British Journal of Medicine & Medical Research
12(1): 1-8, 2016, Article no.BJMMR.21609
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN *international*
www.sciencedomain.org

Weight Management Effects of a Mixture of Conjugated Linoleic Acid and L-Carnitine in Diet Induced Obese Rats

Maryam Nazari[1], Majid Karandish[1*], Mohammad-Taha Jalali[2] and Ali-Hossein Saberi[3]

[1]Nutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[2]Hyperlipidemia Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[3]Department of Medical Genetic, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Authors' contributions

This work was carried out in collaboration between all authors. Authors MK and AHS designed the study and wrote the protocol. Authors MN and MTJ managed laboratory affaires. Author MN wrote the first draft of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/21609
Editor(s):
(1) Nurhan Cucer, Erciyes University, Medical Biology Department, Turkey.
Reviewers:
(1) Adeline Chia, Taylor's University, Malaysia.
(2) Trent W. Nichols, Veterans Administration Hospital, USA.
(3) Rashida Parveen, University Of Agriculture Faisalabad, Pakistan.
(4) Anonymous, University of New Mexico, Mexico.
(5) Anonymous, Rayat Institute of Pharmacy, Ropar, Punjab, India.
(6) Satoshi Odo, Wayo Women's University, Japan.
Complete Peer review History: http://sciencedomain.org/review-history/12024

Original Research Article

Received 26th August 2015
Accepted 8th October 2015
Published 30th October 2015

ABSTRACT

Aims: To examine simultaneous effects of Conjugated Linoleic Acid (CLA) and L-carnitine (LC) on weight gain in diet induced obese rats.
Study Design: Experimental study.
Place and Duration of Study: Department of Nutrition, Faculty of Para-Medical Sciences, Ahvaz Jundishapur University of Medical Sciences (January 2014 to January 2015).
Methodology: Forty male Wistar rats were randomly divided into two groups: Normal fat diet

**Corresponding author: E-mail: mkarandish@yahoo.com;*

(n=8), and High fat diet (HFD) (n=32). After eight weeks, the second group maintained HFD and was subdivided into 4 categories: Corn Oil group, 500 mg CLA, 200 mg LC, and 500 mg CLA+ 200 mg LC (all doses per kg body weight), which were administered by oral gavage for four weeks. Body weights were measured and recorded weekly by means of a digital scale. SPSS Version 16 was used for statistical analysis.

Results: At the end of eighth week, a significant difference in weights was observed between HFD (295.43±5.36 gr) and NFD (246.38±6.48 gr) group. After four weeks, LC significantly reduced weight gain by 7.5% (*P* = .047). Trend of weight gain in CLA and LC + CLA groups were decelerated (24 and 25 gr respectively), but it was statistically insignificant (*P* = .08, .12 respectively).

Conclusion: Findings of this experimental study showed that a high fat diet led to obesity and combined LC and CLA could decelerate weight gain to some extent. However, it needs further work to validate reliability in human.

Keywords: Conjugated linoleic acid; high fat diet; L-carnitine; obesity.

1. INTRODUCTION

The worldwide prevalence of obesity which is defined as excessive amount of body fat has nearly doubled between 1980 and 2008 [1,2]. This multifaceted condition is followed by serious medical, social and psychological consequences. It is estimated that 1-10% of health costs are contributed to obesity comorbidities [3,4].

From various strategies that have been used to manage obesity including diet, exercise, behavior modification, medications and surgery, pharmacotherapy may produce a more rapid weight loss but approved drugs for obesity management are limited in variety and long-term effectiveness. Further, serious side effects such as hypertension, insomnia and diarrhea make limit their widespread usage. However, dietary supplements for weight loss have attracted lots of attention [5,6]. These products are popular because they are advertised and also because of being natural and easily accessed [7,8].

Fat burners refer to categories of nutritional supplements that are claimed to increase energy expenditure by enhancing fat metabolism and oxidation, decreasing fat absorption, increasing weight loss and prevention of weight regain after weight loss [9]. L-carnitine (LC) and Conjugated Linoleic Acid (CLA) are two of the most common fat burner supplements.

