

Weight loss and delayed gastric emptying following a South American herbal preparation in overweight patients

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Abstract

Background Obesity and overweight may soon affect more than half of the population in some regions of the world and are associated with diabetes, hypertension and other diseases that cause morbidity, mortality and high health-care expenditure. No one approach, whether dietetic management, medication, or commercial weight loss programme, can alone solve the problem – all potential treatments need to be investigated and exploited. Among the herbal preparations known to non-western cultures are materials which may have applications in modulating physiological processes which influence gut motility, food intake and energy balance. One such mixed herbal preparation is ‘YGD’ containing Yerbe Maté (leaves of *Ilex paraguayensis*), Guarana (seeds of *Paullinia cupana*) and Damiana (leaves of *Turnera diffusa* var. *aphrodisiaca*).

Aims This study had two distinct aims: to determine the effect of a herbal preparation ‘YGD’ containing Yerbe Maté, Guarana and Damiana on gastric emptying; to determine the effect of the same preparation on weight loss over 10 days and 45 days and weight maintenance over 12 months.

Methods Gastric emptying was observed using ultrasound scanning in seven healthy volunteers following YGD and placebo capsules taken with 420 mL apple juice. Body weight was observed before and after 10 days of treatment with three YGD capsules or three placebo capsules before each meal for 10 days in 44 healthy overweight patients attending a primary health care centre. Forty-seven healthy overweight patients entered a double-blind placebo-controlled parallel trial of three capsules of YGD capsules before each main meal for 45 days compared with three placebo capsules on body weight. Body weight was monitored in 22 patients who continued active (YGD capsules) treatment for 12 months.

Results The herb preparation YGD was followed by a prolonged gastric emptying time of 58 ± 15 min compared to 38 ± 7.6 min after placebo ($P = 0.025$). Body weight reductions were 0.8 ± 0.05 kg after YGD capsules compared to 0.3 ± 0.03 kg after placebo capsules over 10 days, and 5.1 ± 0.5 kg after PGD capsules compared to 0.3 ± 0.08 kg after placebo over 45 days. Active treatment with YGD capsules resulted in weight maintenance of the group (73 kg at the beginning and 72.5 kg at the end of 12 months).

Conclusions The herbal preparation, YGD capsules, significantly delayed gastric emptying, reduced the time to perceived gastric fullness and induced significant weight loss over 45 days in overweight patients treated in a primary health care context. Maintenance treatment given in an uncontrolled context resulted in no further weight loss, nor weight regain in the group as a whole. The herbal preparation is thus shown to be one that significantly modulates gastric emptying. Further clinical studies with dietetic monitoring of energy intake, dietary quality, satiety ratings, body weight and body composition are now indicated, and examination of the active principles contained in the three herbal components may prove rewarding.

Introduction

Obesity and overweight are the main challenge to health and well-being of most populations over the next 20 years. More than half of the populations of some regions of the world may soon be affected (James & Ralph, 1999). Obesity and overweight are associated with diabetes mellitus, hypertension and other diseases that cause morbidity, mortality and high health-care expenditure (Oster *et al.*, 1999). No one approach, whether dietetic management, medication or commercial weight loss programme, can alone solve the problem – all potential treatments need to be investigated and, if shown to be effective, exploited.

Among the herbal preparations known to non-western cultures are materials which may have applications in modulating physiological processes which influence gut motility, food intake and energy balance. The herbal treasure house of South America offers one such mixed herbal preparation 'YGD' containing Yerbe Maté (leaves of *Ilex paraguayensis*), Guarana (seeds of *Paullinia cupana*) and Damiana (leaves of *Turnera diffusa* var. *aphrodisiaca*). These herbs have long been used in folk medicine in South America and

Mexico, as herbs with diverse effects (Hill, 1952; Schery, 1954; Bradley, 1992). However no controlled studies of the effects on body weight and the mechanisms involved have yet been published.

Obesity and overweight are caused by a multitude of factors (Hill & Melanson, 1999). While they are the consequence of a disturbance of the energy balance equation, many factors influence the nature of food and its digestibility, appetite and susceptibility to satiation, upper-gut motility and its influence on food intake, intestinal factors influencing absorption and subsequent metabolic responses, efficiency of metabolic pathways and futile cycling, hormonal responsiveness of adipose tissue at different sites, and central responsiveness to peripheral signals from adipose tissue. This multitude of factors creates many opportunities for influencing the processes that lead to obesity.

