

## **5HT1A receptor antagonists enhance the functional activity of fluoxetine in a mouse model of feeding.**

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Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. 5HT1A autoreceptors regulate synaptic levels of serotonin. A combination of a 5HT1A receptor antagonist and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a 5HT1A antagonist could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1 mice were trained to drink sweetened condensed milk. Fluoxetine was found to attenuate milk drinking, in a dose-dependent manner, at doses greater than 10 mg/kg, i.p. A 10 mg/kg dose of fluoxetine, which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a 5HT1A/beta adrenergic receptor antagonist or with LY206130, a more selective 5HT1A receptor antagonist. These treatment paradigms resulted in significant attenuation of the consumption of sweetened condensed milk. Since fluoxetine has been shown to be useful in the treatment of eating disorders and to promote weight loss in obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a 5HT1A receptor antagonist could be of clinical utility in the treatment of eating disorders and obesity. Copyright 1998 Elsevier Science B.V.

PMID: 9507085 [PubMed - indexed for MEDLINE]

1: Nippon Yakurigaku Zasshi 1976;72(1):23-30

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## **[Pharmacological studies on 5-hydroxy-L-tryptophan (L-5HTP). Interaction between L-5HTP and p-CPA]**

[Article in Japanese]

**Ohmori K, Kojima T, Marumo H.**

The effect of tryptophan hydroxylase inhibitor p-CPA and 5-HT precursor L-5HTP on conditional avoidance response and 5-HT content in rat brain was examined with the following results: Continuous administration of p-CPA improved acquisition of conditional avoidance response and retarded the loss acquired response. Body weight gain was suppressed at the low level. When the conditional avoidance response of the rats reached a certain level, it was suppressed by giving L-5HTP at the doses of 25 and 50 mg/kg in the rats given p-CPA, but no effect was observed in the rats given CMC. The 5-HT content in brain was reduced to 22% of control value by a single administration of p-CPA 316 mg/kg, but it rapidly recovered to a normal level with L-5HTP administration. From the above results, it was demonstrated that the presence or absence of p-CPA loading causes a significant difference in the appearance of behavior alteration in a rats following administration of L-5HTP.



1: Altern Med Rev 1998 Aug;3(4):271-80

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## **5-Hydroxytryptophan: a clinically-effective serotonin precursor.**

**Birdsall TC.**

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5-Hydroxytryptophan (5-HTP) is the intermediate metabolite of the essential amino acid L-tryptophan (LT) in the biosynthesis of serotonin. Intestinal absorption of 5-HTP does not require the presence of a transport molecule, and is not affected by the presence of other amino acids; therefore it may be taken with meals without reducing its effectiveness. Unlike LT, 5-HTP cannot be shunted into niacin or protein production. Therapeutic use of 5-HTP bypasses the conversion of LT into 5-HTP by the enzyme tryptophan hydroxylase, which is the rate-limiting step in the synthesis of serotonin. 5-HTP is well absorbed from an oral dose, with about 70 percent ending up in the bloodstream. It easily crosses the blood-brain barrier and effectively increases central nervous system (CNS) synthesis of serotonin. In the CNS, serotonin levels have been implicated in the regulation of sleep, depression, anxiety, aggression, appetite, temperature, sexual behaviour, and pain sensation. Therapeutic administration of 5-HTP has been shown to be effective in treating a wide variety of conditions, including depression, fibromyalgia, binge eating associated with obesity, chronic headaches, and insomnia.

Publication Types:

- Review
- Review, Tutorial

PMID: 9727088 [PubMed - indexed for MEDLINE]

1: Am J Clin Nutr 1992 Nov;56(5):863-7

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## **Eating behavior and adherence to dietary prescriptions in obese adult subjects treated with 5-hydroxytryptophan.**

**Cangiano C, Ceci F, Cascino A, Del Ben M, Laviano A, Muscaritoli M, Antonucci F, Rossi-Fanelli F.**

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Previous observations have shown that oral administration of 5-hydroxytryptophan (5-HTP) without dietary prescriptions causes anorexia, decreased food intake, and weight loss in obese subjects. To confirm these data over a longer period of observation and to verify whether adherence to dietary restriction could be improved by 5-HTP, 20 obese patients were randomly assigned to receive either 5-HTP (900 mg/d) or a placebo. The study was double-blinded and was for two consecutive 6-wk periods. No diet was prescribed during the first period, a 5040-kJ/d diet was recommended for the second. Significant weight loss was observed in 5-HTP-treated patients during both periods. A reduction in carbohydrate intake and a consistent presence of early satiety were also found. These findings together with the good tolerance observed suggest that 5-HTP may be safely used to treat obesity.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial

PMID: 1384305 [PubMed - indexed for MEDLINE]

1: Int J Obes Relat Metab Disord 1998 Jul;22(7):648-54

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## **Effects of oral 5-hydroxy-tryptophan on energy intake and macronutrient selection in non-insulin dependent diabetic patients.**

**Cangiano C, Laviano A, Del Ben M, Preziosa I, Angelico F, Cascino A, Rossi-Fanelli F.**

Department of Clinical Medicine, University of Rome La Sapienza, Italy.

