was calculated using unpaired t- test or Mann Whitney test based on the distribution of data. In case of within group comparison, data were analysed using paired *t*-test or Wilcoxon test depending upon the distribution of data. *P* values of less than 0.05 were considered as statistically significant difference between and within treatment groups.

## Results

### Disposition of subjects

Of the 102 subjects screened, a total of 96 subjects were enrolled in the study. Of these, 64 subjects were randomly assigned to the chitosan group and 32 to the placebo group. Five subjects from chitosan group and one from placebo group were lost to follow-up; while three subjects from chitosan group and one from placebo group withdrew their consent during the course of the study. A total of 86 subjects completed the study. Figure 1 describes the disposition of the study subjects.

### Demography& subject characteristics

Baseline demographic characteristics (mean ± SD) for subjects in the chitosan group were, age 35.53 (± 11.23) years; weight and height 80.13 (± 11.47) kg and 1.61 (± 0.10) m, respectively and for the placebo group were, age 36.28 (± 10.49) years; weight and height 80.54 (± 12.68) kg and 1.61 (± 0.09) m,respectively. There was no significant difference between the baseline demographics of study participants in each treatment group (Table 1). A total of 15 subjects in chitosan group and 6 subjects in placebo group had hypertension, diabetes mellitus, dyslipidemia or their combination.

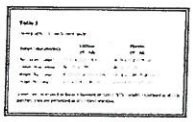


Table 1

Demographics of study participants

### Efficacy analyses

Reduction in the mean body weight over a period of 45 and 90 days intervention for chitosan and placebo group was assessed. In chitosan group, body weight was reduced from 80.13 ± 11.47 kg at baseline to 77.75 ± 11.56 at day 45 and 76.89 ± 11.88 kg at the end of 90 days, which was statistically significant ($p < 0.0001$) when compared with baseline measurements. While in placebo group the body weight was 80.54 ± 12.68 kg at baseline, which minimally changed to 80.89 ± 12.15 kg at 45 days and 80.76 ± 12.31 kg at the end of 90 days of treatment, which was statistically non-significant. It is noteworthy that in chitosan group, the percentage of subjects who reduced body weight in the range of up to 2 kg, 2–4 kg and >4 kg was 54.2 % ($n = 32$), 28.8 % ($n = 17$) and 10.2 % ($n = 6$) at the end of day 45 and 10.7 % ($n = 6$), 48.2 % ($n = 27$) and 33.9 % ($n = 19$) at the end of day 90, respectively. While in the placebo group, the percentage of subjects who reduced body weight in the same range was 41.9 % ($n = 13$), 12.9 % ($n = 4$) and 0 % ($n = 0$) at day 45 and 40.0 % ($n = 12$), 10.0 % ($n = 3$) and 3.3 % ($n = 1$) at the end of day 90, respectively. Only about 6.8 % ($n = 4$) subjects at day 45 and 7.1 % ($n = 4$) subjects at day 90 were non-responders in chitosan group, while in placebo group, the percentage of non-responders were 45.2 % ($n = 14$) and 46.7 % ($n = 14$) subjects at day 45 and day 90, respectively.

In chitosan group, the mean change in body weight was -1.78 ± 1.37 kg (range: -5.30 to 0.80 kg) and -3.10 ± 1.95 kg (range: -9.00 to 1.90 kg) at day 45 and day 90, respectively. These results were significantly different ($p < 0.0001$) as compared to placebo where mean change in body weight was -0.31 ± 1.30 kg (range: -3.00 to 2.50 kg) and -0.33 ± 1.51 kg (range: -4.60 to 2.80 kg), respectively (Fig. 2).Table 2 shows the comparison between body weights in both the groups.

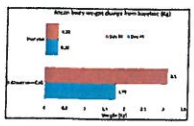


Fig. 2

Mean body weight changes from baseline

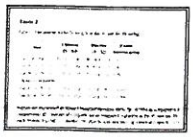


Table 2

Effect of treatments on body weight at day 45 and day 90 (in Kg)

### Other study parameters

Table 3 describes the absolute values of each study parameters at baseline, at day 45 and day 90 and Table 4 describes the change in each parameter at day 45 and day 90 from baseline.

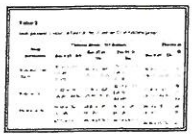


Table 3

Study parameters values at baseline, day 45 and day 90 in treatment groups

Table 4

Mean change from baseline in study parameters

Mean BMI decreased significantly ($p < 0.0001$) over the period of 90 days in chitosan group (30.93 ± 2.69 at baseline to 30.20 ± 2.90 at day 45 and 29.71 ± 3.07 at day 90), while in placebo group it was decreased minimally but was not significant ($p = 0.3846$) as compared to baseline values (30.91 ± 2.72 at baseline to 30.95 ± 2.62 at day 45 and 30.83 ± 2.64 at day 90) (Table 3). Mean change in the reduction of BMI from baseline was significantly higher in chitosan group on day 45 and day 90 as compared to subjects receiving placebo (Table 4).In chitosan group the mean changes in BMI at day 45 were found to be in the range of -2.15 to +0.32 (mean -0.69), while the same for placebo was in a range of -1.19 to +1.01 (mean -0.11). After 90 days of administration, there was a further reduction in BMI in chitosan group which was in the range of -3.65 to +0.73 (mean -1.20) as compared to -1.81 to +1.14 (mean -0.11) in placebo group.

Similarly, body fat was significantly reduced ($p < 0.0001$) in subjects administered with chitosan at the end of 90 days (37.88 ± 6.86, 37.36 ± 7.03 and 36.65 ± 7.25 at baseline, day 45 and day 90 respectively) (Table 3), while it was increased slightly in placebo group ($p = 0.5684$). However, there was no statistical difference between both treatments at any time points. Mean changes in body fat reduction from baseline in chitosan group as compared to placebo group at day 45 (-0.38 ± 1.17 % vs-0.11 ± 1.12 %) and day 90 (-0.98 ± 1.27 % vs-0.05 ± 0.98 %) were significantly different (Table 4). This mean change in body fat reduction was in the range of -6.60 to +2.80 % and -6.80 to +2.60 % in chitosan group, while in placebo group it was -3.70 to +2.80 % and -2.70 to +2.30 % at day 45 and day 90, respectively.

