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INFLUENCE OF PSYCHOTROPIC DRUGS AND β-DIETHYLAMINOETHYL-DIPHENYLPROPYLACETATE (SKF 525-A) ON MESCALINE-INDUCED BEHAVIOR AND ON TISSUE LEVELS OF MESCALINE IN MICE*

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Abstract—The effects of psychotropic drugs or SKF 525-A on mescaline-induced behavior and on the brain, plasma, liver and eye levels of mescaline were studied in mice. Lower doses of promazine (10 mg/kg), trifluoperazine (1 mg/kg) and diazepam (2 mg/kg) were not effective antagonists of mescaline-induced (25 mg/kg) increased locomotor activity or scratching responses. Mesoridazine (10 mg/kg) and diazepam (20 mg/kg) partially prevented mescaline-induced gross behavior, effectively blocked scratching responses to mescaline, produced no catalepsy and did not elevate tissue mescaline contents. Higher doses of trifluoperazine (5 and 15 mg/kg), mesoridazine (30 and 45 mg/kg) and promazine (30 mg/kg) blocked not only the activity-increasing effects of mescaline but also the normal locomotor movements; with the exception of 30 mg/kg of mesoridazine, these treatment schedules induced a cataleptic-like state and markedly enhanced tissue levels of mescaline. SKF 525-A potentiated the mescaline-antagonizing effects and mescaline-retaining activity of several compounds listed. In the doses indicated, imipramine (5, 20 and 50 mg/kg), desmethylimipramine (20 mg/kg), trifluoperazine sulfoxide, promazine sulfoxide (15 mg/kg), promethazine (15 and 30 mg/kg) and SKF 525-A (50 mg/kg) were not effective antagonists of mescaline-induced increased locomotor activity or scratching responses.

Phenothiazines are known antagonists of the hallucinogens. In a recent study, Shah *et al.* [1] have shown that, although 15 mg/kg chlorpromazine (CPZ) blocks the mescaline-induced altered behavior in mice, it induces a cataleptic-like state, marked hypothermia and enhances brain and tissue mescaline concentrations [2]. Sulser and Dingell [3] first furnished evidence that CPZ, in low doses, potentiates and prolongs the amphetamine effects in rats and that this is associated with a marked and prolonged elevation of amphetamine levels in the brain due to an inhibition of the metabolism of amphetamine by CPZ. Tricyclic antidepressants also enhance and prolong various behavioral effects elicited by amphetamine in rats by inhibiting the aromatic hydroxylation of amphetamine [4–8].

β-Diethylaminoethyl diphenylpropylacetate hydrochloride (SKF 525-A) has been shown to modify the actions and metabolism of several drugs; e.g. it prolongs the hypnotic action of hexobarbital in rats and mice [9], enhances the analgesic action of methadone, meperidine, morphine and codeine [10], and blocks metabolism of CPZ *in vivo* and *in vitro* in rats [11] and rabbits [12]. Δ^1-tetra-hydrocannabinol prolongs barbiturate sleeping time in mice and this effect is augmented by SKF 525-A [13].

The effects of piperidine and piperazine phenothiazines, benzodiazepines and tricyclic antidepressants on the mescaline-induced altered behavior and on the tissue levels of the hallucinogen have not been investigated. In the present study, dose–response relationships on antagonism and interactions between mescaline and several such psychotropic drugs were investigated. Since SKF 525-A blocks the metabolism of several compounds, the combined effect of this agent and the psychotropic drugs was also examined.

MATERIALS AND METHODS

Drugs. [8-^{14}C]mescaline hydrochloride (sp. act., 4·53 mCi/m-mole) was purchased from New England Nuclear (Boston, Mass.). The chemical and radio-chemical purity was checked in our laboratory by column and thin-layer chromatography and found to be approximately 97 per cent. Thin-layer chromatograms displayed a single peak when scanned by the radiochromatogram scanner (Packard model 7201). Nonlabeled mescaline hydrochloride was obtained from Sigma Chemical Co. (St. Louis, Mo.) and had a purity of over 99 per cent. The [8-^{14}C]-mescaline was prepared in 0·9% saline and diluted with unlabeled drug to a specific activity of 2·64 μCi/mg of mescaline hydrochloride. The following drugs were received as gifts: trifluoperazine dihydrochloride, trifluoperazine sulfoxide, promazine sulfoxide and SKF 525-A hydrochloride from Smith, Kline & French Laboratories (Philadelphia, Pa.); promazine hydrochloride from Wyeth Laboratories (Philadelphia, Pa.); mesoridazine from Sandoz Pharmaceuticals (Hanover, N.J.); promethazine from the Lannett Co., Inc. (Philadelphia, Pa.); desmethylimipramine hydrochloride and imipramine hydrochloride from Geigy Pharmaceuticals (Ardsley, N.Y.); diazepam from Hoffmann–La Roche (Nutley, N.J.).

