Advancement in Medicinal Plant Research
Vol. 4(3), pp. 73-82, July 2016
ISSN: 2354-2152
Full Length Research Paper

Double-blind, randomized, placebo-controlled, bicentric clinical investigation to evaluate the benefit and tolerability of Redusure IQP-AK-102 in reducing body weight in overweight and obese subjects

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Accepted 30 June, 2016

ABSTRACT

Appetite regulation plays an important role in weight management. Dietary fibres can enhance satiety sensation due to their unique physicochemical properties. This study evaluated the benefit and tolerability of Redusure IQP-AK-102, a patent pending fibres composition for achieving weight loss in overweight and obese Caucasians on hypocaloric diet. Eligible subjects were randomized to take either IQP-AK-102 or identical looking placebo with 250 ml of water 30 to 60 min before breakfast, lunch and dinner for 12 weeks. The primary efficacy endpoint of the study was the difference of mean body weight change after 12 weeks, between the IQP-AK-102 and the placebo groups. Other endpoints measured during the study included changes in body composition (body fat mass and body fat content), waist and hip circumferences, food cravings, satiety, as well as safety and tolerability endpoints. A total of 119 subjects, aged between 18 and 65 years old, who were overweight and obese (BMI of 25 to 35 kg/m^2) were enrolled and randomized. IQP-AK-102 supplementation demonstrated a significant mean body weight reduction compared to placebo after 12 weeks [3.53 kg (SD 2.28) and 0.14 kg (SD 1.84) respectively, $p < 0.001$)]. A significant difference in mean body weight reduction was observed as early as after 4 weeks of IQP-AK-102 consumption [1.01 kg (SD 1.43) versus 0.25 kg (SD 1.17) respectively]. Other efficacy endpoints also showed significant differences between the two intervention groups by the end of the study. No clinically significant changes in blood profiles, clinical chemistry and blood pressure were noted throughout the 12-week study. There was no significant difference in the proportion of subjects that reported adverse events in both study groups. Administration of IQP-AK-102 in conjunction with good dietary and exercise habits for 12 weeks promotes significant weight loss in overweight and obese but otherwise healthy subjects. IQP-AK-102 also shows good safety and tolerability profile.

Keywords: Weight loss, satiety, dietary fibre, overweight, obesity.

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INTRODUCTION

Overweight and obesity are increasingly difficult to overcome. There is a continuous rise in the prevalence of overweight and obesity in the last 3 decades and worldwide obesity has more than doubled since 1980. According to figures published by WHO, in 2014, more than 1.9 billion adults above 18 years of age are overweight and of these 600 million are obese, which is a whopping 39% and 13% of world population, respectively

(WHO, 2015). Obesity is a complex health issue with contribution from multiple factors, including genetics, behavior, lifestyle etc. The fundamental cause of overweight and obesity is an energy imbalance between calories consumption and expenditure. A chronic surplus in energy intake results in body fat deposition and body weight gain, and ultimately results in the increased risk for diabetes and cardiovascular diseases [NHLBI, 1998; USDHHS, 2001]. On the other hand, overweight and obesity, and their associated non-communicable diseases, can mostly be prevented if the energy intake can be managed. Various strategies have been proposed to reduce the calories intake, including behavioral interventions, low-calorie diets, and the use of appetite regulating agents.

Appetite regulation plays an important role in determining food intake. It is a complex process influenced by biological, behavioral and environmental stimuli. Satiation, defined as the process of feeling full and subsequent stopping of food consumption during eating, reduces hunger and limits the energy consumptions during meals. On the other hand, satiety or more precisely intermeal satiety delays the onset and possibly reduces the consumption of the next meal (Gerstein et al., 2004). Besides pharmaceutical drugs, the potential use of dietary fibre as ingredient for promoting satiety is well recognized due to its unique physicochemical properties. High viscosity and bulking food components such as dietary fibres are expected to elicit stronger satiation/satiety than macronutrients or clear liquids (Edwards and Gardia, 2009). Dietary fibre has been known to enhance the sensation of satiety in the upper gut by increasing gastric distension and delaying gastric emptying, which subsequently reduces the food intake (Halford and Harold, 2012; Lyon and Kacinik, 2012). An increased consumption of dietary fibre is shown to correlate directly with the reduction of body weight and fat (Kromhout et al., 2001; Liu et al., 2003; Ludwig et al., 1999).

The investigational product is formulated with Redusure IQP-AK-102, a proprietary, patent pending composition of three soluble fibres which includes purified glucomannan, kappa-carrageenan and xanthan gums. All of these ingredients are known individually as high molecular weight polysaccharides.

Glucomannan, derived from the tuberous roots of the plant *Amorphophallus konjac,* is one of the most viscous dietary fibre known. It has the ability to absorb up to 50 times its weight in water (Doi, 1995). Following absorption of water, glucomannan bulks up into a viscous gel that is low in energy density, which delays gastric emptying and slow glucose delivery to the intestinal mucosa, thereby reducing dietary calories uptake and resulting in promotion of satiety and satiation, leading to weight loss (Keithley and Swanson, 2005; McCarty, 2002).

In numerous clinical studies, glucomannan has shown its efficacy for inducing weight loss in both adults and children. The satiating effect of a dietary soluble fibre like glucomannan has been corroborated by various intervention studies in demonstrating the clinical effect of dietary fibre in weight management (Slavin and Green, 2007; Gemen et al., 2011; Howarth et al., 2001; Pereira and Ludwig, 2001). Observations from clinical studies also support the role of glucomannan as an adjunct therapy to exercise program or low calorie diet program; suggesting that weight loss in treatment of obesity are more effective than taking glucomannan alone (Birketvedt et al., 2005; Cairella and Marchini, 1995; Kraemer et al., 2007).