Visceral fat significantly decreased ($p < 0.0001$) in subjects administered with chitosan at day 45 (10.47 ± 3.38 %) from baseline (10.80 ± 3.52). This further decreased to 9.71 ± 3.33 % at the end of 90 days administration (Table 3). In placebo group, however, visceral fat remained unchanged at day 45 (10.55 ± 2.75 %) and at the end of 90 days (10.43 ± 2.87 %). Again, when compared between treatments, the values were statistically non-significant. But when mean changes in reduction of visceral fat from baseline was compared (Table 4), it was observed that chitosan showed significantly higher ($p < 0.001$) reduction in visceral fat as compared to placebo on day 90 (1.28 ± 1.12 % vs 0.43 ± 0.85).

We found that muscle mass decreased in chitosan group (47.52 ± 9.62, 46.74 ± 9.50 and 46.84 ± 9.57 at baseline, day 45 and day 90 respectively) and increased in placebo group over a 90-days administration (46.95 ± 10.79, 47.04 ± 11.17 and 47.50 ± 11.01 at baseline, day 45 and day 90 respectively) (Table 3). However, there was no significant difference between treatments ($p = 0.581$, 0.798, 0.969 at day 0, 45 and 90 respectively). But when mean changes in muscle mass from baseline was compared, it was found that at day 90 there was significant difference ($p = 0.0008$) between the groups (-0.74 ± 1.57 vs. -0.08 ± 1.16). This can also be observed by reduction of muscle mass in the range of -11.50 to +1.20 in chitosan group as compared to -3.20 to +3.10 in placebo group at day 90 (Table 4).

The reduction in body weight caused a comparable decrease in anthropometric measurement as well. There was significant mean reduction in upper abdominal circumference, hip circumference and waist circumference at day 45 ($p < 0.0001$) and day 90 ($p < 0.0001$) from baseline in subjects treated with chitosan capsules (Table 3). On the contrary, there was no statistical significant reduction in upper abdominal circumference, hip circumference and waist circumference in patients treated with placebo on day 45 and day 90. Mean change in reduction from baseline in upper abdominal circumference (-0.92 ± 1.25 and -2.17 ± 1.98 vs. -0.35 ± 0.95 and -0.50 ± 1.10), hip circumference (-1.05 ± 1.05 and -2.07 ± 1.51 vs. -0.41 ± 1.14 and -0.66 ± 1.24) and waist circumference (-0.91 ± 1.68 and -1.97 ± 2.20 vs. -0.64 ± 1.22 and -0.90 ± 1.47) was significantly ($p < 0.0001$) greater in subjects treated with chitosan than with placebo at day

45 and day 90, respectively (Table 4). There was no significant change in waist to hip ratio in both treatment groups at day 45 and day 90 (-0.0027 ± 0.02 and -0.0010 ± 0.02 vs. -0.0035 ± 0.01 vs.-0.0033 ± 0.01 at p = 0.091 and 0.768).

HbA1c level at baseline was compared with post-administration measurements at day 45 and day 90 to assess the efficacy of chitosancapsules. In this study, HbA1c level was significantly decreased at day 45 (5.72 ± 0.78 %) and day 90 (5.74 ± 0.83 %) in chitosan group as compared to its baseline value (5.89 ± 0.83), which was statistically significant ($p = 0.0327$). However, within placebo group there was statistically significant reduction ($p = 0.0334$) observed at day 45 only as compared to its baseline values, while at day 90 it again increased and was statistically non-significant ($p = 0.8269$) as compared to its baseline values (Table 5). Further analysis revealed that, there were 17 subjects whose HbA1c levels were above 6 % (mean: 6.55 %; range: 6 to 8.2 %) while the remaining subjects had HbA1c levels below 6 % (mean: 5.47 %; range: 4.3 to 5.9 %) at baseline. After 90 day treatment with chitosan, HbA1c level significantly decreased in those17 subjects (mean: 6.04 %; range: 5.1 to 6.8 %) while in the remaining subjects, it was unchanged throughout the study period (mean: 5.48 %; range: 4.7 to 5.9 %). This shows that chitosan was effective in reducing HbA1c levels in subjects who were having higher glycaemic value initially, while subjects with normal glycaemic levels were unaffected.

Table 5

Comparison in lipid profile (TG, HDL, LDL and VLDL) and HbA1C levels

Analysis of daily food intake for the period of 15 days (day 1–5, day 41–45 and day 86–90) for calorie intake showed there was no significant change, in either group, during this study. The mean caloric intake in chitosan group for day 1–5 was 1784 kcal, for day 41–45 was 1797 kcal and for day 86–90 was 1750 kcal. While the same for placebo group was 1761 kcal, 1701 kcal and 1677 kcal, respectively.

### Safety analyses

Lipid levels in both treatment groups are described in Table 5. Although LDL levels increased in chitosan group at day 45 and in placebo group at day 90, in general the results were clinically non-significant as this increase in LDL can be attributed to only two of the subjects; one in chitosan group and one in placebo group who showed transient increase in their LDL levels.

The SF-36 analysis shows that the mean PCS score and mean MCS score obtained in chitosan group at day 0 were 40.99 ± 6.51 and 48.34 ± 6.77, respectively and at day 90 were 51.32 ± 7.23 and 49.10 ± 7.08, respectively. The mean PCS score and mean MCS score obtained in placebo group at day 0 were 41.26 ± 5.78 and 46.16 ± 7.77, respectively and at day 90 were 43.19 ± 7.50 and 47.45 ± 6.60, respectively.Assessment of Quality of Life (QoL) using SF-36 questionnaire showed statistical significant ($p < 0.0001$) increase in QoL score in subjects from chitosan group as compared to the placebo group from baseline to day 90, which depicts improvement in the QoL (Table 6).

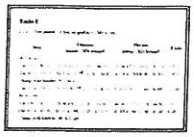


Table 6

Effect of treatment groups on quality of life score

There were a total of 10 adverse events (AEs) recorded during the study period: four in placebo group and six in chitosan group. In chitosan group reported AEs were common cold, hypertriglyceridemia, body ache, constipation (2 subjects) and hypertension, while in placebo group, the reported AEs were mild headache (2 subjects), hypertriglyceridemia and fracture. All adverse events were mild in nature and unrelated to the study treatment.There was no statistically significant difference in laboratory parameters (SGOT, SGPT, serum creatinine and urea) from baseline to day 90 in both chitosan and placebo groups. No dropout was observed due to AEs, which states that overall the study treatment was safe and well tolerated by all study subjects.

## Discussion

This study demonstrates that administration of chitosan (KiOnutrime-CsG® capsules, 500 mg, 5 capsules/day in three divided doses) results in a significant mean weight loss of about 3 kg without diet restriction over a period of 90 days.

