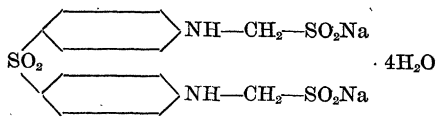
SCIENTIFIC APPARATUS AND LABORATORY METHODS

DIASONE. A NEW AND ACTIVE CHEMOTHERAPEUTIC AGENT

DISODIUM formaldehyde sulfoxylate diaminodiphenylsulfone, designated as Diasone, has the following chemical structure:



It was synthesized by us in 1937.[1,2] Diasone is water soluble, forming fairly concentrated solutions, stabilized by the addition of small quantities of sodium bicarbonate. For years the writer was interested in the detoxifying effect of sodium formaldehyde sulfoxylate upon arsphenamine,[3] the toxicity of which was greatly diminished without proportionate reduction of the therapeutic effect. In other words, the ratio of $\frac{\text{maximum tolerated dose}}{\text{minimum therapeutic dose}}$ was shifted in favor of neoarsphenamine, which is a sodium formaldehyde sulfoxylate derivative of arsphenamine. This has been conspicuously demonstrated in rat trypanosomiasis, rabbit syphilis and human syphilis.

We found that the same improvement in the ratio $\frac{\text{maximum tolerated dose}}{\text{minimum therapeutic dose}}$ occurred when we combined 4,4′-diaminodiphenylsulfone with sodium formaldehyde sulfoxylate. The reduction in toxicity was found to be most impressive. The diaminodiphenylsulfone is known to be toxic to mice, which tolerate at most a single oral dose of 0.200 gms per kilogram of body weight.[4] The maximum tolerated dose of Diasone given to mice by mouth is much larger, namely 4 grams. Rats tolerate a single dose of 7 grams per kilo and rabbits 3½ grams per kilo. Dogs 30 to 40 pounds in weight which were given 60 consecutive daily doses of 1 gram each tolerated the drug without loss in weight or any visible disturbance.

As to the therapeutic efficiency, we found that mice, infected with the streptococcus hemolytic strain C 203 and treated with Diasone by the drug food method, were cured—the drug proving to be as effective as sulfanilamide. In similar experiments, performed on mice infected with pneumococcus type II, Diasone appeared to be almost as effective as sulfadiazine.

The most important therapeutic property of this chemical compound, however, manifests itself in experimental tuberculosis. Since 1938,[5] various investigators became interested in sulfanilamide in the treatment of tuberculosis in guinea pigs. Feldman and Hinshaw[6] extended this observation to sulfapyridine and finally to a derivative of diaminodiphenylsulfone, known as Promin.[7] Callomon[8] found Diasone to be decidedly less toxic than Promin. When mortality and histological changes due to tuberculosis in guinea pigs were considered, Diasone produced the most beneficial therapeutic results among various compounds administered, including Promin. Feldman, Hinshaw and Moses[9] also found Diasone to be an effective therapeutic agent in experimental tuberculosis.

With its background of low toxicity and effectiveness in experimental infection, this drug gives promise of favorable clinical application in tuberculosis.

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[1] The chemistry of Diasone is described in a paper by G. W. Raiziss, R. Clemence and M. Freifelder, entitled "Synthesis and Chemical Properties of Diasone." To be published.

[2] A similar product was simultaneously and independently prepared, using a different method, by H. Bauer and S. M. Rosenthal, "Studies in Chemotherapy" VII. Some new sulphur compounds active against bacterial infections, *Pub. Health Rep.*, 53: 40, 1938.

[3] G. W. Raiziss, J. F. Schamberg and J. A. Kolmer, *Proc. Soc. Exp. Biol. and Med.*, 5: 18, 1921. G. W. Raiziss and M. Falkov, *Jour. Biol. Chem.*, 5: 46, March, 1921.

[4] G. W. Raiziss, M. Severac and J. Moetsch, "The Toxicity and Therapeutic Effectiveness of Diasone." To be published.

[5] G. A. H. Buttle and H. J. Parish, "Treatment of Tuberculosis in Guinea Pigs with Sulphanilamide," *Brit. M. J.*, 2: 776, 1938.

[6] W. H. Feldman and H. C. Hinshaw, *Proc. Staff Meet. Mayo Clin.*, 14: 174, 1939.

[7] W. H. Feldman, H. C. Hinshaw and H. E. Moses, *Proc. Staff Meet. Mayo Clin.*, 15: 695, 1940; 16: 187, 1941.

[8] F. F. T. Callomon, *Am. Rev. Tuberculosis*, 52: 1, January, 1943.

[9] W. H. Feldman, H. C. Hinshaw and H. E. Moses, *Arch. of Pathology*, 36: 64–73, July, 1943.

BOOKS RECEIVED

FERNALD, MERRITT LYNDON and ALFRED CHARLES KINSEY. *Edible Wild Plants of Eastern North America.* Illustrated. Pp. xiv + 452. Idlewild Press. $3.00.

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KOLTHOFF, I. M. and E. B. SANDELL. *Textbook of Quantitative Inorganic Analysis.* Illustrated. Pp. xvii + 794. The Macmillan Company. $4.50.

REMICK, A. E. *Electronic Interpretations of Organic Chemistry.* Illustrated. Pp. v + 474. John Wiley and Sons. $4.50.

SHAND, S. JAMES. *Eruptive Rocks. Their Genesis, Composition, and Classification, with a Chapter on Meteorites.* Illustrated. Pp. xvi + 444. John Wiley and Sons. $5.00.

TREWARTHA, GLENN T. *An Introduction to Weather and Climate.* Illustrated. Pp. xi + 545. McGraw-Hill Book Company. $4.00.