precipitating the halide with silver nitrate. To verify that no bromide was carried down by the protein precipitation, similar experiments were done in which radioactive sodium bromide was injected into mice or added to organs *in vitro*, and these showed that on the average 91 per cent of the bromine was found in the silver precipitate. The fraction of bromine in the blood and kidney that was inorganic increased during the first two hours after intravenous injection and then remained constant at 93 per cent. The amount of inorganic bromide in the liver is shown in Fig. 2 and is seen to be constant.

These results suggest that the drug is rapidly absorbed and metabolized by the liver, about half the bromine being liberated as inorganic bromide, the remainder as one or more organic metabolites. Most of the latter are rapidly excreted in the fæces. These conclusions are borne out by metabolism experiments after subcutaneous injection of the drug. It was found that after several days, 95 per cent of the bromine in the urine was inorganic, but only 43 per cent in the fæces.

These experiments show that this œstrogen is rapidly broken up after absorption, but give no indication as to whether œstrogenic action is due to small amounts of unchanged drug, or to one of the metabolites formed. In particular, the effect may well be due to a metabolite which does not contain bromine.

The investigation was extended by the administration of triphenylbromoethylene to two human subjects. In one case the drug was given subcutaneously in oil, in the other orally, and the activity in the blood and the elimination in urine and fæces was followed. The few results obtained are consistent with the view that the metabolism of the drug in the human subject is similar to that in the mouse.

The full results will be reported elsewhere.

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Mode of Action of Basic Antibacterial Substances

That spermine and streptomycin "do not affect the respiration of yeast and thus have no direct bactericidal activity", as stated by Massart[1], is a conclusion with which many will not agree. Apart from the dangers inherent in applying to bacteria results which have been obtained with yeast, there are few grounds for supposing that the facility with which a drug can impair bacterial respiration bears any simple relation to its growth-inhibiting properties. Indeed, Ferguson and Thorne[2] have shown that the order in which six aminoacridines repress the respiration of *B. coli* (when the substrates were glucose, pyruvic acid, lactic acid, asparagin or oleic acid) bears no obvious relation to the order of their activity in retarding the growth of this bacterium.

Some will also question Massart's conclusion that 'polymerization' (that is, micelle formation) makes an important contribution to the antibacterial action of his test substances (trypaflavine, methylene blue, crystal violet and quinine) by increasing their effective molecular weight.

In the acridine series (of which trypaflavine is a member) the critical micelle concentration has been investigated by one of us (R. J. G.) using three criteria: (i) deviation from Beer's Law; (ii) conductimetric maxima; and (iii) formation of blue colour with potassium tri-iodide. It was found that this concentration often lay well above the minimal antibacterial concentration. Furthermore, it is easy to point out pairs of closely related drugs where a rise in critical micelle concentration is accompanied by heightened antibacterial activity. For example, 5-amino-1-methylacridine, because of a steric effect, does not reach its critical micelle concentration until the solution is twice as concentrated as is necessary in the case of 5-aminoacridine; yet the former is bacteriostatic, for example, to *Streptococcus pyogenes*, at half the minimal effective concentration of the latter[3].

Prof. Massart's argument depends upon the assumption that the critical micelle concentrations of spermine and streptomycin are higher than those of quinine and the dyes. Although the highly polar character of spermine and streptomycin makes this likely, no actual figures have been published.

It has often been observed that, in a series of cationic substances, an increase in the molecular weight goes parallel with increased antibacterial activity (Albert[4], quoted by Massart through Dubos[5]), and the following explanation of this phenomenon has been given. "This requirement of size is to provide a sufficiently great area for adsorption; it depends on the fact that increase in the number of atoms in a molecule increases its Van der Waals' attraction, while the kinetic energy of translation, which is the force tending to remove the molecule, is independent of molecular size"[3]. However, the forces used up by trypaflavine and other dyes in micelle formation are scarcely likely to be available for combination with the bacterial receptors.

It is appreciated that, in a series of amines, some physical properties are dependent upon the presence of micelles (for example, the formation of a blue colour with potassium tri-iodide). But other properties, particularly those which involve accumulation at a surface, are at a maximum when micelles are absent (for example, foaming[6]).

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