Procedures on animals. Swiss–Webster albino mice (30–33 g) of either sex were used. All drugs were freshly prepared in 0·9% saline and were injected i.p. in a volume of 0·5 ml. The doses reported are uncor-

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rected for their salts. Saline or SKF 525-A was administered 1 hr prior to the psychotropic drugs under test; mescaline was injected 30 min later. Control animals received injections of saline twice, followed by mescaline. In a separate experiment, mice injected with mescaline were given promazine 45 min later.

Gross behavior and locomotor activity. The experiments were conducted in the morning in a room thermoregulated at 23·0 ± 0·5°. The gross behavior of animals was observed for the entire period. One mouse was placed in a Plexiglass cage (39 cm long, 25·5 cm wide and 15·5 cm high) and the locomotor activity was monitored using an Animex activity meter type 0 (Farad Electronics, Stockholm, Sweden). The settings of tuning at 40 μA and of sensitivity at 30 μA were used throughout these studies. A control count was monitored for 30 min before injection of a drug; animals that gave an average of 350 counts/10 min were used. After each injection a 3-min period was allowed before the actual counting. The activity was recorded individually in 10-min periods for a total of 90–120 min. Each experimental run included four mice (sometimes two). The animals were sacrificed 3 hr after the injection of mescaline. Blood was collected for the separation of plasma. Whole brain, liver and eyes were promptly removed and frozen on dry ice. Plasma and tissues were stored at −20° for 18–24 hr before they were analyzed for mescaline and its major metabolite, 3,4,5-trimethoxyphenylacetic acid (TMPA).

Extraction and counting of radioactivity. The radioactivity in the plasma and tissues was extracted successively with 5 and 3 ml of chilled 0·4 N perchloric acid [14]. After centrifugation in the cold, the clear supernatants were adjusted to pH 5·8 with 5 N potassium carbonate solution; the salt of potassium perchlorate was removed in the cold by centrifugation. An aliquot of 0·5 ml was added to 10 ml of Bray's scintillation fluid [15] for a count of total ^{14}C in tissue and plasma homogenates. The remaining portion of the extract was poured on columns 50 mm long with an internal diameter of 4·2 to 4·5 mm and containing Dowex 50W-X_4, 200–400 mesh, previously buffered at pH 5·8 with phosphate buffer. The procedure for the separation of mescaline from its principal deaminated metabolite, TMPA, is reported elsewhere [16, 17]. The overall recovery of mescaline through the extraction and isolation procedure ranged between 74 and 88 per cent. The radioactivity was counted in a Nuclear Chicago Mark II liquid scintillation spectrometer using ^{133}Ba as an external standard. The efficiency of the counting system ranged between 85 and 90 per cent. All the data were corrected for recovery and for counting efficiency. The levels of mescaline and TMPA are reported as μg/g of wet weight tissue or μg/ml of plasma.

Mesoridazine assay. The levels of mesoridazine were determined according to the method of Pacha [18] using an Aminco–Bowman spectrophotofluorometer; the concentrations are reported as μg/g of wet weight tissue or μg/ml of plasma.

Statistics. The levels of mescaline, TMPA and mesoridazine were calculated as the mean ± S.D. The statistical significance of differences between mean values was determined with a two-tailed Student's *t*-test, and a P value of 0·05 or less was considered significant.

RESULTS

Gross behavior and locomotor activity. Within 30 min of mescaline administration, the animals exhibited gross behavioral changes characterized by agitation, slight increase in ventilation, moderately increased activity and occasional head shaking or scratching with paws of sides and areas around the nose. The effects were most intense 60 min after drug administration and continued up to 90 min. Subsequently, the animals were inactive and had incoordinated movements of the hind legs.

