

phosphate contents within the individual mammalian orders (Ungulata, Carnivora, Rodentia). In red blood cells produced in the earlier (foetal) ontogenetic stage the specific differences are assumedly even less distinct.

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Zusammenfassung

Die bisherigen Angaben eines reichen organischen säurelöslichen Phosphatgehalts der Erythrozyten können für junge Tiere nicht verallgemeinert werden.

Bei zahlreichen Säugerarten zeigen die Erythrocyten der Neugeborenen infolge einer sehr niedrigen Konzentration von Phosphoglycerinsäure einen Gehalt an organischem, säurelöslichem Phosphat, der unter demjenigen des ausgewachsenen Tieres liegt.

Wir stellen weiterhin fest, dass die bedeutenden Spezies-Unterschiede der Adulttiere in frühen Ontogenesephasen kaum hervortreten.

The Anti-Tumour Activity of 6-Azaauracil Riboside

It has recently been found in this Laboratory¹, and also independently by HANDSCHUMACHER and WELCH², that 6-azauracil inhibits the growth of a number of microorganisms. In the case of *Escherichia coli*, the inhibitory effect has a competitive character and may be cancelled by the addition of uracil, cytosine and uridine³. 6-Azaauracil has a marked inhibitory effect on a number of experimental cancer tumours⁴. It has been observed that when *Escherichia coli* is cultivated in the presence of 6-azauracil, some 6-azauracil riboside is formed; the formation of small amounts of the riboside has also been detected with *Streptococcus fecalis*⁵. Preliminary experiments have revealed pronounced cancerostatic effects of 6-azauracil riboside⁶; a detailed examination has not hitherto been possible due to lack of material.

More recently we have devised a method for the production of 6-azauracil riboside by a fermentation procedure which has made possible experiments *in vivo*⁷.

We first examined the effect of 6-azauracil riboside on Ehrlich's ascites tumours in subcutaneous form in white mice (strain H). Mice (weight 20 g) were subcutaneously inoculated with 0.2 ml of a diluted 8 days old ascites Ehrlich tumour (about 13×10^6 cells). Chemotherapy was

started on the fifth day following transplantation. The riboside was applied in physiological solution in 0.2 ml lots subcutaneously as far as possible from the tumour inocula. The daily dose of the drug given for 7 days amounted to 500, 250 and 50 mg pro 1 kg of weight of the test animal. 24 h after the last dose the tumours were taken out and weighed.

The results are given in the Table.

	Weight of tumor	P	Slowing down of growth of experimental tumour in %
Controls	348 ± 40.3		
500 mg azauracil riboside/kg	96.3 ± 11.5	< 0.01	72
Controls	559 ± 68.5		
250 mg azauracil riboside/kg	194.5 ± 21	< 0.01	65
50 mg azauracil riboside/kg	365.5 ± 52	0.037	35
* Controls	1169 ± 102		
500 mg azauracil/kg. . . .	890 ± 73	0.03	24

* The experiment with 6-azauracil is reported for comparison.

Our experiments show that in the 500 mg/kg dose 6-azauracil riboside is about 3 times more effective than 6-azauracil administered in the same concentration. When compared on a mole per mole basis, the riboside may be seen to be some 6 times more active than 6-azauracil itself. It should be noted, on the other hand, that 6-azauracil riboside has only a relatively weak inhibitory effect on the growth of *Escherichia coli*. It may be assumed that the mechanism of action of the two antimetabolites against tumour and microbial cells differs somewhat in character.

Dr. HÁVA and Mr. JANKŮ in the Pharmacological Laboratory of this Institute have found that the toxicity of 6-azauracil riboside, like that of 6-azauracil, is very low: a daily dose of 500 mg/kg, administered intraperitoneally for 8 days to white mice (strain H), had no adverse effects.

Clinical experiments with 6-azauracil riboside are now in progress.

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Zusammenfassung

Es wird die cancerostatische Wirkung des 6-Azaauracil-ribosids auf die subkutane Form des Ehrlich-Aszites-Tumors beschrieben und festgestellt, dass 6-Azaauracil-ribosid ungefähr 6mal wirksamer ist als 6-Azaauracil.

Die Hemmbarkeit der inhibitorischen Adrenalin- bzw. Noradrenalinwirkung durch Adrenolytika

Im Gegensatz zu den exzitatorischen Effekten des Adrenalins gelang die antagonistische Beeinflussung inhibitorischer Effekte durch Adrenolytika überzeugend nur am spontan arbeitenden Kaninchendarm. Für eine Gruppe dieser Substanzen, die β -Haloalkylamine, war der Nachweis eines Antagonismus bisher überhaupt nicht möglich.

¹ F. ŠORM and J. ŠKODA, Chem. listy 50, 827 (1956); Coll. Czechosl. chem. Comm. 21, 487 (1956).

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³ J. ŠKODA and F. ŠORM, Chem. listy 50, 1165 (1956); Coll. Czechosl. chem. Comm. 21, 1328 (1956).

⁴ F. ŠORM, A. JAKUBOVIČ, and L. SLECHTA, Exper. 12, 271 (1956). T. M. HAKALA, L. W. LAW, and A. D. WELCH, Proc. Amer. Ass. Cancer Res. 2, 113 (1956). – J. ŠABLÍK and F. ŠORM, Neoplasma 4, 113 (1957). – H. KEILOVÁ and F. ŠORM, Neoplasma 4, 204 (1957).

⁵ J. ŠKODA, V. F. HESS, and F. ŠORM, Exper. 13, 150 (1957); Chem. listy 51, 1195 (1957); Coll. Czechosl. chem. Comm. 22, 1330 (1957).

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⁷ J. ŠKODA and F. ŠORM, Biochim. biophys. Acta (in press).