UNIVERSITI PUTRA MALAYSIA

EFFECTS OF CONJUGATED LINOLEIC ACID SUPPLEMENTATION AFTER WEIGHT LOSS PROGRAM ON BODY WEIGHT STATUS AND METABOLIC PARAMETERS AMONG OVERWEIGHT IRANIANS

HANIEH FOULADI

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By

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Thesis Submitted To The School Of Graduate Studies, Universiti Putra Malaysia, In Fulfilment Of The Requirements For The Degree Of Master Of Science

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EFFECTS OF CONJUGATED LINOLEIC ACID SUPPLEMENTATION AFTER WEIGHT LOSS PROGRAM ON BODY WEIGHT STATUS AND METABOLIC PARAMETERS AMONG OVERWEIGHT IRANIANS

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Chair : Associate Professor Loh Su Peng, PhD
Faculty : Medicine and Health Sciences

Obesity is a crucial health related issue among human beings, and investigation to find a solution has been one of the most popular topics among researchers. Although there are some lifestyle changes and strategies to control obesity, using supplement or medication to help people lose weight is still under review. Conjugated linoleic acid (CLA) is one of the supplements that have been studied in the last decades to determine its impact on the weight loss, fat mass reduction, and energy expenditure, but the CLA's mechanism of action is still unclear. The objective of this study is to determine the effect of CLA supplementation and combination of CLA and exercising on anthropometric measurements, lipid profiles, and inflammatory biomarkers.

This study was a randomized controlled trial, and subjects were randomly assigned to participate in one of three groups named Control, CLA (the group receiving CLA supplementation without exercise), and CLA+E (the group that receive CLA supplementation in addition to exercising); two groups received 3 grams of CLA supplement which included a mixture of the bioactive isomers 50% cis-9, trans-11 and 50% trans-10, cis-12, but one of them was put on a moderate-intense training, and the control group neither received CLA supplement, nor was put on any training exercise. A total of 60 participants were recruited for each group (n=180), and the duration of study was 12 weeks. All the participants were on a moderate-balanced restricted calorie diet which was arranged to make them lose 4-6kg during 12 weeks of intervention, and the moderate intensity training was defined as walking with the speed of 5.5-6 km/h at least 160 minutes per week.

171 subjects completed their participation (Response Rate = 95%), and in comparison with the baseline body weight, Body Mass Index (BMI), Body Fat Mass (BFM), and waist to hip ratio of the CLA and CLA+E groups had a significant decrease ($P < 0.05$) with average BFM loss being 10.3% and 12% among CLA and CLA+E, respectively, compared to 2.7% among Control group. As for the biochemical analysis, the blood free fatty acid increased and high density lipoprotein decreased in CLA group which was an unfavorable effect of

CLA supplementation. Although the supplementation alone appeared to have some non-desirable effects on the mentioned blood tests, this change did not occur among the exercise group.

As a conclusion, supplementation with conjugated linoleic acid among overweight Iranians for 12 weeks reduced the BFM with some adverse effects on blood profiles which can be controlled through a moderate-intense exercise.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
Sebagai memenuhi keperluan untuk ijazah Master Sains

KESAN SUPLEMEN ASID LINOLEIK KONJUGASI PADA STATUS BERAT BADAN DAN PARAMETER METABOLIK SELEPAS PROGRAM PENURUNAN BERAT BADAN DI KALANGAN RAKYAT IRAN BERLEBIHAN BERAT BADAN

Oleh

HANIEH FOULADI

Ogos 2015

Pengerusi : Professor Madya Loh Su Peng, PhD
Fakulti : Perubatan dan Sains Kesihatan

Obesiti adalah isu berkaitan kesihatan yang penting dalam kalangan manusia, dan penyiasatan untuk mencari penyelesaian telah menjadi salah satu topik yang paling popular dalam kalangan penyelidik. Walaupun terdapat beberapa perubahan gaya hidup dan strategi untuk mengawal obesiti, penggunaan supplemen atau ubat-ubatan untuk membantu orang ramai mengurangkan berat badan masih dalam kajian. Asid linoleik konjugasi (CLA) adalah salah satu suplemen makanan yang telah dikaji dalam dekad yang lalu untuk menentukan kesannya terhadap kehilangan berat badan, pengurangan jisim lemak, dan penggunaan tenaga, tetapi tindakan mekanisme CLA masih tidak jelas. Dalam kajian ini, objektif kajian ini adalah untuk menentukan kesan suplemen CLA dan gabungan CLA dan bersenam pada pengukuran antropometri, profil lipid dan biomarkers inflamasi.

