silicotungstic, phosphotungstic, and phosphomolybdic. These are (i) anticoagulant activity in vitro and in vivo (*3*); (ii) the ability to elicit the appearance of plasma clearing factor activity (*3*). The work discussed in this report demonstrates that these inorganic substances also resemble heparin in their ability to inhibit crystalline beef pancreas ribonuclease. In addition, dextran sulfate (*4*) and two sulfated pectic acid derivatives which possess anticoagulant activity (*5*) were also found to be potent ribonuclease inhibitors.

Ribonuclease activity was determined by the spectrophotometric method of Kunitz (*6*) at *p*H 5.0. Each of the substances was brought to *p*H 5.0 before addition to the test system. The polyacids were commercial products.

The data given in Table 1 demonstrate that all five of the polyacidic substances inhibit ribonuclease activity under these conditions. Relative inhibitory activity seems to fall in the general order: dextran sulfate > sulfated pectic acid amide > sulfated pectic acid methyl ester > silicotungstate > phosphomolybdate. In general, the sulfated polysaccharides were more active than the inorganic polyacids.

Since pepsin has the lowest isoelectric point of any known protein (*7*), a sample was inactivated by alkali treatment (*8*), then adjusted to *p*H 5.0. This material showed very little ribonuclease inhibitory activity. This result is in marked contrast to the inhibition obtained by Vandendriessche (*2*) with polyaspartic acid and indicates that proper spacing of the polyacidic groups is also an important characteristic of this type of ribonuclease inhibitor (*9*).

Table 1. Inhibition of ribonuclease (RNase) by polyacids.

Amt. added (mg/4 ml)	RNA added (mg/4 ml)	Decrease in A_{300} between 1 and 5 min. after mixing	Relative RNase activity (%)
	Silicotungstate		
None	0.9	0.038	100
0.20	0.9	0.002	5
0.10	0.9	0.008	21
0.08	0.9	0.014	37
0.06	0.9	0.021	55
0.04	0.9	0.034	89
0.02	0.9	0.035	92
	Phosphomolybdate		
None	0.9	0.035	100
0.6	0.9	0.035	100
0.8	0.9	0.023	66
0.8	1.2	0.034	97
	Dextran sulfate		
0.2	0.9	0.001	3
0.1	0.9	0.004	11
0.02	0.9	0.012	34
	Sulfated pectic acid methyl ester		
None	1.2	0.036	100
0.10	1.2	0.012	34
0.05	1.2	0.025	71
	Sulfated pectic acid amide		
0.05	1.2	0.020	57
	Inactivated pepsin		
None	1.2	0.042	100
(1.0)	1.2	0.038	90

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Antihypertensive Effects of an Aldosterone Antagonist

A new synthetic steroid was recently described (*1*) that antagonized the renal excretory effects of aldosterone and deoxycorticosterone acetate (DCA) in rats (*2*) and man (*3*): 3-(3-oxo-17β-hydroxy-4-androsten-17α-yl)propionic acid γ-lactone (SC-5233). It was of interest to examine the ability of this compound to prevent and reverse the experimental hypertension produced in rats by DCA.

In the first experiment, two groups of eight 1-month-old Sprague-Dawley rats were implanted with a 20-mg DCA pellet and offered 0.86-percent NaCl as drinking fluid. In addition, one group received SC-5233, 10 mg/kg per day subcutaneously for 19 days, and the other group received the solvent (propylene glycol). Blood pressures (*4*) were taken periodically under standard "double-blind" conditions. No differences between the blood pressures of the two groups were observed after 1, 5, or 10 days of treatment. However, on the 15th and 18th days, the mean pressure of the treated group was 168 mm, while that of the untreated group was 177 and 181; these differences were significant (*5*) at the 5- and 1-percent levels, respectively. Because of these results, investigations are under way to determine whether SC-5233 will prevent the production of adrenal-regeneration hypertension (*6*), which may involve hyperreactivity to aldosterone (*7*).

Additional experiments were performed on metacorticoid hypertensive rats (*8*), which are no longer under the active metabolic influence of DCA (*9*). This form of experimental hypertension resembles essential hypertension in man, particularly with regard to the pharmacology, physiology, and pathology of the two diseases (*10*).

For acute studies, SC-5233 was injected into 12 metacorticoid rats, and the blood pressures were recorded before and 2, 4, and 6 hours after injection. Twelve hypertensive control rats received the solvent. It was found that the compound had a hypotensive action when it was administered by both the oral and parenteral routes (Table 1).

For chronic studies, two groups of six metacorticoid rats drinking saline were observed for 7 days and then injected with SC-5233 or the solvent for 19 days. The total dose of SC-5233 over this period was 800 mg/kg (subcutaneously). Blood pressures were recorded five times during the pretreatment week, 14 times during treatment, and twice after; SC-5233 caused a significant decrease of pressure, which was reversed after the cessation of therapy (Table 2). This experiment was subsequently repeated at a dosage of 280 mg/kg in 14 days, with the same results.

The ability of SC-5233 to block the pressor action of DCA is consistent with its ability to block the renal excretory actions of DCA and aldosterone (*2, 3*). However, its hypotensive action in metacorticoid hypertensive rats can hardly be due to the same process, since such rats are no longer being subjected to DCA overdosage (*9*). Additional evidence is provided by the finding that we have been unable to uncover any activity of the 19-nor derivative of SC-5233 in blocking the pressor action of DCA in saline-fed rats or in lowering the blood pressure of metacorticoid hypertensive rats, in spite of the fact that this deriva-

Table 1. Acute hypotensive action of SC-5233 in metacorticoid rats.