Kappa-carrageenan, commonly used in processed food or drugs as stabilizer, thickener, and gelling agent, was co-formulated due to its intrinsic thickening and gelling properties. Animal study performed on carrageenan reported that oral administration of 10% carrageenan causes 12.17% body weight reduction in rats (Wang and Yang, 1997). This study provides preliminary evidence that kappa-carrageenan may be effective in promoting satiety and weight loss.

Xanthan gum also shows similar benefits in literature. In 1983, an unpublished double-blinded study was conducted on overweight subjects (JECFA, 1987). Subjects were randomized into two groups that received either 1.0 g xanthan gum or placebo (paraffin oil) three times a day, 30 min before each meal for three weeks. The results confirmed that xanthan gum could cause slow but significant weight loss in overweight subjects. In addition, an animal study conducted by Osilesi et al. indicated that xanthan gum could lower the rate of gastric emptying in rat (Osilesi et al., 1984). This result further supports the potential of xanthan gum in increasing satiety via slowing gastric emptying.

Although evidence support the efficacy of the 3 individual fibres in promoting weight loss via appetite control, the combination of the fibres was found to interact in a synergistic manner, resulting in greater swelling to form a thick, highly viscous and strong indigestible gel structure in the stomach. Hence an optimized, patent pending composition of the 3 fibres was developed as Redusure IQP-AK-102. The objective of this placebo controlled, double blind study was to investigate the clinical benefit of IQP-AK-102 in weight loss through promoting satiety and managing appetite in overweight and obese subjects.

MATERIALS AND METHODS

Study participants

Male and female Caucasian subjects between the ages of 18 and 65 years who were overweight and obese ($25 \leq BMI \leq 35$ kg/m^2) with a desire for weight loss were invited to participate in this parallel, double-blind, randomized placebo-controlled clinical trial. All enrolled subjects being in generally good health were required to commit and adhere to the recommended diet of 3 main meals a day and regular physical activity, including during the run-in period. They were also required to have had consistent stable weight for

the past 3 months prior to the study. Subjects who were on stable concomitant medications were included, but the use of other weight loss products during the study were strictly prohibited. Women of child-bearing age had to agree to use appropriate birth control methods throughout the active study period.

Exclusion criteria for the study were: known sensitivity to the ingredients of IQP-AK-102; presence of any active gastrointestinal disease; bariatric surgery; abdominal surgery within the last 6 months prior to the study; history of eating disorders; serious organ or systemic diseases such as diabetes mellitus, cardiac diseases, renal conditions; osteoporosis; acute or chronic psychiatric diseases; use of any medication that could influence GI functions such as antibiotics, laxatives, opioids, anticholinergics, or anti-diarrheals (must have stopped 3 months before study starts); use of medication that could influence weight loss (e.g. antidepressant) in the last three months; history of abuse of drugs, alcohol or medication; smoking cessation within the 6 months prior to this study; participation in similar studies or weight loss programs within the 6 months prior to this study; participation in other studies within the last 4 weeks.

Written informed consent to participate, understanding of the study requirements and willingness of compliance were obtained from all subjects who were included in the study. The clinical investigation was approved by the ethics committee of the Charité Universitätsmedizin Berlin and was performed in compliance with the principles of the World Medical Association (Declaration of Helsinki), the EU recommendations for Good Clinical Practice (CPMP/ICH/135/95), ICH E6 (R1) and EN ISO14155: 2011.

Experimental design and intervention

The clinical investigation was a 14-weeks (2 weeks run-in phase and 12 weeks treatment phase), double-blind, randomized, placebo-controlled parallel group study conducted on overweight and obese subjects at two investigation sites (bicentric) in Germany from July 2013 to July 2014.

All subjects were instructed to maintain a nutritionally balanced mildly hypocaloric diet composed of 50% carbohydrate, 30% fat and 20% protein throughout the 14 weeks duration. The mildly hypocaloric diet was estimated for each subject based on 20% reduction of their basal daily energy needs. This was estimated from their sex, age, height and actual body weight according to the Institute of Medicine's equations for estimating energy requirements and was corrected for mild to moderate daily physical activities by a factor A (Institute of Medicine, 2005). Additionally, participants were encouraged to have regular physical activity (30 min of moderate intensity physical activity such as walking or cycling). Subjects had to record their calorie intake and physical activities in a diary.

The 2 weeks run-in phase was designed to adapt the subjects to the mildly hypocaloric diet and to confirm their adherence to the diet plan. On completion of the run-in phase, eligible subjects were randomized to receive IQP-AK-102 or placebo. Randomization was done using a block size of 4; the randomization code was created by the independent statistician prior to the start of the study. The investigators received sealed envelopes for each randomized subject containing allocation information (IQP-AK-102 or placebo) in case emergency unblinding is required for safety reasons.

IQP-AK-102 and the placebo were administered as capsules (produced by InQpharm Europe Ltd. in a GMP certified facility in Germany) of identical physical appearance in terms of size, shape, colour and opacity. Each IQP-AK-102 capsule contained purified konjac glucomannan, kappa-carregeenan, and xanthan gum and excipients. The placebo capsule contained microcrystalline cellulose and other excipients. During the entire treatment phase, eligible subjects were assigned to receive either 2 capsules of IQP-AK-102 or placebo, 30 to 60 min before the three main meals (breakfast, lunch and dinner) with a full glass of water (250 ml).

Measurements

Body weight (kg) was measured in subjects wearing underwear and no shoes using calibrated weighing scales (Tanita BC-420 SMA) at screening visit (Visit 1, that is, 2 weeks before baseline), at baseline and every 4 weeks until the study was completed. Difference in mean change in body weight from baseline to final visit (after 12 weeks of treatment) between the IQP-AK-102 and the placebo arms was the primary efficacy endpoint. Body fat content (% and kg) and fat free mass (kg) were measured by bio-impedance method using Tanita BC-420 SMA.

