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Subcutaneous Administration of Cortin Compounds in Solid Form to the Rat.

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Numerous substances having a low solubility in the body fluids have been administered experimentally by implanting them in solid form within the body tissues. We have administered to rats solid forms of extracts of adrenal cortex and 3 pure crystalline compounds which are identified in the literature as A, B, and E.[1]

In Experiment 1, ten male rats having a range in body weight of from 100 to 110 g were matched into pairs and were all adrenalectomized in single-stage aseptic operations. At the time of adrenalectomy a single crystal of compound E which did not exceed 2 mg in weight was implanted subcutaneously into one animal of each pair. The 5 untreated control animals developed symptoms of adrenal insufficiency and died at intervals of 5, 6, 10, 10, and 12 days after operation. The animals which had received the single implants of compound E died at intervals of 15, 20, 23, 23, and 28 days after operation.

For Experiment 2, a total extract of cortin was prepared for implantation. Compounds A, B, E, and some biologically inactive compounds were removed by fractionation. A sample of 330 cc was evaporated to dryness in a vacuum at 40°C. It was redissolved in absolute alcohol and again dried. This was repeated with acetone and the residue of 105 mg was dissolved in alcohol with 400 mg of cholesterol. The mixture was dried by warming in a stream of air. The residue was moistened with alcohol and thoroughly mixed. It was dried in a vacuum desiccator, again moistened with alcohol and compressed into pellets. Twelve male rats having body weights of from 60 to 70 g were closely matched into pairs and all were completely adrenalectomized. A single pellet was implanted under the skin of the dorsal neck region in one animal of each pair. The control animals developed symptoms of adrenal insufficiency and died at intervals of 3, 5, 5, 8, and 10 days after operation. Those animals which had received the pellets grew in a normal manner. Four

[1] Mason, H. L., Hoehn, W. M., McKenzie, B. F., and Kendall, E. C., *J. Biol. Chem.*, 1937, **120**, 719.

weeks after operation these animals were killed and the pellets removed, dried and weighed. The data for these animals are presented in Table I.

TABLE I.
Data on Adrenalectomized Rats Maintained by Subcutaneous Pellets Containing Cortin.

Experimental condition	Body weight, g		Weight of pellet, mg	
	Initial	Final	Initial	Final
Cortin pellets *in situ* 28 days	68	184	52.9	43.0
	69	172	45.2	40.0
	70	196	39.5	31.0
	70	170	44.0	33.5
	70	177	49.8	39.5
Compound B pellets *in situ* 21 days	68	100	60.2	58.0
	65	135	55.3	51.5
	60	124	55.2	53.0
	68	116	44.5	42.0
	60	121	46.3	43.5

For Experiment 3, compound B was prepared for implantation. One hundred milligrams of B and 400 mg of cholesterol were dissolved together in chloroform. The additional procedures for preparing the pellet were identical with those following the mixture of cholesterol and the total cortin extract in Experiment 2. Twelve rats weighing 60 to 70 g were matched into pairs and all of the animals were completely adrenalectomized. At the time of operation a single pellet was implanted subcutaneously in the dorsal neck region. The 6 untreated rats died at intervals of 5, 6, 6, 6, 7, and 7 days after operation. Those animals which received pellets grew in a normal manner. They were killed 3 weeks after operation and the pellets were removed, dried and weighed. The data are presented in Table I.

Atrophy of the adrenal cortex and of the thymus[2] occurs after the oral administration of large amounts of cortin to normal male rats. In Experiment 4, atrophy of the adrenal cortex was produced by the administration of cortin in solid form. Normal male rats each having an initial weight of 180 g were used. Among such animals the range in weight of pairs of adrenal glands is from 22 to 32 mg with an average of 27 mg. The range of thymus weights is 280 to 540 mg with an average of 410 mg. Each rat was killed one week after the implantation of the pellets. The adrenal glands, the thymus and the pellets were removed and weighed. Twelve milligrams of pure compound A lost 7.5 mg weight. The adrenal glands weighed

[2] Ingle, D. J., Higgins, G. M., and Kendall, E. C., *Anat. Rec.*, 1938, **71**, 363.

14.5 mg and the thymus 101 mg. Twelve milligrams of pure compound E lost 6.5 mg weight. The adrenal glands weighed 19 mg and the thymus 188 mg. Pellets containing 20% cortin (containing all of the compound E and some of compounds A and B which were present in the original total extract) and 80% cholesterol were prepared as in Experiment 2. These pellets were implanted into 4 rats. One pellet weighing 54 mg lost 6.5 mg during one week. The adrenals weighed 30 mg and the thymus 433 mg. Two pellets having a total weight of 95.5 mg lost 26.5 mg in one week. The adrenals weighed 27 mg and the thymus 425 mg. Four pellets weighing 220 mg lost 37 mg in one week. The adrenals weighed 17 mg and the thymus 68 mg. Six pellets having a total weight of 302 mg lost 52 mg in one week. The adrenals weighed 15 mg and the thymus 63 mg.

Our data suggest that cortin compounds may be more efficiently utilized when administered to the rat in this manner than when given by the other usual methods. However, there may be appreciable errors in our evaluations of the extent of loss of cortin material by weighing. There may have been a differential absorption of the cortin compounds and of the cholesterol from the pellets and there may have been a cellular infiltration of the pellet which masked the true weight loss to some degree.

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Phagocytosis of Leishman-Donovan Bodies by Leukemic Blood Cells.

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Since kala-azar produces characteristically a marked leukopenia in patients, it seemed interesting to know what effect this infection might produce on the blood picture of patients with chronic myelogenous leukemia. As we had no opportunity to observe this in patients, we thought it worthwhile to study the reaction of leukemic blood cells *in vitro* on Leishman-Donovan bodies, *i. e.*, their phagocytic activity. Incidentally it is also of interest to find out what the relative phagocytic activity of various types of leukemic blood cells is, especially in view of the fact that leukemic patients in general do not