INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com ISSN 2230 – 8407

Research Article

RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED CLINICAL STUDY TO EVALUATE THE EFFECTS OF GARCINIA CAPLETS IN OBESE SUBJECTS

Tripathy P.C.[1], Karmahapatra P B.[2], Palaniyamma D.[3]*

[1]Professor, Department of Post Graduate Studies in Kayachikitsa (Medicine), IPGA and R and S SP Hospital, Kolkata, India

[2]Department of Post Graduate Studies in Kayachikitsa (Medicine), IPGA and R and S SP Hospital, Kolkata, India

[3]Medical advisor, The Himalaya Drug Company, Makali, Tumkur Road, Bangalore, Karnataka, India

*Corresponding Author Email: dr.palani@himalayahealthcare.com

Article Received on: 19/05/13 Revised on: 03/06/13 Approved for publication: 17/07/13

DOI: 10.7897/2230-8407.04740

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

ABSTRACT

Obesity and its concomitant health risks are among the most common conditions managed by health care practitioners. The limited long-term effectiveness of conventional weight management has led to researching alternative medicine and one which is widely accepted is the herbal products by virtue of its safety in long term use. The study was conducted to evaluate effect of caplet of Garcinia extract with reference to reduction in BMI and skin fold thickness in obese individuals. This study was performed according to a double-blind, randomized, placebo-controlled, design. Subjects aged 18 to 60 years with Obesity as decided by BMI > 25 Kg/m^2 to 35 Kg/m^2 falling in the category of overweight and class I obesity were included in the study. A total of 110 individuals participated in the study. Subjects were randomly assigned into two groups of 55 each to receive treatment for 4 months with Garcinia or matching placebo at a dose of 1 caplet twice daily. All the subjects completed the study as stipulated. At the end of 4 months, Garcinia group had significant reduction in BMI and skin fold thickness when compared to the placebo group and baseline values respectively. No severe adverse effect was observed at any time in the study period. Compliance to treatment was good. It is therefore expected that Garcinia may be useful for the prevention and reduction of obesity.

Keywords: Obesity, Garcinia, BMI, Skin fold thickness.

INTRODUCTION

Obesity has reached epidemic proportions globally, with more than 1 billion adults overweight - at least 300 million of them clinically obese - and is a major contributor to the global burden of chronic disease and disability. Often coexisting in developing countries with under-nutrition, obesity is a complex condition, with serious social and psychological dimensions, affecting virtually all ages and socioeconomic groups.[1]

The last 25 years have seen a great increase in the incidence of obesity, both in the Western world and in developing third world countries.[2] Obesity is a very common chronic disease worldwide, resulting principally from a disturbance in energy balance. Of importance, the rate of severe obesity (BMI 40 kg/m^2) is rising exponentially in the industrialized world. Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in metres (kg/m2). As per WHO's International Classification of adult underweight, overweight and obesity according to BMI, a person is said to have normal BMI if it is in the range of 18.50 - 24.99. If BMI is ≥ 25.00, it is termed as overweight or pre obese. BMI ≥ 30.00 is regarded as obese, in which 30.00 - 34.99 is called class I obesity, 35.00 - 39.99 is class II obesity and ≥ 40.00 is class III obesity.[3]

The obesity epidemic moves through a population in a reasonably consistent pattern over time and this is reflected in the different patterns in low- and high income countries. In low income countries, obesity is more common in people of higher socioeconomic status and in those living in urban communities. It is often first apparent among middle-aged women. In more affluent countries, it is associated with lower socioeconomic status, especially in women and rural communities.[4,5] The sex differences are less marked in affluent countries and obesity is often common amongst adolescents and younger children.

Homogenisation and westernisation of the global diet has increased the energy density[6] and this is particularly a problem for the poor in all countries who are at risk of both obesity and micronutrient deficiencies[5].

In general, the causes of weight gain and abdominal weight gain are the same and it is the characteristics of the individuals (such as sex, age, menopausal status) that influence the distribution of the fat that is gained. At a macronutrient level, there is no evidence that energy from fat is more fattening than the same amount of energy from carbohydrate or protein. At a dietary level, there is still debate about the effects of diet composition on unhealthy weight gain and more research is needed in this area. However, it was considered that the overall evidence from the randomised controlled trials was convincing that a high intake of energy-dense foods (which are often also micronutrient poor) promotes unhealthy weight gain[7].