Kajian ini adalah percubaan terkawal rawak, dan subjek dibahagikan secara rawak untuk mengambil bahagian dalam salah satu daripada tiga kumpulan yang dinamakan Kawalan,, CLA (kumpulan yang menerima suplemen CLA tanpa senaman), dan CLA + E (kumpulan yang menerima suplemen CLA dan senaman); dua kumpulan menerima 3 gram bahan CLA yang termasuk campuran isomer bioaktif 50% cis-9, trans-11 dan 50% trans-10, cis-12, tetapi salah satu kumpulan menjalani senaman yang intensiti sederhana dan kumpulan kawalan tidak menerima suplemen CLA, dan tidak menjalani apa-apa senaman. Seramai 60 peserta telah diambil bagi setiap kumpulan (n=180), dan tempoh kajian adalah 12 minggu.. Semua peserta mengamalkan pemakanan seimbang kalori sederhana yang disarankan untuk mereka mengurangkan 4-6kg berat badan dalam masa 12 minggu kajian dan latihan intensiti yang sederhana ditakrifkan sebagai berjalan dengan kelajuan 5,5-6 km/jam sekurang-kurangnya 160 minit setiap minggu.

171 subjek berjaya menamatkan kajian (kadar respon = 95%). Perbandingan dengan nilai sebelum kajian, berat badan, indeks jisim badan, lemak jisim badan, dan nisbah pinggang dan pinggul kumpulan CLA dan CLA+E menunjukkan

penurunan yang signifikan (P <0.05), dengan penurunan purata lemak jisim badan menjadi 10.3% dan 12% di kalangan CLA dan CLA + E , masing-masing, berbanding 2.7% di kalangan kumpulan Kawalan. Bagi analisis biokimia, darah asid lemak bebas menunjukkan peningkatan dan lipoprotein ketumpatan tinggi berkurangan dalam kumpulan CLA. Ini merupakan kesan yang kurang baik daripada suplemen CLA. Walaupun suplemen sahaja nampaknya mempunyai beberapa kesan yang tidak baik atas ujian darah tersebut, namun perubahan ini tidak dilihat bagi kumpulan senaman.

Sebagai kesimpulan, suplemen melalui asid linoleik kinjugasi dalam kalangan rakyat Iran yang berlebihan berat badan selama 12 minggu mengurangkan jisim lemak badan dengan beberapa kesan buruk kepada profil darah yang boleh dikawal melalui senaman intensiti sederhana.

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.

I certify that a Thesis Examination Committee has met on (August 5 2015) to conduct the final examination of (Hanieh Fouladi) on her thesis entitled "Effects of Conjugated Linoleic Acid Supplementation after Weight Loss Program on Body Weight Status and Metabolic Parameters among Overweight Iranians" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

Members of the Thesis Examination Committee were as follows:

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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Signature: _____

Member of Supervisory Committee: Assoc. Professor Dr. Azrina Azlan

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LIST OF ABBREVIATIONS

CLA	Conjugated Linoleic Acid
EFA	Essential Fatty Acid
EE	Energy Expenditure
AA	Arachidonic Acid
RCT	Randomized Control/Clinical Trial
AM	Anthropometric Measurement
BA	Biochemical Analysis
BFM	Body Fat Mass
FFM	Fat Free Mass
LBM	Lean Body Mass
BMC	Body Mass Composition
WHR	Waist to Hip Ratio
WC	Waist Circumference
SFT	Skin Fold Thickness
BW	Body Weight
H	Height
BMI	Body Mass Index
FBS	Fasting Blood Sugar
TG	Triglyceride
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
VLDL	Very Low Density Lipoprotein
CRP	C-Reactive Protein
TNF- α	Tumor Necrosis Factor- α
IL-6	Interleukin-6
FFA	Free Fatty Acid
CHO	Carbohydrate
Group	Protein
CrM	Creatine Monohydrate
UCP-2	Uncoupling Protein-2
WAT	White Adipose Tissue
CVD	Cardiovascular Disease
RQ	Respiratory Quotient
SD	Standard Deviation
ID No	Identification Number
FIFO	First In First Out
USD	United States Dollar

CHAPTER 1

INTRODUCTION

1.1 Study Background

Nowadays, obesity is one of the major health issues around the world, and researchers have not found any concrete solution for this situation yet although it has been mentioned that a cogent way to control this issue is a healthy lifestyle and diet. During the last two decades the prevalence of overweight and obese people has been increased due to the modern and sedentary lifestyle that people even in developing countries are getting used to it.

Obesity is a global problem which the education level and socio-economic status of the countries affects its prevalence all around the world (Fontaine, Redden, Wang, Westfall, & Allison, 2003; Organization, 2000). The least prevalence is found in rural China and Japan, and the most is related to some African countries. This range varies from 5% to 75% which shows a substantial difference (Caballero, 2001, 2005). Recent data from the National Health and Nutrition Examination Survey in the United States indicated that more than one-third of adults are obese, with no gender difference, but according to the ethnic origin some fluctuations have been reported (Ogden, Carroll, Kit, & Flegal, 2014).

In Iran, the prevalence of obesity is increasing. A recent review article indicated that the prevalence of obesity for Iranians who aged less than 18 years old is 5.5%, and for the older population reported as 21.5%. The gender difference is a concern as obesity prevalence percentages are considerably higher among women. This difference is assumed to be the effect of sedentary lifestyle which is seen frequently among Iranian women (Kelishadi, Haghdoost, Sadeghirad, & Khajehkazemi, 2014; Mirzazadeh, Sadeghirad, Haghdoost, Bahreini, & Kermani, 2009).