Other endpoints measured at each of these visits 5 visits, were the change in waist and hip circumferences, the subjects' global feeling of satiety and changes in food craving. The waist circumference (cm) was measured at the level midway between the lateral lower rib margin and the iliac crest (Guy-Grand et al., 2004; Berne, 2005), while hip circumference (cm) was measured as the maximal circumference over the buttocks. Subjects' feeling of satiety (subsequent to the three main meals) was judged by the subjects on the basis of a 4 point rating scale: 0 = "no"; 1 = "slightly"; 2 = "moderate"; and 3 = "strong". For evaluation of changes in food cravings, the validated food craving questionnaire (FCQ, German version) was utilized (Halford and Harold, 2012). The food craving questionnaire contained 15 items and was completed by subjects at the study site during visits 2 to 5. Assessment was based on the following 5-point Likert scale: 1 = "I do not agree at all"; 2 = "I do not agree"; 3 = "Neutral"; 4 = "I agree"; and 5 = "I highly agree". Additionally, at baseline and during the follow up visits at week 4, 8 and 12, subjects' diaries were checked for their calorie intake and physical activities and treatment compliance monitored by counting the investigational product (IP) returned by the subjects at each follow-up visit.

For safety assessment, complete blood count and clinical chemistry, blood pressure and adverse events were monitored. Fasting blood samples were taken at baseline and at the end of the study. Blood samples were transported on the same day in cooler boxes to a central laboratory for analysis of hemogram (hemoglobin, hematocrit, erythrocytes, thrombocytes, and leucocytes) and clinical chemistry (total cholesterol, triglycerides, alanine transaminase, aspartate aminotransferase, gamma-GT, alkaline phosphatase, bilirubin, creatinine, uric acid, urea, glucose, LDL-cholesterol, HDL-cholesterol, thyroid stimulating hormone (TSH)). HbA1c was only measured at the screening visit. Blood pressure and heart rate were assessed by routine methods with subjects seated. Information on adverse events (AE) was recorded at each visit. Investigators assessed the causality of adverse event and intake of IP reported by subjects if any AE had occurred.

During the last visit, the global evaluation of benefit and tolerability were assessed by both the investigators and the subjects based on a questionnaire.

Statistical methods

All data were analysed using the SPSS Statistic software, version 19.0 (SPSS, Chicago, IL). The sample size estimation referred to the examination of the primary objective (mean difference of weight losses between the 2 study groups) by the non-parametric Mann-Whitney U-test for a significance level of 5% (two-sided) and a power of 80%. According to results from published studies (Guy-Grand et al., 2004; Berne, 2005), a difference of 1 kg over 12 weeks is expected, however the standard deviations varied. As such, to meet the span of the observed standard deviations, an effect size of 0.6 kg was adopted. With this, and an estimated 20% drop-out rate, a minimum of 59 subjects were required for each study group.

All the primary, secondary and tolerability endpoints received an

explorative examination and were descriptively assessed. The primary endpoint was analyzed with the non-parametric Mann-Whitney-U test using the rank sums of the individual changes in body weight. The influence of the baseline values was analyzed with analysis of variance. All secondary endpoints and further endpoints were also treated with non-parametric tests. Between-groups comparisons were performed using the Mann-Whitney-U test while the Wilcoxon test was used for analyses of changes within the groups. The Chi^2 test was used to compare frequency of distribution.

As the study extended over a period of several visits, the progression of the primary and secondary endpoint values over the course of the study was analyzed using analysis of variance for repeat measurements. All tests were performed with a significance level (type 1 error) of 5.0% (two-tailed test) or of 2.5% for the one-tailed test. All values were presented as mean ± standard deviation (SD) unless indicated otherwise.

RESULTS

A total of 159 subjects from 2 investigational centres were screened for eligibility. Of these, 119 subjects were randomized and assigned to the 2 treatment groups (IQP-AK-102 group, n = 60; placebo group, n = 59) (Figure 1). 111 subjects were included in the intention-to-treat (ITT) and safety and tolerability analysis. From this group, 102 subjects who completed the study without major protocol deviations were included in the per protocol (PP) population. For the primary endpoints, an analysis was performed on both ITT and PP populations.

There were no statistically significant differences among the treatment groups with respect to baseline and demographic characteristics (Table 1). The two groups were well balanced in terms of gender, age, body weight, height and BMI.

In general, treatment compliance monitored by the investigator by counting IP returned by the subjects in the ITT population at each follow-up visit at weeks 4, 8 and 12, was equally high for both IQP-AK-102 and placebo groups with a mean of 99.6% (SD 4.9) and 100.6% (SD 4.9) respectively. No statistically significant differences were found in both groups in relation to expected intake (p = 0.551).