The non-fatal, but debilitating health problems associated with obesity include respiratory difficulties, chronic musculoskeletal problems, skin problems and infertility. The more life-threatening problems fall into four main areas: CVD problems; conditions associated with insulin resistance such as type 2 diabetes; certain types of cancers, especially the hormonally related and large-bowel cancers; and gallbladder disease[1]. Raised BMI also increases the risks of cancer of the breast, colon, prostrate, endometrium, kidney and gallbladder.

Chronic overweight and obesity contribute significantly to osteoarthritis, a major cause of disability in adults. Although obesity should be considered a disease in its own right, it is also one of the key risk factors for other chronic diseases together with smoking, high blood pressure and high blood cholesterol.

It is well established that cardiovascular disease has an inflammatory component. The present narrative review explores the role of adipose tissue distribution, morphology and function as potential mediators of the link between inflammation and cardiovascular disease. Evidence that abdominal obesity is a key driving force behind a constellation of atherothrombotic inflammatory abnormalities linked to insulin resistance and often referred to as the metabolic syndrome is also reviewed. It is also proposed that the amount of visceral adipose tissue and the liver fat content are important factors responsible for the link between abdominal obesity and features of the metabolic syndrome. It is suggested that the inflammatory profile associated with excess visceral adipose tissue/liver fat may be a consequence of the relative inability of subcutaneous adipose tissue to expand through hyperplasia and to act as a protective metabolic sink storing the chronic energy surplus resulting from a positive energy balance (overnutrition or lack of physical activity or both).[8]

Obesity is characterized by sympathetic nervous system (SNS) predominance in the basal state and reduced SNS responsiveness after various sympathetic stimuli, such as cold exposure, postural changes, mental effort, caffeine, alcohol and nicotine intake, and hypoglycemia[9,10]. Weight loss and exercise are the first line therapy for obesity[11] and also reduce related SNS over activity.[12]

Despite the seeming inexorable progression of this disease; there have been limited advances in the pharmacotherapy of this condition. Of the newest introductions to the obesity drug portfolio, Orlistat, which acts to prevent dietary fat absorption, and Sibutramine, which seems to affect both arms of the energy balance equation, were the first new chemical entities to be introduced for the treatment of obesity in 30 years.

The limited long-term effectiveness of conventional weight management, including behavioral therapy,[13] is the impetus of major efforts aimed at developing alternative pharmacologic[14] and surgical weight reduction treatment strategies.[15] A rapidly growing therapeutic area, and one widely embraced by the general public, is the use of herbal weight loss products.

Herbal medicines have been extensively used in recent years for chronic and lifestyle related disorders. The fruit of *Garcinia cambogia* is one such drug in the obesity management that has been traditionally used in food preparation and cooking for many centuries with no toxicity. Garcinia and its active ingredient, HCA (hydroxycitric acid) have been extensively studied for effectiveness in inhibiting lipogenesis, suppressing appetite and encouraging weight-loss in experimental models.[16]

Obtained from extracts of related plants native to India, mainly *Garcinia cambogia* and *Garcinia indica*, hydroxycitric acid was first identified by Watson and Lowenstein[17,18] in the late 1960s as a potent competitive inhibitor of the extramitochondrial enzyme adenosine triphosphate–citrate (pro-3 S)-lyase. These investigators and others subsequently demonstrated both *in vitro* and *in vivo* that hydroxycitric acid in animals not only inhibited the actions of citrate cleavage enzyme and suppressed de novo fatty acid synthesis,[19] but also increased rates of hepatic glycogen synthesis,[20] suppressed food intake,[21] and decreased body weight gain.[22]

Although hydroxycitric acid appears to be a promising experimental weight control agent, studies in humans are limited and results have been contradictory.[23-27]

Objectives of the Study

To evaluate the effects of Garcinia Caplets in the management of obesity

Study design

The present study was a randomized, double-blind, placebo controlled clinical trial.

