

Chlorpromazine-lysergic acid diethylamide antagonism

SIR,—Lysergic acid diethylamide (LSD) produces an increase in the 5-hydroxytryptamine (5-HT) content of rat brain (Freedman, 1961; Freedman & Giarman, 1962), which may be related to many of its central effects like tremors, excitement and hallucinations (Udenfriend, Weissbach & Bogdanski, 1957; Giarman & Freedman, 1965). It is also known that chlorpromazine antagonizes the LSD-induced behavioural effects in man and animals (Ray & Marrazzi, 1960) and the EEG changes in dogs (Djahanguiri & Guiti, 1966). We therefore examined the effect of chlorpromazine on the LSD-induced increase in the brain 5-HT.

Adult albino rats, 100–150 g, were injected intraperitoneally with LSD (0.25 mg/kg) and chlorpromazine (0.15 mg/kg). In one group of rats, LSD and chlorpromazine were given simultaneously; the second group had LSD followed by chlorpromazine after 10 min; a third group were given chlorpromazine 10 min before the LSD. Control animals had normal saline. The rats were killed $\frac{1}{2}$ hr after the administration of drugs and the brain (excluding the olfactory lobe, cerebellum and pituitary glands) rapidly removed. The 5-HT was extracted by the method of Amin, Crawford & Gaddum (1954) and assayed on the oestrous uterus of the rat (Parratt & West, 1957).

TABLE 1. EFFECT OF CHLORPROMAZINE ON LSD-INDUCED INCREASE IN THE 5-HT CONTENT OF RAT BRAIN

Drugs	Dose mg/kg	Time interval in hr	No. of rats	Brain 5-HT content in $\mu\text{g/g} \pm \text{s.e.}$	Probability P
Control	—	$\frac{1}{2}$	10	0.38	—
LSD	0.25	$\frac{1}{2}$	9	0.48 ± 0.03	<0.01
Chlorpromazine	0.15	$\frac{1}{2}$	7	0.37 ± 0.05	<0.05
LSD + Chlorpromazine	0.25 + 0.15	$\frac{1}{2}$	6	0.47 ± 0.006	<0.01
LSD (after 10 min) followed by Chlorpromazine	0.25 + 0.15	$\frac{1}{2}$	6	0.45 ± 0.04	<0.01
LSD followed by Chlorpromazine (after 10 min)	0.25 + 0.15	$\frac{1}{2}$	8	0.46 ± 0.07	<0.05

The results (Table 1) show that pre-, simultaneous or post-administration of chlorpromazine does not modify the LSD-induced increase in brain 5-HT, even though according to Ray & Marrazzi (1960) it does antagonize the behavioural effects of the hallucinogen. This finding is in agreement with Hess & Doepfner (1961) who, pretreating rats with a monoamine oxidase inhibitor and then giving tryptophan, concluded that it was possible to produce alterations in brain 5-HT levels without corresponding changes in behaviour.

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Polyhedral emulsion particles

SIR,—In 1965, irregular polyhedral particles were reported in a semi-solid emulsion system (Groves & Scarlett, 1965) and it was suggested that they may have arisen in areas of localized close packing within the system which produced distortion of the molten oil phase droplets at elevated temperatures, the shape being retained when the droplets cooled and solidified. However, the fact that close packing could occur in a system with a disperse ratio of 0.225 was of interest since this would not be anticipated until the concentration approached a value of approximately 0.74, the theoretical limit for a system consisting of equal diameter spheres.

We have now examined systems similar to the emulsion system previously investigated and consisting of an oil phase of equal parts by weight of ceto-stearyl alcohol and liquid paraffin dispersed in 0.5% w/w aqueous cetrimide solutions. A series of dispersions containing different amounts of the oil phase were prepared under standardized conditions. The molten oil phase at 70° was added to the aqueous phase at the same temperature and stirred with a high speed laboratory stirrer (Silverson, fitted with homogenizer head) until the mixture had cooled to 30°, when the stirrer was switched off and cooling allowed to proceed undisturbed to room temperature.

Samples were withdrawn and particle size distributions measured with a Coulter Counter Model A (Industrial) fitted with a 70 μ orifice tube. Results are summarized in Table 1.

TABLE 1. PARTICLE SIZE DISTRIBUTIONS OF THE DISPERSIONS PREPARED WITH DIFFERENT DISPERSE PHASE RATIOS. MEASURED WITH A COULTER COUNTER MODEL A (INDUSTRIAL) FITTED WITH A 70 μ ORIFICE TUBE (GROVES, 1966)

Dispersion phase ratio (weight)	Particle size distribution parameters ¹	
	D50 (μ)	Standard deviation
0.01 ²	2.75	3.20
0.05	3.40	2.03
0.10	5.30	1.89
0.15	5.00	1.90
0.20	4.65	1.87
0.30	4.85	2.06
0.40	8.30	1.92
0.50	8.50	2.00
0.55 ³	8.00	2.21

¹ From a logarithmic probability plot of the cumulative weight percent distribution.

² The data on this sample is unreliable since microscope examination showed that most particles were below the limit of detection of the Counter under the conditions of measurement.

³ Attempts to prepare systems more concentrated than 0.55 were not successful.

Using a photomicrographic technique, at least 1,000 particles from each sample were classified visually as either spherical or non-spherical and the results are shown in Fig. 1.