LC, a vitamin-like compound that is synthesized from the essential amino acids lysine and methionine translocates long chain fatty acids in the form of esters of L-carnitine (acyl-carnitine) into the mitochondria matrix where β-oxidation occurs [10,11]. Carnitine palmitoyltransferase I (CPTI) on the outer membrane catalyzes the transfer of long-chain fatty acids into the cytosol from Coenzyme A (CoASH) to L-carnitine, which is the rate limiting step in fatty acid oxidation. On the inner mitochondrial membrane, carnitine palmitoyl transferase II (CPTII) catalyzes the transfer of fatty acids from L-carnitine to free CoA in the mitochondrial matrix, where metabolic conversion by β-oxidation yields propionyl-CoA and acetyl-CoA. This is known as the L-Carnitine shunt [12,13].

It seems that in carnitine deficient situations (although it is rare) most of the dietary lipids cannot be metabolized as an energy source an and therefore leads to obesity [10,11,14,15]. Wutzke and Lorenz have shown that LC supplementation causes a significant increase in β-oxidation of fatty acids without any changes in protein synthesis and breakdown rates in slightly overweight subjects [16]. Despite wide use of LC for obesity management, there is inconsistent evidence that it alters fuel metabolism or enhances weight loss in healthy subjects [9].

CLA, another frequently studied fat burner, is a group of positional and geometric isomers of linoleic acid with conjugated double bonds that seems to have anti-obesity properties [17]. Findings of studies about CLA effects on body fat storage were based on different animal models and CLA isomers [18]. On the other hand CLA was not reported to have any effect on fullness, appetite and satiety in human studies [19,20]. Results of studies on human subjects have shown that the magnitude of CLA effect is negligible and does not seem to be clinically important since weight loss from baseline was less than 5% [21]. However a meta-analysis of 18 human studies about CLA efficacy concluded that CLA in large doses has modest but

significant reductive effect on weight which is equivalent to 0.2 to 3 g/kg body weight in mice. Additionally, that study attributed the inconsistency of results to lacked statistical power because of short treatment duration, few subjects or both [22].

Though LC and CLA supplements, as weight loss promoters, have a widespread use nowadays, administration of them for reducing body fat and weight, is still a controversial issue. Also, even though different molecular targets for both treatment and prevention of obesity have been introduced, targeted monotherapy has not shown successful effects. Thus, targeting multiple metabolic pathways simultaneously with several natural compounds to attain synergistic or additive effects might be a hopeful approach to address obesity by different mechanisms.

LC and CLA are in a close metabolic inter-relationship and few studies have clarified the similar or complementary role of them in fat metabolism [23]. For example, LC transports long-chain fatty acids across mitochondrial and facilitates their β-oxidation, while CLA by increasing the activity of CPT is known to facilitate fatty acid may account for its fat partitioning effects. Incorporating CLA into LC to produce novel CLA ester may offer advantages for use as a pharmaceuticals [24]. In addition, in several researches single effect of these two supplements in obesity management have been investigated but potential effects of combined CLA and LC on obesity have not been examined yet. Such idea has been reported in a patent [25] but to the best of our knowledge no study on this topic has been published yet. The aim of present study is comparing the separate effects of LC and CLA with combination of them on weight gain in diet induced obese rats. High fat diet (HFD) was used to create the obesity model in rats.

2. MATERIALS AND METHODS

2.1 Experimental Details

Forty male albino rats of Wistar strain with 8 weeks age from Laboratory Animal Unit of Jundishapur University of Medical Sciences, Ahvaz, Iran weighing 150-200 g were housed in groups of four per cage and maintained on a 12-h light: dark cycle at 22℃ and the relative humidity at 50±5%. The animals were placed on normal chow diet for the first week for acclimation with new environmental conditions. Then they were randomly assigned into 2 different diets:

- Normal Fat Diet (NFD) all over the study (semi-purified normal fat diet) (n=8).
- High Fat Diet (HFD) all over the study (semi-purified high fat diet) (n=32).