Time of treatment	Blood pressure (mm)	
	SC-5233	Controls
*Experiment A**		
Before injection	190	190
2 hr after injection	169†	194
4 hr after injection	170†	192
6 hr after injection	166†	193
Experiment B‡		
Before injection	188	188
2 hr after injection	166§	194
4 hr after injection	162§	192
6 hr after injection	160§	194

* A, 20 mg/kg subcutaneously (eight rats per group).
† $P < 0.01$ that change in pressure equals that of controls (*5*).
‡ B, 200 mg/kg by gavage (four rats per group).
§ $P < 0.05$ that change in pressure equals that of controls (*5*).

Table 2. Chronic hypotensive action of SC-5233 in metacorticoid rats; SC-5233 was administered on days 8 to 27, inclusive.

Day	Blood pressure (mm)	
	SC-5233	Controls
1–7	184–208	182–210
9	176*	189
11	169†	190
15	162†	191
17	158†	181
21	153†	179
23	157*	177
25	155†	180
28	160*	177
32	174	183

* $P < 0.05$ that change of pressure equals that of controls (5).
† $P < 0.01$ that change of pressure equals that of controls (5).

tive is considerably more potent than SC-5233 in blocking the renal excretory effects of DCA (2). Apparently the renal mineralocorticoid-blocking and the antihypertensive properties of SC-5233 are not directly related. Instead, the latter property might be mediated by the reversal of some internal electrolyte disturbance that had been instituted by the temporary treatment with DCA, such as an increase in the intracellular sodium compartment (11–13).

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Lack of Competitive Inhibition between Beef and Monkey Growth Hormones in Rhesus Monkeys

The demonstration that growth hormone obtained from monkey pituitary glands is physiologically effective in the rhesus monkey while that from beef glands is not (1, 2) led to the finding of distinct physicochemical differences between the molecules of the two growth hormones (3). These results suggested the possibility that beef growth hormone, which is inactive in the monkey, might mask the effects of monkey growth hormone on nitrogen retention by competing for "effector sites" when the two molecules are administered concurrently to hypophysectomized rhesus monkeys.

Two immature male monkeys (*Macaca mulatta*) which had been hypophysectomized approximately 1 year before were placed on a nitrogen balance regimen, as previously described (2). Following a control period, each animal received daily intramuscular injections of monkey pituitary growth hormone (prepared by A. E. Wilhelmi) at a dosage of 1 mg/kg; one animal was treated for 7 days, the other for 9 days. This was followed by a 10-day control period. On the following day each monkey received an intramuscular injection of 10 mg of beef growth hormone (4) per kilogram. In the succeeding week each animal was given daily intramuscular injections of beef growth hormone (10 mg/kg) and monkey growth hormone (1 mg/kg). Daily nitrogen balance determinations were made throughout the control and experimental periods. The mean daily nitrogen retention and its standard error were calculated for each period.

The results obtained for each of the hypophysectomized monkeys were essentially the same and are illustrated in Fig. 1 with data from one of them. The anabolic effect of the monkey growth hormone preparation was not significantly reduced by the concurrent administration of beef growth hormone in a ratio of 10:1 by weight.

In both experiments a slight tendency toward a reduction in nitrogen retention when both hormones were administered was noted. This reduction, however, was not stastistically significant. It would seem from the foregoing data that the specificity of the "effector sites" for growth hormone action in the monkey is such that beef growth hormone in relatively large quantities, although physiologically inert in this species, does not mask the action of the monkey growth hormone molecule. These "effector sites" in the rat do not exhibit such specificity, since in this animal monkey and beef growth hormones are equally effective (2, 5).

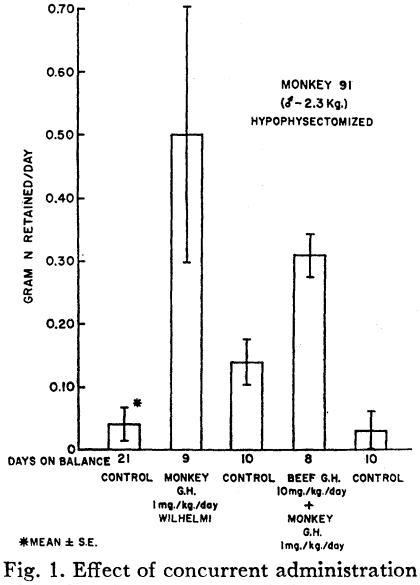

Fig. 1. Effect of concurrent administration of beef and monkey growth hormones on nitrogen retention in a hypophysectomized rhesus monkey.

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Microbiological Fractionation of the Hydrogen Isotopes

Mass spectrometric analyses of bacterially generated gas made in early 1956 as an adjunct to U.S. Geological Survey studies of Bahama Banks sediments unexpectedly revealed a high concentration of light hydrogen (protium), presumably with segregation elsewhere of the heavy isotope deuterium. Further investigation is intended, but meanwhile it seems advisable to record our findings to date in sufficient detail to provide a point of departure for others who may be interested (1).

As a part of a comprehensive plan of study of Bahamas sediments collected by