ersichtlich, dass, im Gegensatz zu N-Lost, weder SP-G noch SP-I den Thymidineinbau hemmen. Bei SP-I ist sogar nach $2^1/_2$ h eine leichte, allerdings nicht signifikante Förderung erkennbar.

Von einem Teil der Kulturen wurden Ausstriche angefertigt und davon Autoradiogramme (Stripping-Film Kodak AR. 10) hergestellt. Die Auszählung der markierten Zellen und der Silberkörner nach Exposition ergab mit den Werten der Tabelle übereinstimmende Resultate.

Der Wirkungseintritt von SP-G und SP-I ist sehr rasch, schon 30–45 min nach Substanzzugabe sind keine späten Mitosephasen mehr auffindbar; in den hier erwähnten Versuchen wurde demnach der Thymidineinbau zu einem Zeitpunkt gemessen, da die volle Mitosehemmung längst eingetreten war. Da die Generationszeit der P-815-Zellen sehr kurz ist (unter günstigsten Bedingungen ca. 8 h[9], üblicherweise 10–14 h), ist nach etwas mehr als 6 h rund die Hälfte der Zellen in Mitose eingetreten. Dass der Thymidineinbau nach 6stündiger Einwirkung von SP-I nicht gehemmt ist, deutet darauf hin, dass auch bei in Mitose arretierten Zellen die DNS-Synthese weitergehen kann. Morphologische Beobachtungen über die Entstehung von Polyploidie bei P-815-Mastocytomzellen nach Einwirkung von Podophyllumstoffen[10] bestätigen diese Annahme. Es kann somit geschlossen werden, dass die Podophyllum-Cytostatica SP-G und SP-I den während der Interphase (Ruhezellen) stattfindenden Thymidineinbau nicht beeinträchtigen, sondern ihre Wirkung auf den Zellteilungsprozess als solchen beschränken. Längere Versuchszeiten wurden nicht gewählt, da sich dann infolge Absterbens von Zellen usw. nicht genau kontrollierbare Sekundäreffekte einstellen.

Summary. SP-G and SP-I, two podophyllum preparations with spindle poison activity, were tested for their effect on ^{3}H-thymidine incorporation into P-815 mastocytoma cells *in vitro*. Concentrations which inhibited cell multiplication completely did not affect DNA-synthesis as measured by thymidine incorporation.

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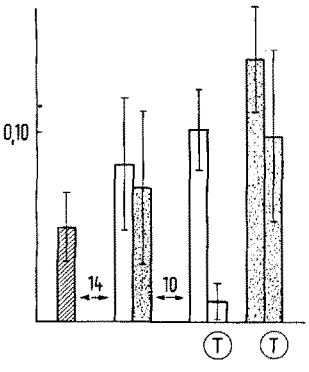
The Effect of Thyroxine on the Formation of Oxidation Products of Lipids by Rat Liver Tissue under Different Nutritional Conditions

The antioxidant effect of thyroxine has been described by Bunyan et al.[1] and Kaufman et al.[2]. It seemed of interest to establish whether the effect of thyroxine on the rate of formation of lipid oxidation products can be modified by the nutritional state. This might be biologically important, as both the formation of peroxides and nutrition are considered to be amongst the factors which influence the ageing of the organism[3].

Five-month-old rat males weighing 200–240 g were fed before the experiment on a diet of the following composition: 700 g bruised wheat, 100 g dry milk powder, 150 g casein, 30 g crushed alfalfa hay, 15 g $CaCO_3$, 50 g fat (100%), 7.5 g liver oil, 2.5 g NaCl and an amount of water sufficient to obtain a pasty consistence. Before the experimental period each rat was given 13 g of the dry diet of similar composition daily. Then the rats were divided into two groups. One group was fed *ad libitum* (they consumed, on an average, 10 g of the wet diet per 100 g body weight), the other group was fed 5 g of the wet diet per 100 g body weight. Fourteen days after the start of the controlled feeding, one part of the group of rats fed *ad libitum* and one part of those undernourished were injected subcutaneously daily for 10 days with 30 μg thyroxine per 100 g body weight injection solution Roche. The controls were injected with saline solution (0.03 ml per 100 g body weight) subcutaneously. The rats were given water *ad libitum*. Each subgroup included 6 rats. 24 h after the last injection the rats were killed by decapitation. The oxidation products of lipids were determined in the liver homogenates by means of 2-thiobarbituric acid (TBA) test, using a modified method of Placer and Slabochová[4]. After the removal of the liver, 1 g of the tissue was cut into small pieces, which were homogenized with 3 ml of ice-cold phosphate buffer pH 5.9 by means of a Potter-Elvehjem type homogenizer (15 strokes, rotation of the plunger 1500 revolutions per min) under simultaneous cooling. An aliquot (0.2 ml) of the homogenate was added to 5 ml of phosphate buffer, pH 5.9; immediately after, or after a 1 h incubation (37°C), the mixture was stirred and 2 ml of 10% trichloracetic acid were added; after 10 min the mixture was filtered,



Ordinate: extinctions. Hatched column: rast before the experiment. Solid columns: rats fed *ad libitum*. Open columns: undernourished rats. T: rats after the administration of thyroxine.