The diets were prepared freshly twice a week and were stored in 4℃. They were a modification of the AIN-93 Purified Diets for Laboratory Rodents [19]. Different ingredients of the original diets were purchased and mixed. Cellulose was replaced by wheat bran in formulation in this study and margarine was added in place of a proportion of corn starch to reach 60% of diet from fat. Details about the proportional composition of each group-specific diet are presented in Table 1. NFD according to AIN-93M formula contained 75% carbohydrate, 14% protein and 10% fat. To prepare HFD, we increased the fat content of diet to 60% and in order to keep protein portion (14%), 26% of diet supplied from carbohydrate. Soybean oil and margarine were used equally. Different parts of carbohydrate composition as AIN-93M formula were calculated and mixed with other ingredients. Palatability and efficacy of the diets were confirmed in a 45 days pilot study with 8 rats.

Animals had free access to food and water. Body weight was measured and recorded weekly by means of a digital scale (MFD By OHAUS CORP, Florham Park N.J.).

On the eighth week, HFD group was randomly subdivided into 4 categories (n=8 in each) to receive the main interventions as follows for 4 weeks:

- Control group, which received 500 mg/kg body weight corn oil.
- CLA group, which received 500 mg/kg body weight CLA as a 50:50 isomer blend of c-9, t-11 and t-10, c-12 CLA.
- LC group, which received 200 mg/kg body weight LC.
- CLA + LC group that received 500 mg/kg body weight CLA+ 200 mg/kg body weight LC.

The CLA used in this study was Tonalin (Natural Factors, USA) which contains free fatty acids containing about 80% conjugated linoleic acid.

Table 1. Modified* American Institute of Nutrition diet composition

Ingredients in 1 kg diet	Normal fat diet (g)	High fat diet (g)
Corn starch	465.6	237
Casein *(>85% protein)*	140	200
Dextrinized corn starch	155	78
Sucrose	100	50
Soybean oil	40	185
Margarine	0	185
Fiber	50	50
Mineral mix (AIN-93M-MX))	35	35
Vitamin mix (AIN-93-VX)	10	10
L-Cystine	1.8	3
Choline bitartrate	2.5	2.5
Tert-butylhydroquinone	0.008	0.01
Total energy (kcal)	3600	5700

**AIN-93M Purified Diets for Laboratory Rodents [26] was modified. Fiber was replaced by wheat bran in formulation*

LC was Levocarnitin (So.Se PHARM, Italy) which contains 1gr LC per 10 mL solution. Protocol and doses of agents in this study were in accord with previous investigations [22,25,27].

This experiment was carried out in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals (NIH Publications No. 80-23) revised 1996 and the guidelines provided by the ethical committee of experimental animal care at Jundishapur University of medical sciences (NRC9204).

2.2 Statistical Analyses

All statistical tests were performed with the use of SPSS (Statistical Package for Social Sciences version 16.0; SPSS Inc, Chicago) and a $p < 0.05$ was statistical significance level. Results are expressed as means ± standard error of the mean (SEM). Normality and homogeneity of variances were tested with Kolmogrov-Smirinov. One-way ANOVA, followed by LSD test was used to compare mean differences in body weight.

3. RESULTS AND DISCUSSION

- Body weights of animals in NFD group was not different from HFD groups at the baseline. At the end of eighth week, body weight increased significantly in HFD-fed rats compared to NFD group (Table 2). HFD-induced obese rats weighed 20% more than animals in NFD group.
- After four weeks treatment with LC, weight gain reduced significantly. Trend of weight gain in CLA and LC + CLA groups was decelerated in comparison with HFD group, however they were not statistically significant (Table 3).

The present study was designed to gain more insight into the effects of co-administration of CLA and LC on weight changes. Our purpose was to achieve an obesity model by feeding a synthetic high fat diet in eight weeks followed by mentioned treatment period for four weeks in Wistar rats. This model simulates a tangible clinical case of obesity and also obesity treatment that its duration is safe and recommended in previous investigations [5,28].

Despite the reported beneficial effects of separate treatments with LC and CLA on body weight, no additive or synergistic effect on weight control was observed in this experiment. However Chopra reported such synergistic activity in treating overweight and obesity [25].

