Potentiation of methamphetamine aggregate toxicity in mice by *diethyldithiocarbamate*

SIR,—Diethyldithiocarbamate (DDTC), a metabolite of disulfiram, inhibits the enzyme dopamine-β-hydroxylase, causing an increase in dopamine and a decrease of noradrenaline in mouse brain (Hashimoto, Ohi & Imaizumi, 1965). It has been postulated that dopamine release is a mechanism for amphetamine-induced locomotor stimulation and stereotyped behaviour (Rossum & Hurkmans, 1964; Randrup & Jonas, 1967). If dopamine release also is involved in methamphetamine-induced aggregate toxicity, DDTC should potentiate the effects of submaximal doses of methamphetamine.

Groups of 10 male CF # 1 mice, 18–22 g, were housed in covered plastic cages (30 cm × 15 cm × 13 cm). The LD50 for methamphetamine aggregate lethality was 6 mg/kg, intrapenitoneally, and this dose was used in all experiments. DDTC was administered intraperitoneally 30 min before methamphetamine and deaths were counted 24 hr later.

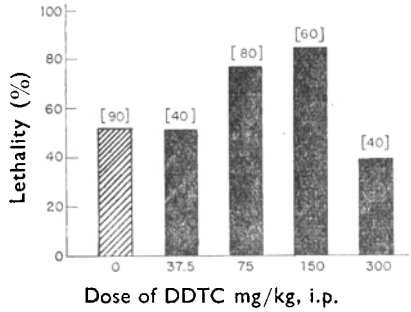

FIG. 1. The influence of DDTC on the aggregate lethality produced by methamphetamine, 6 mg/kg, i.p. Total number of mice used for each dose of DDTC is in brackets.

As shown in Fig. 1, DDTC, 75 and 150 mg/kg, significantly *increased* the aggregate lethality of methamphetamine. The levels of significance as determined by the Fisher Exact Probability test were $P < 0.005$ and $P < 0.001$, respectively (Siegel, 1956). These doses of DDTC (75 and 150 mg/kg) do not affect overt behaviour in mice and are well below its LD50 (1500 mg/kg) (Hald, Jacobsen & Larsen, 1952). DDTC 300 mg/kg markedly depressed spontaneous motor activity in normal mice, which may explain why further potentiation of methamphetamine was not seen at this dose.

DDTC (75 and 150 mg/kg), which significantly increased methamphetamine lethality, also reverses reserpine-induced hypothermia (Barnett & Taber, 1968); whereas, DDTC, 37·5 mg/kg, was ineffective in both procedures. These two effects of DDTC can be explained by its ability to increase brain dopamine content.

It has been postulated that the cause of amphetamine aggregate lethality is increased motor activity (Greenblatt & Osterberg, 1961) or hyperthermia (Greenblatt & Osterberg, 1961; Menon & Dandiya, 1967). Since DDTC (75–300 mg/kg) produces hypothermia in normal mice (Barnett & Taber, 1968), it seems likely that it potentiates methamphetamine aggregate lethality by increasing the locomotor stimulant rather than the hyperthermic effects of methamphetamine.

Department of Pharmacology,
Schering Corporation,
Bloomfield, New Jersey, U.S.A.

ALLEN BARNETT
ELLEN PESCHEL

April 1, 1968

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Crystallization in polyhedral emulsion particles

SIR,—During an investigation of the properties of emulsions, preparations were made by adding a mixture of cetyl alcohol in liquid paraffin at 65° to an aqueous solution of sodium dodecyl sulphate at the same temperature and stirring with a Silverson mixer until cold. The systems used were liquid paraffin 100 g, water 300 g and:

	A	B	C	D	E	F	G	H	I
Sodium dodecyl sulphate ..	0·8	1·2	1·6	2·0	2·4	2·8	3·2	3·6	4·0 g
Cetyl alcohol ..	7·2	10·8	14·4	18·0	21·6	25·2	28·8	32·4	36·0 g

Non-spherical particles were observed microscopically in each cooled emulsion, even though the concentration of alcohol in liquid paraffin was sufficiently low to ensure that the globules were essentially liquid. These deformed globules varied in shape from flattened spheres to polyhedra, and contained anisotropic crystals which lay along the straight sides of the globules. Crystals were formed even though the alcohol to liquid paraffin ratio was much less than 8:5, which has been quoted as the minimum ratio for crystallization in similar systems by Groves & Scarlett (1965). The crystals I observed were usually acicular but occasionally flat and hexagonal. They were not easily visible in ordinary light but showed up clearly when a specimen was mounted between crossed polars. The system of lowest emulsifier concentration (A) contained some large globules

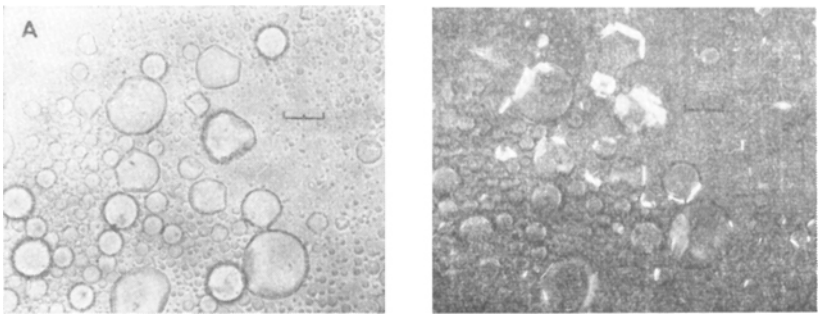

FIG. 1. Photomicrographs of System A mounted in 50% v/v glycerol in water. (a) Ordinary light (b) crossed polars. One division = 10 μ.