Primary and Secondary Endpoints

The predefined primary endpoints were reduction in the BMI and skin fold thickness. The predefined secondary endpoints were to identify incidence of adverse effects if any and overall compliance to the drug under investigation.

Inclusion and Exclusion Criteria

Individuals of both the sex aged between 18 to 60 years with Obesity as decided by BMI > 25 Kg/m^2 to 35 Kg/m^2 falling in the category of overweight and class I obesity were included in the study. Only those individuals willing to sign informed consent were included. Individuals with other endocrinal disorders like hypothyroidism, Cushing's syndrome, Type I or Type II Diabetes mellitus, serious systemic or psychiatric illnesses, hypertension, clinically significant medical condition, were taking prescription medications or appetite suppressants on a regular basis, had a history of alcohol or other drug abuse, were allergic to any of the study products were excluded. Those with a known history of other complication of obesity like cardiovascular events, etc were also excluded from the study. Pregnant and lactating women were not included in the study.

METHODOLOGY

Selection of Volunteers

The present study was a randomized, double-blind, placebo controlled clinical trial. The duration of the study was 4 months and the 'Institutional Ethics Committee' approval was obtained before study initiation. A total of 110 individuals who were obese with a BMI > 25 Kg/m^2 to 35 Kg/m^2 according to the subject selection criteria and those who were willing to sign the informed consent form were included in the study.

Diet

Regularity in diet was recommended to all the subjects throughout the study. They were asked to divide their regular diet into three meals a day and keep it constant throughout the study period. They were also advised to maintain a stable physical activity. However, Diet compliance was not quantitatively measured during the study.

Study Drugs

The subjects were divided into two groups: and the Group 1 (n=55) received 1 caplet of Garcinia twice daily for 4 months. Group 2 (n=55) received similar looking placebo at the same dose for 4 months.

Study Procedure

One hundred and ten subjects from IPGA and R and S SP Hospital, Kolkata, India were selected for the clinical trial. Subjects attending the hospital who were obese were detailed the nature of the study and their written informed consent was obtained. All the subjects were clinically examined before the trial. The subjects received either Garcinia or placebo by randomization using a random number table at a dose of 1 caplet twice daily for 4 months. The subjects were

assessed at the end of 2 months, 3rd month and 4th month. Assessment was done on the basis of parameters like BMI, mid axillary Skin fold thickness. Skin fold thickness was measured by Skin fold calipers and values expressed in millimeters (mm). Adverse effects as volunteered by the subjects were recorded in the case record forms.

Statistical Analysis

The results were analyzed statistically for BMI by between the group analysis using Unpaired ''t'' test. Skin fold thickness in obese subjects as compared to the respective baseline values, by repeated measures of ANOVA. The values are expressed as mean ± SD. The differences were considered significant at $p < 0.05$. Data was analyzed using Graph Pad Prism, Version 4.03 for windows, Graphpad Software, San Diego, California, USA.

Table 1: Demographic Data (on entry)

S. No	Parameter	Garcinia	Placebo
I.	Age in years (Mean ± SD)	35.3 ± 9.15	38.5 ± 8.42
II.	Sex (M / F)	34 / 21	28 / 27
III.	Diet (Veg / Non veg)	25 / 30	26 / 29

Table 2: BMI in Obese Subjects

Group	BMI (Kg/m^2)			
	At entry	2nd month	3rd month	4th month
Garcinia caplets (n = 55)	30.12 ± 3.13	28.01 ± 3.14	26.35 ± 3.02	24.75 ± 2.99
Placebo (n = 55)	30.36 ± 3.01	29.41 ± 3.12	28.95 ± 3.10	28.53 ± 3.16
Significance	NS	$p < 0.021$	$p < 0.0001$	$p < 0.0001$

Statistical analysis: Unpaired ''t'' test for between the group analysis NS- Not significant