Upper gut motility influences appetite and satiety, but there is still debate about whether gastric emptying is faster in obese subjects compared to non-obese controls. Some investigators (Wisén & Johansson, 1992) have found no significant differences in gastric emptying between lean and obese subjects while others (Gryback *et al.*, 1996) found a significantly shorter emptying

in obese compared to normal-weight subjects. It has been suggested that obese subjects may absorb dietary energy more rapidly than non-obese (Wisén & Johansson, 1992) and manipulation of upper gut motility is a therapeutic option which merits further investigation.

Trends in health care suggest an increasing use of herbal preparations in the Western world over the coming decades – clearly any herbal preparation with effects on weight control would be useful. The effect of the herbal mixture containing Yerbe Maté, Guarana and Damiana on gastric emptying, and on body weight in a controlled primary health care setting for 45 days was thus investigated.

Methods and materials

The herbal preparation and placebo

Guarana, a dough made from the seeds of *Paullinia cupana*, which grows in Brazil and Venezuela, contains 3–6% caffeine, 5–8.5% tannins, 7.8% resins, 2–3% lipid, 0.06% saponin, 5–6% starch and 1.5% colouring agents (Schery, 1954). Yerbe Maté is an extract of *Ilex paraguayensis* from Brazil, Argentina and Paraguay containing 1–1.5% caffeine, 4–10% tannins and 3% resins and lipids (Hill, 1952). Damiana is obtained from the leaves of the plant *Turnera diffusa* var. *aphrodisiaca* from California, Mexico, Brazil and Bolivia and contains ethereal oils, resins and tannins (Bradley, 1992). The herbal extracts were obtained as powders. The components were mixed and prepared in capsules (Jemo-pharm A/S, Hassevej 1, DK 4780 Stege, Denmark) each containing 112 mg Yerbe Maté, 95 mg Guarana and 36 mg Damiana extract. In this paper this preparation is referred to as 'YGD capsules'.

Placebo capsules were prepared using matched capsules with lactose contents.

Gastric emptying

Subjects

The gastric emptying study was carried out in Denmark by one of us (T.A.). Seven healthy normal-weight volunteers, six women and one man, with no

previous history of pregnancy or gastrointestinal disease, were instructed not to drink coffee or to smoke cigarettes on the day of the study.

Study design

Each volunteer was examined twice, once after receiving three YGD capsules and once after receiving three placebo capsules containing lactose, the treatment order being randomized. The study was performed in a double-blind manner: neither subject nor observer was aware of the treatment used. The subjects fasted for 8 h before the study and the emptiness of the stomach was confirmed by ultrasound scan before commencement (emptiness being defined as a gastric volume of less than 10 mL). The placebo or 'YGD caps' were ingested with 20 mL apple juice and 15 min later 400 mL apple juice was also ingested (this point was defined as time zero).

Every 5–10 min ultrasound scanning was performed as described below until the stomach was empty. Gastric emptying time (GET) was defined as the elapse of time between ingestion of 400 mL apple juice and the time when the fundus and body of the stomach was completely empty as shown by a gastric volume of less than 10 mL. The gastric volume was calculated by placing a computer-generated intragastric ellipsoid on each of the ultrasound scan pictures (Fig. 1). The gastric volume was calculated as the ellipsoid volume. The results of measurements of gastric volume were noted immediately and checked later by playback of the videotapes. After completion of all the measurements and volume calculations, the treatment code was opened and the calculated values for placebo and YGD-treated groups were compared by an independent observer.

Gastric volume and emptying evaluated by ultrasound scanning

Gastric volume and emptying was determined by ultrasound examination of the stomach using a 3.5-MHz curved array transducer and an Aloka 630 standard unit employing a modification of the techniques described by Holt *et al.* (1980) and Bateman & Whittingham (1982). Continuous scans were performed by switching the transducer between two alternate projections. The first



Figure 1 Ultrasound scan with computer-generated ellipsoid superimposed.

projection was an oblique upward view with the transducer positioned under the left curvature allowing the gastric fundus, body and antrum to be inspected, and the second was a transverse view across the epigastrium with a slight upward direction viewing the antrum, pylorus and the duodenal bulb. The two projections ensured very clear visual estimation of the volume (see Fig. 1). All examinations were recorded on videotape and still pictures were taken every 5 min.

