dissociation among acute anorexiant activity, vasopressor activity, or subjective effects. A significant contrast between diethylpropion and *d*-amphetamine is the oral-to-parenteral potency ratios where diethylpropion is twice as potent orally as subcutaneously, while, in contrast, oral and subcutaneous *d*-amphetamine were nearly equipotent.

The relative potency estimates in these studies correspond to those determined by other investigators. The relative potency of ⅛ (diethylpropion as *d*-amphetamine) in man for decreases in caloric intake (Table II) corresponds to the acute anorexiant potency estimates of Gylys and his colleagues[11] of ⅛ in rats and ⅓ in dogs for oral diethylpropion and *d*-amphetamine. Boxill and his colleagues[2] estimated diethylpropion 1/10 as potent as *d*-amphetamine as a vasopressor in anesthetized dogs; they, too, observed differences in potency estimates for routes of administration in that diethylpropion may have been relatively more potent by intraduodenal administration than by intravenous administration. In man, Jonsson and colleagues[13] estimated 50 mg of oral diethylpropion equal to 10 mg of oral *d*-amphetamine as a euphoriant.

Existing data suggest that the greater oral effectiveness of diethylpropion may be attributable to greater conversion of diethylpropion to an active metabolite. In man orally administered diethylpropion is metabolized through sequential N-deethylation, reduction of the ketone, parahydroxylation of the benzene ring, oxidative cleavage of the nitrogen, and conjugate formation resulting in 21 identified and 2 unidentified metabolites.[19] Metabolites formed by N-deethylation or reduction of the ketone have been synthesized and demonstrated to have anorectic, stimulant, and vasopressor activity in animals.* Blood samples taken ½, 2, and 4 hours after oral administration of 400 mg. of diethylpropion and subcutaneous administration of 600 mg of diethylpropion in one subject not in the crossover study indicated that at these times the levels of diethylpropion were higher following subcutaneous than following oral administration.*

Demonstration of amphetamine-like subjective effects, euphoria, and physiologic effects coupled with reports[3, 4, 11, 14, 18, 21] of compulsive drug-seeking behavior and psychoses indicate that diethylpropion is appropriately classified as an amphetamine-like drug. Relating the abuse potential of diethylpropion to amphetamine-like agents held to have high abuse potential is difficult since diethylpropion has been marketed for a decade and a half with extremely few reports of abuse. Relating the abuse potential of diethylpropion to centrally active sympathomimetic amines with little or no recognized abuse potential is even more difficult. Ephedrine, a centrally active sympathomimetic amine widely available with almost no abuse, clearly produces amphetamine-like subjective effects, euphoria, and physiologic effects,[16] at least when administered subcutaneously.

Diethylpropion is available only as a 25 mg tablet or 75 mg Dospan (a mucilaginous gel in aqueous solution designed to retard release). As a parenteral euphoriant, the 25 mg tablet would be equivalent to 1 to 2 mg of *d*-amphetamine. It would be necessary to dissolve a large, if not impossible, number of tablets to achieve doses equieuphoric to doses of amphetamine reported for intravenous abuse. Comparatively, the standard 25 mg tablet of ephedrine administered parenterally would be equieuphoric to 5 mg of parenterally administered *d*-amphetamine.[16] Similar considerations of the 75 mg Dospan preparation leads to a conclusion of low likelihood of parenteral abuse. This estimate of low parenteral abuse potential is supported by

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