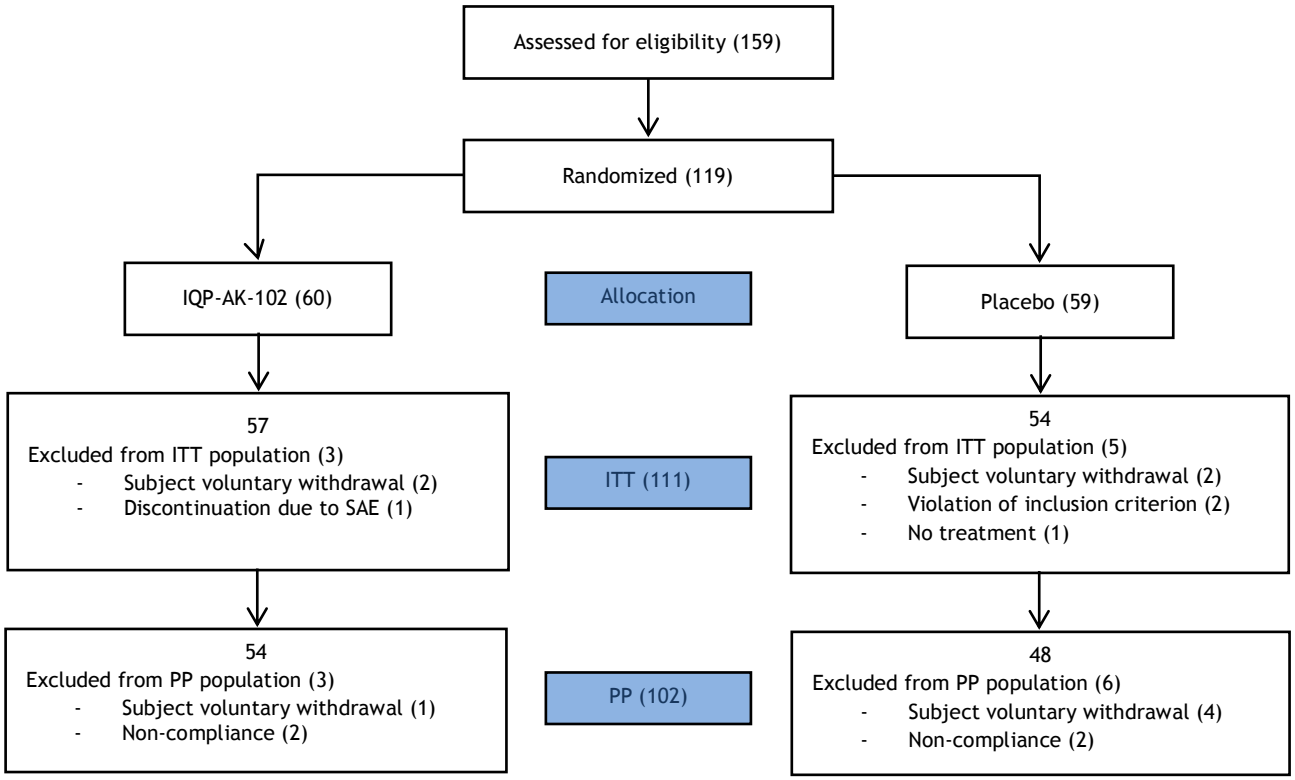

Figure 1. Study design and disposition of subjects.

Efficacy

Body weight changes of subjects were analyzed over the 12 weeks study duration. The weight loss was progressive and constant throughout the treatment period in the IQP-AK-102 group (Figure 2). The difference in body weight loss between the IQP-AK-102 and placebo subjects was significant from week 4 onwards (p = 0.005) where a mean reduction of 1.01 kg (SD 1.43) was achieved in the IQP-AK-102 group compared to 0.25 kg

Table 1. Baseline and demographic characteristics of Intention-to-Treat (ITT) population (n = 111).

Parameter		Intention-to-treat population (n = 111)		P-value
		IQP-AK-102 group (n = 57) mean (SD)	Placebo group (n = 54) mean (SD)	
Gender	Males	17 (29.8%)	11 (20.4%)	0.252
	Females	40 (70.2%)	43 (79.6%)	
Age (Years)		47.9 (SD 12.3)	46.3 (SD 10.5)	0.271
Body weight (kg)		83.0 (SD 12.4)	80.8 (SD 8.8)	0.606
Body fat mass (kg)		29.4 (SD 7.4)	28.9 (SD 6.3)	0.938
Body fat content (%)		35.5 (SD 7.5)	35.8 (SD 6.8)	0.781
Height (cm)		169.3 (SD 9.6)	168.2 (SD 9.0)	0.927
BMI (kg/m^2)		29.3 (SD 2.7)	29.0 (SD 2.1)	0.960
Waist circumference (cm)		101.6 (SD 10.7)	97.9 (SD 7.0)	0.032
Hip circumference (cm)		109.6 (SD 8.2)	108.3 (SD 7.8)	0.272