When injected alone, the following drugs in the doses indicated did not disrupt the normal behavioral pattern or locomotor movements measured by Animex: diazepam (2 mg/kg), promazine (10 mg/kg), mesoridazine (10 mg/kg), trifluoperazine (1 mg/kg), trifluoperazine sulfoxide (15 mg/kg), promazine sulfoxide (15 mg/kg), promethazine (15 and 30 mg/kg), imipramine (20 mg/kg), desmethylimipramine (20 mg/kg) and SKF 525-A (50 mg/kg). Diazepam (20 mg/kg) and mesoridazine (30 mg/kg) moderately decreased the normal activity, whereas promazine (30 mg/kg), mesoridazine (45 mg/kg) and trifluoperazine (5 and 15 mg/kg) almost completely blocked the normal behavior and locomotor activity. The degree of tranquilization varied with the dose and the drug.

Pretreatment with 2 mg/kg of diazepam, 1 mg/kg of trifluoperazine, 15 mg/kg each of trifluoperazine sulfoxide and promazine sulfoxide, 15 and 30 mg/kg of promethazine, 20 mg/kg each of imipramine and desmethylimipramine and 50 mg/kg of SKF 525-A and pre- and post-treatment with 10 mg/kg of promazine did not affect mescaline-induced altered behavior. Diazepam (20 mg/kg) and mesoridazine (10 mg/kg) partially prevented mescaline effects. The scratching responses and head shaking were considerably diminished; the animals were less excited but not tranquilized or drowsy and responded to sound stimuli. While no cataleptic-like state appeared, an incoordination of the hind legs continued. Promazine (30 mg/kg), mesoridazine (30 and 45 mg/kg) and trifluoperazine (5 and 15 mg/kg) effectively prevented all forms of mescaline-induced behavioral changes; with the exception of 30 mg/kg of mesoridazine, these treatments induced a cataleptic-like state, drowsiness and loss of body movement.

A combination of SKF 525-A with 30 mg/kg of promazine or 15 mg/kg of trifluoperazine did not produce any effect on mescaline-induced behavior in addition to that observed with the phenothiazine alone, probably because the anti-psychotic drug by itself produced a complete blockade at the doses employed. A combination of SKF 525-A with 10 mg/kg of promazine or 10 mg/kg of mesoridazine more effectively blocked the mescaline-induced changed behavior than did either phenothiazine given alone. Trifluoperazine sulfoxide (15 mg/kg), promazine sulfoxide (15 mg/kg), promethazine (15 and 30 mg/kg), imipramine (20 mg/kg) and desmethylimipramine (20 mg/kg) injected 1 hr after SKF 525-A produced no inhibitory effects of mescaline-induced changed behavior.

Animex. Figure 1 illustrates the data on the locomotor activity. The control count for the initial

