

Effect of Litramine (IQP-G-002AS) on Weight Loss in Overweight and Obese US Population: A Randomised, Double-Blind, Placebo-Controlled Study

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Abstract

Background

Previous studies have shown that Litramine was effective in weight loss for overweight and obese subjects.

Objective

To further validate the weight loss effect of Litramine compared to placebo in US population.

Methods

Double-blind, randomised, placebo-controlled study conducted over 14 weeks including 2 weeks run-in. Overweight and obese subjects were randomly allocated to either Litramine™ or the placebo group. Primary endpoint was the comparison of the difference in body weight (lbs) at baseline and after 12 weeks of treatment with Litramine™ versus placebo.

Results

The Litramine group lost significantly more weight in comparison to the placebo group who gained weight instead (-2.53 lbs vs 2.56 lbs, $p < 0.001$).

Conclusion

Litramine is safe and efficacious for body weight loss.

Keywords: Litramine; Weight loss; IQP-G-002AS

Abbreviations: lbs: Pounds; BMI: Body Mass Index

Introduction

Since 1980, worldwide obesity has more than doubled with an estimated 10% of world population classified as obese [1]. It is projected that by 2048, all American adults will become overweight or obese based on 2012 trends [1]. In 2010, overweight and obesity were estimated to cause 3.4 million deaths worldwide [2]. This epidemic has also placed higher burdens on healthcare systems, as those who are obese are at higher risk for many serious health conditions such as cardiovascular diseases, type 2 diabetes and certain cancers [3-5].

Weight loss reduces morbidity risk in metabolic diseases. The INTERHEART study found that a sustained weight loss of just 5-10% can have a positive impact on metabolic and cardiovascular risks [6]. The same amount of weight loss can also reduced progression of diabetes and improve diabetes control [7,8]. Body weight can be influenced by complex factors such as genetics and metabolism but one of the main contributory factor is positive energy balance. According to a recent analysis, increased food energy supply has been implicated as a major driver of this global epidemic

[9]. Treatments that aim to reduce caloric intake and absorption of dietary fat can be considered as effective approaches to reducing weight [10].

The investigational product, Litramine (IQP-G-002AS) is a patented natural fibre complex derived from *Opuntia ficus-indica*, that has been enriched with additional soluble fibre from *Acacia sp.* Litramine has been standardised for its lipophilic activity, where 1g of Litramine binds to 10g of fats. In the gut, Litramine forms fat-fibre complexes which are indigestible thus reduces calories uptake. Its mechanism of action has been largely described in other studies [11,12]. There have been two previous studies which confirmed that Litramine is safe and efficacious for weight loss and weight maintenance [12,13]. This study was conducted to further validate the efficacy of Litramine as a weight loss supplement under a different study set up of a US population.

Method and Procedure

Trial Design

This double-blind, randomised, placebo-controlled study was conducted over 14 weeks including a 2-week run-in period at a study center in California, USA. Subjects were randomly allocated in 1:1 ratio to either the Litramine or the placebo group. All subjects gave written informed consent voluntarily. The clinical investigation was approved by the Western Institutional Review Board® (Olympia WA), and was performed in compliance with EN ISO 14155, the Declaration of Helsinki, and the Guideline for Good Clinical Practice (CPMP/ICH/135/95).

Eligible subjects included overweight and obese subjects (BMI 25-35 kg/m²) between the ages of 18 to 60 years who are accustomed to three main meals per day, with a consistent and stable body weight 3 months prior to study enrolment. Women of childbearing age were required to use appropriate birth control methods during the duration of study. Subjects who had known sensitivity to the ingredients in the investigational product were excluded from the study. Other exclusion criteria included subjects with a history of medical disorders that may affect body weight (such as diabetes mellitus, Cushing's disease etc.), presence of any active gastrointestinal (GI) disease or malabsorption disorders, history of GI surgery, history of eating disorders, history of cardiac disease or renal disease, pregnant and lactating women and subjects on medication that could influence GI function. Subjects using other anti-obesity products are excluded unless such medications were discontinued 3 months prior to the study initiation. Subjects who were taking daily dietary supplements were allowed to participate, provided that they stop taking the supplements 2 weeks before the start of the study. Subjects were also excluded if they were currently on any diet regimen (such as low carbohydrate, low fat or high protein diets), or in case they undergo more than 3 hours of strenuous physical activity per week.

At screening visit, subjects first provided their informed consent. Inclusion and exclusion criteria were then assessed. A detailed medical history was obtained from each of the subjects and a physical examination was conducted by the investigator. Body weight and blood pressure measurement were also taken. Subjects then underwent a two-week washout period of any previous dietary supplement intake, and kept a diary on food intake and satiety. Subjects who are compliant (>85%) in completing the diary were included.

