Behavioral Pharmacology II

1527 PHARMACOLOGY

EFFECTS OF THREE POTENTIAL INSECT REPELLENT COMPOUNDS ON AVOIDANCE BEHAVIOR OF RATTUS RATTUS. William M. Smith, Jr. USAEHA, Edgewood Arsenal, APG, Md. 21010. (Sponsor: LTC M. Steinberg)

Three compounds proposed for use by humans as insect repellents were tested for detrimental effects on rats trained to avoid electric shock. ED_{50}'s ("effect dose" for 50% subjects) were determined for the following: Carbamide (cyclohexamethylene carbamide), Sulfonimide (N-butylsulfonimidocyclohexamethylene), and Pentadecane (3,6,9,trioxapentadecan-1-OL). Subjects were given four training trials of paired shock and white noise tone. Subjects escaped the aversive stimuli by running into a larger, "safe" compartment adjacent to the shock chamber. The animals were next tested for avoidance responding in the presence of a 20-sec tone, followed by electric shock if no response was made. Those animals which avoided the shock "passed" the criterion test, and were injected intraperitoneally with a test compound. After a predetermined interval (15 min to one hour), subjects were given another avoidance trial. Avoidance responses and failures were recorded. The following ED_{50}'s were determined in this test situation: Carbamide - 300 mg/kg (22 rats); Sulfonimide - 400 mg/kg (22 rats); Pentadecane - 100 and 200 mg/kg (33 rats tested). It was concluded that Pentadecane should be submitted to more definitive tests for behavioral toxicity, due to its relatively low ED_{50}.

1528 PHARMACOLOGY

BEHAVIORAL ACTIVITY OF CATNIP AND ITS CONSTITUENTS: NEPETALIC ACID AND NEPETALACTONE. JOHN W. HARNEY*, JOHN D. LEARY*, AND IVAN B. BAROFSKY. MASSACHUSETTS COLLEGE OF PHARMACY, BOSTON, MA. 02115

Catnip has been reported to be abused by humans, although little or no experimental data are available to account for its usage. In four experiments catnip oil, nepetalic acid, and nepetalactone were tested for behavioral and toxicologic effects. The LD_{50} of catnip, nepetalic acid, and nepetalactone were determined, in mice, to respectively be 1300 mg/Kg, 1085 mg/Kg, and 1500 mg/Kg. Catnip oil (500 mg/Kg), and nepetalic acid (125 mg/Kg) were found to produce a 100% increase in the hexobarbitol sleeping time of mice. Rats trained on Sidman avoidance schedule showed a significant decrease in performance following ip injections of catnip oil (500-750 mg/Kg), nepetalic acid (125-250 mg/Kg), and nepetalactone (500-750 mg/Kg). Rats, which were trained to avoid, developed a behavioral tolerance after they were given 750 mg/Kg of catnip oil for 10 consecutive days. The results demonstrate that catnip can be behaviorally active in species other than insects and felines, and that nepetalic acid was the most active of the compounds tested.

1529 NUTRITION

A PEPTIDE MODULATOR FOR THE STEP DOWN INDUCER, CATABATHMOPHOBIN. Helene N. Guttman and Roman Czuper*. Dept. Biol. Sci., Univ. Ill. at Chi. Circle, Chicago, Il. 60680.

Rats step off small, low platforms in 10 secs. When the floor upon which they step down (SD) is electrified, rats learn, in one trial, to remain on the platform. Catabathmophobin (CATA) is a dialyzable, rat brain oligopeptide synthesized concomitant with SD avoidance learning (Guttman and Gronke, Psychon. Sci. 24, 107, 1971) but not synthesized by animals yoked for contingent shock. CATA is bioassayed by the transfer method in which peptide is injected into naive rats or mice and their latency to SD measured in the absence of either punishment or reward. Brains of rats reestablished for SD for 1-5 addnl. days continue to contain about the same amount of CATA whereas reestablishment for a total of 10-15 days results in disappearance of isolatable CATA and the appearance of a new oligopeptide. This new peptide, when injected into recipient rodents along with effective doses of CATA, annuls the transfer effects of CATA. A peptide nodulator of the dark avoidance transfer effect also has been isolated and it is not identical with the CATA modulator.