According to the past studies, LC keeps its anti-obesity effect when it is administered in combination with other compounds like arginine, caffeine, soy isoflavones [29], extract of Garcinia Cambogia [30] and herbal mixture extract [28]. This effect of LC might be mediated via induction of lipolysis, fatty acid oxidation and down-regulation of both $PPAR_{gamma}$ and adipose-specific fatty acid binding protein (aP2) adipogenesis [31]. In spite of evidence and a few relevant proposed mechanisms about positive effects of LC on fat metabolism, no fat mass or weight loss was seen after 8 weeks of LC administration accompanied by aerobic training in moderately obese women in Villani et al. [32] study which made such relation doubtful.

Table 2. Effect of NFD and HFD on rats body weight during eight weeks

Group	n	Baseline weight (g)	*P*	Eight-week weight (g)	*P*
NFD	8	170.00±3.91		246.38±6.48	
HFD	32	176.04±4.02	.26†	295.43±5.36	.000§

Values are expressed as means ± standard error. †: Insignificant weight difference between NFD and HFD at baseline. §: Significant weight difference between NFD and HFD at eighth week. NFD: Normal Fat Diet, HFD: High Fat Diet

Table 3. Effect of LC, CLA and LC+CLA on body weight and weight gain rate during four weeks treatment in obese rats

Group	n	Eight-week weight (g)	*P**	Twelve-week weight (g)	*P*	Difference (g)	*P*
NFD	8	246.38±6.48		271.62±8.03		25.2 (10.2%)	
HFD	8	297.12±13.16	.000	336.43±15.10	.000	39.31 (13.23%)	.000
LC	8	294.38±7.60	.828	316.68±11.8	.219	22.3 (7.5%)	.04†
CLA	8	288.71±8.27	.522	312.71±9.62	.150	24 (8.31%)	.08
MIX	8	285.86±6.19	.392	310.86±7.43	.121	25 (8.74%)	.12

Values are expressed as means ± standard error.
**All P are expressed in comparison with HFD except for first (.000) which is between HFD and NFD group.*
†: Significant difference between LC and HFD in weight gain during four week (P =.04).
CLA: Conjugated Linoleic Acid, LC: L-carnitine, NFD: Normal Fat Diet, HFD: High Fat Diet

However our results were consistent with Wutzke and Lorenz study that demonstrated a significant increase in β-oxidation of fatty acids by LC supplementation in slightly overweight subjects [16].

According to some studies, LC can exacerbate symptoms of hypo-thyroidism as it might inhibit thyroid hormone entry into the nucleus of cell [33] and thus, it can act as a peripheral antagonist of thyroid hormone action [34,35]. Hence, it will lower metabolic rate which may lead to inefficiency of LC in weight loss.

On the other side, inefficacy of CLA supplement in weight control has been reported by large body of data while different mechanisms have proposed for possible anti-obesity effects of CLA including lipolysis augmentation, promotion of preadipocyte apoptosis via increase of TNFα mRNA and increase of uncoupling protein 2 (UCP2), adipogenesis inhibition and reduction of preadipocyte differentiation [36–38].

Additionally, two main conjugated isomers of linoleic acid, cis-9, trans-11-C 18:2 and trans-10, cis-12-C, have been shown that they are not only poor substrates for the mitochondrial oxidation pathway, but also interfered the oxidation rate of other fatty acids at a step close to the launch of the β-oxidative cycle [39]. Therefore the synergetic effect on weight loss by LC combination with CLA may have been blunted in the Wistar rats.

Our results confirmed that LC limits weight gain on a high fat diet in comparison with control group (7.5% vs. 13.2%, respectively) and unexpectedly CLA or LC+CLA did not show a significant effect on diminishing weight gain (Table 3). The only indicator of weight change in our study was body weight while body fat is a more sensitive criterion for assessing obesity in animals, since Wood et al. [40] reported that rats which were fed a high-fat diet for 10 weeks displayed a 10% increase in total body weight but a 35–40% increase in total body fat compared with the animals fed a NFD. The source of fat which was used (plant origin) might also affect the results, for instance, because SFA of plant origin might not be as effective as SFA of animal origin in developing obesity [41].