The observed weight loss in chitosan group is in contrast to only 0.3 kg weight loss in placebo group. Also significant was the percentage of subjects who lost between 5 and 10 % of body weight after 90 days compared to placebo group (32.4 and 3.3 %, respectively). Although some studies demonstrated that reduction in body weight by administration of chitosan can be achieved in individuals given a hypocaloric or standardized diet [14, 29], other studies show efficacy of chitosan for persons without diet restrictions [10, 23, 30, 31]. The results of our study confirm that indeed significant weight loss can be achieved in subjects adhering to a non-restrictive diet [10, 23, 30, 31]. Reasons for the difference in results in our study with other reported studies could be difference in diets, dosage and timing of chitosan administration or protocol variability such as life style recommendations.

One factor which is important to consider is the timing of chitosan ingestion before meals. It is typically recommended that chitosan supplements be ingested approximately 15 min to 1 h prior to a meal in order to allow sufficient time for chitosan to dissolve in the stomach acid[18]. In our study, the dosage was one capsule 15 min before breakfast and two capsules each 15 min before lunch and dinner. This allowed sufficient time for it to dissolve properly and efficiently bind the fats present in the meal, which resulted in observed weight loss.

Body weight gain and increase in BMI are the key clinical features of obesity. BMI correlates fairly well with total body fat on a population basis [32]. The overweight (BMI 25.0 to 29.9 $kg/m^2$) and obese (BMI $\geq$30 $kg/m^2$) individuals have higher body fat together with increased risk of cardiovascular and other metabolic disorders. In this study we found that after 90 day administration with chitosan, there was 10.91 fold reduction in BMI compared to placebo group. The implications of this result are that the subjects, who were initially classified as obese, can now be defined as overweight as their mean BMI fell below 30 $kg/m^2$.

It is well known that weight reduction in subjects with obesity has a marked effect on the regulation of lipolysis [33] and weight loss shows good correlations with several of the circumferences [34] that were measured in present study. Also, in one of the gastric bypass study conducted by Sjostrom and colleagues [35], it was found that the profound weight loss experienced by the subjects resulted from a global decrease in body fat rather than localised loss. Also, hypocholesterolemic properties of chitosan decrease the risk of atherosclerosis and other cardiovascular dysfunctions [36]. Chitosan, by the virtue of its property to bind fat and triglycerides, may also have caused the disturbances in regulation of lipolysis resulting in lowering of body fat and visceral fat observed in our study.

Reduction of muscle mass by chitosan was observed in this study which is reduced in an average of 0.74 kg over a period of 90 days. Although there is a statistically significant reduction, this has not produced any clinically relevant adverse effects over a period of 90 days.

It is already reported that chitosan can regulate lipids with benefit on anthropometric parameters [37]. Also, in one of the study conducted over a period of five years, it was confirmed that weight gain and weight loss are associated with changes in the anthropometric measurements and waist to hip ratio (WHR) in both genders [38]. The reduction in body composition and anthropometric parameters observed in our study can be attributed to general reduction in body weightpossibly due to reduction in fat absorption [39] by chitosan.

Practically no significant change was observed in serum triglyceride, LDL and VLDL throughout the test period while HDL was slightly increased in chitosan group (non-significant). It is well known that Low-density lipoproteins (LDL) are considered as important risk factors for cardiovascular diseases (CVD), while highdensity lipoproteins (HDL) are well recognized for their putative role in reverse cholesterol transport [40]. Since HDL-cholesterol is more metabolisable into bile acid than LDL-cholesterol [41], it is presumed that a deficiency of bile acid in the body due to binding with chitosan would accelerate the conversion of cholesterol to bile acid, which may result in an increase of HDL-cholesterol. In a similar previous study where effects of chitosan was studied on lipids and lipoproteins, it was found that chitosan increased HDL level up to 14 % during the 4-month study period [42].

Obesity is a multi-factorial disorder, which is often associated with many other significant diseases such as diabetes, inflammation, hypertension and other cardiovascular diseases; there is a consistent graded relationship between increased BMI and prevalence of non-insulin dependent diabetes mellitus (NIDDM) and insulin resistance [43]. It is established that inflammation, diabetes and obesity are interrelated and a person with diabetes are predisposed to obesity and metabolic syndrome. HbA1C reflects the long-term glycaemic level and is a marker for progression of diabetes. In the present study, we observed that chitosan was able to lower the HbA1C level to less than 6 % during the 90-days study period. It has been reported that chitosan significantly reduced postprandial blood glucose levels in both animal and in

vitro models [44] as well as in humans [45]. This may the reason for the observed decrease in HbA1c levels in our study. Interestingly, this reduction was mainly observed in subjects who were initially having high HbA1C levels, while subjects with normal HbA1C levels at baseline were unaffected by chitosan. However, more clinical studies are required to confirm this effect of chitosan in large diabetic population.

The results of SF-36 QoL score showed that there was significant improvement in mean PCS score in chitosan group which reflects improvement in physical morbidity and adaptation to obesity. However, mean MCS score failed to improve with the treatment. This may be due to failure to evaluate the impact that excess weight would have on obesity-specific aspects of QoL score during the baseline evaluations [46]. This might explain why no effect of decrease in BMI was detected on MCS despite it being recognised that people who are overweight or obese are more likely to suffer from discrimination and depression [47]. Another possible explanation may be that people who are very overweight and obese may need to loose in excess of 10 % of their body weight in order to experience a positive impact on QoL [48]. However, only one of the subjects in our study showed weight loss of more than 10 %, thus explaining the differences in PCS and MCS score.

## Conclusion

In summary, we conclude that KiOnutrime-CsG® capsule, containing 500 mg of chitosan from fungal origin, was able to reduce the mean body weight up to 3 kg during the 90-days study period. Together with this, there was also improvement in body composition, anthropometric parameters and HbA1C, reflecting overall benefits for the overweight individuals. Additionally, there was also improvement in QoL score. KiOnutrime-CsG® capsulewas also found to be safe and well tolerated by all study participants.

## Availability of supporting data

The data set(s) supporting the results of this article is (are) included within the article.

## Acknowledgements

We are thankful to all the subjects who gave their consent to participate in this trial, without which this work was not possible.

## Abbreviations

| | |
|---|---|
| BMI | body mass index |
| HbA1C | glycated haemoglobin |
| IASO | International Association for the Study of Obesity |
| IOTF | International Obesity Task Force |
| QoL | quality of life |
| WHR | waist to hip ration |

## Footnotes

**Competing interests**

The author(s) declare that they have no competing interests.

