4719

The Actions of Synthetic Salicyluric Acid.

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The occurrence of a natural salicyluric acid in the body, and its significance as a detoxification product, after administration of salicylates, analogous to hippuric acid after benzoates, have been much discussed but not conclusively settled. Owing to previous negative results by one of us[1] with chemical methods of isolation from urines, it was attempted to obtain indirect evidence on the question by a study of the pharmacological actions of synthetic salicyluric acid. The pure compound was synthesized according to E. Fischer's method[2] by Dr. Robert T. Dillon of the California Institute of Technology, Pasadena, to whom our thanks are due.*

It was found that synthetic salicyluric acid was comparatively stable *in vitro*, since it was not hydrolyzed in incubated buffer-salt solutions with hydrion concentrations falling within the range of body fluids, and in these solutions containing ferments, yeast and bile-salts. Some hydrolysis occurred in solutions of pH 2 and 14 and complete hydrolysis in strong acids and alkalies.

On the other hand, the compound suffered marked hydrolysis in its passage through the body, since from one-half to three-fourths of the total excreted salicyl in urines of human subjects (6) consisted of ordinary salicylate. The total salicyl excretion was about 88% of the total administered (from 4 to 28 gm.). The effects on urinary nitrogenous metabolites were variable or insignificant. The symptoms of salicylism in human subjects were weak, even with the highest oral doses, but in white mice, white rats, pigeons and a dog (total, 89 animals) typical symptoms of salicyl poisoning were demonstrated after hypodermic and intravenous administrations. The M.F.D. in the majority or 60% of the mice was 1.13 gm., and in rats 3 gm., per kilo. The toxicity in mice was proportional to the amount of liberated salicylate, assumed from the results on urinary partition, and corroborated by the actual toxic dose of salicylate.

Accordingly, the results obtained indicate that significant quanti-

[1] Hanzlik, P. J., *J. Pharm. Exp. Therap.*, 1917, x, 461.

[2] Fischer, E., Ber., 1909, xlii, 215.

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ties of salicyluric acid can not be expected in the body after administration of salicylates, and therefore, the alleged biochemical rôle of the compound is not sustained. This agrees with the negative results of chemical isolation, and also with the vast majority of results on excretion which show that the salicylates are excreted mainly unchanged.

4720

Duck Disease Studies. III. Salt Content of Soils in Disease and Non-disease Areas.*

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It has been shown[1] that oral administrations of certain inorganic salts, alone or in combination, are definitely toxic for ducks. The greatest toxicity in these experiments was found in sodium chloride and sodium sulphate mixtures containing in addition either magnesium or bicarbonate *together with nitrate ions.* The symptoms exhibited by the birds after feeding with these mixtures resembled in many respects those noted in "duck disease". The salt composition of soils from disease and non-disease areas was studied to attempt to correlate these experimental findings with the naturally occurring condition.

Soil samples were obtained from the following areas:

A. Disease Areas. 1. San Joaquin Valley (West of Pond, Calif.). 2. Tule Lake (Modoc County, Calif.). 3. Government Sump (South of Klamath Falls, Ore.).

B. Non-disease Areas. 1. San Joaquin Valley (Los Banos area). 2. Isolated ponds south of Klamath Falls, Ore.).

All samples were taken near the surface of the soil and within a few yards of the water's edge. Analyses were made on water extracts. Carbonate, bicarbonate, and chloride were determined by titration. Calcium, magnesium, and sulphate were approximated

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[1] Shaw, P. A., PROC. SOC. EXP. BIOL. AND MED., 1929, xxvii, 6.