disintegrating ascites cells which were seen to be under all stages of destruction.

Two weeks following the aspiration of fluid, and 3 weeks following the last insult of irradiated and Tween 80 treated cells, the experimental mice and a control group were injected i.p. with 0.2 ml of a cell suspension of normal ascites cells which were treated with Tween 80 as above but without irradiation. This treatment has been shown previously to make no difference in the normal growth of this tumor in host mice[10]. The control group and the experimental group were allowed to remain for observation. Food and water were available ad libitum to each group.

In 2 separate experiments, employing 5 mice in a preliminary study and a larger group of 10 mice in control and experimental series the control mice all died as a result of tumor development in the usual period of about 2 weeks (Table). The surviving experimental mice remain tumor free in the first experiment after 4 months. In the second experiment 1 mouse died of unknown causes with 9 mice remaining normal in all aspects 2 months after the injection of viable Ehrlich ascites tumor cells.

It is apparent that the immunization procedure involving the use of Tween 80 treatment of cells killed by irradiation must unmask cell surface antigens and permit specific antibody formation leading to rejection of the tumor. It has been shown that Tween 80 removes phospholipids from the cell membrane with a resultant change in cell permeability[9]. It seems likely that such a treatment, at the same time, exposes the cell surface glycoprotein antigens. It remains to be determined if the mouse serum contains specific antibodies directed against the exposed cell surface antigens of the Ehrlich ascites cells. A preliminary study with the use of fluorescein labelled serum globulin of the experimental mice has shown that it does bind specifically to Tween 80 treated cells. This aspect of the problem is under further investigation.

Zusammenfassung. Nach i.p. Injektionen von mit Tween 80 behandelten Ehrlich-Lettré Ascites Krebszellen immunisierten Mäusen ergab sich bei diesen eine Widerstandsfähigkeit gegenüber Transplantaten von lebensfähigen Tumorzellen, woraus geschlossen wird, dass diese Behandlung die spezifischen Antigene der Zelloberfläche freisetzt.

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Inhibition of Thyroid Function Following the Administration of Metopiron (SU-4885)

Pharmacological effects of metopiron (SU- 4885, Ciba) are generally believed to produce a specific inhibition of 11-β-hydroxylation of steroids by the adrenal cortex followed by a compensatory increase of pituitary ACTH secretion[1]. An investigation into the effect of prolonged treatment with metopiron (SU-4885) on the hypothalamo-hypophysial neurosecretory system has led to the observation that this drug can produce more subtle effects on spermatogenesis[2,3].

In view of this finding, we decided to investigate the effect of this compound on pituitary thyrotrophic function. The effect of the goitrogenic action of metopiron (SU- 4885) was investigated in bat (*Rhinopoma* and *Taphozous*) and desert rat (gerbil). The criteria used in this investigation were 1. Thyroid weight and its microscopic structure. 2. Collection of radioactive iodine by the thyroid gland. 3. Protein-bound radioiodine (Pb I^{131}) conversion rate.

Materials and methods. Rhinopoma kinneari (Wroughton); *Taphozous perforatus*. In *Rhinopoma* and *Taphozous*, the testis is at its peak from late January till the end of April in the arid zone region of Rajasthan, India (KUMAR)[4].

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Effect of metopiron (SU-4885) on the thyroid radioiodine uptake

Group No.	Treatment		No. of days	Total dose (mg)	Body weight	Average thyroid wt. (mg)[b]	Thyroid weight (mg/100 g body wt.)	I^{131} uptake[a] (c/min/thyroid)	Normal (%)	CR (%)	Statistical comparison
	Rhinopoma										
1	None	(10)	–	–	23 ± 1	1.74 ± 0.1	6.3 ± 2.1	615972	100	–	$P < 0.01$ compared
2	Metopiron	(10)	6	15	26 ± 2	2.23 ± 0.1	8.6 ± 0.4	917654	149	–	with group 1
	Taphozous										
3	None	(10)	–	–	39 ± 2	4.40 ± 2.0	11.1 ± 2.7	753000	100	66	$P < 0.001$ compared
4	Metopiron	(10)	8	40	45 ± 1	9.40 ± 2.8	20.9 ± 1.6	1105000	147	30	with group 3
	Gerbil										
5	None	(10)	–	–	71 ± 5	3.30 ± 0.4	4.6 ± 0.4	183410	100	60	$P < 0.01$ compared
6	Metopiron	(10)	10	100	82 ± 6	6.40 ± 0.2	7.8 ± 0.4	272688	149	36	with group 5

Figures in parentheses indicate the number of animals examined. [a] 5 and 10 μCi carrier free I^{131} was injected in bat and gerbil respectively [b] ± Standard error.