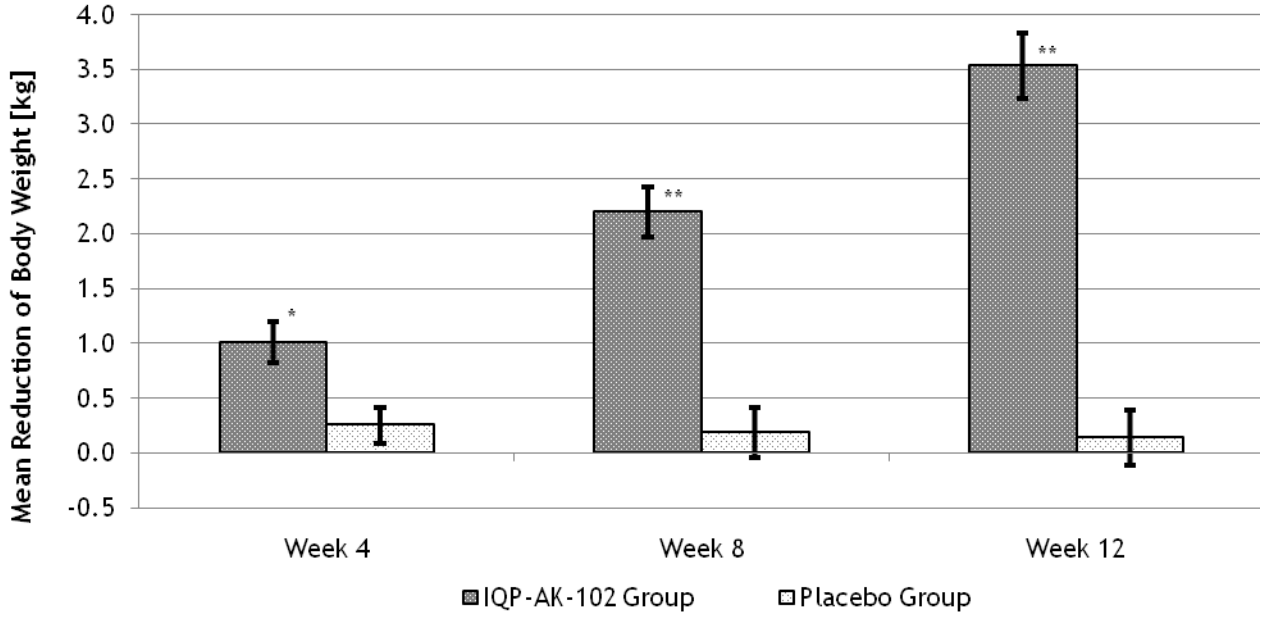

Figure 2. Reduction in mean body weight (kg) over time during the course of the 12-week study. The reduction was measured relative to baseline mean body weight of the ITT population. Asterisks indicate significant difference between IQP-AK-102 and placebo (derived from the Mann-Whitney U Test), * p = 0.005; ** p < 0.001. Error bars expressed as mean ± SEM.

(SD 1.17) in the placebo group. By the end of the study at week 12, body weight reduction from baseline was 3.53 kg (SD 2.28) in the IQP-AK-102 group compared to 0.14 kg (SD 1.84), p < 0.001 in the placebo group. Correspondingly, in the PP population (n = 102), subjects in the IQP-AK-102 lost significantly more weight compared to the placebo group (mean of 3.73 kg (SD 2.12) versus mean of 0.14 kg (SD 1.82), p < 0.001) (Table 2).

Additionally, a total of 72.0% of subjects (n = 57) achieved more than 3% weight reduction at week 12 in the IQP-AK-102 group compared to 14.9% in the placebo group (n = 54) (p < 0.001). In the IQP-AK-102 group, 43.9% of the subjects achieved more than 5% weight reduction at week 12 as compared to 1.9% in the placebo group (p < 0.001).

Subgroup analyses revealed that body weight changes from baseline to the final visit at week 12 between the treatment and placebo group as well as the total population (ITT) were not significantly different between subjects of varying baseline BMI (overweight and obese) and subjects gender. Similarly, there were no statistically significant differences between subjects of the study sites 1 and 2 in the changes in body weight from baseline to the final visit at week 12, in the total population or in the treatment group. However, there was a statistically

Table 2. Mean (SD) Weight Loss from Initial Body Weight at Week 12. P-value was derived from the parametric independent t-test. Positive values represent reduction, negative values represent increment.

Parameter	Reduction in body weight (kg) at Week 12 Mean (SD)		P-value
	IQP-AK-102 group	Placebo group	
Intended to treat analysis (n = 111)	3.53 (SD 2.28)	0.14 (SD 1.84)	<0.001
Per-protocol analysis (n = 102)	3.73 (SD 2.12)	0.14 (SD 1.82)	<0.001

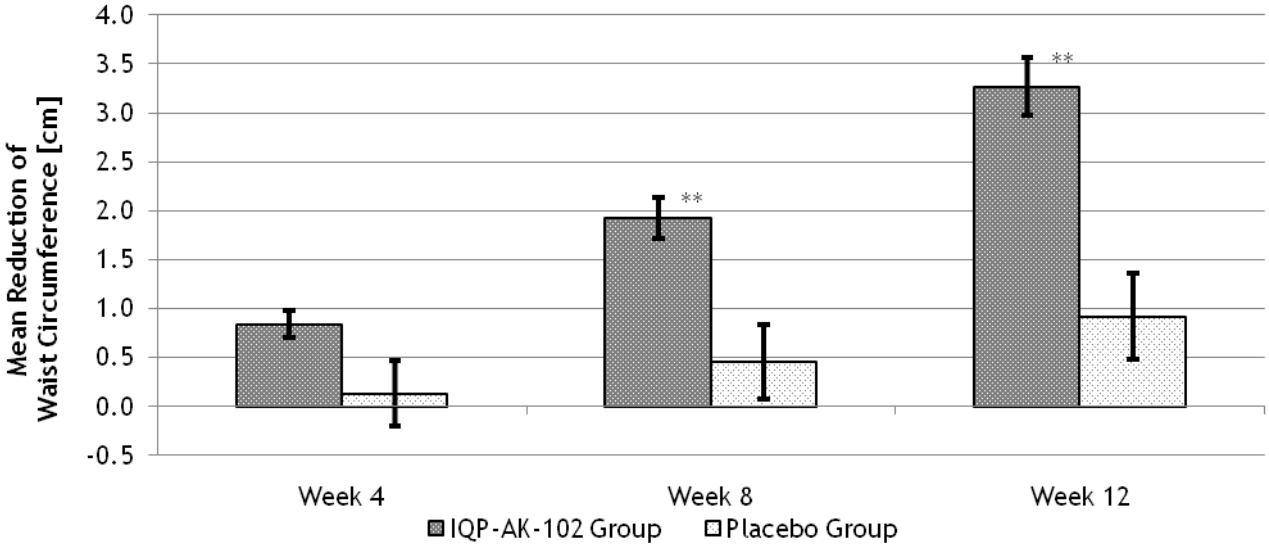

Figure 3. Reduction in mean waist circumference (cm) over time during the course of the 12-week study. The reduction was measured relative to baseline waist circumference of the ITT population. Asterisks indicate significant difference between IQP-AK-102 and placebo (derived from the Mann-Whitney U Test), ** p < 0.001. Error bars expressed as mean ± SEM.

significant difference in the placebo group.

