was given, sustained hypertension developed in older rats with intact kidneys, and with relatively small dosage of DCA. Moreover, none of the latter rats died during the experimental interval, nor was gross evidence of toxicity observed in these animals, confirming the protective action of potassium in the DCA-treated animal(10-12).

Although most all of the pressor and toxic actions of DCA heretofore have been studied in reference to the cation, sodium, the importance of potassium in this same relation cannot be overlooked. Indeed, both these, as well as our earlier findings(8), strongly suggest that the presence of adequate amounts of the latter cation is essential for the development of hypertension in the rat, whether the latter is induced by the administration of DCA or by interference with renal hemodynamics.

Summary. Significant hypertension was produced by DCA in intact, older rats given excess potassium, in contrast with the failure of hypertension to persist in similarly treated rats but receiving excess sodium. Potassium deficiency abolished the pressor action of DCA in rats. The results of these studies also indicated that the effects of DCA on the blood pressure were far more profoundly influenced by experimental variation of the potassium intake than that of sodium.

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Received July 13, 1951. P.S.E.B.M., 1951, v78.

Work Performance of Adrenalectomized Rats Given Cortisone and 17-hydroxycorticosterone by Continuous Intravenous Injection. (18980)

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The biologic activity per unit weight of 17-hydroxycorticosterone has been found to be greater than that of 17-hydroxy-11-dehydrocorticosterone (cortisone) when assayed by the Ingle work-test(1,2) and by the liver glycogen deposition test(2). All biologic assays of the adrenal cortical steroids have been based upon the response to intermittent injection. Since there are some differences in the physical properties of the steroids the possibility must be considered that the apparent differences in potency are based upon differences in the rate of absorption from the site of injection or in the speed of inactivation of the compound after it enters the body fluids. Accordingly we have determined the biologic response per unit weight of 17-hydroxycorticosterone and of cortisone by administering each steroid by continuous intravenous injection to rats under the conditions of the Ingle work-test. In these experiments 17-hydroxycorticosterone had approximately twice the potency of cortisone.

Methods. Male rats of the Sprague-Dawley strain were maintained on Archer Dog Pellets until they reached a weight of 200 ± 2 g. The work test was carried out according to Ingle(3). The animals were anesthetized with phenobarbital sodium and cyclopal sodium and were subjected to the stimulation of muscle immediately following removal of both adrenal glands and both kidneys. The quadriceps muscle of the left hind leg was weighted with 100 g. A Nerve Stimulator, Model B, Upjohn, was used to deliver 5 pulses per second. The duration of each pulse was 20 milliseconds and the intensity was 20 milliamperes. The distance the weight was lifted was recorded on automatic work adders. Each recorder revolution represented approxi-

1. Ingle, D. J., and Kuizenga, M. H., *Endocrinology*, 1945, v36, 218.

2. Pabst, M. L., Sheppard, R., and Kuizenga, M. H., *Endocrinology*, 1947, v41, 55.

3. Ingle, D. J., *Endocrinology*, 1944, v34, 191.

TABLE I. Work* Performance of Adrenalectomized-Nephrectomized Rats Given Adrenal Cortical Steroids by Continuous Intrav. Inj. Total recorder revolutions. Averages and stand. dev. of averages.

Dose steroid, mg/24 hr/rat	Cortisone		17-hydroxycorticosterone	
	No. of rats	Total work	No. of rats	Total work
.1	15	11051 ± 700	15	13732 ± 863
.25	15	12396 ± 1447	15	22975 ± 1625
.5	15	21192 ± 1855	15	26408 ± 1716
1	16	28515 ± 2665	16	35074 ± 2027

* Each recorder revolution represents approximately 400 g-centimeters of work.

mately 400 gram-centimeters of work. Stimulation was continued until muscular responsiveness was lost. The animals were enclosed in a temperature cabinet with the temperature constant at 28 ± 0.5°C. The two steroids were each dissolved in water containing 5% ethanol, 0.9% sodium chloride and the potassium salt of crystalline penicillin G (Upjohn). The fluid load was 20 cc per 24 hrs per rat and the penicillin dose was 5000 units per 24 hrs per rat. The injections were made into the jugular vein by means of a continuous injection machine which was incorporated into the fatigue apparatus. By means of this apparatus 12 rats can be studied simultaneously.

Experiments and results. The two compounds were compared at dosage levels of .1, .25, .5 and 1.0 mg per rat per 24 hrs. The compounds were equally represented in each individual experiment. Each position on the fatigue apparatus and each automatic recorder was represented equally among the rats receiving each compound.

The group averages and the standard deviations of the averages are summarized in Table I. At each dosage level the average amount of work done by the rats treated with 17-hydroxycorticosterone was significantly greater than the average amount done by the rats treated with cortisone. In these experiments the potency per unit weight of 17-hydroxycorticosterone appears to be about twice that of cortisone, *i.e.*, in order to duplicate the work performed at a given dose of 17-hydroxycorticosterone it was necessary to give twice as much cortisone. This estimate may differ from the true ratio of activity due to errors in sampling.

