CHEMOTHERAPY OF TUBERCULOSIS

Part I. Synthesis of Possible Lipophilic Chemotherapeuticals of the Sulphonamide and Sulphone Series derived from Fatty Acids, including those of the Chaulmoogra Group

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Received October 15, 1949

(Communicated by Major-General Sir S. S. Sokhey, Kt., F.A.Sc.)

The present state of our knowledge in the Chemotherapy of Tuberculosis, the significance of the results of testing the drugs *in vitro* and *in vivo*, and the peculiar pathological features of the disease have been described by us recently.[1] In accordance with the ideas, work has been undertaken to synthesise compounds that are likely to act powerfully on the tubercle bacilli both *in vitro* and *in vivo*.

For the discovery of drugs lethal to the tubercle bacilli, there are three methods that could be followed:—

(1) to start from a compound showing action on the tubercle bacilli and by introducing substituents attempt to arrive at a more powerful drug; (2) to examine a cross-section of compounds belonging to diverse groups and structures to detect the structural features associated with tuberculocidal activity and (3) to design inhibitors that could effectively interfere with any of the vital nutritional, metabolic or respiratory processes of the bacilli so as to cause death; these inhibitors could be designed only on the basis of the knowledge of the chemistry of the abovementioned processes. We have undertaken work employing all these methods and the compounds synthesised are presented in this and the succeeding communications. The testing of the compounds is under way.

Of the numerous compounds and substances tested so far for their curative action in experimental tuberculosis, only derivatives of sulfanilamide and 4:4′-diaminodiphenyl sulphone as well as the antibiotic streptomycin, have shown very significant protective action. But these compounds have not shown the same degree of protection in tuberculosis and leprosy clinically. The synthesis and study of lipophilic derivatives of sulphanilamide and 4:4′-diaminodiphenyl sulphone were undertaken to try out whether this would lead to any compound or compounds with better protective action.

The present communication is concerned with the synthesis of some simple *fatty* acyl derivatives of the sulfanilamides in clinical usage and 4:4′-disubstituted diphenyl sulphones. Among the fatty acids used in this exploratory study, hydnocarpic acid has been chosen as the representative