After 12 weeks, subjects treated with IQP-AK-102 lost a mean of 3.27 cm (SD 2.20) in waist circumference versus 0.92 cm (SD 3.24) in the placebo group. The difference in waist circumference between the two groups was statistically significant (p < 0.001) (Figure 3). Similarly, subjects treated with IQP-AK-102 achieved 3.37 cm (SD 2.72) loss in hip circumference, compared to 1.07 cm (SD 1.12) in the placebo group at the end of the study. The outcome proved to be statistically significant (p < 0.001) (Figure 4).

Apart from losing significant body weight, subjects in the IQP-AK-102 group also achieved significant reduction in body fat content (BFC) at the end of the 12-week study compared with baseline, with mean reduction difference of 1.76% (SD 3.44) (Figure 5). In comparison, subjects in the placebo group achieved a loss in BFC by 0.08% (SD 1.90) at the end of the study. The difference in body fat content between the two groups was statistically significant (p = 0.002).

In terms of actual fat loss, the IQP-AK-102 group lost 2.51 kg (SD 3.16) (p < 0.001) whereas the placebo group did not lose any significant fat weight [0.05 kg (SD 1.95), p = 0.825] (Figure 6). A statistically significant mean reduction was also observed as early as week 8 where subjects from the IQP-AK-102 group experienced 1.80 kg (SD 2.35) mean reduction of fat mass, in comparison with the mean decrease of 0.11 kg (2.02) in the placebo group (p < 0.001).

The feeling of satiety was evaluated by the subjects on the basis of a 4 point rating scale: 0 = “no”; 1 = “slightly”, 2 = “moderate” and 3 = “strong” after consumption of three main meals. The differences in the feeling of satiety between the IQP-AK-102 and placebo groups were statistically significant after 4, 8 and 12 weeks of treatment. 86.0% of subjects in the IQP-AK-102 group reported to have a moderate or strong feeling of satiety after 4 weeks compared to 59.2% in the placebo group (p = 0.007). A moderate or strong feeling of satiety was reported by 94.7% of subjects in the IQP-AK-102 group both after 8 and 12 weeks of treatment compared to 59.3% in the placebo group (p < 0.001 respectively).

Safety/tolerability

Based on analysis of blood profiles, clinical chemistry and blood pressure of the subjects, no clinically significant

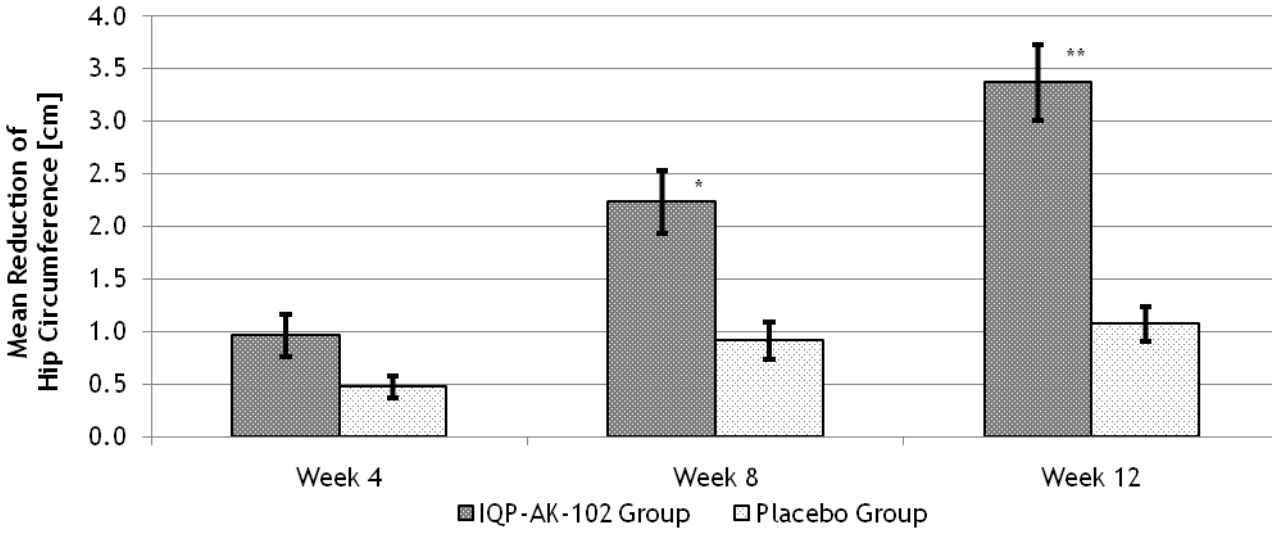

Figure 4. Reduction in mean hip circumference (cm) over time during the course of the 12-week study. The reduction was measured relative to baseline hip circumference of the ITT population. Asterisks indicate significant difference between IQP-AK-102 and placebo (derived from the Mann-Whitney U Test), * p = 0.001; ** p < 0.001. Error bars expressed as mean ± SEM.