OBJECTIVE: In obese patients, brain serotonergic stimulation via orally administered 5-hydroxy-tryptophan

(5-HTP), the precursor of serotonin, causes decreased carbohydrate intake and weight loss. Since diabetes mellitus is associated with depressed brain serotonin, hyperphagia and carbohydrate craving, we hypothesized that in diabetic patients, orally administered 5-HTP stimulates brain serotonergic activity and thus normalizes eating behaviour. To test this hypothesis, we investigated whether in diabetic patients: 1) predicted brain serotonin concentrations are depressed as a result of decreased availability of the precursor, tryptophan; and 2) oral 5-HTP is effective in reducing energy and carbohydrate intake. **SUBJECTS AND METHODS:** 25 overweight non-insulin dependent diabetic outpatients were enrolled in a double-blind, placebo-controlled study, and randomized to receive either 5-HTP (750 mg/d) or placebo for two consecutive weeks, during which no dietary restriction was prescribed. Energy intake and eating behaviour, as expressed by macronutrient selection, were evaluated using a daily diet diary. Plasma amino acid concentrations and body weight, as well as serum glucose, insulin and glycosylated haemoglobin were assessed. **RESULTS:** 20 patients (nine from the 5-HTP group and 11 from the Placebo group) completed the study. Brain tryptophan availability in diabetic patients was significantly reduced when compared to a group of healthy controls. Patients receiving 5-HTP significantly decreased their daily energy intake, by reducing carbohydrate and fat intake, and reduced their body weight. **CONCLUSIONS:** These data confirm the role of the serotonergic system in reducing energy intake, by predominantly inhibiting carbohydrate intake, and suggest that 5-HTP may be safely utilized to improve the compliance to dietary prescriptions in non-insulin dependent diabetes mellitus.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial

PMID: 9705024 [PubMed - indexed for MEDLINE]

1: Int J Obes Relat Metab Disord 1998 Jul;22(7):648-54

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## **Effects of oral 5-hydroxy-tryptophan on energy intake and macronutrient selection in non-insulin dependent diabetic patients.**

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Publication Types:

- Clinical Trial
- Randomized Controlled Trial

PMID: 9705024 [PubMed - indexed for MEDLINE]

## **The effects of oral 5-hydroxytryptophan administration on feeding behavior in obese adult female subjects.**

**Ceci F, Cangiano C, Cairella M, Cascino A, Del Ben M, Muscaritoli M, Sibia L, Rossi Fanelli F.**

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Nineteen obese female subjects with body mass index ranging between 30 and 40 were included in a double-blind crossover study aimed at evaluating the effects of oral 5-hydroxytryptophan administration on feeding behavior, mood state and weight loss. Either 5-hydroxytryptophan (8 mg/kg/day) or placebo was administered for five weeks during which patients were not prescribed any dietary restrictions. Feeding behavior was investigated by means of a questionnaire designed to establish the onset of anorexia and related symptoms. Food intake was evaluated using a three-day diet diary. BDI, SI, STAI-T, and STAI-S were used to assess mood state. The administration of 5-hydroxytryptophan resulted in no changes in mood state but promoted typical anorexia-related symptoms, decreased food intake and weight loss during the period of observation.

Publication Types:

- Clinical Trial
- Controlled Clinical Trial

PMID: 2468734 [PubMed - indexed for MEDLINE]

### **)L-Tryptophan/5-Hydroxytryptophan (Oxitriptan).**

Several human studies with 5HTP, the precursor of serotonin, have found good weight loss results with 5HTP. (18,19) There is evidence that some humans compulsively snack on CHO foods to feel better. The large insulin releases generated by such "carbo-bingeing" preferentially increase tryptophan/serotonin in the brain, temporarily reducing anxiety and depression in such people. (20) By providing an alternative, non-insulin-driven way to increase brain serotonin, L-Tryptophan, supplements may help reduce weight not only by reducing total caloric intake, but especially by reducing CHO intake, thus lessening hyper-insulinemia/insulin resistance. In the 1992 Italian study (19), 300mg/5HTP supplements may help reduce weight not only by reducing total caloric intake, but especially by reducing CHO intake, thus lessening hyperinsulinemia/insulin resistance. In the 1992 Italian study, (19) 300mg 5HTP 3 times daily before meals reduced women's caloric intake over a twelve week period from 3232 cal/day to 1273 cal/day, while reducing CHO intake from 350gm/day to 150gm/day. Weight dropped an average of eleven pounds. (The study did use special enteric-coated 5HTP capsules to prevent gut irritation) Ed [IAS provides same Italian 5HTP]. Taking 1000-1500mg L-Tryptophan at bedtime, or 50-100mg 5HTP before meals may reduce CHO-craving and intake.