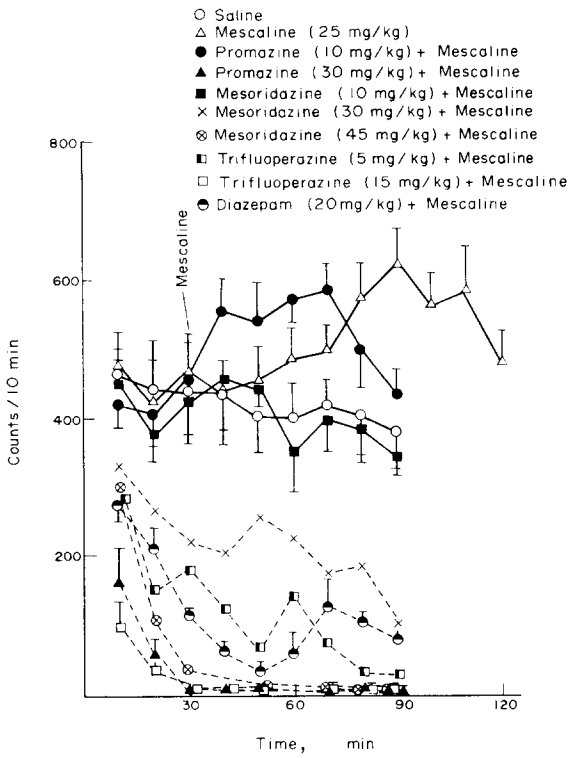

Fig. 1. Modification by several psychotropic drugs of the effects of mescaline on locomotor activity in mice. Psychotropic drugs were administered i.p. 30 min prior to [8-^{14}C]mescaline (25 mg/kg; shown by arrow). Motor activity was recorded for successive 10-min periods using an Animex activity meter. Each point represents the mean ± S. D. (vertical lines) of four experiments. (Where averages from two experiments were obtained, S. D. values are not shown.)

10-min session was 463 ± 47 and for the 90-min session 382 ± 54. Mescaline moderately increased the activity: the 10-min count for the 90-min session (60 min after mescaline injection) was over 1·5 times ($P < 0·001$) that of saline controls. Mescaline-induced increased activity was not blocked by the prior administration of 15 mg/kg of trifluoperazine sulfoxide, 15 mg/kg of promazine sulfoxide, 15 and 30 mg/kg of promethazine, 20 mg/kg of imipramine, 20 mg/kg of desmethylimipramine, 50 mg/kg of SKF 525-A and by lower doses of diazepam (2 mg/kg) and trifluoperazine (1 mg/kg) (not shown in Fig. 1). In mice pretreated with 10 mg/kg promazine, mescaline caused an initial increase (30- to 70-min sessions) followed by a slight decrease in the activity. Mesoridazine (10 mg/kg) did not completely abolish the locomotor activity but did prevent the activity-increasing effect of mescaline; the 10-min count for the 40-min session or thereafter was not significantly different from the corresponding sessions for saline-treated controls. Higher doses of promazine (30 mg/kg), mesoridazine (30 and 45 mg/kg), trifluoperazine (5 and 15 mg/kg) and diazepam (20 mg/kg) markedly decreased the locomotor activity; injections of mescaline apparently had no effect. Pretreatment with SKF 525-A potentiated the effects of 10 mg/kg of mesoridazine or promazine; the combined treatments blocked not only the activity-increasing effect of mescaline but also the normal locomotor activity (not shown in Fig. 1).

Mescaline and TMPA levels. Concentrations of mescaline and TMPA, as μg/g or μg/ml, in the controls and phenothiazine-treated mice 3 hr after the injection of [^{14}C]mescaline are shown in Fig. 2. Pretreatment with 10 mg/kg of promazine caused small but significant increases in mescaline levels in the plasma, brain ($P < 0·005$) eye and liver ($P < 0·001$). Small significant increases were also seen in the brain ($P < 0·05$) and eye ($P < 0·005$) when 10 mg/kg of promazine was injected 45 min after mescaline. Pretreatment with 30 mg/kg of promazine raised mescaline concentrations from 4-fold in the brain to 9-fold in the eye. With lower doses of mesoridazine (10 and 30 mg/kg) or trifluoperazine (1 mg/kg, not shown) the tissue mescaline contents were not significantly affected ($P > 0·1$ to 0·5), the exception being the eye levels with 30 mg/kg mesoridazine ($P < 0·001$). With higher doses, the levels of mescaline were significantly increased in the brain and eye following trifluoperazine (5 mg/kg; $P < 0·005$) and in the plasma, brain, eye and liver following trifluoperazine (15 mg/kg; $P < 0·001$) and mesoridazine (45 mg/kg; $P < 0·001$). The levels of TMPA were unaltered or increased somewhat by various treatments.

The plasma, brain and hepatic levels of mescaline in mice pretreated with 15 mg/kg of promazine sulfoxide, 15 mg/kg of trifluoperazine sulfoxide, 20 mg/kg of imipramine, 15 mg/kg of promethazine and 2 and 20 mg/kg of diazepam were not significantly different ($P > 0·1$ to 0·5) from those of the control (Fig. 3); with the exception of the lower dose of diazepam, these treatment schedules significantly elevated mescaline contents in the eye ($P < 0·005$ to 0·05). Imipramine in doses of 5 or 50 mg/kg neither prevented mescaline-induced gross behavioral changes nor increased tissue mescaline levels (not reported in Fig. 3). Desmethylimipramine (20 mg/kg) and promethazine (30 mg/kg) significantly raised plasma, brain, eye and hepatic concentrations of mescaline ($P < 0·001$ to 0·01).