**Authors' contribution**

VRT participated in analyses and interpretation of data, performed the statistical analyses, and writing, revising, and finalizing the manuscript. MCS participated in design of the study, analyses and interpretation of data, performed the statistical analyses, and revising and finalizing the manuscript. AD participated in design of the study, and revising and finalizing the manuscript. VM participated in design of the study, and revising and finalizing the manuscript. RBS participated as investigator in the study, involved in subject recruitment, their compliance and acquisition of the data. PHZ participated as investigator in the study, involved in subject recruitment, their compliance and acquisition of the data. JVT participated as investigator in the study, involved in subject recruitment, their compliance and acquisition of the data. All authors have read and approved the final manuscript.

## Contributor Information

VR Trivedi, Email: llun@ved:otliam.

MC Satia, Email: llun@ved:otliam.

A. Deschamps, Email: llun@ved:otliam.

V. Maquet, Email: llun@ved:otliam.

RB Shah, Email: llun@ved:otliam.

PH Zinzuwadia, Email: llun@ved:otliam.

JV Trivedi, Email: llun@ved:otliam.

## References

1. Sengupta K, Mishra AT, Rao MK, Sarma KV, Krishnaraju AV, Trimurtulu G. Efficacy and tolerability of a novel herbal formulation for weight management in obese subjects: a randomized double blind placebo controlled clinical study. Lipids Health Dis. 2012;11(122):11–122. [PMC free article] [PubMed]

2. Nammi S, Koka S, Chinnala KM, Boini KM. Obesity: an overview on its current perspectives and treatment options. Nutr J. 2004;3:3. doi: 10.1186/1475-2891-3-3. [PMC free article] [PubMed] [Cross Ref]

3. Taylor RW, Keil D, Gold EJ, Williams SM, Goulding A. Body mass index, waist girth, and waist-to-hip ratio as indexes of total and regional adiposity in women: evaluation using receiver operating characteristic curves. Am J Clin Nutr. 1998;67(1):44–49. [PubMed]

4. About Obesity [http://www.worldobesity.org/site_media/uploads/IASO-Advocacy-toolkit-Oct13.pdf]

5. Daniels S. Pharmacological treatment of obesity in paediatric patients. Paediatr Drugs. 2001;3(6):405–410. doi: 10.2165/00128072-200103060-00001. [PubMed] [Cross Ref]

6. Daniels SR, Arnett DK, Eckel RH, Gidding SS, Hayman LL, Kumanyika S, et al. Overweight in children and adolescents: pathophysiology, consequences, prevention, and treatment. Circulation. 2005;111(15):1999–2012. doi: 10.1161/01.CIR.0000161369.71722.10. [PubMed] [Cross Ref]

7. Brenot F, Herve P, Petitpretz P, Parent F, Duroux P, Simonneau G. Primary pulmonary hypertension and fenfluramine use. Br Heart J. 1993;70(6):537–541. doi: 10.1136/hrt.70.6.537. [PMC free article] [PubMed] [Cross Ref]

8. Rizzo M, Perez-Martinez P, Nikolic D, Montalto G, Lopez-Miranda J. Emerging approaches for the treatment of hypertriglyceridemia. Expert Opin Pharmacother. 2013;14(14):1869–1873. doi: 10.1517/14656566.2013.823402. [PubMed] [Cross Ref]

9. Astrup A. Dietary composition, substrate balances and body fat in subjects with a predisposition to obesity. Int J Obes Relat Metab Disord. 1993;17(3):S41–S42. [PubMed]

10. Schiller RN, Barrager E, Schauss AG, Nichols EJ. A randomized, double-blind, placebo-controlled study examining the effects of a rapidly soluble Chitosan dietary supplement on weight loss and body composition in overweight and mildly obese individuals. J Am Nutraceut Assoc. 2001;4:42–49.

11. Mesa Ospina N, Ospina Alvarez SP, Escobar Sierra DM, Rojas Vahos DF, Zapata Ocampo PA, Ossa Orozco CP CP. Isolation of chitosan from Ganoderma lucidum mushroom for biomedical applications. J Mater Sci Mater Med. 2015;26(3):135. doi: 10.1007/s10856-015-5461-z. [PubMed] [Cross Ref]

12. Pittler MH, Abbot NC, Harkness EF, Ernst E. Randomized, double-blind trial of chitosan for body weight reduction. Eur J Clin Nutr. 1999;53(5):379–381. doi: 10.1038/sj.ejcn.1600733. [PubMed] [Cross Ref]

13. Muzzarelli RAA. Chitin. Oxford, England: Pergamon Press; 1977.

14. Mhurchu CN, Poppitt SD, McGill AT, Leahy FE, Bennett DA, Lin RB, et al. The effect of the dietary supplement, Chitosan, on body weight: a randomised controlled trial in 250 overweight and obese adults. Int J Obes Relat Metab

Disord. 2004;28(9):1149–1156. doi: 10.1038/sj.ijo.0802693. [PubMed] [Cross Ref]

15. Sugano M, Fujikawa T, Hiratsuji Y, Nakashima K, Fukuda N, Hasegawa Y. A novel use of chitosan as a hypocholesterolemic agent in rats. Am J Clin Nutr. 1980;33(4):787–793. [PubMed]

16. Nauss JL, Thompson JL, Nagyvary J. The binding of micellar lipids to chitosan. Lipids. 1983;18(10):714–719. doi: 10.1007/BF02534538. [Cross Ref]

17. Ebihara K, Schneeman BO. Interaction of bile acids, phospholipids, cholesterol and triglyceride with dietary fibers in the small intestine of rats. J Nutr. 1989;119(8):1100–1106. [PubMed]

18. Kanauchi O, Deuchi K, Imasato Y, Kobayashi E. Increasing Effect of a Chitosan and Ascorbic Acid Mixture on Fecal Dietary Fat Excretion. Biosci Biotechnol Biochem. 1994;58(9):1617–1620. doi: 10.1271/bbb.58.1617. [Cross Ref]

19. Maezaki Y, Tsuji K, Nakagawa Y, Kawai Y, Akimoto M, Tsugita T, et al. Hypocholesterolemic Effect of Chitosan in Adult Males. Biosci Biotechnol Biochem. 1993;57(9):1439–1444. doi: 10.1271/bbb.57.1439. [Cross Ref]

20. Sciutto AM, Colombo P. Lipid-lowering effect of chitosan dietary integrator and hypocaloric diet in obese subjects. Acta Toxicol Ther. 1995;16(4):215–230.