The most remarkable point in our study was that LC restrictive effect on weight gain, was stronger than CLA and also significant. Nature of the dietary fat, level of fats, duration of treatment, mixed isomer form of CLA and animal species might affect the energy expenditure role of LC and CLA [42]. Inconsistency of results might come from improper ratio of CLA to LC that was 2 in our experiment. Also, ineffectiveness of simultaneous use of CLA and LC may be relevant to hypothyroid properties of LC which was mentioned above.

Extrapolation of such studies to human needs further investigation, modifying study design which may result in more precise evidence; for

example longer intervention period, using different isomers of CLA, survey of dose dependent relationship (both CLA and LC) and assessment of food intake. Although it seems that the t10, c12 isomer is effective as an anti-adiposity agent, but this isomer could induce insulin resistance marginally [22,43]. Moreover it is suggested to consider some biochemical parameters in next such co-administrative researches.

4. CONCLUSIONS

In conclusion, CLA and LC have a beneficial effect on rat body weight control. Though this effect is slight, but in longer durations this effect may be noticeable. Like most other supplements definite evidence is not available for CLA and LC together.

To the extent of our knowledge this is the first study which investigated the effects of co-administration of CLA and LC as two fat burners on weight changes. It should be noted that some studies have used combination of these supplements as a single dose but their synergistic or additive effect was not examined yet. Due to the failure of most simple pharmaceutical interventions in obesity control, it is rational to evaluate co-administration of supplements which are metabolically interrelated to achieve stronger approach to address obesity. Because list of weight loss supplements is growing up (that are not in parallel to increase in scientific foundation) further exact investigations are needed.

CONSENT

It is not applicable.

ACKNOWLEDGEMENTS

This paper is issued from the PhD thesis of Maryam Nazari and financial support was provided by Ahvaz Jundishapur University of Medical Sciences (Grant number NRC 9204). The authors would like to thank Mr. Mehdi Shirinasab for his help in laboratory analysis and Dr. Azadeh Saki for her statistical advices.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. Lancet 2011;377:557–67.
2. Katherine M. Flegal, Margaret D. Carroll, Cynthia L. Ogden LRC. Prevalence and trends in obesity among US adults, 1999-2008. JAMA. 2010;303:235–41.
3. Seidell JC. Worldwide Prevalence of obesity in adults. In: Bray GA, Bouchard C, editors. Handbook of obesity. 3th ed. London: Taylor & Francis Group. 2013; 47-57.
4. Padula WV, Allen RR, Nair KV. Determining the cost of obesity and its common comorbidities from a commercial claims database. Clin Obes. 2014;4:53–8. DOI: 10.1111/cob.12041.
5. Odo S, Tanabe K, Yamauchi M. A pilot clinical trial on l-carnitine supplementation in combination with motivation training: effects on weight management in healthy volunteers. Food Nutr Sci. 2013;4:222.
6. Bray GA. Medical therapy for obesity. Mt Sinai J Med A J Transl Pers Med. 2010; 77:407–17.
7. Blanck HM, Khan LK, Serdula MK. Use of nonprescription weight loss products: Results from a multistate survey. Jama. 2001;286:930–5.
8. Blanck HM, Serdula MK, Gillespie C, Galuska DA, Sharpe PA, Conway JM, et al. Use of nonprescription dietary supplements for weight loss is common among Americans. J Am Diet Assoc. 2007; 107:441–7.
DOI: 10.1016/j.jada.2006.12.009.
9. Jeukendrup AE, Randell R. Fat burners: Nutrition supplements that increase fat metabolism. Obes Rev. 2011;12:841–51. DOI: 10.1111/j.1467-789X.2011.00908.x.
10. Dwyer JT, Allison DB, Coates PM. Dietary supplements in weight reduction. J Am Diet Assoc. 2005;105:80–6.
DOI:http://dx.doi.org/10.1016/j.jada.2005.02.028
11. Osorio JH. Supplementation with carnitine for weight loss: A biochemical approach. Colomb Med. 2011;42:529–35.