Table 3: Skin Fold Thickness(mm) in Obese Subjects

Parameter	Garcinia caplets (n = 55)				Placebo (n = 55)			
	At entry	2nd month	3rd month	4th month	At entry	2nd month	3rd month	4th month
Triceps	29.52 ± 9.37	28.23 ± 8.59	26.23* ± 6.52	25.50* ± 7.56	29.24 ± 8.32	29.0 ± 8.24	28.32 ± 8.10	28.10 ± 7.82
Subscapular	32.10 ± 8.70	31.32 ± 8.20	30.24 ± 6.23	30.20* ± 9.60	32.24 ± 8.50	31.98 ± 8.24	31.12 ± 7.96	31.83 ± 7.68
Mid axillary	33.40 ± 9.63	30.28 ± 8.65	29.62 ± 6.12	31.30* ± 8.36	33.20 ± 9.23	32.96 ± 9.12	32.84 ± 8.92	31.87 ± 7.54

*$p < 0.05$ as compared to the respective baseline values, by repeated measures of ANOVA

RESULTS

Demographic data of the study with respect to age, sex and diet habits of the subjects at entry is given in Table 1. Mean age of the subjects at entry was comparable in both the groups. In Garcinia group, the mean age was 35.3 ± 9.15 years and in placebo group, it was 38.5 ± 8.42 years. All the subjects completed the study. The Garcinia caplets produced a significant reduction in the BMI and skin fold thickness. The subjects in Garcinia group had BMI 30.12 ± 3.13 at entry which gradually reduced to 26.35 ± 3.02 at the end of 3 months and further to 24.75 ± 2.99 in the 4th month of treatment. The subjects in placebo group had BMI 30.36 ± 3.01 at entry which reduced to28.95 ± 3.10 at the end of 3 months and to 28.53 ± 3.16 in the 4th month. The effect of treatment with Garcinia had significant reduction in BMI with a significance of $p < 0.021$, at the end of 2nd month, and $p < 0.0001$ at the end of 3rd and 4th months when compared to the placebo values (Table 2).

The skin fold thickness in subjects reduced significantly in Garcinia treated group when compared to the Baseline values with a significance of $p < 0.05$. The mean triceps score which was 29.52 ± 9.37 at entry in the Garcinia group reduced to 25.50 ± 7.56 at the end of 4th month of treatment. Whereas, in the placebo group, the mean triceps score reduced from 29.24 ± 8.32 at entry to 28.10 ± 7.82 at the end of treatment. The mean Subscapular score which was 32.10 ± 8.70 at entry reduced to 30.20 ± 9.60 at the end of the treatment. In the Baseline values, the mean Subscapular score reduced to 31.83 ± 7.68 from 32.24 ± 8.50 at the end of treatment with placebo. Similarly reduction in the mean mid axillary score was also found to be significant in the Garcinia group as compared to Baseline values (Table 3). There were no adverse effects either reported or observed during the study and the compliance to the treatment was good.

DISCUSSION

Medical treatment for obesity by contemporary medicine has encountered limitations owing to a range of adverse drug reactions for medications. In 2010 the FDA noted the concerns that Sibutramine increases the risk of heart attacks and strokes in patients with a history of cardiovascular disease. Other frequently encountered side effects are dry mouth, paradoxically increased appetite, nausea, strange taste in the mouth, upset stomach, constipation, trouble sleeping, dizziness, drowsiness, menstrual cramps/pain, headache, flushing, or joint/muscle pain.

Orlistat usage is associated with gastrointestinal related various adverse events along with incidence of renal failure due to oxalate deposition in kidneys.[10] Phentermine is an amphetamine like stimulant. Generally, Phentermine appears to be relatively well tolerated. It can produce side effects consistent with its catecholamine-releasing properties, e.g., tachycardia (increased heart rate) and elevated blood pressure, but the incidence and magnitude of these appear to be less than with the amphetamines. Because phentermine acts through sympathomimetic pathways, the drug may increase blood pressure and heart rate. It may also cause palpitations, restlessness and insomnia. Additionally, phentermine has the potential to cause psychological dependence. After short term use, tolerance begins and can be followed by rebound weight gain.[10]

The present study indicates the clinical efficacy of Garcinia caplets in the management of obesity. Garcinia clinically has been used for a very long time to reduce blood cholesterol levels and increase metabolism and thus used for weight loss. Garcinia is known to support normal appetite levels, supports normal fat and carbohydrate metabolism and supports normal glycogen production and body weight. The present study has evaluated the safety and efficacy of Garcinia caplets. This

study also indicates that Garcinia caplet is well tolerated and safe in obese subjects. The BMI and skin fold thickness reduced significantly in obese subjects and the treatment was well tolerated by all the subjects.

