CHEMOTHERAPY OF BACTERIAL INFECTIONS

IX. Synthesis of Some Sulphathiazole Derivatives

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Considerable attention is being given in recent times to the discovery of sulphanilamide derivatives for the treatment of infections of the typhoid-cholera-dysentery group. A drug to be ideal for these intestinal infections should, besides possessing very strong bacteriostatic and bactericidal action against the organism concerned, remain localised in the intestine with little of it being absorbed from there into the blood stream. Such a drug should be harmless even with very high concentrations in the intestine because the toxic effects produced by the drugs are mainly the results of their high concentrations in the blood. Basing on this principle, Marshall *et al.*[1] brought forward sulphanilylguanidine as a drug suitable for the treatment of the intestinal infections. Though there are fairly good reports on the treatment of bacilliary dysentery with this drug, it does not impress on us to be as excellent as sulphanilamide or sulphathiazole in their respective spheres of action (compare for example[2]). We attempted therefore to prepare other compounds which may fulfil the criteria mentioned above.

It has previously been reported[3] from this laboratory that sulphathiazole protects mice against septicæmia due to *B. typhosum* and that it shows distinct bacteriostasis against *V. cholerœ in vitro* in as low a concentration as 3 mg. per cent., while sulphanilamide even in 10 mg. per cent. shows no bacteriostasis. The disadvantage of this drug for our present purpose is that it is very rapidly absorbed from the intestine so that it is difficult to attain very high concentrations of this in the intestine without increasing correspondingly the concentration in the blood to dangerous limits. So we sought to prepare derivatives of sulphathiazole of such a type that the original therapeutic activity may not be much impaired and at the same time its absorption from the intestine will considerably be reduced. The poor absorption of sulphaguanidine from the intestine which is alkaline in pH, appeared to us to be due to its insolubility in alkali and so we attempted to prepare derivatives of sulphathiazole of formula (I) or (II).