This report presents findings relative to the morphine-like properties of three drugs, d-propoxyphene napsylate, azidomorphine, and butorphanol and to the assessment of three amphetamine congeners, d-benzphetamine, dl-fenfluramine, and chlorphentermine. Brief reference will be made to a peculiar effect of amphetamine on blood pressure.

SECTION I: MORPHINE-LIKE DRUGS

d-Propoxyphene

This drug (Darvon®) is a morphine-like analgesic. In recent years, the napsylate salt of this agent has been utilized to maintain or detoxify heroin dependent patients[1,2,3,4,5] where it was felt that the drug had certain advantages over methadone, i.e., 1) a lower abuse liability; 2) milder degree of physical dependence produced; and 3) greater acceptance by some patient categories. Fraser and Isbell[6] demonstrated some years ago that the hydrochloride salt of d-propoxyphene had morphine-like effects in man, since the drug produced both miosis and morphine-like subjective effects and suppressed morphine abstinence. Moreover, in direct addiction studies, the hydrochloride produced morphine-like physical dependence. Although d-propoxyphene was less potent than morphine, it was relatively more toxic.

Oral doses of 800-1600 mg of d-propoxyphene napsylate have been recommended for detoxification and/or maintenance of heroin addicts. Larger doses produce untoward manifestations such as convulsions and a toxic psychosis. It is of interest, therefore, to determine the degree of morphine-like activity produced by d-propoxyphene napsylate in this dose range and to determine if this activity is sufficient to suppress abstinence in subjects physically dependent upon 60 mg of morphine/day.

Nine non-dependent subjects were administered the following conditions in random order at weekly intervals: morphine sulfate (10, 20 mg subcutaneously); d-propoxyphene hydrochloride (210, 420, and 600 mg, orally); d-propoxyphene napsylate (310, 620, and 700 mg orally); and placebo (oral capsule and saline, s.q.). To maintain double blind conditions, subjects received both the oral and subcutaneous conditions simultaneously with appropriate substitution of active drug.

One and one-half mg of d-propoxyphene napsylate and 1.0 mg of the hydrochloride contains equal amounts of d-propoxyphene base. Prior studies[7] have shown that d-propoxyphene, 600 mg, orally, produces effects equivalent to a 20 mg subcutaneous injection of morphine sulfate; and this dose of d-propoxyphene hydrochloride is not convulsive in man. Therefore, 900 mg of the napsylate salt was presumed to be the maximum dose that should be studied. However, during a preliminary dose run-up, 750 mg of d-propoxyphene napsylate produced nervousness, anxiety, apprehension and hyperreflexia (effectively antagonized by naloxone in one subject). For this reason, the