21. Giustina A, Ventura P. Weight-reducing regimens in obese subjects: effects of a new dietary fiber integrator. Acta Toxicol Ther. 1995;16(4):199–214.

22. Ventura P. Lipid lowering activity of chitosan, a new dietary integrator. Chitin Enzymology. 1996;2:55–62.

23. Kaats GR, Michalek JE, Preuss HG. Evaluating efficacy of a chitosan product using a double-blinded, placebo-controlled protocol. J Am Coll Nutr. 2006;25(5):389–394. doi: 10.1080/07315724.2006.10719550. [PubMed] [Cross Ref]

24. Ho SC, Tai ES, Eng PH, Tan CE, Fok AC. In the absence of dietary surveillance, chitosan does not reduce plasma lipids or obesity in hypercholesterolaemic obese Asian subjects. Singapore Med J. 2001;42(1):6–10. [PubMed]

25. Pokhis K, Bitterlich N, Cornelli U, Cassano G. Efficacy of polyglucosamine for weight loss-confirmed in a randomized double-blind, placebo-controlled clinical investigation. BMC Obes. 2015;2(25):015–0053. [PMC free article] [PubMed]

26. Abelin J, Lassus A. L-112 Biopolymer - Fat binder as a weight reducer in patients with moderate obesity. Helsinki: Medical research report performed at ARS Medicina; 1994.

27. Ware JE, Kosinski M, Kellar SD. SF-36 physical and mental health summary scales: a users manual. 2. Boston, MA: The Health Institute, New England Medical Centre; 1994.

28. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ. 1993;306(6890):1437–1440. doi: 10.1136/bmj.306.6890.1437. [PMC free article] [PubMed] [Cross Ref]

29. Veneroni G, Veneroni F, Contos S, Tripodi S, De Bernardi M, Guarino C, et al. Effect of a new chitosan dietary integrator and hypocaloric diet on hyperlipidemia and overweight in obese patients. Acta Toxicologica et Therapeutica. 1996;17:53–70.

30. Wadstein J, Thom E, Heldman E, Gudmunsson S, Lilja B: Biopolymer L112, a chitosan with fat binding properties and potential as a weight reducing agent: a review of in vitro and in vivo experiments. In: *Chitosan per os - from dietary supplement to drug carrier*. Edited by A.A.Muzzarelli R: Atec Edizioni, Grottammare; 2000: 65–76.

31. Cornelli U, Belcaro G, Cesarone MR, Cornelli M. Use of polyglucosamine and physical activity to reduce body weight and dyslipidemia in moderately overweight subjects. Minerva Cardioangiol. 2008;56(5 Suppl):71–78. [PubMed]

32. American College of Cardiology/American Heart Association Task Force on Practice Guidelines, Obesity Expert Panel Expert panel report: Guidelines (2013) for the management of overweight and obesity in adults. Obesity. 2014;22(S2):S41–S410. doi: 10.1002/oby.20660. [PubMed] [Cross Ref]

33. Kopelman PG. The effects of weight loss treatments on upper and lower body fat. Int J Obes Relat Metab Disord. 1997;21(8):619–625. doi: 10.1038/sj.ijo.0800458. [PubMed] [Cross Ref]

34. Bray GA, Greenway FL, Molitch ME, Dahms WT, Atkinson RL, Hamilton K. Use of anthropometric measures to assess weight loss. Am J Clin Nutr. 1978;31(5):769–773. [PubMed]

35. Sjostrom L, Narbro K, Sjostrom D. Costs and benefits when treating obesity. Int J Obes Relat Metab Disord. 1995;19(6):S9–S12. [PubMed]

36. Kerch G. The Potential of Chitosan and Its Derivatives in Prevention and Treatment of Age-Related Diseases. Mar Drugs. 2015;13(4):2158. doi: 10.3390/md13042158. [PMC free article] [PubMed] [Cross Ref]

37. Patti AM, Katsiki N, Nikolic D, Al-Rasadi K, Rizzo M. Nutraceuticals in Lipid-Lowering Treatment: A Narrative Review on the Role of Chitosan. Angiology. 2015;66(5):416–421. doi: 10.1177/0003319714542999. [PubMed] [Cross Ref]

38. Caan B, Armstrong MA, Selby JV, Sadler M, Folsom AR, Jacobs D, et al. Changes in measurements of body fat distribution accompanying weight change. Int J Obes Relat Metab Disord. 1994;18(6):397–404. [PubMed]

39. Deibert P, Konig D, Vitolins MZ, Landmann U, Frey I, Zahradnik HP, et al. Effect of a weight loss intervention on anthropometric measures and metabolic risk factors in pre- versus postmenopausal women. Nutr J. 2007;6:31. doi: 10.1186/1475-2891-6-31. [PMC free article] [PubMed] [Cross Ref]

40. Garcia-Rios A, Nikolic D, Perez-Martinez P, Lopez-Miranda J, Rizzo M, Hoogeveen RC. LDL and HDL subfractions, dysfunctional HDL: treatment options. Curr Pharm Des. 2014;20(40):6249–6255. doi: 10.2174/1381612820666140620154014. [PubMed] [Cross Ref]

41. Halloran LG, Schwartz CC, Vlahcevic ZR, Nisman RM, Swell L. Evidence for high-density lipoprotein-free cholesterol as the primary precursor for bile-acid synthesis in man. Surgery. 1978;84(1):1–7. [PubMed]

42. Rizzo M, Giglio RV, Nikolic D, Patti AM, Campanella C, Cocchi M, et al. Effects of chitosan on plasma lipids and lipoproteins: a 4-month prospective pilot study. Angiology. 2014;65(6):538–542. doi: 10.1177/0003319713493126. [PubMed] [Cross Ref]

43. O'Rahilly S. Science, medicine, and the future. Non-insulin dependent diabetes mellitus: the gathering storm. BMJ. 1997;314(7085):955–959. doi: 10.1136/bmj.314.7085.955. [PMC free article] [PubMed] [Cross Ref]

44. Jo SH, Ha KS, Moon KS, Kim JG, Oh CG, Kim YC, et al. Molecular Weight Dependent Glucose Lowering Effect of Low Molecular Weight Chitosan Oligosaccharide (GO2KA1) on Postprandial Blood Glucose Level in SD Rats Model. Int J Mol Sci. 2013;14(7):14214–14224. doi: 10.3390/ijms140714214. [PMC free article] [PubMed] [Cross Ref]