Compared to controls, 50 mg/kg of SKF 525-A caused significant increases in mescaline levels in the brain, liver, eye ($P < 0·001$) and plasma ($P < 0·025$) (Fig. 4). The mescaline contents in the tissues of mice treated with SKF 525-A, SKF 525-A plus promazine sulfoxide, SKF 525-A plus trifluoperazine sulfoxide and SKF 525-A plus desmethylimipramine were not significantly different ($P > 0·1$ to 0·5), the exception being the eye content with the latter combination ($P < 0·005$). Alone, neither 10 mg/kg of mesoridazine nor 15 mg/kg of promethazine significantly raised mescaline levels (Figs. 2 and 3), but in combination with SKF 525-A, the levels were markedly enhanced ($P < 0·001$) (Fig. 4). Promazine (10 mg/kg) when injected individually caused small but significant increases in mescaline contents (Fig. 2) and, in the presence of SKF 525-A, produced further rises ($P < 0·001$) (Fig. 4) comparable to those produced by a 30 mg/kg dose of promazine (Fig. 2).

Mesoridazine levels. To determine the effects of SKF 525-A on the tissue levels of mesoridazine, groups of mice were injected either with saline or SKF 525-A followed by mesoridazine (10 mg/kg) and mescaline as reported in Materials and Methods; con-

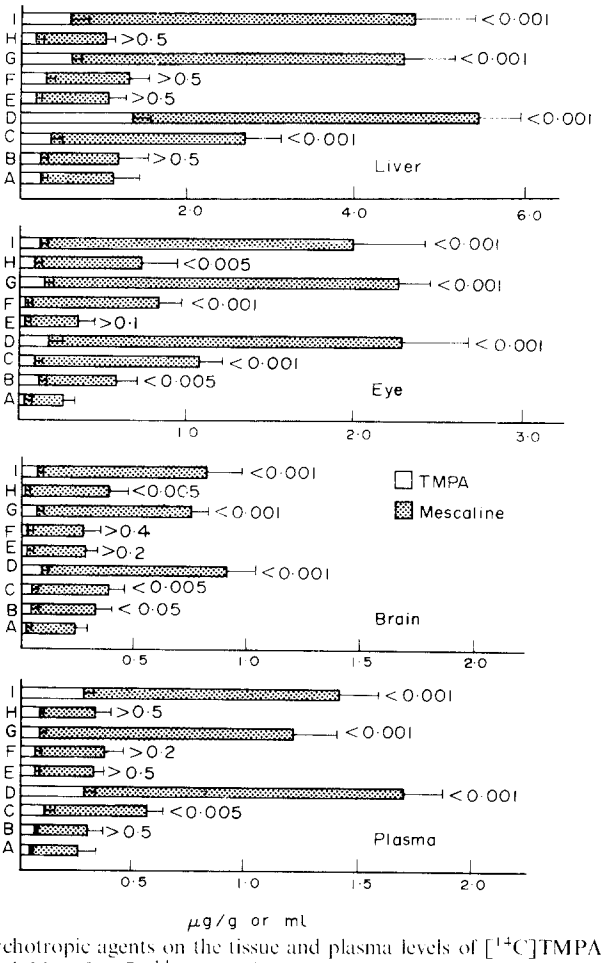

Fig. 2. Effects of psychotropic agents on the tissue and plasma levels of [^{14}C]TMPA and [^{14}C]mescaline in mice sacrificed 3 hr after [8-^{14}C]mescaline (25 mg/kg, i.p.). Drugs were injected 30 min prior to (C to I) or 45 min after (B) mescaline. Each value represents the mean ± S. D. (horizontal lines) of at least four (sometimes six to eight) experiments. P values are calculated for mescaline; each value is compared against the saline mescaline control. The significance of the differences is shown in the figure. A = saline mescaline control; B = promazine (10 mg/kg); C = promazine (10 mg/kg); D = promazine (30 mg/kg); E = mesoridazine (10 mg/kg); F = mesoridazine (30 mg/kg); G = mesoridazine (45 mg/kg); H = trifluoperazine (5 mg/kg); I = trifluoperazine (15 mg/kg).

