(±)-1-(2,5-dimethoxy-4-ethylthiophenyl)-2-aminopropane (ALEPH-2), a novel putative anxiolytic agent lacking affinity for benzodiazepine sites and serotonin-1A receptors

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Serotonergic behavioral responses, effects on motor activity and core temperature, and binding properties of the novel putative anxiolytic amphetamine derivative (±)1-(2,5-dimethoxy-4-ethylthiophenyl)-2-aminopropane (ALEPH-2), were examined in rodents in order to elucidate the mechanism underlying its anxiolytic-like effect. After peripheral administration in rats, ALEPH-2 induced some symptoms of the serotonergic syndrome, e.g. forepaw treading and flat body posture. Additionally, a decrease in motor activity was observed. No significant effects on the number of head shakes were observed after injection, although high inter-subject variability was noted. Higher doses of ALEPH-2, in the range exhibiting anxiolytic properties (4 mg/kg), elicited significant hypothermia in mice. The affinity of the drug for 5-HT(2A/2C) receptors ([3H]ketanserin sites) was in the nanomolar range (K(i) = 173 nM), whereas for 5-HT(1A), benzodiazepine sites, and GABA(A) receptors, the affinity was micromolar