Body weight changes over 10 and 45 days

The effect on body weight of 10 days treatment with the herb preparation (YGD capsules) and placebo (lactose-containing capsules) was recorded in a double-blind pilot study (undertaken by J.F.) of 44 healthy subjects attending a primary health care practice in France for treatment of mild to moderate overweight. None of these patients took any drugs and none was following any specific diet. The patients were instructed to take three capsules with a large glass of water 15 min before the main meals and they were asked to take great care not to change their normal food habits. Any side-effects were also noted. They were weighed at the beginning and end of 10 days treatment.

Patients were not asked to record dietary intake as this would have influenced behaviour – adding a second variable to the intervention.

The effect on body weight of 45 days treatment with the herb preparation (YGD capsules) and placebo was also studied in a double-blind parallel study of 47 patients. These subjects also attended the general practice for mild moderate overweight (BMI range 25.8–30.4) but were otherwise healthy. They did not take any medicinal drug or diet before or during the study. The subjects, who were between the ages of 20 and 60 years, were randomly allocated to active treatment (YGD capsules) (15 women, nine men, average age 38.2 years) and placebo (17 women, six men, average age 38.6 years).

In view of the good response in the YGD group, and following enquiry by the subjects it was agreed to provide YGD to that group for a longer period. This was not originally planned and was not intended to be a controlled trial.

Weight maintenance over 12 months following initial weight loss

Twenty-two of the 24 patients who had taken YGD in the studies referred to above continued active

treatment for 12 months. Each subject was reviewed monthly in a primary health care practice, was weighed and on each occasion was given a month's supply of YGD capsules.

Statistical analysis and research ethics review

Comparison of the measurements of gastric emptying times after YGD and placebo capsules was performed by the Mann-Whitney test for paired samples (a P -value of < 0.05 was considered statistically significant). Other comparisons were undertaken using the t -test for paired samples where appropriate. The studies were approved by the Local Research Ethics Committee.

Results

Rate of gastric emptying measured by ultrasound scanning

The mean (\pm SD) Gastric emptying times (GET) were 38 ± 7.6 min following placebo capsules and 58 ± 15 min following YGD capsules, corres-

ponding to a mean 53% increase of GET following YGD capsules (Fig. 2). The prolongation of gastric emptying was statistically significant ($P = 0.025$). In all cases GET was prolonged following YGD capsules, increases ranging from 15% to 58%.

Body weight over 10 and 45 days

In the study over 10 days the 22 subjects who received placebo (baseline BMI $24.9\text{--}29.0$ kg m^{-2}) showed a mean (\pm SEM) decrease in body weight of 0.3 ± 0.03 kg while the 22 subjects who received the test compound (baseline BMI range $25.1\text{--}29.5$ kg m^{-2}) showed a decrease of 0.8 ± 0.05 kg.

In the study over 45 days, the 24 subjects receiving the YGD capsules showed a mean (\pm SEM) decrease in body weight of 5.1 ± 0.5 kg, and the 23 subjects receiving the placebo capsules showed a mean (\pm SEM) decrease of 0.3 ± 0.08 kg (Fig. 3).

Effect on weight maintenance after an initial weight loss

Twenty-two subjects (10 women and 12 men) completed the 12-month uncontrolled maintenance

