower symmetry. In the case of the crystals in the corona

of *Narcissus*, the structural identity with synthetic  $\beta$ -carotene<sup>4-6</sup> is proved by X-ray and electron diffraction analysis. Although the geometry of the electron diffraction patterns is almost indistinguishable from hexagonal, its reflections can be identified with those from the planes of the monoclinic lattice of  $\beta$ -carotene. The face of the plate-shaped crystals corresponds to (102).

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## Magnesium Pemoline and Ehrlich Tumor: Tumor Animal versus Tumor Cell Survivals

In an earlier report, the results of a pilot study dealing with the effect of Magnesium Pemoline on the survival of mice with Ehrlich tumor was presented<sup>1</sup>. The drug not only slows down the mortality rate, but also enhances the life span of the tumor animals. Subsequent cytological studies on the tumor taken from the injected mice showed a marked alteration of the growth pattern and morphology of the tumor cells with or without the additional effect of X-irradiation<sup>2</sup>. In this paper we are comparing the survival rates between the animal population and the cell population.

**Methods.** As usual, there were 3 runs in each experiment; each run involving 180 CF<sub>1</sub> male mice, 50–60 days old (20–22 g). The animals were divided randomly into 6 groups as indicated in the Table.

Magnesium Pemoline and whole-body X-irradiation were administered 72 h after tumor inoculation for 5 consecutive days. 6 cytological specimens were collected from all 6 groups every other day, starting from the first day after drug injection and X-ray exposure. 3 animals from each group were chosen randomly and used for the cytological specimens. Smears taken were then spread on a number of glass slides and fixed in ether alcohol mixture 50:50 before staining. As the basis for comparisons, tumor cells collected from control group (Group I)

<sup>1</sup> H. LEVAN and D. L. HEBRON, *Experientia* 24, 830 (1968).

<sup>2</sup> H. LEVAN, P. BURLAKOW and D. L. HEBRON, *Oncologia*, in press (1969).

Groups	Magnesium pemoline treatments	X-Irradiation
Control (I)	Tragacanth only	Sham
Experimental (II)	0.7 mg/kg per day for 5 days	Sham
Experimental (III)	14 mg/kg per day for 5 days	Sham
Control (IV)	Tragacanth only	100 r/day for 5 days
Experimental (V)	0.7 mg/kg per day for 5 days	100 r/day for 5 days
Experimental (VI)	14 mg/kg per day for 5 days	100 r/day for 5 days

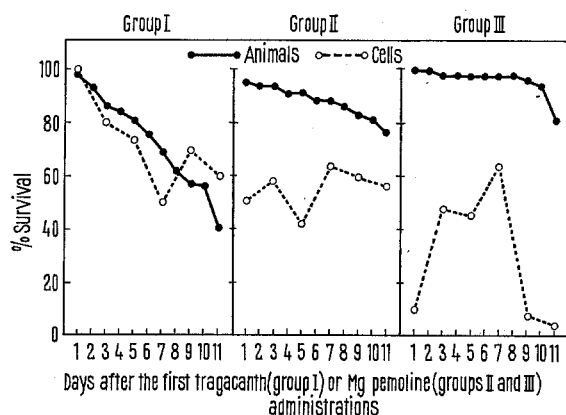


Fig. 1. Survival percentage of tumor bearing mice and Ehrlich tumor cells treated with Magnesium Pemoline.

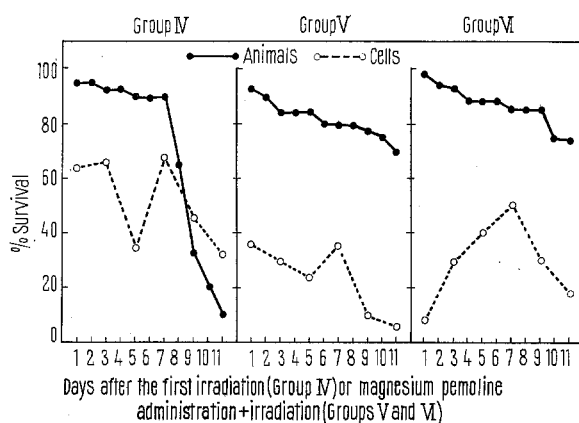


Fig. 2. Survival percentage of tumor bearing mice and Ehrlich tumor cells treated with Magnesium Pemoline and irradiation.

