

for use in mines, tunnels, etc., shall have been developed, it seemed advisable to present a preliminary account of the work. Due acknowledgements will be made in a later, more detailed, publication.

The principles involved may, perhaps, be set forth more clearly by considering CO_2 as the contaminating gas. It is well known that CO_2 has narrow regions of strong absorption and emission near 2.7 and 4.4 μ in the infrared. According to the first procedure tried, radiations from a jet of hot CO_2 are passed through an absorbing chamber and are focused on a thermopile. Since the radiations from hot CO_2 are largely absorbed only by cold CO_2 , it is evident that CO_2 in the absorbing chamber would reduce the intensity of the radiations falling on the thermopile—other gases and vapors in the chamber being ignored. The actual apparatus is sketched in Fig. 1, where J is a small

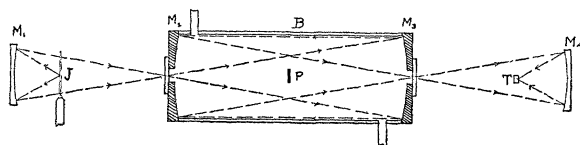


Fig. 1.

jet of hot CO_2 whose radiations, after leaving the concave mirror M_1 , are focused on the absorbing chamber B. This consists of a brass tube (30 cm long and 6 cm in diameter) whose ends are closed by the concave mirrors M_2 and M_3 —each supplied with a central hole 1 cm in diameter. As is evident, these mirrors make it possible to send the radiation through the tube three times. Direct transmission through the tube is prevented by the introduction of a small baffle at P. The system is made gas-tight by waxing windows of fluorite or rock-salt over the holes in the mirrors. The mirror M_4 focuses the emergent radiations on a thermopile T, which is connected to a sensitive galvanometer.

The results obtained are confined largely to CO_2 . Using as source the radiations emitted by the hot CO_2 found in the non-luminous portion of a small gas-jet (burning in a water-cooled jacket) it was found that less than one part of CO_2 in a million of air could be detected. By employing a jet of hot CO_2 as the source, water-vapor in the absorbing chamber was completely ignored.

This procedure was soon found to suffer from a number of serious defects such as (1) lack of constancy of the source, (2) inability to heat all gases and vapors to a sufficiently high temperature without bringing about decomposition, (3) lack of exact agreement of the spectral regions of emission of the hot gas and of absorption of the cold gas.

Accordingly, a second procedure was evolved. Here,

radiations from an incandescent nichrome spiral at J are passed through the absorbing chamber and are allowed to fall on a closed but (infrared) transparent receiver T filled with CO_2 . As long as the absorbing chamber is free from CO_2 , the gas in the receiver will be heated, due to the selective absorption of the radiations near 2.7 and 4.3 μ . If, however, some CO_2 be admitted to the absorbing chamber, this gas will absorb, prematurely, some of the radiations which, previously, had heated the receiver. As a result, the temperature of the latter will drop. The first of these selective receivers consists of a brass capsule whose ends are closed with plates of rock-salt. After filling with CO_2 through a suitable side tube, this is connected to an improvised stethoscope. By mounting a phonic wheel at M_2 and raising the rate of interruption to about 200 per sec. a fairly loud sound is heard by applying the stethoscope to the ears. Evidently the CO_2 in the receiver is periodically heated by the direct absorption of radiant energy. Eventually this sound is to be amplified so that, upon replacing the loud-speaker by a portable galvanometer, sound-intensity may be translated into galvanometer deflections.

A second and more immediately useful receiver was constructed on the idea that if a polished thermopile were introduced into an infrared-transparent receiver filled with CO_2 and if the thermopile junctions were shielded from direct radiation, then the adjacent CO_2 would be heated by radiation and would, by diffusion, heat the junctions of the thermopile.

This receiver showed high sensitivity as well as selectivity. Having filled the receiver with CO_2 , ordinary illuminating gas, free of CO_2 , was allowed to fill the absorbing chamber to atmospheric pressure. In spite of the fact that illuminating gas contains methane and carbon monoxide, both to the extent of 20 per cent. or more, no measurable absorption could be detected. When, on the other hand, the receiver was filled with CO_2 -free illuminating gas, the effect was enormous.

Obviously, the highest degree of selectivity is achieved by using as source a jet of hot gas or vapor x whose radiations fall on a selective receiver filled with x; the presence of x between source and receiver will be recognized decisively.