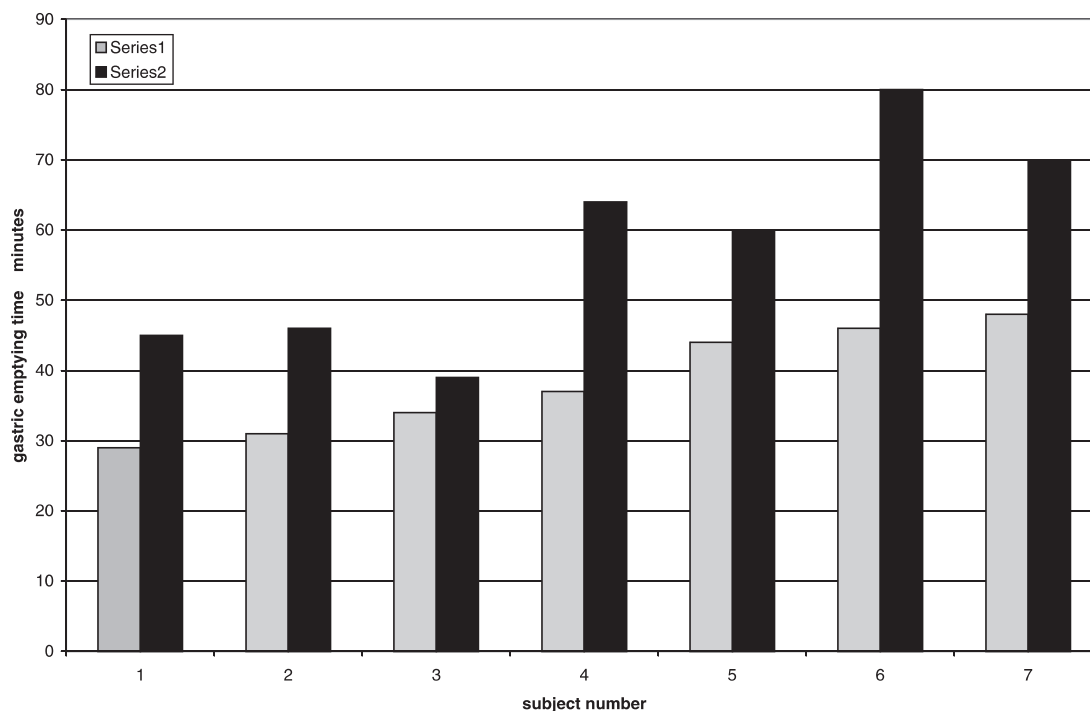


Figure 2 Gastric emptying time following treatment with the herbal preparation (YGD capsules) and placebo capsules.

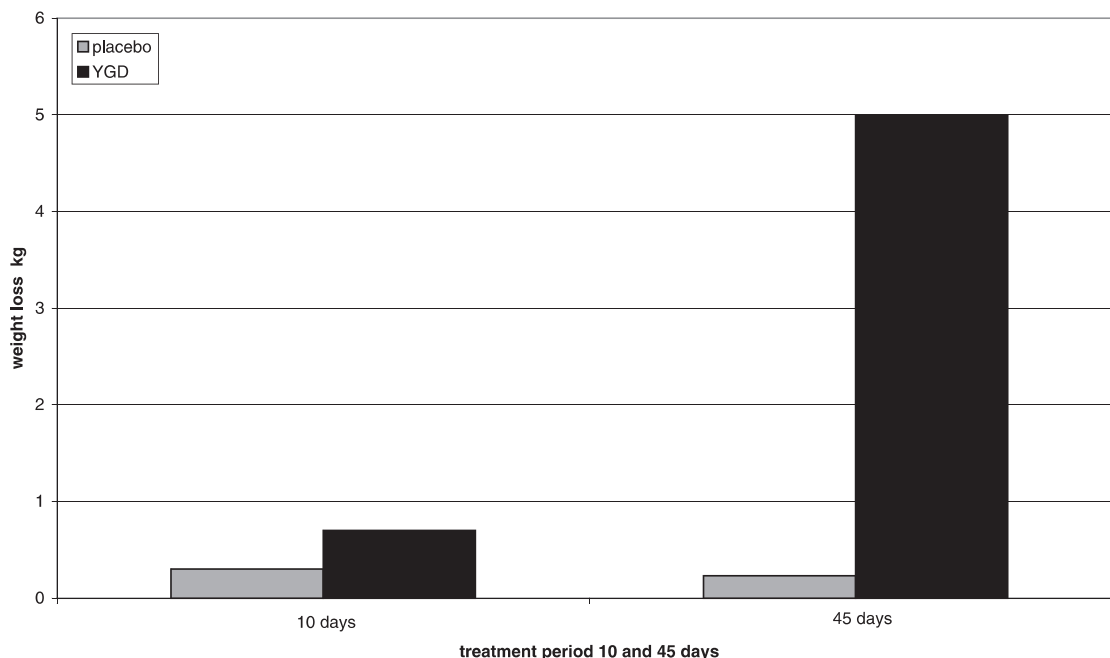


Figure 3 Mean weight change (kg) after 10 days of treatment with placebo ($n = 22$) or herbal preparation (YGD) ($n = 22$) and after 45 days of treatment with placebo ($n = 24$) or herbal treatment (YGD) ($n = 24$).

treatment. Mean body weight was 73 kg (range 57–85 kg) at the commencement and 72.5 kg (range 58–87 kg) at the end of the period.