3 days after tumor inoculation were used. All other experimental techniques were previously described<sup>1,2</sup>.

**Results.** From Figure 1, one observes that the survival curves for both tumor cells and animals in group I are very consistent. 11 days after tragacanth administration and sham-irradiation (14 days after tumor transplantation) the animal population in this group dropped from 100% to 40% while the cell population decreased to only 60%. After this same period of time, the percents of animal survival in group II (0.7 mg/kg Mg Pemoline) and group III (14 mg/kg Mg Pemoline) were both about 80%. The survival patterns of the tumor cells in these 2 groups, however, were quite different. The percent variation of group II was quite stable around 55% while that of group III varied between 5% and 75%. Here one can see obviously the effect of the drug on the tumor cells.

In Figure II, the additional effect of X-irradiation is shown. Group IV treated only with X-ray without drug exhibited typical reaction of tumor cells to radiation. The animals in this group were no doubt under dual stress of both tumor expansion and irradiation. Only 10% of the mice survived 11 days after tumor transplantation. The average tumor cell survival was about 50% and thus was comparable with the percentage of cell survival in group II treated with the low dose of Magnesium Pemoline. There was no significant difference in the percent survival of animals in both group V (treated with 0.7 mg/kg of Mg Pemoline + radiation), and group VI (treated with 14 mg/kg of Mg Pemoline + radiation). Although the average tumor cell survival percentages of these 2 groups were not very far apart (about 5% difference), the pattern of their reaction to the combination of irradiation and Mg Pemoline seemed to vary with the drug doses employed.

**Discussions.** Comparing the percent survival between the animals and the tumor cells in all 4 experimental groups (II, III, V, VI), one notes no significant difference in the animal mortality of these groups. The effect of Magnesium Pemoline on the survival of the tumor cells, however, is not the same when used alone or in combination with irradiation. In an earlier report<sup>3</sup> we observed radiation-like effect of Mg Pemoline on the morphology of Ehrlich tumor cells at low drug dose with the presence of giant cells. This is now confirmed by the almost identical average percent of cell survivals between group II and group IV (54% and 51% respectively). Better results were obtained, however, when either the drug was administered concurrently with irradiation at low dose or administered alone at high dose. At the drug dose of 14 mg/kg employed in this experiment, the presence of radiation did not enhance significantly the survival rate of the animals or kill the tumor cells any faster. Again, further studies on various types of tumors are necessary before one could tell whether Magnesium Pemoline is really useful in cancer therapy. If so, this property, along with the radioprotective effect of the drug reported earlier<sup>3-6</sup> would make Magnesium Pemoline a very valuable compound in both radiodiagnosis and therapy.

**Zusammenfassung.** Es wird der Überlebensprozentsatz von mit Magnesiumpemolin behandelten Tumorzellen und Tumormäusen nach und ohne Röntgenbestrahlung verglichen: Die Substanz erhöht die Überlebensrate der Tiere und verändert das Wachstumsbild der Tumorzellen. Magnesiumpemolin während der Bestrahlung in niedriger Dosis oder ohne Bestrahlung in hoher Dosis erzielt beste Werte.

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<sup>3</sup> H. LEVAN, *Experientia* 23, 1058 (1967).

<sup>4</sup> H. LEVAN, *Experientia* 24, 477 (1968).

<sup>5</sup> H. LEVAN and D. L. HEBRON, *J. pharm. Sci.* 57, 1033 (1968).

<sup>6</sup> H. LEVAN, *Int. J. clin. Pharm. Ther. Toxic.* 6, 514 (1968).