Eligible subjects received either two tablets (1g) of Litramine or matching placebo, to be taken three times a day after each main meal. The placebo tablet was identical in appearance to the Litramine tablet but contained 500 mg of microcrystalline cellulose as replacement for the active ingredient. Tablets were packed into bottles and labeled by an independent pharmacist for each subject according to the randomisation schedule. Both the investigators and the subjects were not informed of the treatment allocation throughout the study.

Subjects were followed up through scheduled visits with the investigators on week 4, 8 and 12. At each visit, subjects were required to fast for 10 hours prior to the visit. This was to minimise influence from recent food consumption on measurements.

All subjects were counselled after each study visit to maintain a nutritionally balanced diet according to USDA recommendation. However no formal dietary restriction or any behavioral modification programmes were applied to simulate "free-living conditions". The subjects were asked to keep a diary documenting their daily intake of the investigational product and also their food intake. Subjects were also asked to complete the Stanford Exercise Behavioural scale [14], which is used to determine the level of exercise that the subject had undertaken.

End Points

The primary endpoint of this study was the comparison of the the difference in body weight (lbs) at baseline and after 12 weeks of treatment with Litramine™ versus placebo in overweight and obese subjects. Body weight was measured using a calibrated weighing scale in subjects wearing underwear and no shoes at screening, baseline and subsequently at 4-week intervals.

Secondary endpoints included changes in mean waist circumferences, body mass index (BMI) and mean body fat mass. Waist circumference (inches) was measured at the level midway between the lateral lower rib margin and the iliac crest. Body fat content was measured by bioimpedance method using validated electronic weighing scales.

Safety Parameters

Safety assessment included measurement of vital signs such as resting blood pressure, heart rate (beats per minute), body temperature (°F) and respiratory rate (breaths per minute). The subjects were asked open-ended questions to establish any adverse effects at each visit. All adverse effects were recorded regardless of causality.

Statistical Analyses

Demographic and baseline characteristics of efficacy and safety variables were assessed based on descriptive statistics. All primary and secondary variables, as well as safety variables were evaluated as relative change within the groups. For all statistical analyses, a level of significance of p<0.05 was assumed. All values are presented as mean (SD) unless indicated

otherwise. Efficacy and safety data were analyzed based on modified per protocol data, which was defined as subjects who had at least one post-dose visit completed. All statistical analyses were done using the SPSS Statistic software, V19.0 (SPSS, Chicago, IL).

Results

A total of 217 subjects were screened with 99 subjects being randomised into two groups. 3 subjects were excluded after randomisation due to non-compliance. 9 subjects in the Litramine group and 10 subjects in the placebo group did not turn up for the 2nd follow up visit and were thus excluded from analysis. All remaining subjects attended all clinic visits as planned. The baseline characteristics are shown in Table 1 below. There were no significant differences between both groups.

Parameter	Litramine (n=48)	Placebo (n=48)
Gender		
Male	15	16
Female	33	32
Age (years)	38.33 (11.38)	39.63 (11.19)
Weight (lbs)	186.93 (33.26)	185.28 (22.37)
Height (inches)	65.50 (3.88)	66.12 (3.56)
BMI (kg/m ²)	30.45 (3.38)	29.76 (2.47)

Table 1: Baseline characteristics of randomised subjects. Values are presented as mean (SD).

Figure 1 shows mean body weight of the subjects throughout the study. The mean body weights of the subjects at baseline were 190.06 (SD 28.66) lbs in the Litramine group and 185.74 (SD 31.91) lbs in the placebo group. There is a trend towards weight reduction in the Litramine group compared to the placebo group. At the end of week 12, mean body weight in the Litramine group was 187.53 (SD 28.87) lbs vs 188.30 (SD 33.16) lbs in the placebo group. The Litramine group lost significantly more weight than the placebo group compared to the placebo group who gained weight instead (Table 2). In terms of percentages, those taking Litramine actually lost 1.33% of their initial body weight compared to those on placebo who gained 1.38% instead (Figure 2).

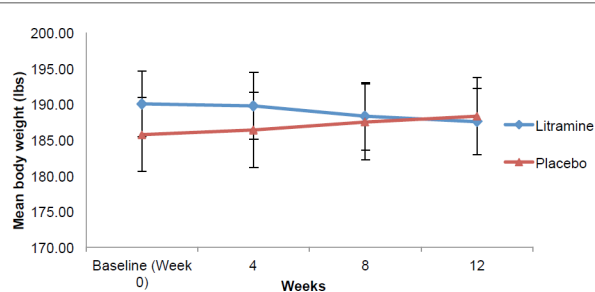


Figure 1: Body weight reduction over time (Error bars represent SEM)