In 1883 von Lippmann isolated hydroxycitric acid, a minor constituent of sugar beets.[28] More than half a century later, in 1941, Martius and Maué [29] discovered that the (+) isomer of a racemic hydroxycitric acid mixture is attacked by the enzyme isocitrate dehydrogenase. The (−) hydroxycitric acid isomer of hydroxycitric acid was first isolated by Lewis and Neelakantan in 1964,[30] and by 1969 Watson and colleagues[31] reported the powerful inhibition by (−) hydroxycitric acid of citrate cleavage enzyme.

Evidently, the additional hydroxyl group's steric position, compared with citric acid, enhances its binding affinity and competitively inhibits catalytic action by the enzyme. Citrate, entering the cytoplasm from mitochondria, cannot be cleaved to release acetyl coenzyme A, the substrate for de novo fatty acid synthesis.

Garcinia contains citrine, an extract that is 50-60 % HCA (hydroxycitric acid), which inhibits an enzyme that helps the body synthesize fat for storage in adipose tissue. HCA promotes energy, inhibits lipogenesis, lowers the production of cholesterol and fatty acids, increases the production of glycogen in the liver, suppresses appetite and increases the body's production of heat by activating the process of thermogenesis.

Earlier experimental studies have shown that Serum insulin and leptin levels in treated mice were lower than those of control mice in two groups of female Std ddY mice that were fed either a high sucrose diet or the same diet with 3.3 % *Garcinia cambogia* extract for 4 weeks.[32]

Garcinia cambogia extract increased the release of tritium-labeled serotonin from cultured brain cortex slices in a dose-dependent manner. The maximum release of serotonin was comparable to a response elicited by K+ depolarizing stimuli. This may suggest why HCA seems to work best for people who overeat when they are anxious or stressed, as it will give the same calming effect that they get from food[33].

Garcinia cambogia extract (1 g/kg body weight) inhibited the rise in lipid levels in both serum and liver tissue induced by ethanol and also prevented ethanol-induced peroxidative damage in male albino rats for 45 days.[34] Rats pretreated with *Garcinia cambogia* extract at 1 g/kg body weight, at days 7 and 15 prior to ulcer induction with hydrochloric acid and ethanol, significantly reduced the number of lesions and showed a decrease in lipid peroxidative damage in animals orally administered HCl and ethanol.[35]

When the glycogen stores are reasonably full, additional carbohydrates are then converted into excess of extramitochondrial Acetyl CoA required for fatty acid synthesis using ATP Citrate lyase enzyme. (-)-Hydroxycitric acid [(-)-HCA] is the principal acid of fruit rinds of *Garcinia Cambogia* (-)-HCA was shown to be a potent inhibitor of ATP citrate lyase. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates.[16]

This added glycogen load in the liver stimulates a longer lasting neuro-signal from the liver to the brain, indicating satiety (satisfaction), thus helping to suppress appetite longer. (-)-HCA as weight-controlling agent.[16]

Owing to a substantial increase in glucose uptake by working muscle, glucose homeostasis during sustained aerobic exercise requires a several fold increase in hepatic glucose output. As exercise continues and liver glycogen declines, an increasing proportion of this elevated glucose output must be provided by gluconeogenesis. Increased gluconeogenic efficiency in trained individuals is a key adaptation promoting increased endurance, since failure of hepatic glucose output to keep pace with muscle uptake rapidly leads to hypoglycaemia and exhaustion.[16]

Pre-administration of (-)-hydroxycitrate, may aid endurance during post-absorptive aerobic exercise by promoting gluconeogenesis. Carnitine and bioactive chromium may potentiate this benefit. The utility of this technique may be greatest in exercise regimens designed to promote weight loss.[16]

CONCLUSION

With the present literature and clinical data available on Garcinia, it may be regarded as a promising product for obesity management in view of its safety and efficacy in the management of obesity. Observations from the present clinical study indicates that obese subjects treated with Garcinia caplets showed reduction in BMI and skin fold thickness from 2nd month onwards and significant improvement by the end of 3rd and 4th month of treatment. There were no adverse effects either reported or observed during the study period and overall compliance to the study was good. Hence it can be concluded that Garcinia may be beneficial in individuals with obesity.