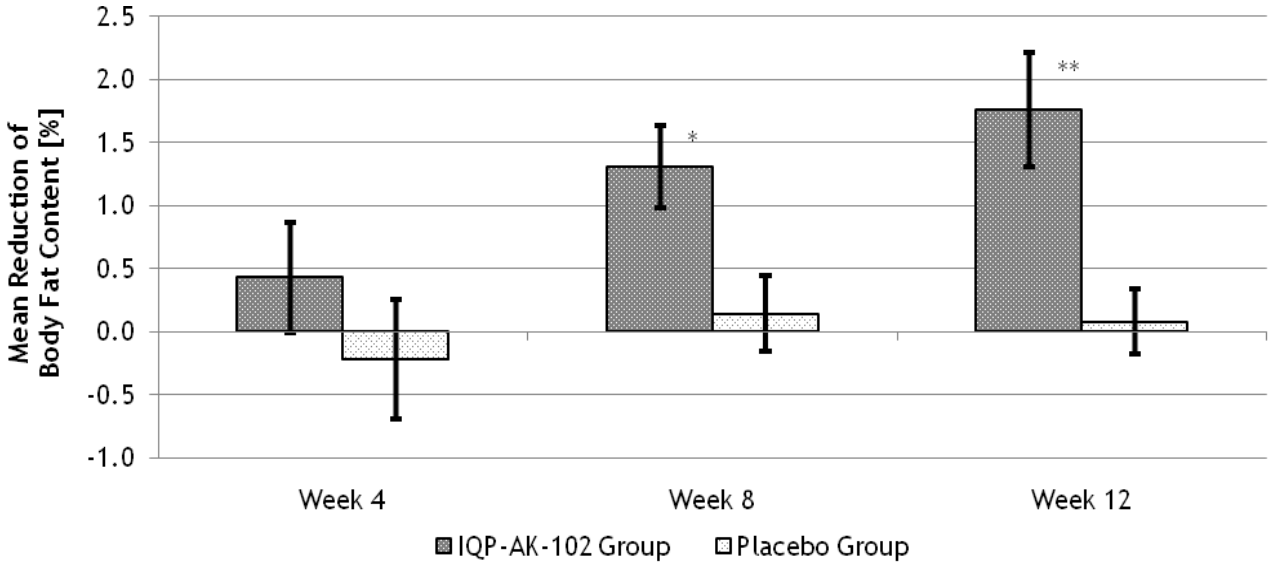

Figure 5. Reduction in mean body fat content (BFC) (%) over time during the course of the 12-week study. The reduction was measured relative to baseline body fat content of the ITT population. Asterisks indicate significant difference between IQP-AK-102 and placebo (derived from the Mann-Whitney U Test), * p = 0.003; ** p = 0.002. Error bars expressed as mean ± SEM.

changes were noted throughout the 12-week study. At the end of the study, both subjects and investigators rated the tolerability of IQP-AK-102 as “very good” or “good” in 100% of the cases, while for the placebo group, the tolerability was rated “very good” or “good” in 97.7% and 97.8% of the cases by investigators and subjects respectively. There was no statistically significant difference in the assessment of tolerability by both the investigators (p = 0.420) and subjects (p = 0.514) between the IQP-AK-102 group and placebo groups.

There was no significant difference in the proportion of subjects in the IQP-AK-102 group and placebo group who reported adverse events (AEs) (p = 0.903). During the study, 29 AEs were documented in 26 subjects. AEs included common cold, toothache, cold, skin abscess at the breastbone area, acute infections of the upper respiratory tract, dorsalgia, constipation, dental extraction, nausea, flatulence, macular degeneration, urinary tract infection, headache, headache with nausea, gastrointestinal complaints, prostate cancer, right sided

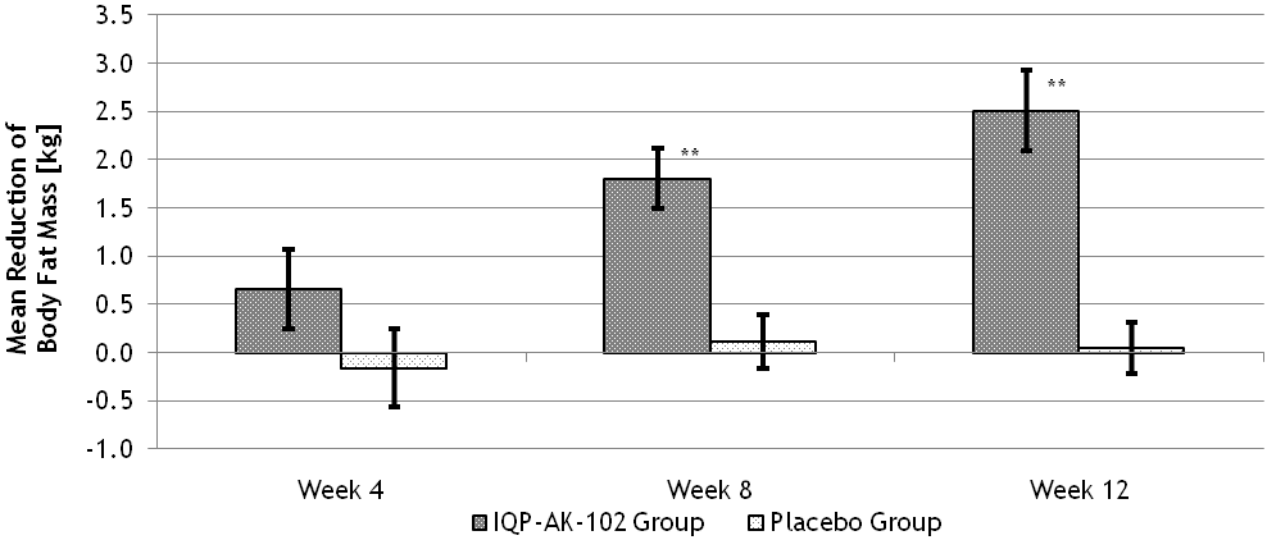

Figure 6. Reduction in mean body fat mass (BFM) (kg) over time during the course of the 12-week study. The reduction was measured in relative to baseline body fat mass of the ITT population. Asterisks indicate significant difference between IQP-AK-102 and placebo (derived from the Mann-Whitney U Test), ** $p < 0.001$. Error bars expressed as mean ± SEM.

contusion of knee after stair fall, migraine, gastrointestinal with nausea and vomiting, bronchitis, feverish common cold, distortion of the right knee joint, allergic rhinitis and cough. Most AEs were not serious or severe. The only one serious AE (SAE) reported was prostate cancer. However, none of the AEs were related to the investigational product.

