

## METHOD AND COMPOSITION FOR REDUCING WEIGHT

The present invention relates generally to the treatment of obesity by means of the internal administration of pharmaceuticals. More particularly, the invention pertains to the improved administration of L-Dopa with or without a decarboxylase inhibitor plus a potentiator, Molindone, to treat obesity.

### BACKGROUND OF THE INVENTION

The health problems associated with the widespread problem of obesity need not be elaborated. A need exists for pharmaceutical treatments which are effective for the treatment of obesity in mammals with a minimum of undesirable side effects. By "obese warm-blooded animal" is meant a human or other mammal which is more than 10 percent overweight as judged by contemporary medical standards. Many treatments have been proposed for obesity. For example, U.S. Pat. No. 3,867,539 to Henkin describes a treatment wherein anorexia is produced by administration of histidine to the obese patient. However, no effective pharmaceutical treatment is believed in widespread use due to a lack of either lasting effectiveness or of undesirable side effects.

### DESCRIPTION OF THE PRIOR ART

L-Dopa is the trivial name for the naturally occurring compound L-3, 4-dihydroxyphenylalanine, which is commercially available—its synthesis having been reported in the literature (Yamada et al., *Chem. Pharm. Bull.*, 10:693 (1962)).

The most widely recognized therapeutic use of L-Dopa is in the treatment of Parkinson's disease. The mechanism of L-Dopa in the treatment of this disease is attributed to its presumed role in the correction of an imbalance of dopamine and acetylcholine in the basal ganglia, a biochemical defect associated with Parkinsonism.

L-Dopa has also been used as a treatment of ethanol withdrawal symptoms, as reported in the U.S. Pat. No. 3,995,058 to Hammond et al. The treatment of paralysis agitans with L-Dopa and with mixtures of L-Dopa and benzodiazepines is reported in U.S. Pat. No. 3,984,545 to Frills, Jr. et al. Therapeutic use of L-Dopa in the treatment of depression, sleep production in mice, supranuclear palsy and hepatic coma has also been reported.

It has been reported by Leonor Rivera-Calimlim, et al. in *The Journal of Pharmacology and Experimental Therapeutics*, 184:2 Sept. 18, 1972 that daily administration of L-Dopa causes weight reduction in rats. Weight loss in Parkinson patients treated long term with L-Dopa has also been reported, T Vardi etc. L-Dopa induced weight reduction is believed to be the result of several factors including altered absorptive capacity of the gut, loss of appetite, enhanced lipid metabolism and/or basal metabolism. (There have also been reports showing that L-Dopa induces weight gain).

Molindone hydrochloride is the trivial name of 3-ethyl-6,7 dihydro-2-methyl 5 morpholinomethyl indol-4(5H) one hydrochloride, which is described in U.S. Pat. No. 3,491,093 and is commercially available from Endo Laboratories under the trademark "Moban" and from Abbott Laboratories under the trademark "Lindone".

Molindone has an action which resembles that of major tranquilizers causing reduction of spontaneous locomotion aggressiveness, suppression of a conditional response and antagonism of the bizarre stereotyped behavior and hyperactivity induced by amphetamines. Heretofore, Molindone was prescribed primarily for the treatment of schizophrenia. Recommended human dosages generally range from 15 to 225 mg. per day, although 800 mg. has been administered in one case.

It has been reported by George Gardos and Jonathan Cole in *The American Journal of Psychiatry* 134:3, March 1977, that Molindone has caused weight loss in schizophrenics. A usual clinical course in schizophrenics is for improvement of patient's clinical condition to be accompanied by weight gain and deterioration to be accompanied by a corresponding weight loss. Gardos and Cole reported that when schizophrenic patients were administered Molindone, improvements of their clinical conditions were achieved without accompanying weight gain and in most cases by significant weight loss. There are also reports showing weight gain and improved appetite in Molindone treated patients, e.g., Sugarmann & Herrmann, *Chem. Pharm. Ther.* 8:261-65, 1967.

### SUMMARY OF THE INVENTION

It has been found that simultaneous administration of L-Dopa, with or without a decarboxylase inhibitor, plus Molindone hydrochloride results in weight loss substantially in excess of that which would be expected by the additive effects of the drugs individually and that the combination of L-Dopa and Molindone is a unique combination demonstrably superior as an anti-obesity composition to doses of either drug alone. The effective dosage of the two drugs in combination is reduced to levels that can be tolerated without the undesirable side effects of the higher dosage required if the drugs were administered singly.

### DETAILED DESCRIPTION OF THE INVENTION

Molindone and L-Dopa, each of which have previously been known to cause weight reduction in warm-blooded animals, have been found to have a synergistic effect when used in combination with each other. It has been found that Molindone functions as a potentiator to significantly increase the weight reducing functions of L-Dopa or L-Dopa compositions. Although the term "L-Dopa" is used throughout the application, it should be construed to include other known compounds in chemically equivalent amounts which are converted in the body to L-Dopa, such as known precursors, i.e., pro-L-Dopa.

Dopamine, which is formed by the decarboxylation of L-Dopa, is the chemical which actually associates with the brain receptors to produce the pharmaceutical effects associated with L-Dopa. The amount of dopamine available to the brain is generally provided by the L-Dopa which decarboxylizes within the brain. The action of the Molindone potentiates the effect of the dopamine in the brain or peripherally.

Accordingly, the L-Dopa is preferably used in combination with a stabilizer, such as an L-Dopa decarboxylase inhibitor, to prevent premature metabolism and breakdown of the L-Dopa which may occur in the gut mucosa or elsewhere before reaching the brain. The level of L-Dopa required is reduced if the L-Dopa is administered in stabilized form, and it is known to stabi-