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THE AVERSIVE, ANXIOLYTIC-LIKE, AND L-TYPE CALCIUM CHANNEL DEPENDENT PSYCHOSTIMULANT EFFECTS OF PULEGONE

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Introduction. Pulegone is a monoterpenic compound found in many plants. This compound is found in *Mentha piperita* L. (peppermint) essential oil and is the main constituent of *Mentha pulegium* L. (pennyroyal) and *Ziziphora clinopodioides* (blue mint bush) essential oils (60%-90%). *M. piperita*, *M. pulegium* and *Z. clinopodioides* are pharmacologically and toxicologically important worldwide. The behavioral effects of pulegona have only recently gained attention in the field, and pulegone has been shown to possess psychostimulant effects that are sensitive to dopamine receptor antagonists. Therefore, considering the important role of dopamine in the regulation of both movement and reward, we hypothesized that pulegone has both psychostimulant and reward properties. Since natural products that contain a large amount of pulegone have been used as sedatives, we also investigated the possible anxiolytic-like actions of this substance. Moreover, we also analyzed pulegone for the sensitivity of the psychostimulant effects to the $GABA_A$ receptor and to L-type Ca^{2+} channel blockage, aimed at evaluating pharmacological similarities between pulegone and the classical depressant ethanol.

Material and Methods. The experiments were conducted using male Swiss mice treated with pulegone or a vehicle. General mouse activity (locomotion, rearing, grooming and immobilization) was determined in the open field. The anxiolytic-like activity, motor coordination and strength force were evaluated using the elevated plus maze (EPM), rotarod test and grasping test, respectively. The motivational properties of pulegone were evaluated by pairing the drug effects on the mice with the less preferred compartment (previously determined) of a conditioned place preference (CPP) apparatus. The

Results and Discussion. Pulegone increased mouse locomotor activity and immobilization time. Verapamil, but not haloperidol or picrotoxin, decreased the psychostimulation induced by pulegone. Pulegone also decreased grooming and rearing behaviors and caused motor incoordination and weakness at high doses. Pulegone increased the time spent by mice in the open arms of the EPM, and flumazenil pre-treatment did not alter this effect. Pulegone either produced no CPP or induced conditioned place aversion. Thus, pulegone has a dose-dependent dual effect on mouse behavior, which acts as either a stimulant or a depressant. The stimulant effect appears to be unrelated to dopamine D2 receptor activation but it does depend on the opening of the voltage-dependent L-type Ca^{2+} channel. Moreover, pulegone possesses negative reinforcing properties and has anxiolytic-like effects that are unrelated to the benzodiazepine site of the $GABA_A$ receptor. Our data provide some

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explanation of the pharmacological and toxicological actions ascribed to pulegone-containing essential oils and highlight the use of verapamil in selected cases of intoxication with this natural compound.

References.

Umezu, T.; *Pharmacol Biochem Behav*, **2010**, 94, 497-402.