DISCUSSION

Animal and human studies for each individual ingredient in IQP-AK-102 which includes glucomannan, kappa-carrageenan and xanthan gum, showed potentials in providing fibre bulk, which can create a sense of satiety and eventually lead to significant weight reduction. However, to date, this is the first randomized, double-blind, placebo-controlled trial to demonstrate the weight loss effect of these ingredients in combination.

In this study, the supplementation of IQP-AK-102 contributed to weight loss as indicated by a superior body weight reduction compared to placebo in as early as week 4 of consumption in this study. At the end of the 12 weeks study, subjects who consumed IQP-AK-102 experienced significantly more reduction in mean body weight in comparison to subjects who were on placebo [3.53 kg (SD 2.28) versus 0.14 kg (SD 1.84), $p < 0.001$]. Additionally, 43.9% of the subjects lost more than 5% body weight at week 12 in the IQP-AK-102 group as compared to 1.9% in the placebo group ($p < 0.001$). Furthermore, body fat reduction of subjects on IQP-AK-102 was also superior compared to that of the placebo group beginning from week 8 of the treatment period. Statistically significant waist and hip circumference reductions were observed in IQP-AK-102 subjects after 8 weeks. The reduction of waist circumference, which is a key indicator of central obesity, is linked to the risk reduction of cardiovascular diseases, dyslipidemia, and diabetes mellitus (Janssen et al., 2004; Grievink et al., 2004).

In general, supplementing with dietary fibre is thought to facilitate weight management by enhancement of satiety through various mechanisms. It is postulated that soluble fibres provides bulk by increasing viscosity in the gastrointestinal tract, which can cause a delay in intestinal transit time. Consequently, the delay in gastric emptying will lead to an increase in gastric distension (Kristensen and Jensen, 2011), which subsequently promotes satiety (Cecil et al., 1999). In the current study, a moderate or strong feeling of satiety was reported by significantly more subjects in the IQP-AK-102 group compared to the placebo group after 12 weeks (94.7% vs 59.3%, $p < 0.001$). This supports the satiety enhancement effect of IQP-AK-102. Additionally, increased viscosity of intestinal content may also retard macronutrient absorption from the small intestine (Kristensen and Jensen, 2011; Weickert and Pfeiffer, 2008) thus leads to reduce calories uptake and weight loss.

The effect of body fat reduction may be directly correlated with the weight loss reported in the study. However, it is possible that the prebiotic effect of fibres helps in modulating body fat percentage (Ramnani et al., 2012), particularly in obese subjects (Parnell and Reimer, 2009). In general, fermentation of soluble fibres by colonic bacteria is much greater in comparison to that of insoluble fibres. It appears that via gut fermentation, such fibres or more specifically the products of colonic

fermentation [short-chain fatty acids (SCFA)], have the ability to decrease adipocyte size and adiposity by increased lipolysis in animal models (Keenan et al., 2006; Cani et al., 2005; Dewulf et al., 2011).

Supplementation with fibre can lead to dilution of energy density of food (Roy et al., 2003), thus limiting spontaneous intake of energy (Saris, 2003). A review by Pereira and Ludwig (2001) also concludes how dietary fibre may play a role in satiety and energy intake. In our study, despite a positive effect on weight loss which was linked to satiety enhancement, it was difficult to discern if solely calorie intake was reduced following intake of IQP-AK-102 and caused to the observed weight loss, or if additional micro-biome related effects did also play a role, as the energy intake was not accounted for to such a detailed level.

The present study included Caucasian men and women who are overweight or obese ($25.1 \leq BMI \leq 35.1$ kg/m^2), in a broad age range of 21 to 65 years old. The design of the study may however limit the generalization of the findings to non-Caucasian populations.

The study was also limited by a 12-week treatment period, and no follow-ups were included to observe the weight maintenance effect of IQP-AK-102. Rebound weight gain has been observed in longer-term weight management studies (Sjöström et al., 1998; Davidson et al., 1999), thus respective future investigation would be indicated to explore the long-term weight loss and weight maintenance effects of IQP-AK-102.

There was a high compliance rate to the IP consumption (>99%). No statistically significant difference in compliance was found between the IQP-AK-102 and placebo groups in both the per-protocol population. This indicates that IQP-AK-102 dosing regime (2 capsules, 3 times daily) is generally well tolerated and optimum weight loss is achievable under real-life conditions. There were no product related serious adverse events reported and no clinically significant changes in the safety parameters.

Conclusions

IQP-AK-102 is efficacious for body weight management in conjunction with good dietary and exercise habit. Together with a good safety and tolerability profile, we conclude that IQP-AK-102 is an effective and safe intervention for body weight reduction in overweight and obese but otherwise healthy subjects.

ACKNOWLEDGEMENTS

InQpharm Group Europe Ltd. funded the study. The authors express their appreciation to Norman Bitterlich for his contributions and valuable assistance in this study. The trial is registered on clinicaltrials.gov (No: NCT01905956).

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Citation: Bongartz U, Uebelhack R, Grube B, Chong P-W, Alt F 2016. Double-blind, randomized, placebo-controlled, bicentric clinical investigation to evaluate the benefit and tolerability of Redusure IQP-AK-102 in reducing body weight in overweight and obese subjects. Adv Med Plant Res, 4(3): 73-82.