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OXIDATION-REDUCTION POTENTIALS AND THE MODE OF ACTION OF SULFANILAMIDE

THE report by Shaffer¹ concerning a possible relationship between the potentials developed by certain

¹ SCIENCE, 89, 547-50, June 16, 1939, and Cold Spring Harbor Symposia on Quantitative Biology, 7, 1939, to be published.

oxidation products of sulfanilamide and its therapeutic activity contains much that is suggestive. Certainly it is reasonable to suppose that some oxidation of sulfanilamide occurs in the body. Furthermore, it is possible that the oxidation products account for the therapeutic effect. But that the high potentials reported by Shaffer are due to oxidation products of sulfanilamide and are responsible for the activity of the drug is open to question.

We believe that these apparently abnormally high potentials are attributable not to any oxidation products of sulfanilamide, but to the oxidizing agents used. For example, if to a dilute solution of sulfanilamide a dilute solution of ceric sulfate is added gradually as in a titration, some cerous sulfate will be formed almost immediately. As a result, a potential due to the cerous-ceric system will be established. Eventually all the ceric sulfate from any one addition will be reduced by the sulfanilamide. The reaction would be very slow in dilute solutions, however, and, if fresh additions of ceric sulfate were made before all the previous portion was reduced, a fairly steady potential would result. This should be particularly true if the rate of addition of ceric sulfate approximated its rate of reduction. Since the E_0 of the cerous-ceric system is -1.46 volts,² it would not be surprising to find high potentials. Most of the other effective oxidizing agents mentioned by Shaffer show potentials of the same order of magnitude.

The method used in our experiments was briefly as follows:

A standard Beckman Model G pH meter was used to record oxidation-reduction potentials. The cell was equipped with a saturated calomel half-cell, gold and platinum electrodes, a mechanical agitator, nitrogen inlet tube and 50 cc burette. Before, and at intervals during the course of the work, this set-up was checked with quinhydrone at various pH values. The results in all cases checked to within the limits of the instrument (± 3 millivolts).

A typical experiment involved the titration of 100 cc of 0.001 M sulfanilamide dissolved in 1.0 N sulfuric acid (pH 0.8) with 0.001 M ceric sulfate in 1.0 N sulfuric acid. By plotting observed potentials against cc of ceric sulfate added, curves were obtained which showed the same "plateau potentials" reported by Shaffer. If, however, the rate of addition of ceric sulfate was varied, differences in the "plateau potential" of as much as 70 millivolts were obtained. The same drift in potentials was also observed. This could be demonstrated more strikingly when 0.01 M ceric

sulfate was employed. No "plateau potential" was obtained in this case, the potentials falling very rapidly to a limiting value.

It was possible to plot potentials against the time following the addition of a given amount of 0.01 M ceric sulfate. Smooth curves were obtained which appeared to be a direct indication of the rate of oxidation of sulfanilamide. With some refinements, it is possible that this method might be applied to a quantitative study of the rate of oxidation of aromatic amines. Preliminary studies on several compounds, including sulfapyridine, p,p'-diamino diphenyl sulfone and o- and m-amino benzene sulfonamide were made by means of this technique. This work was carried out with the idea that rate or ease of oxidation might be a factor in chemotherapeutic activity. However, no significant difference in the rate of oxidation of the above compounds could be demonstrated by this method, at least not with as strong an oxidizing agent as ceric sulfate.

With 0.008 M hydrogen peroxide and 0.0001 M Fe^{++} at pH 4.6 we were unable to obtain the same high potentials. The results were very erratic and seemed to depend largely on the condition of the electrodes. Potassium permanganate gave much the same results as ceric sulfate except that no definite end-point could be established. For the results on potassium permanganate we are indebted to Dr. A. Moos, of the Lederle Laboratories, Inc., Pearl River, N. Y.

It might be argued that the rapid drop in potential when higher concentrations of ceric sulfate were employed was due to the rapid disappearance of the intermediate oxidation products of sulfanilamide responsible for the potentials. However, when a reverse titration was carried out, by adding 5- or 10-cc portions of 0.001 M sulfanilamide to 100 cc of 0.002 M ceric sulfate, the potentials at equilibrium were in good agreement with those calculated for a cerous-ceric system on the basis of four equivalents of ceric sulfate to one of sulfanilamide. The number of equivalents was determined by the normal titration method as described by Shaffer and was close to four.

Finally, we found that, on standing for 48 hours, a solution of 100 cc of 0.001 M sulfanilamide in 1.0 N sulfuric acid, to which was added 15 cc of 0.01 M ceric sulfate, developed a single electrode potential which was close to -0.6 volt. Since the gold and platinum electrodes checked as usual, we have assumed that this was a true equilibrium potential. The value obtained in this way was of the same order of magnitude as the potential reported by Conant and Lutz³ for the system phenyl hydroxylamine-nitrosobenzene. We have determined this equilibrium potential for several therapeutically active and "inactive" compounds. Of the

² Kunz, *Jour. Am. Chem. Soc.*, 53: 101, 1931. The sign convention of Lewis and Randall, "Thermodynamics," McGraw-Hill Book Company, New York, N. Y., Chapter XXX, 1923, is used in this report.