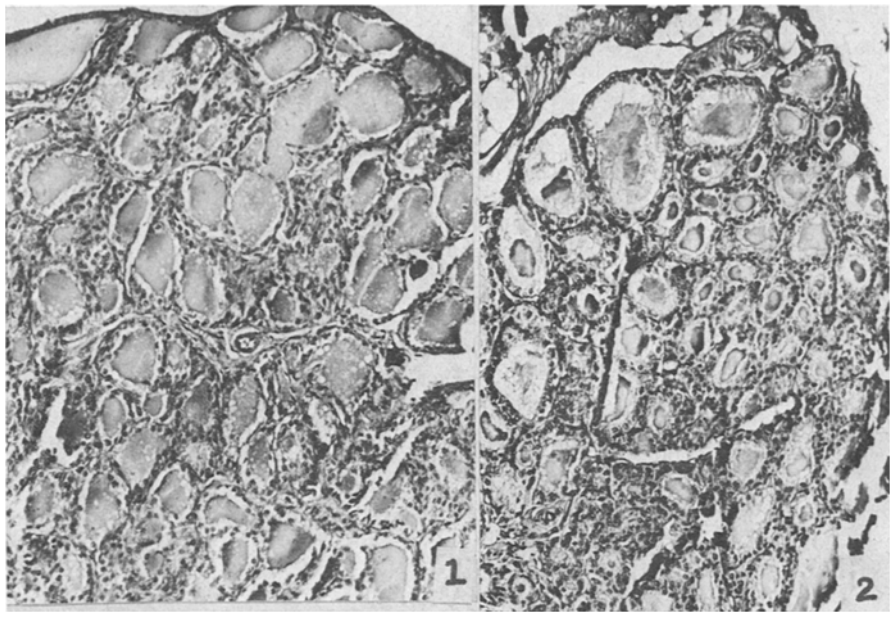

Fig. 1. Thyroid follicles of a control gerbil. HE, ×80.

Fig. 2. Thyroid follicles showing depletion of colloidal material (metopiron 100 mg HE, ×80).

The bats were caught from the surroundings of Amber Fort in the month of February and March, 1971. The healthy males were housed in wire cages in groups of 20. They were acclimatized in the laboratory for at least 7 days at 23 ± 1 °C. The bats were treated with metopiron (SU- 4885, CIBA) (*Rhinopoma:* 2.5 mg/day for 6 days; *Taphozous:* 5 mg/day for 8 days). The drug was administered s.c. in the pelvic region. An equal number of males received 0.1 ml of distilled water each day and served as controls.

Indian Gerbil (*Meriones hurrianae Jerdon*). A group of 10 male gerbils weighing 77 ± 4 g were injected with metopiron 10 mg/day for a period of 10 days. The drug was injected s.c. in the pelvic region. The animals were given rat food and water ad libitum. An equal number of controls received normal saline water.

An injection of carrier-free NaI^{131} was given i.p. (in a dose of 5 μCi per bat and 10 μCi per gerbil, contained in a volume of 0.5 ml). After 48 h the animals were sacrificed, and 2–3 ml of blood were withdrawn into a heparinized syringe from the vena cava under ether anesthesia. Following withdrawl of blood, the thyroid with underlying trachea was removed, dissected free of fat, and connective tissue and weighed on a Mettler's balance. These organs were then immediately put into a 10 ml vial containing 400 ml of a solution of 3 parts Bouin's fluid and 1 part of 1% NaI. Counting of I^{131} was done in a well type scintillation counter.

Protein-bound radioiodine (Pb I^{131}) was determined according to the method of GHOSH et al.[5]. The conversion ratio was calculated as follows[6]:

$$CR = \frac{\text{serum Pb } I^{131} \text{ cpm}}{\text{serum Pb } I^{131} \text{ cpm} + \text{serum } I^{131} \text{ cpm}} \times 100$$

Results. It is believed that the progressive decline in radioiodine concentration of the thyroid is an index of the rate of hormone secretion by the thyroid[7]. It is seen in the Table that the total radioactivity in the thyroid gland is significantly, higher in the metopiron-treated bat and gerbil than in the controls. This denotes a decrease in the rate of discharge of thyroid hormone after metopiron administration. A significant increase in thyroid weight was noticed in all the metopiron-treated groups (Table).

The rate of conversion of administered inorganic radioiodine into protein-bound radioiodine of the plasma has been used to evaluate thyroid activity following metopiron administration. Metopiron produced a significant decrease in the protein-bound radioiodine conversion rate (Table). This denotes that metopiron acts on thyroid gland function directly.

Thyroid microscopic structure. Metopiron (SU- 4885) treatment for 10 days in gerbil induced marked changes in the microscopic thyroid structure. As thyroid weight increased, cell height did too (mean cell height, metopiron: 10.56 ± 0.16 μm control: 9.12 ± 0.25 μm) and the colloid became more dilute and highly vacuolated (Figures 1 and 2). The largest glands were virtually devoid of colloid.