45. Kim HJ, Ahn HY, Kwak JH, Shin DY, Kwon YI, Oh CG, et al. The effects of chitosan oligosaccharide (GO2KA1) supplementation on glucose control in subjects with prediabetes. Food Funct. 2014;5(10):2662–2669. doi: 10.1039/C4FO00469H. [PubMed] [Cross Ref]

46. Ni Mhurchu C, Bennett D, Lin R, Hackett M, Jull A, Rodgers A. Obesity and health-related quality of life: results from a weight loss trial. N Z Med J. 2004;117(1207):U1211. [PubMed]

47. Onyike CU, Crum RM, Lee HB, Lyketsos CG, Eaton WW. Is obesity associated with major depression? Results from the Third National Health and Nutrition Examination Survey. Am J Epidemiol. 2003;158(12):1139–1147. doi: 10.1093/aje/kwg275. [PubMed] [Cross Ref]

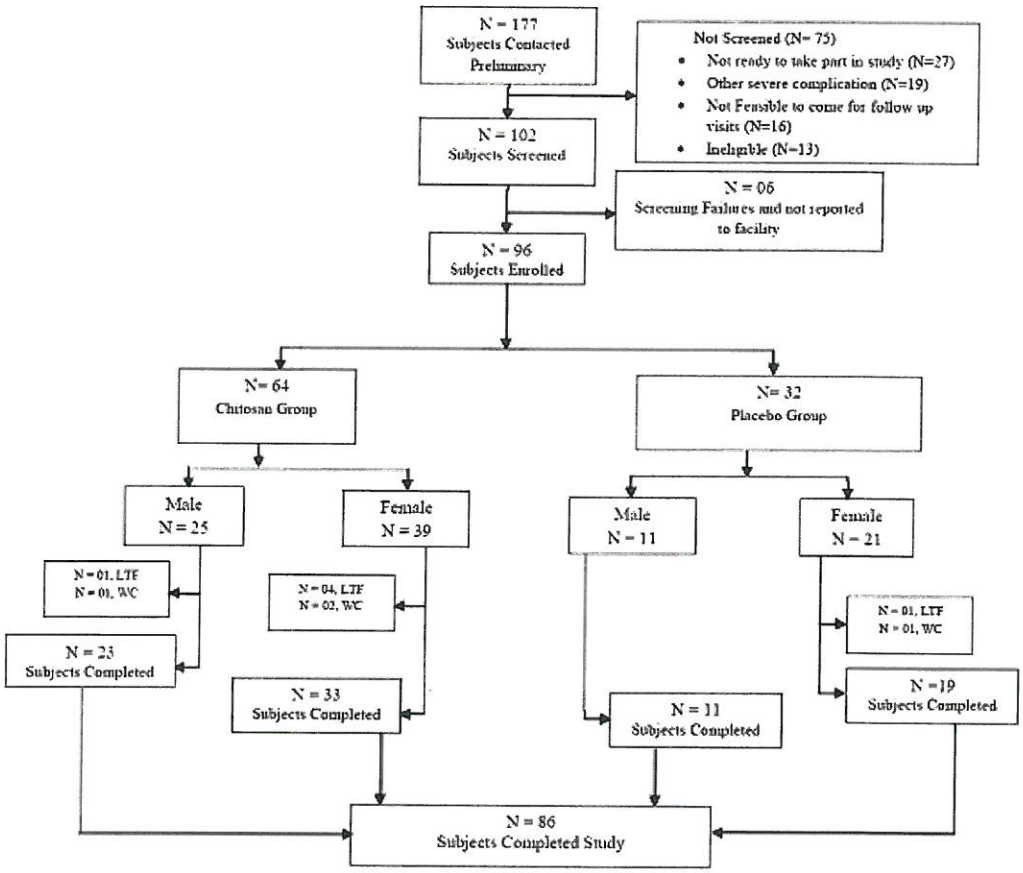
48. Kaukua JK, Pekkarinen TA, Rissanen AM. Health-related quality of life in a randomised placebo-controlled trial of sibutramine in obese patients with type II diabetes. Int J Obes Relat Metab Disord. 2004;28(4):600–605. doi: 10.1038/sj.ijo.0802591. [PubMed] [Cross Ref]

Articles from Nutrition Journal are provided here courtesy of **BioMed Central**

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


<< Prev Fig. 1 Next >>

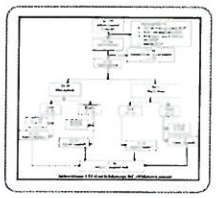
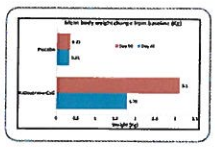
## Fig. 1




**Abbreviations: LTF–Lost to follow-up; WC –Withdrawn consent**

Disposition of subjects

## Images in this article

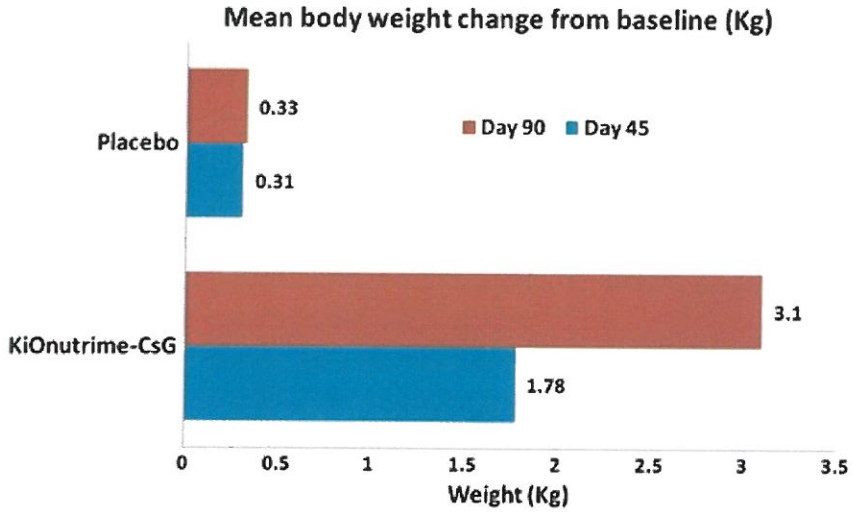



Click on the image to see a larger version.

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8

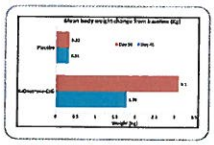

<< Prev Fig. 2 Next >>

## Fig. 2




Mean body weight changes from baseline

## Images in this article

Click on the image to see a larger version.