12. Vaz FM, Wanders RJA. Carnitine biosynthesis in mammals. Biochem J 2002;361:417–29.
DOI: 10.1042/0264-6021:3610417.
13. McGarry JD, Brown NF. The mitochondrial carnitine palmitoyltransferase system—from concept to molecular analysis. Eur J Biochem. 1997;244:1–14.
14. Cha YS. Effects of L-carnitine on obesity , diabetes, and as an ergogenic aid. Asia Pac J Clin Nutr. 2008;17:306–8.
15. Flanagan JL, Simmons PA, Vehige J, Willcox MDP, Garrett Q. Role of carnitine in disease review. Nutrition & Metabolism. 2010;1–14.
16. Wutzke KD, Lorenz H. The effect of l-carnitine on fat oxidation, protein turnover, and body composition in slightly overweight subjects. Metabolism. 2004;53: 1002–6.
DOI: 10.1016/j.metabol.2004.03.007.
17. Lehnen TE, Ramos M, Camacho A, Marcadenti A, Lehnen AM. A review on effects of conjugated linoleic fatty acid (CLA) upon body composition and energetic metabolism. J Int Soc Sports Nutr; 2015.
DOI: 10.1186/s12970-015-0097-4.
18. Watras AC, Buchholz AC, Close RN, Zhang Z, Schoeller DA. The role of conjugated linoleic acid in reducing body fat and preventing holiday weight gain. Int J Obes (Lond). 2007;31:481–7.
DOI: 10.1038/sj.ijo.0803437.
19. Zambell KL, Keim NL, Van Loan MD, Gale B, Benito P, Kelley DS, et al. Conjugated linoleic acid supplementation in humans: Effects on body composition and energy expenditure. Lipids. 2000;35:777–82.
20. Medina EA, Horn WF, Keim NL, Havel PJ, Benito P, Kelley DS, et al. Conjugated linoleic acid supplementation in humans: Effects on circulating leptin concentrations and appetite. Lipids. 2000;35:783–8.
21. Onakpoya IJ, Posadzki PP, Watson LK, Davies LA, Ernst E. The efficacy of long-term conjugated linoleic acid (CLA) supplementation on body composition in overweight and obese individuals: A systematic review and meta-analysis of randomized clinical trials. Eur J Nutr 2012;51:127–34. doi:10.1007/s00394-011-0253-9.
22. Whigham LD, Watras AC, DA S, Whigham LD, Watras AC, Schoeller DA. Efficacy of conjugated linoleic acid for reducing fat mass: A meta-analysis in humans 1, 2. Am J Clin Nutr. 2007;85:1203–11.
23. Li Z, Yang D, Jiang L, Ji J, Ji H, Zeng X. Lipase-catalyzed esterification of conjugated linoleic acid with L-carnitine in solvent-free system and acetonitrile. Bioprocess Biosyst Eng. 2007;30:331–6. DOI: 10.1007/s00449-007-0129-9.
24. Martin JC, Grégoire S, Siess MH, Genty M, Chardigny JM, Berdeaux O, et al. Effects of conjugated linoleic acid isomers on lipid-metabolizing enzymes in male rats. Lipids 2000;35:91–8.
25. chopra RJ. Synergistic conjucated linoleic acid (CLA) and carnitine combination. Pat Appl Publ. 2006;23:1-13.
26. Reeves PG. Committee report AIN-93 purified diets for laboratory rodents: Final report of the American Institute of Nutrition Ad Hoc Writing Committee on the Reformulation of the AIN-76A Rodent Diet. J Nutr. 1993;123:1939-1951.
27. Mingorance C, Gonzalez del Pozo M, Dolores Herrera M, Alvarez de Sotomayor M. Oral supplementation of propionyl-l-carnitine reduces body weight and hyperinsulinaemia in obese Zucker rats. Br J Nutr 2009;102:1145–53.
DOI: 10.1017/S0007114509389230.
28. Amin KA, Nagy MA. Effect of carnitine and herbal mixture extract on obesity induced by high fat diet in rats. Diabetol Metab Syndr 2009;1:17.
DOI: 10.1186/1758-5996-1-17.
29. Murosaki S, Lee TR, Muroyama K, Shin ES, Cho SY, Yamamoto Y, et al. A combination of caffeine, arginine, soy isoflavones, and L-carnitine enhances both lipolysis and fatty acid oxidation in 3T3-L1 and HepG2 cells *in vitro* and in KK mice *in vivo* 1. J Nutr. 2007;2252–7.
30. Kim YJ, Kim KY, Kim MS, Lee JH, Lee KP, Park T. A mixture of the aqueous extract of Garcinia cambogia, soy peptide and L: -carnitine reduces the accumulation of visceral fat mass in rats rendered obese by a high fat diet. Genes Nutr. 2008;2:353–8. DOI: 10.1007/s12263-007-0070-1.
31. Lee MS, Lee HJ, Lee HS, Kim Y. L-carnitine stimulates lipolysis via induction of the lipolytic gene expression and suppression of the adipogenic gene expression in 3T3-L1 adipocytes. J Med Food. 2006;9:468–73.
32. Villani RG, Gannon J, Self M, Rich PA. L-carnitine supplementation combined with aerobic training does not promote weight