REFERENCES

1. Obesity and overweight, Global strategy on diet, physical activity and health, World health organization; 2003.
2. John CC, Jonathan RS Arch, Mohammad T. Anti-obesity drugs: a critical review of current therapies and future opportunities.
3. WHO Global Database on Body Mass Index Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004. Available from: www.who.int/bmi/index.jsp?introPage=intro_3.html.
4. Seidell JC, Rissanen A. Prevalence of Obesity in Adults: The Global Epidemic. In: Bray GA, Bouchard C, eds. Handbook of Obesity (In press); 2004.
5. Pena M, Bacallao J. ed. Obesity and Poverty: A New Public Health Challenge. Washington, DC: Pan American Health Organization (PAHO); 2000.
6. Drewnowski A. Nutrition transition and global dietary trends. Nutrition 2000; 16(7–8): 486–7. http://dx.doi.org/10.1016/S0899-9007(00)00295-1
7. BA Swinburn. Diet, nutrition and the prevention of excess weight gain and obesity, Public Health Nutrition; 7(1A): 123–146. PMid:14972057
8. Després JP. Abdominal Obesity, Inflammation, and CVD, Canadian Journal of Cardiology 2012; 28: 642-652. http://dx.doi.org /10.1016/j.cjca.2012.06.004 PMid:22889821
9. Tentolouris N, Liatis S, Katsilambros N. Sympathetic system activity in obesity and metabolic syndrome. Ann N Y Acad Sci 2006; 1083: 129–152. http://dx.doi.org/10.1196/annals.1367.010 PMid:17148737
10. Angelopoulos N, Goula A, Tolis G. Current knowledge in the neurophysiologic modulation of obesity. Metabolism 2005; 54(9): 1202–1217. http://dx.doi.org/10.1016/j.metabol.2005.04.005 PMid:16125532
11. Leiter LA, Fitchett DH, Gilbert RE. Cardiometabolic Risk Working Group: Executive Committee, Cardiometabolic risk in Canada: a detailed analysis and position paper by the cardiometabolic risk working group. Can J Cardiol 2011; 27(2): 1-33. http://dx.doi.org/10.1016 /j.cjca.2010.12.054 PMid:21459257
12. Mora S, Cook N, Buring JE, Ridker PM, Lee IM. Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. Circulation 2007; 116: 2110–2118. http://dx.doi.org/10.1161/ CIRCULATIONAHA.107.729939PMid:17967770 MCid:PM C2117381
13. National Task Force on the Prevention and Treatment of Obesity. Long-term pharmacotherapy in the management of obesity. JAMA 1996; 276: 1907-1915. http://dx.doi.org/10.1001/jama.276.23.1907 PMid:8968018
14. Bray GA. Use and abuse of appetite suppressant drugs in the treatment of obesity. Ann Intern Med 1993; 119: 707-713. http://dx.doi.org/ 10.7326/0003-4819-119-7_Part_2-199310011-00016 PMid:8363202
15. National Institutes of Health Consensus Development Conference statements: gastrointestinal surgery for severe obesity. Am J Clin Nutr 1992; 55(suppl): 487S-619S. PMid:1733116