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 1

Demographics of study participants

| Subject characteristic | Chitosan ($N = 64$) | Placebo ($N = 32$) |
|---|---|---|
| Age (years) [range] | 35.53 ± 11.23 [19–63] | 36.28 ± 10.49 [18–56] |
| Gender (male /female) | M = 25; F = 39 | M = 11; F = 21 |
| Weight (Kg) [range] | 80.13 ± 11.47 [54.0–106.5] | 80.54 ± 12.68 [59.8–116.0] |
| Height (M) [range] | 1.61 ± 0.10 [1.38–1.82] | 1.61 ± 0.09 [1.47–1.83] |

Values are expressed as Mean ± Standard deviation (SD). Gender expressed as absolute number. $N$ = number of patients. Data are presented as descriptive statistics

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 2

Effect of treatments on body weight at day 45 and day 90 (in Kg)

| Visit | Chitosan ($N=64$) | Placebo ($N=32$) | *P* value between group |
|---|---|---|---|
| Day 0 (n = 64, 32) | 80.13 ± 11.47 | 80.54 ± 12.68 | 0.87 |
| Day 45 (n = 59, 31) | 77.75 ± 11.56* | 80.89 ± 12.15 | 0.43 |
| Day 90 (n = 56, 30) | 76.89 ± 11.88* | 80.76 ± 12.31 | 0.35 |
| Change from baseline | | | |
| Day 45 (n = 59,31) | −1.78 ± 1.37@ | −0.31 ± 1.30 | < 0.0001 |
| Day 90 (n = 56, 30) | −3.10 ± 1.95@ | −0.33 ± 1.51 | < 0.0001 |

Values are expressed as Mean ± Standard deviation (SD); *$p < 0.0001$ as compared to baseline (Within group comparison); @ - statistically significant as compared to placebo at day 45 and day 90; $N$ = Number of subjects in each treatment group. $n$ = number of subjects with non-missing values at respective visit

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 3

Study parameters values at baseline, day 45 and day 90 in treatment groups

| Study parameters | Chitosan (mean ± SD) [range] | | | Placebo (mean ± SD) [range] | | |
|---|---|---|---|---|---|---|
| | Day 0 ($N$ = 64) | Day 45 ($N$ = 59) | Day 90 ($N$ = 56) | Day 0 ($N$ = 32) | Day 45 ($N$ = 31) | Day 90 ($N$ = 30) |
| Body mass Index ($Kg/m^2$) | 30.93 ± 2.69 [26.49 – 35.19] | 30.20 ± 2.90* [25.32 – 35.08] | 29.71 ± 3.07* [24.88 – 35.64] | 30.91 ± 2.72 [26.23 – 34.95] | 30.95 ± 2.62 [26.29 – 34.95] | 30.83 ± 2.64 [26.36 – 35.09] |
| Body fat (%) | 37.88 ± 6.86 [25.20 – 49.50] | 37.36 ± 7.03* [25.00 – 50.30] | 36.65 ± 7.25* [24.30 – 49.40] | 37.96 ± 7.83 [23.70 – 49.30] | 38.02 ± 8.00 [23.70 – 49.30] | 38.07 ± 8.09 [23.50 – 49.10] |
| Visceral fat (%) | 10.80 ± 3.52 [4 – 20] | 10.47 ± 3.3* [4 – 20] | 9.71 ± 3.33* [4 – 20] | 10.53 ± 2.97 [4 – 17] | 10.55 ± 2.75 [5 – 17] | 10.43 ± 2.87 [5 – 17] |
| Muscle mass (Kg) | 47.52 ± 9.62 [32.20 – 68.30] | 46.74 ± 9.50* [32.00 – 64.50] | 46.84 ± 9.57* [31.70 – 64.20] | 46.95 ± 10.79 [34.70 – 81.10] | 47.04 ± 11.17 [35.20 – 83.80] | 47.50 ± 11.01 [35.20 – 83.00] |
| Upper abdominal circumference (cm) | 97.70 ± 7.96 [80.00 – 114.0] | 96.61 ± 7.99* [80.00 – 113.0] | 95.68 ± 8.40* [77.00 – 112.0] | 95.75 ± 9.22 [73.00 – 117.0] | 95.55 ± 9.13 [74.00 – 115.0] | 95.73 ± 9.09 [74.00 – 115.0] |
| Hip circumference (cm) | 110.35 ± 9.30 [89.00 – 130.0] | 109.2 ± 9.77* [88.00 – 128.0] | 108.3 ± 9.96* [88.00 – 128.0] | 108.59 ± 14.80 [48.00 – 138.0] | 109.0 ± 13.91 [50.00 – 138.0] | 108.3 ± 13.79 [50.00 – 137.0] |
| Waist circumference (cm) | 102.80 ± 7.70 [84.00 – 118.0] | 101.7 ± 7.69* [85.00 – 117.0] | 100.5 ± 8.05* [82.00 – 115.0] | 102.72 ± 10.14 [67.00 – 124.0] | 102.2 ± 10.27 [68.00 – 124.0] | 102.3 ± 10.12 [68.00 – 124.0] |
| Waist to hip ratio | 0.93 ± 0.07 [0.80 - 0.95] | 0.93 ± 0.07 [0.80 – 0.97] | 0.92 ± 0.07 [0.79 – 0.96] | 0.96 ± 0.12 [0.75 – 0.98] | 0.94 ± 0.10 [0.74 – 0.98] | 0.95 ± 0.10 [0.82 – 0.98] |

Values are expressed as Mean ± Standard deviation (SD). *$p < 0.0001$ as compared to baseline (Within group comparison). $N$ = Number of patient in each treatment group