Discussion. Increase in thyroid weight has been used as an index of goitrogenic action of methyl thiouracil/propyl thiouracil in rat and guinea-pig[8,9]. It has also been used as an index of thyrotrophin production by the pituitary. In the present investigation goitrogenic action of metopiron (SU- 4885) has been confirmed, using the thyroid weight and histological structure as an index.

The I^{131} content of the thyroid gland was significantly higher in the metopiron-treated groups than in the controls. This was interpreted as being the result of a decrease in the rate of discharge of thyroid hormone, which further supports the supposition of the inhibition of thyroid function after metopiron administration. In addition, a direct effect on the trapping and binding of iodine by the thyroid gland is reflected in a decreased Pb I^{131} conversion rate. The evidence is quite conclusive

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that SU-4885 acts on thyroid gland function directly as well as by influencing pituitary thyrotrophic activity in enhancing I^{131} uptake.

Zusammenfassung. Die Goitrogen-Wirkung des Metopirons (SU- 4885, CIBA) wurde in Feld- und Wüstenmaus mittels radioaktivem I^{131} untersucht. Das radioiodingebundene Protein (Pb I^{131}) war nach SU- 4885 vermindert. Die Zunahme der gesamten Radioaktivität in der Schilddrüse lag bei 49%. Metopiron wirkt als Schilddrüsen-Hemmer.

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Effect of Light and Darkness on the Hypothalamo-Neurohypophyseal System of the Garden Lizard, *Calotes versicolor*

The stimulating effect of light or the inhibitory effect of darkness on the hypothalamic neurosecretory system (HNS) have been reported in fish[1], amphibia[2–5], birds[6] and mammals[7–10]. This investigator is not aware of any report dealing with the effects of light and darkness on the reptilian HNS. Such effect, however, has been studied on the intermediate pituitary lobe of a number of reptiles[11,12] including the garden lizard *Calotes versicolor*[12]. This investigation reports on the effect of light and darkness on the HNS of the same garden lizard, *Calotes versicolor*.

Freshly collected adult garden lizards of both sexes, acclimated to laboratory condition for 3 days, were used. 18 lizards were kept in 2 cages ($8 \times 8 \times 6$ inches) in equal number under continuous illumination at room temperature (31 °C average) for various periods. Illumination was done by a 100 W bulb from a vertical distance of 3 feet from the central base of each cage. Another 18 lizards were kept in continuous darkness while 16 others were maintained as controls at room temperature under natural light and darkness. At least 3 lizards from each experimental as well as control group were sacrificed by quick decapitation at the selected intervals of 1, 3, 5 and 7 days. 6 µm thick sagittal paraffin sections of the aqueous Bouins fixed brain with hypophysis were stained with chrome

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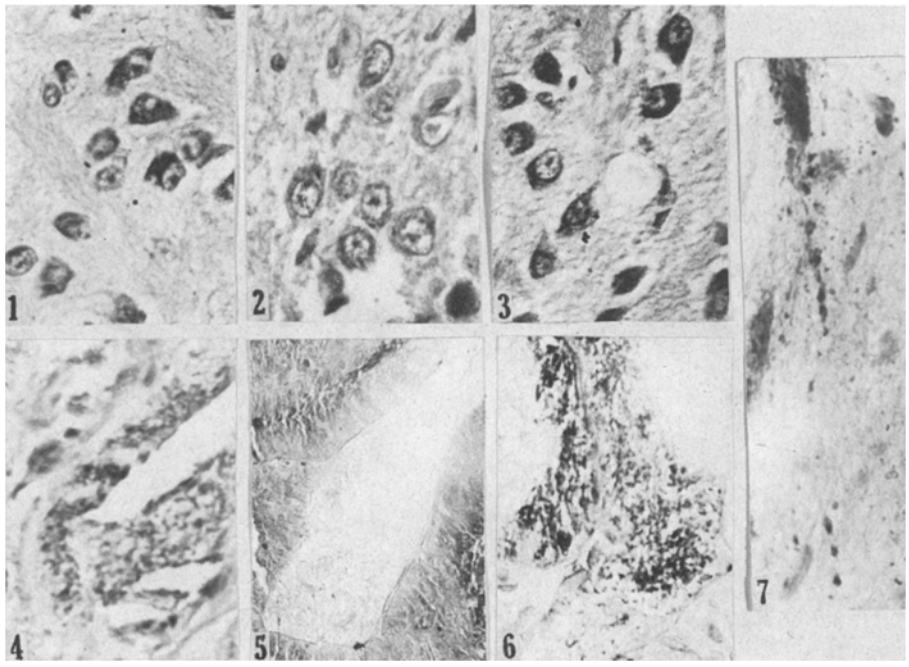

Figs. 1–6. Showing the paraventricular cells and pars nervosa of the control[1,4], illuminated[2,5] and light-obscured[3,6] *Calotes* on day 5. × 315 for Figures 1–3 and × 100 for Figures 4–6.
Fig. 7. Showing the 'beaded' axons in the light-obscured *Calotes* on day 5. × 200.