16. Atul S. A review on *Garcinia cambogia* – A weight controlling agent. IJPRD 2011; 3(10): 13-24.
17. Watson JA, Lowenstein JM. Citrate and the conversion of carbohydrate into fat. J Biol Chem 1970; 245: 5993-6002. PMid:5484459
18. Watson JA, Fang M, Lowenstein JM. Tricarballylate and hydroxycitrate: substrate and inhibitor of ATP: citrate oxaloacetate lyase. Arch Biochem Biophys 1969; 35: 209-217. http://dx.doi.org/10.1016/0003-9861(69)90532-3
19. Lowenstein JM. Effect of (−)-hydroxycitrate on fatty acid synthesis by rat liver *in vivo*. J Biol Chem 1971; 246: 629-632. PMid:5542676
20. Sullivan AC, Triscari J, Neal MO. The influence of (−)-hydroxycitrate on *in vivo* rates of hepatic glycogenesis: lipogenesis and cholesterol-genesis. Fed Proc 1974; 33: 656.
21. Sullivan AC, Triscari J, Hamilton JG, Neal MO. Effect of (−)-hydroxycitrate upon the accumulation of lipid in the rat: appetite. Lipids 1973; 9: 129-134. http://dx.doi.org/10.1007/BF02532137
22. Nageswara Rao R, Sakeriak KK. Lipid-lowering and antiobesity effect of (−) hydroxycitric acid. Nutr Res 1988; 8: 209-212. http://dx.doi.org/10.1016/S0271-5317(88)80024-1
23. Badmaev V, Majeed M. Open field, physician controlled clinical evaluation of botanical weight loss formula citrin. Presented at: Nutracon: Nutriceuticals, Dietary Supplements and Functional Foods; 1995. Las Vegas, Nev.
24. Conte AA. A non-prescription alternative on weight reduction therapy. Am J Bariatr Med.Summer 1993: 17-19.
25. Thom E. Hydroxycitrate (HCA) in the treatment of obesity. Int J Obes 1996; 20(suppl 4): 48.
26. Rothacker DQ, Waitman BE. Effectiveness of a *Garcinia cambogia* and natural caffeine combination in weight loss: a double-blind placebo-controlled pilot study. Int J Obes 1997; 21(suppl 2): 53.
27. Girola M, De Bernardi M, Contos S. Dose effect in lipid-lowering activity of a new dietary intetrator (chitosan, *Garcinia cambogia* extract and chrome). Acta Toxicol Ther 1996; 17: 25-40.
28. Von Lippmann EO. Uber eine neue, im Rübensaft vorkommende Säure. Ber Dtsch Chem Ges 1883; 16: 1078-1081. http://dx.doi.org/10.1002/cber.188301601242
29. Martius C, Maué R. Darstellung, physiologisches Verhalten und Bedeutung der (+) − Oxycitronensäure und ihrer Isomeren. Z Physiol Chem 1941; 269: 33-40. http://dx.doi.org/10.1515/bchm2.1941.269.1.33
30. Lewis YS, Neelakantan S. (−)-Hydroxycitric acid: the principal acid in the fruits of *Garcinia cambogia*. Phytochemistry 1965; 4: 610-625. http://dx.doi.org/10.1016/S0031-9422(00)86224-X
31. Watson JA, Fang M, Lowenstein JM. Tricarballylate and hydroxycitrate: substrate and inhibitor of ATP: citrate oxaloacetate lyase. Arch Biochem Biophys 1969; 35: 209-217. http://dx.doi.org/10.1016/0003-9861(69)90532-3
32. Hayamizu K, Hirakawa H, Oikawa D, Nakanishi T, Takagi T, Tachibana T, Furuse M *et al*. Effect of *Garcinia cambogia* extract on serum leptin and insulin in mice. Fitoterapia 2003; 74: 267-273. http://dx.doi.org/10.1016/S0367-326X(03)00036-4
33. Ohia SE, Olubusayo AS, LeDay AM, Opere CA, Bagchi D. Effect of hydroxycitric acid on serotonin release from isolated rat brain cortex. Res Commun Molec Pathol Pharmacol 2001; 109(3and4): 210-216.
34. Mahendran P, Shyamala Devi CS. The modulating effect of *Garcinia cambogia* extract on ethanol-induced peroxidative damage in rats. Indian Journal of Pharmacology 2001; 33: 87-91.
35. Mahendran P, Sabitha KE, Shyamala Devi CS. Prevention of HCl-ethanol induced gastric mucosal injury in rats by *Garcinia cambogia* extract and its possible mechanism of action. Indian J Exper Biol 2002; 40: 58-62. PMid:12561970

Cite this article as:
Tripathy P.C., Karmahapatra P B., Palaniyamma D. Randomized, double-blind, placebo controlled clinical study to evaluate the effects of Garcinia caplets in obese subjects. Int. Res. J. Pharm. 2013; 4(7):182-186 http://dx.doi.org/10.7897/2230-8407.04740

Source of support: Nil, Conflict of interest: None Declared