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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12. A detailed report by C. M. Kagawa *et al.*, on the pharmacology of SC-5233 is in preparation.
13. The technical assistance of Esther Lacunza and Gladys Powers is gratefully acknowledged.

13 March 1958

## 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*).

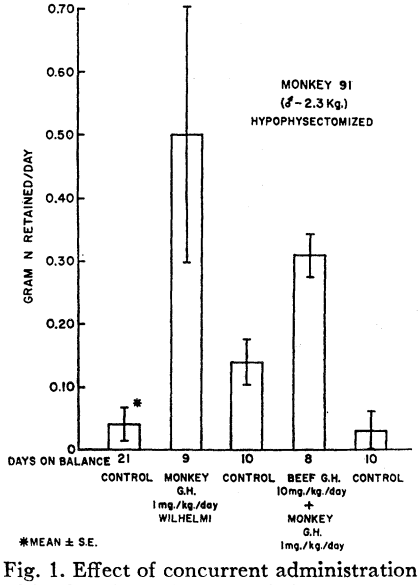


Fig. 1. Effect of concurrent administration of beef and monkey growth hormones on nitrogen retention in a hypophysectomized rhesus monkey.

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5. We wish to express our gratitude to Dr. D. A. McGinty of Parke, Davis & Co., Dr. Mary A. Root of Eli Lilly & Co., Dr. Joseph Seifter of Wyeth, Inc., Dr. R. H. Barnes of the Sharp & Dohme Division of Merck & Co., Inc., and Dr. C. A. Bunde of Pittman-Moore & Co. for generous gifts of monkey pituitary glands. The beef growth hormone (Somar-A) was a gift of the Endocrinology Study Section of the National Institutes of Health. The technical assistance of John Cimerol is gratefully acknowledged. This study was supported by a grant from the American Cancer Society (EDC-18) and a grant from the National Institute of Arthritis and Metabolic Diseases (A-292), National Institutes of Health, U.S. Public Health Service.

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3 February 1958

## 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

Cloud and associates in May 1955, bacteriological analyses of the refrigerated samples were undertaken by Sisler, beginning early in 1956. It was soon observed that a yet unidentified (*2*) facultative aerobe found in teeming abundance in aragonite muds from a mid-bank locality west of Andros Island (Fig. 1, station G4) produced gas vigorously when it was cultured in a dextrose medium (*3*). It seemed likely that this gas was largely $CO_2$, but a check-analysis was sought from the Mass Spectrometry Section of the National Bureau of Standards. That analysis, by Dibeler, showed 26.3 percent carbon dioxide and 63.4 percent hydrogen; the latter, within the resolving power of the apparatus, appeared to consist exclusively of common light hydrogen. The balance was 5.3 percent water vapor, 4.6 percent nitrogen, and 0.4 percent oxygen.

There is, of course, nothing unusual about the concentration of hydrogen by bacteria (*4*). The striking aspect of Dibeler's analysis was its indication that the hydrogen was markedly enriched in the light isotope. The apparent magnitude of the enrichment was so unexpected that an independent analysis of a new gas sample from the same bacterial culture was run by Friedman, on a newly installed Geological Survey mass spectrometer especially designed for study of the hydrogen isotopes. Friedman's results showed that the deuterium was depleted by a factor of 20 over ocean water, rather than by the factor of 3.7 to be expected from evaporation and the equilibrium

$$H_2O + HD \rightleftharpoons H_2 + HDO$$

This situation was so remarkable that hydrogen isotope analyses were later run (by Friedman) on the water of inclusion and the whole dextrose from the same batch that was used in preparation of the culture medium, as well as on a sample of the dextrose formula actually used to prepare the station G4 gas sample, including the mixture of lower Chesapeake Bay water and distilled water employed throughout the tests. Since these three tests all showed normal isotopic abundance, it is certain that the fractionation observed is performed by the bacteria themselves.

Meanwhile, an opportunity had arisen to return to the Bahamas in June 1956, and further work on the hydrogen was deferred pending field observations to determine whether the gas was generated (and fractionated) in place. At the approximate site of station G4 a trap was set to catch any gases moving upward from the sediment into the overlying water. No free gas accumulated in this trap over a 24-hour period, and accidental tipping of the trap prevented analysis of the enclosed water for dissolved gases. Further investigation was not practicable.

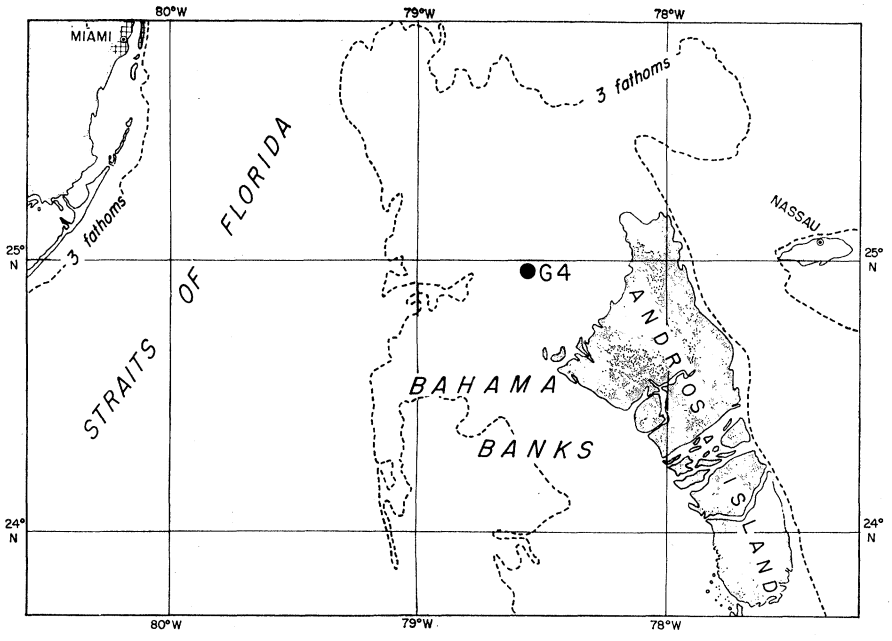


Fig. 1. Index map showing location of station G4.

Regardless of what may happen in nature, however, it is certain that there exist, in at least one site in the calcium carbonate muds west of Andros Island, bacteria that, under appropriate circumstances, can vigorously produce hydrogen gas depleted in deuterium. An estimate of abundance by the minimum dilution technique indicates this bacterium to be present in the top 6 in. of sediment from station G4 in excess of $10^{10}$ units per gram wet weight. This unprecedented abundance might be in part due to bacterial increase during the year in which the sample was refrigerated before study, but control counts of the total number of bacteria in fresh muds indicate that allowance for such increase would not reduce the estimated exponent by more than 2 or 3 at most.

Inasmuch as the gas is depleted in deuterium, the deuterium is presumably concentrated within the interstitial water, the residual nutrients, or the bacteria. Such concentration of the normally scarce heavy isotope, if it should prove feasible to produce it in large-scale viable culture, suggests means to facilitate and reduce the cost of production of heavy water (*5*).

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### References and Notes

1. Publication of this report has been authorized by the director, U.S. Geological Survey, and the director, National Bureau of Standards.
2. Studies are under way to characterize and identify this bacterium, tentatively referred by Sisler to the genus *Pseudomonas*.
3. Composition of the medium was as follows: Bacto-dextrose, 4.0 g; $(NH_4)_2HPO_4$, 0.2 g; $MgSO_4 \cdot 7H_2O$, 0.2 g; $FeCl_3$, 0.2 g; normal sea water, 750 ml; distilled water, 250 ml.
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29 April 1958