trol mice received SKF 525-A–saline–mescaline. They were sacrificed 1·5 and 3·5 hr after mesoridazine. Neither SKF 525-A nor mescaline interfered with the assay when mixed with mesoridazine standards and carried through the extraction procedure. The spectrophotofluorometric readings of extracts from brain, liver and plasma from control mice were negligible. As shown in Table 1, the liver contents of mesoridazine were raised 3 to 4 times ($P < 0·001$) in SKF 525-A-treated mice compared to the levels observed in the non-SKF 525-A-treated mice; in the brain the levels were increased 1·5 times at 1·5 hr ($P < 0·025$) and 2·5 times at 3·5 hr ($P < 0·005$). The plasma levels in SKF 525-A-treated animals were statistically non-significant ($P > 0·4$) compared with those in the non-SKF 525-A group.

DISCUSSION

In the present report the dose–response relationships on antagonism and metabolic interactions between mescaline and a few commonly used psychotropic drugs were examined. One common feature of the benzodiazepine and the representatives of three subgroups of phenothiazine drugs tested was their ability to prevent mescaline from producing any abnormal behavior in a dose-related manner. The aliphatic and piperazine phenothiazines, however, differed from the benzodiazepine and the piperidine phenothiazines in regard to their ability to induce mescaline retention and catalepsy. Among phenothiazines, CPZ is extensively studied for its antihallucinogenic actions. This drug effectively antagonizes mescaline effects in a dose-related manner [2], but induced a few untoward effects such as marked hypothermia, cataleptic-like state and highly elevated tissue levels of mescaline. With certain exceptions, the pharmacologic actions of mesoridazine or thioridazine are in general similar to those of the other phenothiazines. Unlike CPZ, they do not produce the cataleptic-like condition in animals; they are about one-seventh as potent as CPZ in reducing spontaneous motor activity in the mouse and their hypothermic effect in rat is also weaker [19]. Compared to several antischizophrenic drugs of the aliphatic and piperazine groups, the piperidine derivatives elicit the fewest

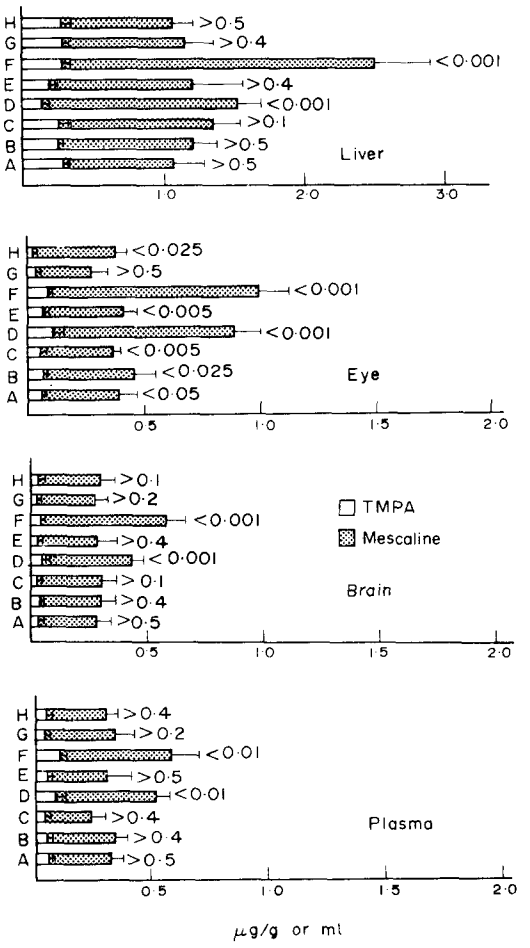

Fig. 3. Effects of tricyclic compounds and diazepam on the plasma and tissue levels of [^{14}C]TMPA and [^{14}C]mescaline in mice sacrificed 3 hr after [8-^{14}C]mescaline (25 mg/kg, i.p.). Drugs were injected 30 min prior to mescaline. Each value is the mean ± S. D. (horizontal lines) of at least four (sometimes six to eight) experiments. P values are calculated for mescaline; each value is compared against the saline mescaline control shown in Fig. 2. The significance of the differences is shown in the figure. A = promazine sulfoxide (15 mg/kg); B = trifluoperazine sulfoxide (15 mg/kg); C = imipramine (20 mg/kg); D = desmethylimipramine (20 mg/kg); E = promethazine (15 mg/kg); F = promethazine (30 mg/kg); G = diazepam (2 mg/kg); H = diazepam (20 mg/kg).

extrapyramidal symptoms and possess greater affinities for the muscarinic cholinergic receptors in the brain [20].