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 4

Mean change from baseline in study parameters

| | Visit | Chitosan (mean ± SD) [range] | Placebo (mean ± SD) [range] | *P* value between groups |
|---|---|---|---|---|
| Body mass index(Kg/m$^2$) | Day 45 ($n$ = 59, 31) | -0.69 ± 0.53@ [-2.15 – 0.32] | -0.11 ± 0.50 [-1.19 – 1.01] | < 0.0001 |
| | Day 90 ($n$ = 56, 30) | -1.20 ± 0.76@ [-3.65 – 0.73] | -0.11 ± 0.59 [-1.81 – 1.14] | < 0.0001 |
| Body fat (%) | Day 45 ($n$ = 59, 31) | -0.38 ± 1.17@ [-6.60 – 2.80] | -0.11 ± 1.12 [-3.70 – 2.80] | 0.034 |
| | Day 90 ($n$ = 56, 30) | -0.98 ± 1.27@ [-6.80 – 2.60] | -0.05 ± 0.98 [-2.70 – 2.30] | < 0.0001 |
| Visceral fat (%) | Day 45 ($n$ = 59, 31) | -0.38 ± 0.71 [-3.0 – 1.0] | -0.19 ± 0.54 [-2.0 – 1.0] | 0.127 |
| | Day 90 ($n$ = 56, 30) | -1.28 ± 1.12@ [-4.0 – 1.0] | -0.43 ± 0.85 [-2.0 – 2.0] | 0.001 |
| Muscle mass (Kg) | Day 45 ($n$ = 59, 31) | -0.48 ± 1.51 [-11.10 – 1.20] | -0.20 ± 0.89 [-2.50 – 2.70] | 0.253 |
| | Day 90 ($n$ = 56, 30) | −0.74 ± 1.57@ [−11.50 – 1.20] | -0.08 ± 1.16 [-3.20 – 3.10] | 0.0008 |
| Upper abdominal circumference (cm) | Day 45 ($n$ = 59, 31) | -0.92 ± 1.25@ [-6.0 – 2.0] | -0.35 ± 0.95 [-3.0 – 1.0] | 0.020 |
| | Day 90 ($n$ = 56, 30) | -2.17 ± 1.98@ [-8.0 – 2.0] | -0.50 ± 1.10 [-3.0 – 1.0] | < 0.0001 |
| Hip circumference (cm) | Day 45 ($n$ = 59, 31) | -1.05 ± 1.05@ [-4.0 – 0.0] | -0.41 ± 1.14 [-4.0 – 2.0] | 0.0024 |
| | Day 90 ($n$ = 57, 30) | -2.07 ± 1.51@ [-6.0 – 2.0] | -0.66 ± 1.24 [-3.0 – 2.0] | < 0.0001 |
| Waist circumference (cm) | Day 45 ($n$ = 59, 31) | -0.91 ± 1.68@ [-8.00 – 6.00] | -0.64 ± 1.22 [-1.00 – 6.00] | 0.027 |
| | Day 90 ($n$ = 57, 30) | -1.97 ± 2.20@ [-8.00 – 7.00] | -0.90 ± 1.47 [-1.00 – 7.00] | < 0.0001 |
| Waist to hip ratio | Day 45 ($n$ = 59, 31) | -0.0027 ± 0.02 [-0.13 – 0.04] | -0.0035 ± 0.01 [-0.03 – 0.03] | 0.091 |
| | Day 90 ($n$ = 57, 30) | -0.0010 ± 0.02 [-0.13 – 0.07] | -0.0033 ± 0.01 [-0.02 – 0.04] | 0.768 |

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 5

Comparison in lipid profile (TG, HDL, LDL and VLDL) and HbA1C levels

| Visit | Chitosan ($N=56$) | Placebo ($N=30$) | $P$ value between groups |
|---|---|---|---|
| TG (mg/dl) | | | |
| Day 0 | 145.2 ± 64.35 | 153.1 ± 76.44 | 0.753 |
| Day 45 | 143.7 ± 76.33 | 160.5 ± 92.92 | 0.494 |
| Day 90 | 138.8 ± 63.81 | 170.3 ± 102.8 | 0.203 |
| HDL(mg/dl) | | | |
| Day 0 | 41.47 ± 7.50 | 42.87 ± 10.28 | 0.448 |
| Day 45 | 44.38 ± 12.01 | 41.14 ± 9.55 | 0.285 |
| Day 90 | 43.17 ± 11.65 | 42.08 ± 10.74 | 0.944 |
| LDL (mg/dl) | | | |
| Day 0 | 106.9 ± 27.80 | 107.2 ± 30.39 | 0.959 |
| Day 45 | 114.9 ± 42.44* ($p=0.0213$) | 113.7 ± 38.66 | 0.746 |
| Day 90 | 109.9 ± 31.64 | 115.6 ± 31.93* ($p=0.0266$) | 0.428 |
| VLDL (mg/dl) | | | |
| Day 0 | 29.04 ± 12.87 | 30.62 ± 15.29 | 0.746 |
| Day 45 | 28.74 ± 15.27 | 32.10 ± 18.59 | 0.494 |
| Day 90 | 27.76 ± 12.76 | 34.07 ± 20.55 | 0.203 |
| HbA1C (%) | | | |
| Day 0 | 5.89 ± 0.83 | 5.89 ± 0.75 | 0.912 |
| Day 45 | 5.72 ± 0.78* ($p=0.0225$) | 5.80 ± 0.68* ($p=0.0419$) | 0.661 |
| Day 90 | 5.74 ± 0.83* ($p=0.0343$) | 5.88 ± 0.57 | 0.138 |

Values are expressed as Mean ± Standard deviation (SD). * = as compared to baseline (Within group comparison).
$N$ = Number of patient in each treatment group

**PMC full text:** Nutr J. 2015; 15: 3.
Published online 2016 Jan 8. doi: 10.1186/s12937-016-0122-8


## Table 6

Effect of treatment groups on quality of life score

| Visit | Chitosan (mean ± SD) [range] | Placebo (mean ± SD) [range] | *P* value |
|---|---|---|---|
| PCS Score | | | |
| Day 0 ($n = 58, 31$) | 40.99 ± 6.51 [22.80 − 56.90] | 41.26 ± 5.78 [33.10 − 57.70] | 0.869 |
| Day 90 ($n = 59, 31$) | 51.32 ± 7.23*@ [32.10 − 61.80] | 43.19 ± 7.50[31.20 − 56.40] | < 0.0001 |
| Change from baseline (PCS Score) | | | |
| Day 90 ($n = 59, 31$) | 10.58 ± 8.07@ [-27.70 − 8.50] | 1.93 ± 5.69 [−17.60 − 6.30] | < 0.0001 |
| MCS score | | | |
| Day 0 ($n = 58, 31$) | 48.34 ± 6.77 [27.20 − 60.50] | 46.16 ± 7.77 [17.70 − 61.90] | 0.173 |
| Day 90 ($n = 59, 31$) | 49.10 ± 7.08 [33.20 − 61.60] | 47.45 ± 6.60 [27.90 − 62.40] | 0.283 |
| Change from baseline (MCS Score) | | | |
| Day 90 ($n = 59, 31$) | 0.98 ± 6.73 [-20.80 − 16.70] | 1.28 ± 8.81 [-34.30 − 10.60] | 0.4755 |

Values are expressed as Mean ± Standard deviation (SD). * = statistically significant as compared to baseline. @ - statistically significant as compared to placebo at day 90. *N* = Number of subjects in each treatment group