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Dear Dr. Novich:

Enclosed are results from studies recently conducted in my laboratory investigating the effects of phenylpropanolamine HCL (PPA) in volunteer research participants.

Two hundred sixteen (216) healthy normotensive volunteers (mean age = 32.3) presenting with various degrees of overweight participated in a double blind, placebo controlled evaluation of the effects of PPA on blood pressure, pulse, and mood. Two dosage forms of PPA were studied (75 mg. sustained release and 25 mg. t.i.d.) in relation to placebo. Subjects in each of four weight categories were randomly assigned to one of three drug conditions. The weight categories were normal weight (n = 36), mildly overweight (n = 72), moderately overweight (n = 72), and severely overweight (n = 36). Subjects received a test medication (either an active product or placebo) three times during a 12 hour testing session. Subjects in one group (Group A) received a 75 mg. sustained release dose on their first medication occasion and placebo capsules on the other two dosing occasions. Subjects in another group received 25 mg. doses at each medication occasion (Group B). Subjects in another group (Group C) received placebo at each measurement occasion. Subjects were studied for a 12 hour testing session.

Measurements of blood pressure (both standing and supine, pulse, and subjective drug effect (using the Addiction Center Research Inventory - ARCI) were obtained 11 times during the session; at baseline (prior to drug administration) and at ½ hr., 1 hr., 2 hr., 4 hr., 4½ hr., 6 hr., 8 hr., 8½ hr., 10 hr., and 12 hr., post initial dosing.

Mixed design analysis of variance revealed no main effects for drug treatment on any of the measures. Subjects in the heavier weight categories consistently showed more rapid pulse rates and higher blood pressure readings than did those of normal or near normal weight. However, no significant differences in drug effect as a function of weight classification were observed. As expected, most measures showed fluctuations over the course of the day (circadian effects), indicating that subjects' physiological and subjective state changed over the course of the session. These changes were not, however, related to the drug treatment condition. Our analyses of peak changes in blood pressure were quite consistent with our overall findings. Only

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2 individuals (one in the 75 mg. SR group and one in the placebo group) showed blood pressure readings greater than 94 mm. Hg. The mean peak difference between placebo and active drug treatment was less than 1 mm. Hg.

Analysis of subjective effects, focusing on a comparison of PPA with those of various other drugs (stimulants, opiates, sedatives), did not suggest a profile characteristic of amphetamine or other stimulant drugs. PPA was not associated with euphoria.

"Side effects" from drug treatment did not differ between treatment groups, in my clinical judgement. In fact, the most remarkable "side effect" -- hallucinations and confusion -- was reported (one day after treatment) by a subject in the placebo treatment condition.

Overall, our results are entirely consistent with the studies recently completed at the Behavioral Pharmacology Research Unit of the Johns Hopkins University School of Medicine: PPA -- in the doses currently approved for marketing -- is not associated with clinically significant hypertensive risk in generally healthy individuals. In addition, no evidence of "abuse potential" was found.

Please do not hesitate to contact me if I can be of further assistance.

Sincerely,



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