Comparatively little is known about the influence of benzodiazepines on mescaline-induced behavioral manifestations or on the metabolism of mescaline. In the present study, the mouse was chosen since both humans and mice lack specific mescaline oxidase enzyme [21]. Diazepam in a dose of 20 mg/kg partially prevented the behavioral responses to mescaline without producing any untoward effect. The interaction between benzodiazepines and amphetamine seems to be different; for example, diazepam (20 mg/kg) significantly prolongs amphetamine-induced stereotyped behavior in rats and elevates brain amphetamine level [22]. Solursh and Clement [23] reported a therapeutic success with benzodiazepines in the treatment of adverse psychedelic reactions to hallucinogens. A recent report by Levy [24] suggests that diazepam behaves like a specific antidote to the psychedelic effects of LSD.

Species differences play an important role in the metabolism of pharmacological agents. In rats the tricyclic antidepressants interfere with the aromatic hydroxylation of amphetamine and enhance and prolong psychomotor stimulatory effects of this drug [5, 6, 25, 26], while in mice where *p*-hydroxylation of amphetamine plays a minor role [27], no potentiation is observed [28, 29]. Hyperactivity caused by *d*-amphetamine is increased with imipramine at doses of 2·5 mg/kg but is decreased at a dose of 20 mg/kg [30]. The potentiating effect of the tricyclic antidepressants has been attributed to the ability of these drugs to cause greater amounts of *d*-amphetamine to enter the brain and to prolong its half-life in the CNS [4]. The present study in mice indicates that doses of imipramine ranging from 5 to 50 mg/kg failed to modify the mescaline effects and its tissue levels. This difference, therefore, appears to be due to species variation in the handling of the drugs.

SKF 525-A, which has little or no pharmacological effect of its own [31, 32], modifies the actions and metabolism of a wide range of chemical compounds [33] by inhibiting microsomal drug-metabolizing enzymes. By employing rabbit liver homogenates, Bhatnagar [12] has shown that SKF 525-A depresses the metabolism of CPZ by inhibiting the mono- and di-demethylation, sulfoxidation and hydroxylation reactions. SKF 525-A intensified the effects of 10 mg/kg of mesoridazine and promazine. The fact that SKF 525-A markedly enhanced the brain and hepatic concentrations of mesoridazine (Table 1) suggests that this drug potentiated the effects of neuroleptics (complete blockade of mescaline-induced behavior and cataleptic-like state) due to the accumulation of more of this phenothiazine following the inhibition of its metabolism by microsomal drug-metabolizing enzymes. The stabilization of biological membranes by SKF 525-A, tranquilizers, antihistamines, barbiturates, steroids and local anesthetics is well documented [34]. The most common physicochemical properties of phenothiazines are associated with their surface activity and high lipid solubilities at physiological pH. Guth and Spirtes [35] have reported the accumulation of CPZ and other phenothiazines at the biological membranes. In other studies, CPZ- and SKF 525-A-mediated inhibition of the uptake of α-aminoisobutyric acid by hepatoma cells was attributed to membrane stabilizing effects of these agents [36].

