It is important, therefore, to choose a suitable dose schedule of polymyxin B for the preferential depletion of tissue histamine in the rat, for prolonged treatment reduces the 5-hydroxytryptamine content of tissues as well as that of histamine. Other potent histamine liberators such as compound 48/80[2,4,5] also release both histamine and 5-hydroxytryptamine, but whilst the release of 5-hydroxytryptamine by compound 48/80 usually precedes that of histamine, with polymyxin B the reverse occurs.

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The Determination of Meprobamate as the Dixanthyl Derivative

SIR,—Roth and others[1] have characterised meprobamate (2,2-di(carbamoyloxymethyl) pentane) by means of its dixanthyl derivative and report only a melting point of 182°. Algeri and others[2] also used the dixanthyl derivative to identify meprobamate, but give no constants for their derivative. We obtained a higher melting point product, by dissolving meprobamate and xanthenol in glacial acetic acid and allowing the solution to stand for 10 hours or more at room temperature[3]. After recrystallisation from hot methanol and drying to constant weight, the nitrogen content of the crystals, which melted at 188° to 189°, was found to be 4·80 per cent. This value agrees with the calculated value of 4·84 per cent for a product of molecular weight 518·42 derived from the reaction of 2 moles of xanthenol and 1 mole of meprobamate.

The spectral absorbance of dixanthyl meprobamate in various solvents showed two maxima at 240 and 289 mμ similar to those shown by solutions of 9-xanthenol. An E (1 per cent, 1 cm.) (λ289 mμ) of 142·5 was found for solutions of the dixanthyl derivative in methanol, ethanol and isopropanol, and was used to calculate the solubility of the compound in saturated solutions of the various solvents shown in Table I.

The best yields of dixanthyl meprobamate were obtained by reacting 0·100 g. of meprobamate with 0·3 g. of 9-xanthenol in 5 ml. of glacial acetic acid, and seeding with 5 to 10 μg. of dixanthyl meprobamate crystals. After standing for 16 hours, 45 ml. of 80 per cent aqueous isopropanol was added to the reaction flasks and the solutions refrigerated for 1 hour. The crystals were transferred to a tared sintered glass filter with 15 ml. of the aqueous isopropanol and dried to constant weight at 100°. The weight of the crystals multiplied by 0·3769 gives

TABLE I

SOLUBILITY OF DIXANTHYL MEPROBAMATE IN VARIOUS SOLVENTS AT 25°

Solvent	g./100 ml.
Methanol	0·040
Ethanol	0·022
Isopropanol	0·013
Butanol	0·027
Glacial acetic acid	0·25
Ether	0·22
Acetone	2·0
Dimethyl formamide	2·0
Dioxane	over 10·0
Chloroform	over 10·0
Benzene	5·0
Isopropanol 72 per cent v/v Glacial acetic acid 10 " " v/v Water 18 " " v/v	0·008
Water	0·0005

the weight of meprobamate recovered as the dixanthyl derivative. The actual yields and the yields corrected for a loss of 4 mg. of dixanthyl meprobamate by solubility are shown in Table II.

TABLE II

RECOVERY OF MEPROBAMATE AS THE DIXANTHYL DERIVATIVE

Test	Recovery per cent	Recovery corrected for solubility per cent	Melting-point uncorrected °C
1	94·48	95·91	187
2	95·05	96·50	188
3	94·78	96·23	188
4	94·78	96·23	188
5	95·39	96·84	188
6	94·29	95·72	188

The nitrogen values for the products from 3 of these tests were 4·90, 4·85 and 4·75 per cent.

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