Discussion

It has been suggested that the stomach plays an important role in regulating delivery of energy and nutrients to the intestinal tract for absorption (Wisen & Hellstrom, 1995). Certainly, extremes of emptying rates perturb the digestive processes: too slow (such as following non-selective vagotomy with an inadequate pyloroplasty) limits food energy intake and results in weight loss, while excessively rapid emptying results in 'dumping' of hypertonic digesta into the small intestine with consequence disturbances of blood volume and rapid swings of blood glucose and insulin, as well as intestinal hurry and diarrhoea. Whether variation in gastric emptying within the 'normal' range has any significant effect on energy intake, rates of digestion and energy balance has not yet been fully addressed. The studies reported here were designed to investigate the effect of a promising South American herbal preparation 'YGD'

containing Yerbe Maté (leaves of *Ilex paraguayensis*) Guarana (seeds of *Paullinia cupana*) and Damiana (leaves of *Turnera diffusa* var. *aphrodisiaca*) which was believed to have potential as an aid to weight reduction by virtue of its effects on gastric emptying.

Several quantitative methods of measuring gastric emptying are available. Gastric emptying has been measured using radioisotope scanning techniques (Hutson & Wald, 1993) and blood samples subsequent to ingestion of a marker of gastric emptying, e.g. using paracetamol (Van Wyk *et al.*, 1995). However, measurement of gastric emptying using ultrasound gastric scanning is an attractive method because of its simplicity and non-invasive nature. The ultrasound method has been used in several ways. There is a rather complex method of regional gastric function measurements (Fujimura *et al.*, 1994) and a somewhat simpler modification with the combined time and ellipsoid volume measurements (Holt *et al.*, 1980; Bateman & Whittingham, 1982) described in this paper. Others have also found ultrasound scanning useful for the evaluation of gastric emptying (Fujimura *et al.*, 1994).

Using this ultrasound scanning technique the herbal preparation YGD was shown to significantly slow gastric emptying. Several normal regulatory mechanisms important for feeding behaviour may explain the effect of YGD. These factors include autonomic nervous regulatory mechanisms as well as gastrointestinal peptides.

The evidence for weight reduction over 10 days and 45 days obtained in a primary health care context suggests that the effect on gastric emptying was sufficient to influence food energy intake. Patients were asked not to change their dietary habits, and were not asked to make any dietary records since this would have influenced their behaviour. It might, however, have been possible to undertake a dietary recall examination at the end of each period to gain some information on dietary intake, but this was not done. The amount of weight lost, equivalent to about 0.75 kg per week, would be regarded as safe, not excessive and sufficient to improve biomarkers of disease in susceptible individuals (Pi-Sunyer, 1996).

In clinical practice, any adjunct or aid to weight loss would only be given in conjunction with sound advice about dietary change, exercise and lifestyle with appropriate monitoring of the patients well-being, and where appropriate measurement of biomarkers such as blood pressure, blood glucose and blood lipids. The evidence provided here for a weight-loss effect without concurrent dietary advice raises the question of whether the herbal preparation would be more effective taken in conjunction with such advice – this needs to be tested. If this preparation were to be used as an ‘over-the-counter’ herbal preparation users should be informed about dietary change, exercise and lifestyle relevant to successful weight loss.

Concern that a herbal preparation of this type if taken long-term might cause continued weight loss to an undesirable degree is dispelled by the evidence presented here that 22 subjects continuing active treatment for 12 months did not lose any more body weight. These subjects did not regain weight either, suggesting an application for YGD in weight maintenance, albeit in an uncontrolled study.

The herbal preparation, ‘YGD’, significantly delayed gastric emptying, reduced the time to perceived gastric fullness and induced significant

weight loss over 45 days in overweight patients treated in a primary health care context. Maintenance treatment given in an uncontrolled context resulted in no further weight loss, nor weight regain in the group as a whole. The herbal preparation is thus shown to be one that significantly modulates gastric emptying. The evidence for induction of weight loss suggests that the preparation may increase satiation and reduce energy intake – but this needs to be tested experimentally. Since moderate weight reduction may be beneficial in improving biomarkers of disease in some patients, this herbal preparation may prove to be an additional new method for facilitating weight loss. Further clinical studies with dietetic monitoring of energy intake, dietary quality, satiety ratings, body weight and body composition are now indicated, and examination of the active principles contained in the three herbal components may prove rewarding.

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