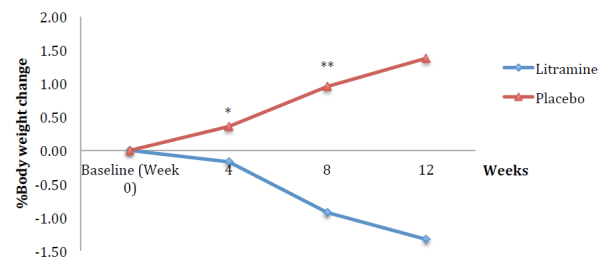


Figure 2: % Body weight reduction over time. *p=0.035, **p<0.000

Table 2: Mean changes in primary and secondary parameters between baseline and week 12

(Negative values represent reduction). Values are presented as mean (SD)

Parameter	Litramine (n=39)	Placebo (n=38)	p-value
Body weight (lbs)	-2.53 (3.75)	2.56 (4.73)	<0.001
BMI (kg/m ²)	-0.41 (0.60)	0.43 (0.75)	<0.001
Waist circumference (inches)	-1.56 (5.98)	0.55 (6.75)	0.213
Body fat (%)	-0.18 (6.71)	-0.44 (4.56)	0.836

BMI

Subjects in the Litramine group had a mean BMI of 30.35 (SD 3.22) kg/m² compared to the placebo group at 30.51 (SD 3.28) kg/m² at baseline. At the end of the study, there was a significant reduction in BMI for subjects in the Litramine at -0.41 (SD 0.60) kg/m² compared to the subjects in the placebo group whose BMI gained slightly at 0.43 (SD 0.75) kg/m² (Table 2) compared to baseline.

Waist Circumference

At baseline, subjects in the Litramine group had a mean waist circumference of 39.40 (SD 4.74) inches while the placebo group had a mean waist circumference of 38.63 (SD 4.16) inches. Although the change in waist circumference measured at the end of the study was not statistically significant between the Litramine and placebo groups, the Litramine group showed a trend towards reduction in waist circumference, whereas the placebo showed an increasing trend.

Body Fat Percentage

After 12 weeks, there was a slight decrease for both Litramine and placebo group, which was not statistically significant. Subjects in Litramine group had their body fat percentage drop by 0.18 (SD 6.71)% while those in placebo group reduced by 0.44 (SD 4.56)%.

Safety and Tolerability

There were no clinically significant changes in mean body temperature, mean blood pressure and mean heart rate during the study. Throughout the study, there were 18 reported cases of adverse events in 12 subjects. Reported cases included upper respiratory tract infections and other common cold symptoms, which were assessed by the investigator not to be related to intake of the study product. There was one case of allergic rash, which was possibly linked to intake of the study product. This reaction was deemed not serious by the investigators and a decision was made to continue with the study. The condition was then resolved after a month. No serious adverse events were reported during the course of the study.

Discussion

In this study, we looked at the use of Litramine as a weight loss aid in conjunction with a balance diet. EU and US guidelines recommend that those who have a BMI > 25 kg/m² should first be counselled on lifestyle changes and nutritional modifications, through reduction of caloric intake, before consideration of other methods.

Litramine works via mechanical and physical means within the gastrointestinal tract. Previous studies have shown Litramine to be effective in weight loss through the binding of dietary fat [12,13]. The fat-fibre complexes formed are not absorbable and prevent further utilisation or storage of the dietary fat in the body, resulting in a lower caloric uptake.

In the current study, there were significant changes in subjects' BMI and weight. Although the weight reduction was short of the 5% weight loss stipulated for significant health risk reduction, it must be borne in mind that this study was conducted with the purpose to investigate the effectiveness of Litramine in a population not instructed to modify their diet or lifestyle. Therefore, this study results reasonably support the conclusion that Litramine is effective in weight loss even if those who are taking it do not apply any stringent behavioural modifications. However, we recommend the intake of the product in combination with a slightly hypocaloric dietary regimen, similar to the conditions applied in the previous clinical trial to achieve a better weight loss effect [12].

Current marketed antiobesity drugs often cause abdominal discomfort and are associated with liver injury, cardiac and psychiatric side effects [15-17]. The lipase inhibitor, Orlistat, which is commonly prescribed and available over the counter to help with weight loss, is reported to cause unpleasant side effects such as oil spotting [15]. In comparison, Litramine is a safe and effective alternative to aid in weight loss. No serious adverse effects were reported during the course of this study. The active in Litramine has long been used as a food source and its safety has also been shown in previous clinical trials [12,13].

Limitations

There was no follow-up performed after termination of the study, and subsequent body weight regain post-study may occur due to the well known "yo-yo" effect in conjunction with dietary interventions. However a previous weight maintenance study conducted with Litramine showed that continuation of the intake over a period of 24 weeks does also support weight maintenance [13].

The study duration was relatively short. Besides measuring weight loss, it was not able to measure effect of Litramine in improving obesity-related health risks.

Conclusion

Evidence from previous studies showed that Litramine is an efficacious mean towards weight reduction. This study reiterates the fact that Litramine can be considered as an effective weight loss tool in combination with a healthy lifestyle.

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