1530 PHARMACOLOGY

ATTENUATION OF CONDITIONED AVERSION FOLLOWING REPEATED ADMINISTRATIONS OF ELECTROCONVULSIVE SHOCK. John R. Vogel. Rorer Res. Labs., Inc., Fort Washington, PA 19034, U.S.A.

Repeated administrations of electroconvulsive shock (ECS) attenuates the suppression of behavior by unavoidable punishment. To further examine the effects of repeated ECS on response suppression, rats were given repeated ECS following establishment of a conditioned aversion to milk. To produce a conditioned aversion, rats were allowed to lick sweetened condensed milk and then were injected with atropine methyl nitrate (1.0 mg/kg, i.p.). Beginning five days later, the rats were given three ECS or sham ECS treatments per day for seven additional days. Following these treatments rats were again tested with milk. Sham treated controls showed a strong aversion to milk, *i.e.*, did not lick. ECS treated rats, on the other hand, licked freely. These results indicated that repeated ECS treatments markedly attenuated aversion to milk. In a subsequent experiment separate groups were tested 1, 7 or 14 days following termination of ECS treatments. In this experiment the conditioned aversion gradually reappeared. Therefore, repeated ECS treatments may temporarily release behavior from suppression by aversive stimuli.

1531 PHARMACOLOGY

USE OF FAMILIAR SUBSTANCES AS DIFFERENTIAL CUES IN AVOIDANCE CONDITIONING. Larry A. Birch* and John F. Wing. Dept. of Psychology, Wittenberg University, Springfield, Oh. 45505

Bait-shyness has been proposed as a behavioral index of toxicity, but many critical variables relating to its effectiveness have not been researched. This study demonstrates the use of familiar (rather than novel) substances, and it compares the cue effectiveness of water, a very familiar substance, with that of saccharin, a less familiar substance. Two experimental groups and their yoked controls were exposed on alternate days to water and saccharin. Immediately following removal of the fluid, one experimental and control group got three injections on successive water days; the other experimental and control group got three injections on successive saccharin days. For experimentals the intraperitoneal injections were 66 mg/kg LiCl and for controls they were 0.9% hypotonic saline. Comparison was made of fluid intake on all days by all groups. Fluid intake dropped significantly for both experimental groups on the conditional liquid days following each injection; but it showed no drop for controls. No statistically significant differences were found between experimental groups, indicating that water, a less-**preferred**, familiar substance can be as effective as saccharin, a more **preferred**, relatively novel substance. Furthermore, this finding suggests that under some conditions absolute novelty of substances is not critical to obtaining bait-shyness.

1532 PHARMACOLOGY

TOLERANCE TO EFFECTS OF Δ-9-TETRAHYDROCANNABINOL (THC) ON FREE-OPERANT SHOCK AVOIDANCE Frederick J. Manning, Walter Reed Army Institute of Research, Washington, D.C. 20012

Albino rats were given extensive experience in free-operant lever-press shock avoidance. THC was administered daily 3 hours prior to avoidance testing, via intragastric intubation, at a dose of 30mg/kg, for 10 to 45 days. Significant drug effects on both response rates and shock rates were seen, but the nature of these effects was highly idiosyncratic. Efforts to relate the nature of these performance changes to aspects of baseline avoidance performance have thus far been unsuccessful. The presence and extent of tolerance was also highly variable across subjects, but might be summarized as follows: whenever the effect of THC was to increase the number of shocks received by the rat, complete tolerance was observed within 6 days; whenever the effect of THC was to decrease the shock rate, no tolerance was observed, even when drug administration was continued for as long as 45 days. In several rats, both of these phenomena were observed: an initial increase in shocks, which quickly disappeared, followed by a decrease in shocks below the pre-drug baseline. The rats continued to perform at this level of proficiency until THC was discontinued, at which point the baseline was reacquired. These data emphasize the importance of the drug's consequences as a determinant of tolerance.