³ *Jour. Am. Chem. Soc.*, 43: 1059, 1923.

active substances, the potentials of sulfanilamide, sulfapyridine and *p,p'*-diamino diphenyl sulfone were measured. The potentials of these fell within a range of 20 millivolts. *o*- and *m*-amino benzenesulfonamide were the "inactive" compounds examined. These two substances gave potentials about 50 millivolts lower than the active compounds.

It must be emphasized that, until more is known about the blood levels obtained and the rate of absorption and excretion of "inactive" compounds, it is not possible to accept them as inactive in theoretical considerations. When an attempt is made to correlate activity, only compounds known to be present in the blood stream for intervals of time and in concentrations comparable with sulfanilamide or sulfapyridine, and under these conditions showing no therapeutic effect, should be considered as inactive. Strangely enough, for this type of work, some well-studied inactive compounds would be highly desirable. It seems possible that attempts of this sort to use some fundamental physical property as a stepping-stone in attacking the problem of correlating chemical structure with chemotherapeutic activity may lead to a more rational basis for the selection of new chemotherapeutic agents. Further work of this general nature will be reported later.

We conclude, on the basis of the following facts, that the "plateau potentials" of Shaffer are a function of the oxidized and reduced forms of the oxidizing agents employed, rather than of the oxidation products of sulfanilamide:

(1) In the presence of excess sulfanilamide the potentials fall rapidly as the oxidized form of the oxidizing agent is exhausted.

(2) Equilibrium potentials are established if partially oxidized solutions of sulfanilamide are allowed to stand for 48 hours.

(3) When an excess of ceric sulfate is present, the equilibrium potentials agree with those calculated for a cerous-ceric system.

(4) The "plateau potentials" can be varied within wide limits, depending on the rate of addition of the oxidizing agent.

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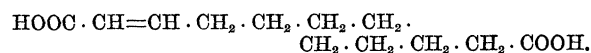
AMERICAN CYANAMID COMPANY,
STAMFORD, CONN.

STRUCTURE AND SYNTHESIS OF A PLANT WOUND HORMONE

In an earlier publication the isolation of a crystalline substance possessing wound hormone activity has been described.¹ This substance, which was isolated from the water extract of green string-beans, possesses

¹ J. English, J. Bonner and A. J. Haagen-Smit, *Proc. Nat. Acad. Sci.*, 25: 323, 1939.

the property of eliciting renewed growth activity in the parenchymatous cells of the bean mesocarp, and its activity may hence be quantitatively determined by the bean test which has been described elsewhere.² Elementary analysis of the crystalline product, together with its molecular weight (by m.p. depression in camphor) leads to the formula $C_{12}H_{20}O_4$, and the equivalent weight by titration indicates a dibasic acid.¹ Upon catalytic hydrogenation a crystalline dibasic acid, $C_{12}H_{22}O_4$, identical with decane-1,10-dicarboxylic acid was obtained. After oxidative degradation of the natural wound hormone, sebacic acid was obtained in good yield. The substance must therefore be 1-decene-1,10-dicarboxylic acid:



This structure has been confirmed by synthesis of 1-decene-1,10-dicarboxylic acid. The resulting product was found to be identical with the natural product both in chemical properties and in physiological activity.

1-decene-1,10-dicarboxylic acid is capable of evoking intensive wound periderm formation in washed discs of potato tuber. It would seem probable therefore that the material with which Haberlandt³ dealt in his early investigations of wound hormone activity in the potato was at least in part 1-decene-1,10-dicarboxylic acid. It would seem appropriate and convenient to refer to this substance as "traumatic acid"⁴ (from Greek *τραύμα* = wound). A detailed report of these investigations will appear elsewhere.

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THE PLASMODIUM OF HEMITRICHIA VESPARIUM (BATSCH) MACBR

SCLEROTIUM collected from a partially decayed log furnished the source of material used in studying certain cytoplasmic elements in the plasmodium of a Mycetozoon species that had been treated with mitochondrial methods of technique.

When exposed to a humid condition in a large dish, the revived sclerotium issued a bright yellow stream of plasmodium on the woody substratum that had been thoroughly moistened. At this stage of development it was impossible to make an accurate determination of the species involved. For over four months the plasmodium was active under the stimulus of food, moisture and slight light, but when exposed to a bright,

² J. Bonner and J. English, *Plant Physiol.*, 13: 331, 1938.

³ G. Haberlandt, *Sitzungsb. d. Königl. Preuss. Akad. d. Wiss.*, 16: 318, 1913.

⁴ Report of work carried out with the aid of the Works Progress Administration, Official Project No. 665-07-3-83, Work Project Number 9809.