Mescaline in doses greater than 20 mg/kg was reported to increase the locomotor activity [37] and scratching responses [38] in mice. It is recognized that there is no known specific pharmacologic test for mescaline. Kulkarni [38] has indicated the importance of scratching responses to mescaline as a convenient and simple procedure for the assessment of the drug-induced behavioral manifestations. The data reported here indicate that the increase in locomotor activity and scratching responses induced by mescaline can be prevented by pretreatment with benzodia-

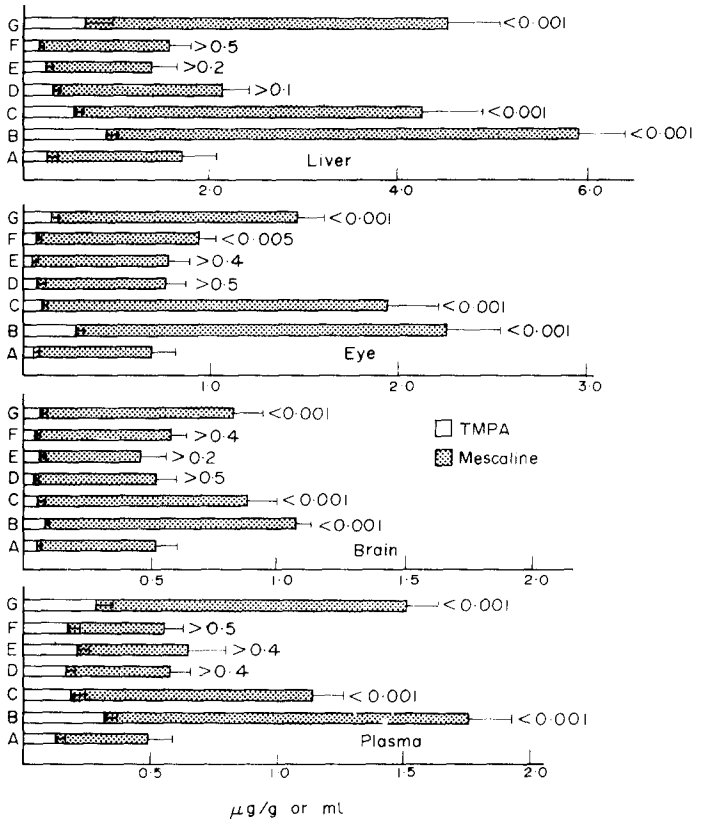

Fig. 4. Combined effects of SKF 525-A (50 mg/kg) and tricyclic drugs on the plasma and tissue levels of [^{14}C]TMPA and [^{14}C]mescaline in mice sacrificed 3 hr after [8-^{14}C]mescaline (25 mg/kg, i.p.). SKF 525-A was administered 1 hr before the tricyclic compound, which was administered 30 min before mescaline. Each value is the mean ± S. D. (horizontal lines) of at least four (sometimes six to twelve) experiments. P values are calculated for mescaline; each value is compared with the SKF 525-A-treated group (A) and this A group is compared with the A group of Fig. 2. The significance of the differences is shown in the figure. A = SKF 525-A; B = SKF 525-A + promazine (10 mg/kg); C = SKF 525-A + mesoridazine (10 mg/kg); D = SKF 525-A + promazine sulfoxide (15 mg/kg); E = SKF 525-A + trifluoperazine sulfoxide (15 mg/kg); F = SKF 525-A + desmethylimipramine (20 mg/kg); G = SKF 525-A + promethazine (15 mg/kg).

Table 1. Levels of mesoridazine in plasma, liver and brain*

Treatment	Plasma (μg/ml)		Brain (μg/g)		Liver (μg/g)	
	1·5 hr	3·5 hr	1·5 hr	3·5 hr	1·5 hr	3·5 hr
Saline mesoridazine mescaline	0·213 ± 0·062	0·105 ± 0·007	0·075 ± 0·017	0·042 ± 0·022	0·364 ± 0·073	0·222 ± 0·044
SKF 525-A mesoridazine mescaline	0·165 ± 0·054	0·096 ± 0·017	0·110 ± 0·013	0·103 ± 0·014	1·009 ± 0·113	0·832 ± 0·095
P value	<0·4	<0·4	<0·025	<0·005	<0·001	<0·001

* Saline or SKF 525-A (50 mg/kg) was injected 1 hr prior to mesoridazine (10 mg/kg) followed 30 min later by mescaline (25 mg/kg). Mice were sacrificed 1·5 and 3·5 hr from the time of mesoridazine injection. The values are mean ± S. D. of four experiments. P values indicate significance of differences between non-SKF 525-A (saline)- and SKF 525-A-treated groups.

zepine and phenothiazine drugs in certain doses: 10 mg/kg of mesoridazine and 20 mg/kg of diazepam seem to be the most reasonable choices.

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