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4 ml of the filtrate were added to 2 ml of TBA solution[5], and heated in a boiling water bath; after refrigeration, the colour was measured using a Lange colorimeter (type IV) against H_2O with a green filter. The absorbencies given in the graph are the differences between the values of the samples without incubation (which varied between 0.000 and 0.028) and the samples after 1 h incubation at 37°C.

The following observations were made: (1) When compared with the situation at the beginning of the experimental period, an increase of the rate of formation of the TBA chromogens was noted in the animals fed *ad libitum* and those undernourished. (2) In the rats fed *ad libitum* which were given thyroxine, a statistically insignificant inhibition of the TBA chromogen formation occurs in comparison with the same control group without thyroxine. (3) In the undernourished rats which were injected with thyroxine, the TBA chromogens were evidently produced more slowly than in both groups without thyroxine, and in the group fed *ad libitum* and treated with thyroxine.

The statistically significant difference in the response to thyroxine emphasizes the importance of the nutritional condition of the experimental animals in the evaluation of the antioxidant effect of the drug examined.

The rate of formation of TBA chromogens during incubation generally depends[6–8] on the content of oxidation substrates (polyunsaturated fatty acid and their derivatives), catalysts and inhibitors (antioxidants), all of which may be influenced by the nutritional state.

Zusammenfassung. Es wurde der Einfluss des Thyroxins auf die Bildung der Oxydationsprodukte von Lipiden in Homogenaten des Rattenlebergewebes bei verschiedenem Ernährungszustand untersucht. Bei den während 24 Tagen unterernährten Ratten, nach 10-tägiger Thyroxinverabreichung (30 µg/100 g Gewicht), wurden im Leberhomogenat deutlich weniger Oxydationsprodukte der Lipide gefunden als bei den Kontrollratten (1. Nahrung *ad libitum* und 2. Nahrung *ad libitum* mit appliziertem Thyroxin).

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The Effects of an Indole Derivative 6-(2'-Aminopropyl Indole) on the General and Coronary Haemodynamics of the Intact Dog

This paper concerns the cardiovascular actions of an indole derivative, a racemic 6-(2'-amino-propyl) indole, synthesized by Sandoz (Basle) and coded as MR 689. It is said not to be a tryptamine derivative, in so far as the side chain is placed in the 6th position of the benzene ring. The drug is said to have antireserpine properties, but it is not an inhibitor of monoamine oxidase[1].

Methods. The effect of the drug was studied in eight dogs. The methods have previously been described in detail[2,3], and include measurement by the Fick principle of cardiac output and coronary flow before and after the administration of the drug; thus after the control measurements, MR 689 (0.5 mg/kg) was dissolved in 15 ml of saline; 5 ml was given initially, 5 ml after 5 min, and 5 ml 10 min after the first intravenous injection. This gave a reasonably steady state of hypertension during which cardiac output and coronary flow were again measured.

Discussion. The results are shown in Tables I–III and suggest that this drug, unlike other indole-alkylyamines[4,5], has little effect upon respiration. The increases in blood oxygen content, and the maintenance of saturation, are due to the increase in haemoglobin. The parallel trends in cardiac output and systemic pressures increase both pressure and flow work, but maintain vascular resistances at control levels. The increase in coronary flow is modest, and coronary vascular resistance is unchanged. The increase in myocardial oxygen extraction (Δ arterial-coronary sinus O_2) is a function of the increase in arterial oxygen.

Table I. General metabolism

Factor	Control	Experimental
Respiratory rate, per min	18±6	17±6
Respiratory volume (l/min)	3.4±1.2	3.7±1.4
Tidal volume (ml)	209±56	250±73
O_2 consumption (ml/min)	123±31	132±34
CO_2 production (ml/min)	97±27	112±35[a]
Exchange ratio (R.Q.)	0.78±0.03	0.84±0.08[a]
Arterial O_2 content (vol. %)	18.3±1.2	20.2±1.5[a]
Mixed venous O_2 content (vol. %)	14.3±2.0	16.6±2.0[a]
Δ Arterial-mixed venous O_2	4.0±0.7	3.6±1.2[a]
Mixed venous CO_2 (vol. %)	48.7±4.6	47.0±4.3[a]
Arterial CO_2 (vol. %)	45.8±4.3	43.3±3.5[a]
Δ Mixed venous-arterial CO_2 (vol. %)	2.9±1.2	3.7±1.2[a]
Haemoglobin (g %)	15.8±1.3	18.0±1.3[a]
Haematocrit	54±4	61±4
pH (units)	7.28±0.05	7.30±0.05

Figures are group means with S.D. Statistical comparison by '*t*' test.
[a] = *p* value of change 0.05 or less.

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