Discussion. These data confirm the earlier observations(1,2) that 17-hydroxycorticosterone is more potent than cortisone per unit weight in supporting the ability of the adrenalectomized rat to work. The difference in quantitative activity is not due to differences in absorption into the body fluids for it remains evident when these steroids are delivered directly into the blood. The possibility remains untested that the quantitative differences in activity are based upon differences in the rate and extent of entry of the steroid from the blood into tissue cells.

The potency of any biologically active compound must always be defined in terms of the conditions under which it is tested. A biologic activity is not a quality which is determined solely by the compound itself but rather is a sign of an interaction with a responsive tissue. Consequently, ratios between the quantitative activities of two or more compounds may be significantly altered by changes in experimental conditions or may even be reversed. The greatest practical interest in 17-hydroxycorticosterone at the present time centers upon the possibility that it may be more effective than cortisone in treating the so-called connective tissue diseases. Although Thorn(4) and his associates have found that 17-hydroxycorticosterone is more effective than cortisone in eliciting eosinopenia in man and Conn(5) has found that 17-hydroxycorticosterone is the more potent of the two compounds in eliciting metabolic changes in man, the preliminary comparisons of the efficacy of the two compounds in the treatment of rheumatoid arthritis have thus far failed to support the hope that 17-hydroxy-

4. Thorn, G. W., and Forsham, P. H., personal communication.

5. Conn, J. W., personal communication.

corticosterone would be superior to cortisone (6).

Summary. Under the conditions of these experiments 17-hydroxycorticosterone was found to have about twice the biologic potency of cortisone in the work performance test on adrenalectomized-nephrectomized male rats.

We wish to express our appreciation to Dr. Augustus Gibson, The Medical Division of Merck and Co., who supplied the cortisone and to Dr. W. J. Haines, Endocrinology Department, The Upjohn Research Laboratories, who supplied the 17-hydroxycorticosterone for these studies.

6. Sprague, R. G., personal communication.

Received July 17, 1951. P.S.E.B.M., 1951, v78.

Nutritive Value of Legume Seeds. XI. Counteracting the Growth Inhibitor of Raw Soybeans.* (18981)

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The existence of a distinct growth-inhibiting factor for the chick in raw soybeans was demonstrated by Ham, Sandstedt, and Mussehl (1). That the soybean growth inhibitor similarly affects the rat has been established subsequently in several reports. One of the objectives of the present writers' investigations of the soybean growth inhibitor (SGI†) has been to answer this question: Is there a factor which will counteract the growth inhibitor of raw soybeans? Results of a search for an anti-SGI† are here described.

Experimental. The substances to be tested for anti-SGI activity replaced an equal weight of starch in the following ration: 25 g autoclaved or raw soybean oil meal, 0.6 g DL-methionine, 2 g salt mixture(2), 0.5 g choline chloride, 0.5 mg thiamine HCl, 0.5 mg Ca pantothenate, 2.5 mg niacin, 0.125 mg pyridoxine HCl, 0.5 mg riboflavin, 5 g cod liver oil, 15 g lard, and corn starch sufficient to make 100 g. The raw soybean oil meal was prepared with a minimum of heat treatment by the solvent process according to the manufacturer's statement. The autoclaved soybean oil meal was prepared from this by autoclaving at 15 lb pressure for 30 minutes. The rations were fed to weanling rats of the Sprague-Dawley strain. Animals of each litter were paired as to sex and initial weight between the 2 experimental rations, autoclaved soybean oil meal plus the material being tested for anti-SGI activity versus raw meal plus the same material. The rats were housed in individual screen-bottom cages with food and water available *ad libitum*. The number of rats fed each ration ranged from 8 to 20, the feeding period from 20 to 42 days. Some of the materials tested for anti-SGI activity are listed in Table I with the average gain per day at the end of 20 days feeding. Longer feeding periods did not affect the results other than to increase statistical significance. Of some 25 materials tested only trypsin powder has been found to be effective in counteracting the growth inhibitor in raw soybeans. Because of the interest in the trypsin inhibitor of raw soybeans, the apparent trypsin inhibitor activity of a mixture of 25 g raw soybean oil meal and 5 g trypsin

* Published with the approval of the Director as Paper No. 539, Journal Series, Nebraska Agricultural Experiment Station. This work was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service. A preliminary report of some of these data was submitted in an abstract to the American Institute of Nutrition, Cleveland, May, 1951.

1. Ham, W. E., Sandstedt, R. M., and Mussehl, F. E., *J. Biol. Chem.*, 1945, v161, 635.

† It is proposed that the abbreviation "SGI'" be used for the soybean growth inhibitor until identification has been accomplished. A factor which counteracts the growth inhibitor will be termed "anti-SGI."

2. Hubbell, R. B., Mendel, L. B., and Wakeman, A. J., *J. Nutrition*, 1937, v14, 273.