K33 2,5-Dimethoxy-4-n-propylthiophenethylamine (2C-T-7) Dose Response Relationship in the Rat

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Attendees will be exposed to a model for studying the pharmacological properties of 2C-T-7 in the rat.

This report will provide novel analytical and behavioral protocols for studying the pharmacological properties of 2C-T-7, a drug that has been recently detected in postmortem cases in the United States.

Sprague-Dawley rats, 200-250 gms, were given 2C-T-7 by intraperitoneal (ip) injection to establish both a lethal and a high pharmacological dose. The doses included 5, 25, 37.5, 50, 70, and 100 mg/kg with a group size of 5. The measurements consisted of behavior, body temperature, and 2C-T-7 tissue concentrations in blood, brain, lungs, liver and heart. 2C-T7 was quantified using a liquid-liquid extraction with trimethoxyamphetamine as internal standard. Tissues were first treated with dilute perchloric acid (8% v/v) then centrifuged. The supernatant was transferred and the pH of the specimens and standards was adjusted to > 10 by addition of ammonium hydroxide. 1-Chlorobutane was added to the standards and specimens and they were placed on a rotary extractor for ten minutes and then centrifuged. The upper solvent layer was transferred to 5.0 mL conical test tubes and the solvent evaporated to dryness using a nitrogen evaporator with a water bath set at 40°C. The dried extracts were reconstituted in 50 uL of chloroform and placed in glass autosampler vials. The samples were then analyzed by gas chromatography-EI mass spectrometry utilizing selected ion monitoring. The instruments and conditions were as follows: Agilent 6890 gas chromatograph, with a 15 meter HP-1MS (100 % methyl polysiloxane), 1.0 mL per minute helium carrier gas flow, 250°C injector port, 300°C detector interface, oven 120°C ramped to 300°C at 20°C per minute. The ions monitored were 226, 255, 183 m/z for 2 C-T-7 with the 226 m/z used as the quantitation ion and 182 m/z for the internal standard.

TABLE 1. Tremors and Convulsions After 2C-T-7 Administration

Dose (mg/kg,ip)	5	25	37.5	50	100
Rats (#)	5	5	5	19	5
Tremor	0	0	2 (40%)	2 (11%)	4 (80%)
Automatisms (Jaw)	0	0	2 (40%)	5 (26%)	2 (40%)
Myoclonic Jerks	0	0	1 (20%)	4 (21%)	3 (60%)
Intermittent	0	0	0	3 (16%)	3 (60%)
Jacksonian-like	0	0	0	1 (5%)	1 (20%)
Tonic-Clonic	0	0	2 (20%)	5 (26%)	5 (100%)

Physiological events resulting from the 2C-T-7 are listed in Table 1. At the 100 mg/kg dose, the animals died in 19.6 ± 10.7 minutes (range 9- 35) from suffocation and/or convulsions. A straub tail followed by a tonicclonic convulsion occurred at 9.6 ± 1.5 minutes (range 7-13). The 50mg/kg ip dose was selected as the high pharmacological dose with one hour being past the absorption phase. Only three out of 90 rats died within that time interval (30, 42,and 55 minutes). Behavioral effects occurred within 2 minutes post 50mg/kg ip dose with peak effects between 30 and 60 minutes; at 17 hours post dosing 30% of the rats still had intermittent tremor and body jerks. No obvious behavior effects occurred post 24 hours. After the 50-mg/kg ip dose there was no significant body temperature change in the 2.5 hour measurement period. A temperature elevation did not occur at any dose. A small (2ºC maximum) but significant decrease occurred after the 5, 25 and 37.5 mg/kg ip dose. 25mg/kg ip dose had greater temperature effects. Lethal 2C-T-7 tissue concentrations after the 100mg/kg dose were 23.9 ± 9.3 µg/ml for blood, 21.3 ± 9.0 µg/gm for brain, for 285.9 ± 156.0 mg/gm lungs 51.4 ± 9.2 µg/gm for heart and 126.3 ± 94.6 µg/gm for liver. Lethality in the rat is an LD_{50} of 69 ± 8 mg/kg with a minimum observed lethal dose at 37.5 mg/kg.

In conclusion, a 2C-T-7 rat model has been established to study the dose-response relationship for 2C-T-7. Future research is needed to elucidate the complete pharmacological profile of this drug.

2C-T-7, Phenethylamine, Behavior

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