Some coalescence of the globules has occurred and long filaments developed which solidified on cooling.

These experiments were repeated with emulsions containing less than 1·0% w/w cetostearyl alcohol. In no case were we able to demonstrate the presence of filamentous structures.

These observations provide some evidence of migration of cetostearyl alcohol and indicate that its ultimate location is dependent on the previous history of the emulsion. In the aqueous phase the fatty alcohol is probably combined with the surfactant in a liquid crystalline state as described by Barry & Shotton (1967) for a similar system. The filamentous structures shown here are not necessarily of precisely the same form as those of the gel to which we earlier attributed the rheological properties of our emulsions (Talman, Davies & Rowan, 1967; 1968), although they are likely to be of the same constitution. The presence of such a gel is indicated by the aggregates of globules which appear to be immobilized within a matrix and are difficult to disperse. The fine structure of the gel has so far evaded detection, undoubtedly due to the limits of resolution of the optical microscope.

Department of Pharmaceutics,
School of Pharmacy,
Brighton College of Technology,
Brighton, BN2 4GJ, England.

F. A. J. TALMAN
E. M. ROWAN (Miss)

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Supersensitivity to tyramine not due to monoamine oxidase inhibition

SIR,—Our observation that chlorobethanidine [1-(*o*-chlorobenzyl)-2,3-dimethylguanidine; BW 392C60], a bretylium-like agent greatly enhanced the responses of the rat isolated vas deferens to tyramine, prompted us to investigate the mechanism involved. Chlorobethanidine differs from bretylium in showing an inhibitory action on monoamine oxidase (Gessa, Cuenca & Costa, 1963). Since most monoamine oxidase inhibitors have been shown to potentiate tyramine responses in a number of preparations (Furchgott, Weinstein & others, 1955; Balzer & Holtz, 1956; Corne & Graham, 1957; Goldberg & Sjoerdsma, 1959; Spano, 1966; Laporte, Jané & Valdecasas, 1968) and it has been postulated that this potentiation is related to monoamine oxidase inhibition (Goldberg & Sjoerdsma, 1959), it could be assumed that the potentiation observed by us could be explained on the basis of its enzyme inhibition. However, taking into account the fact that the doses of chlorobethanidine which determined tyramine enhancement in our experimental conditions were devoid of monoamine oxidase inhibitory activity in the rat heart (Gessa, Cuenca & Costa, 1963), the possibility was entertained that these doses did not inhibit the monoamine oxidase activity of the rat vas deferens. To demonstrate our working hypothesis, the influence of chlorobethanidine on the responses of the rat isolated vas deferens to tyramine or rat vas deferens monoamine oxidase activity, or both, was investigated.

Rats were injected intraperitoneally with different doses of the drug and killed 6 hr later and both vasa were removed. Cumulative dose response curves for

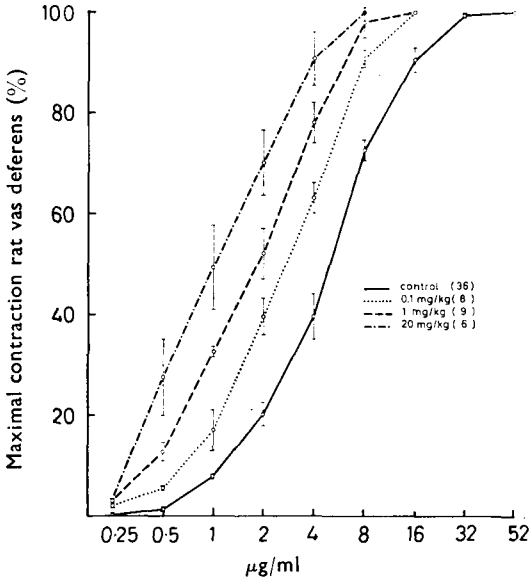

FIG. 1. Modification of the cumulative log concentration-response curves of tyramine by different doses of chlorobethanidine. Rat isolated vas deferens. The mean values and their standard errors are shown. The drug was given 6 hr before the animals were killed. In brackets, the number of experiments.

tyramine were done in controls (36 experiments) and treated animals (23 experiments). Vas deferens monoamine oxidase activity was also measured in some treated animals (Bogdanski, Weissbach & Udenfriend, 1957).

Chlorobethanidine (0·1 mg/kg) greatly enhanced the responses of the rat isolated vas deferens to tyramine (Fig. 1) with the dose response curve clearly shifted to the left. Higher doses (1 and 20 mg/kg) produced a more pronounced supersensitivity (Fig. 1). Vas deferens monoamine oxidase activity in the animals treated 6 hr before with the lower effective doses of the drug (0·1 and 1 mg/kg) showed no difference from that of controls. The 20 mg/kg dose produced 38% inhibition (mean of 3 exp.).

It can then be concluded that the potentiation of the tyramine responses elicited by chlorobethanidine is not related to monoamine oxidase inhibition.

Departamento de Farmacología,
Facultad de Medicina,
Universidad de Barcelona,
Spain.

E. CUENCA
J. FORN
F. G. VALDECASAS

July 28, 1968

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