loss in moderately obese women. Int J Sport Nutr Exerc Metab. 2000;10:199–207.
33. Carolina N, Piga A, Pulita F, Pietroselli D, Cellerino R. Storms Treated With L-carnitine and Low to the Editor: Syndrome following. Am J Med. 2003;115:417–8.
34. Benvenga S, Amato A, Calvani M, Trimarchi F. Effects of carnitine on thyroid hormone action. Ann N Y Acad Sci. 2004; 1033:158–67.
DOI: 10.1196/annals.1320.015.
35. Benvenga S, Ruggeri RM, Russo A, Lapa D, Campenni A, Trimarchi F. Usefulness of L-carnitine, a naturally occurring peripheral antagonist of thyroid hormone action, in Iatrogenic hyperthyroidism: A randomized, double-blind, placebo-controlled clinical trial. J Clin Endocrinol Metab. 2001;86: 3579–94.
36. Simon E, Macarulla MT, Fernandez-Quintela A, Rodriguez VM, Portillo MP. Body fat-lowering effect of conjugated linoleic acid is not due to increased lipolysis. J Physiol Biochem. 2005;61: 363–9.
37. Tsuboyama-kasaoka N, Takahashi M, Tanemura K, Kim H, Tange T, Okuyama H, et al. Conjugated Linoleic acid supplementation reduces adipose tissue by apoptosis and develops lipodystrophy in mice. Diabetes. 2000;49:1534–42.
38. Wang YW, Jones PJH. Conjugated linoleic acid and obesity control: Efficacy and mechanisms. Int J Obes. 2004;28:941–55.
39. Demizieux L, Degrace P, Gresti J, Loreau O, Noël JP, Chardigny JM, et al. Conjugated linoleic acid isomers in mitochondria: Evidence for an alteration of fatty acid oxidation. J Lipid Res. 2002;43: 2112–22.
DOI: 10.1194/jlr.M200170-JLR200.
40. Woods SC, Seeley RJ, Rushing PA, D'Alessio D, Tso P. A controlled high-fat diet induces an obese syndrome in rats. J Nutr. 2003;133:1081–7.
41. Hariri N, Thibault L. High-fat diet-induced obesity in animal models. Nutr Res Rev. 2010;23:270–99.
DOI: 10.1017/S0954422410000168.
42. Choi JS, Jung MH, Park HS, Song J. Effect of conjugated linoleic acid isomers on insulin resistance and mRNA levels of genes regulating energy metabolism in high-fat-fed rats. Nutrition. 2004;20: 1008–17. DOI: 10.1016/j.nut.2004.08.009.
43. Racine NM, Watras AC, Carrel AL, Allen DB, Mcvean JJ, Clark RR, et al. Effect of conjugated linoleic acid on body fat accretion in overweight or obese children. Am J Clin Nutr. 2010;2000:1157–64.
DOI: 10.3945/ajcn.2009.28404.1.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/12024