For many years, human beings find and provide food just to be alive, but nowadays knowledge on nutrition let them not only live for a long time, but also prevent severe or chronic diseases, and stay healthy. Nutrients and their recognition have helped human through this journey. Macro and micro nutrients have been known as the very small parts of food which provide us energy and essentials respectively. Among macronutrients, fat is the most concentrated energy source, as it supplies a part of required energy (each gram of fat supplies 9 Cals), and most importantly body needs it for its vital functions such as growth, heat maintenance, and etc. (Mahan, Escott-Stump, Raymond, & Krause, 2012).

Dietary fats are mostly triglycerides and phospholipids, and the most vulnerable and substantial part of them is fatty acids which can be dispensable or indispensable. Essential fatty acids are fatty acids that humans must ingest since the body requires them for good health, and they are called as essentials as the body cannot synthesize them. Only two fatty acids are known to be essential for

humans: alpha-linolenic acid (an omega-3 fatty acid) and linoleic acid (an omega-6 fatty acid); moreover some others known as conditionally essential like docosahexaenoic acid and gamma-linolenic acid (Mahan et al., 2012).

From the historical point of view, it seems that for the first time Booth who was working on the quality of the milk's fat saw changes in the absorption in the ultra-violet for the fatty acids along with the seasonal changes which was because of the conjugated double bonds (Booth, Kon, Dann, & Moore, 1935; Moore, 1939). In continuation of Booth's investigations almost after 30 years another researcher, Reil, confirmed that the alteration in the cow's milk through a year and different seasons among Canadian cows is obvious. These two points of time were the very first investigations for a clue regarding the Conjugated Linoleic Acid (CLA) (Riel, 1963).

As the prevalence of obesity is undeniable, and it is known that many factors play important roles in the maintenance of healthy weight, for many years, researchers have tried to find a way to help people with their weight management plans. One way of addressing this problem is through finding a beneficial supplement that can help weight loss. Many scientific research have been conducted to evaluate the effects of functional foods and supplementation on obesity; one of these supplements is CLA (L. D. Whigham, Watras, & Schoeller, 2007).

Conjugated Linoleic Acid (CLA) is an isomer for the essential fatty acid Linoleic Acid. This term (CLA) refers to some positional and geometrical isomers of the omega-6 essential fatty acid (linoleic acid) (Eulitz et al., 1999; G. S. Kelly, 2001). Since this fatty acid has some biological effects on human and animals, there is an immense interest to study and find more knowledge about it. For many years, CLA has been known as a fatty acid which is found in the foods that come from ruminants such as dairy products and meat (Aydin, 2009; Eulitz et al., 1999). Research in this field has become even more interesting when it has been found that CLA has got some anticarcinogenic effects among animals, and since then a cornucopia of research has been conducted in this context (S. Chin, Liu, Storkson, Ha, & Pariza, 1992).

As far as CLA's effect on body composition is concerned, it induces loss of body fat in mice (DeLany, Blohm, Truett, Scimeca, & West, 1999; Park et al., 1997; West et al., 1998), rats (Azain, Hausman, Sisk, Flatt, & Jewell, 2000; Yamasaki et al., 1999), pigs (Dugan, Aalhus, Schaefer, & Kramer, 1997; Wiegand, Parrish, Swan, Larsen, & Baas, 2001), and humans (Chen et al., 2012; Mougios et al., 2001; Riserus, Berglund, & Vessby, 2001), and this effect is mostly attributed to the trans-10,cis-12 isomer (Ostrowska, Muralitharan, Cross, Bauman, & Dunshea, 1999), but some other studies declared that the use of moderate doses for a mixture of the two main CLA isomers reduces body fat content, improves plasma lipid profile, and maintains insulin sensitivity (despite a moderate degree of hyperinsulinaemia) without the promotion of inflammatory markers in adipose tissue (Dilzer & Park, 2012; Kennedy et al., 2010; Parra, Palou, & Serra, 2010; Terpstra, 2004).

A review in 2007 stated when the body of evidence is considered as a whole, CLA does have a beneficial effect on human body composition. Although this effect is modest, it could be important if accumulated over time, especially in an environment where continuous, gradual weight gain is the norm in the adult population (L. D. Whigham, Watras, & Schoeller, 2007). Beside the body fat mass reduction impact, in some studies it has been proposed that if the adipose tissue depletion does not get along with an increase in Energy Expenditure (EE) it might result in some adverse consequences in human like hyperlipidemia, hyperglycemia, and lipodystrophy (Kennedy et al., 2010). Additionally, the combination of physical activity -which regulates the EE- and CLA supplementation might be the other side of this hypothesis in which the effectiveness on fat mass reduction might be improved with a better control on biochemical profiles, specially lipid profiles (Kennedy et al., 2010; Kreider, Ferreira, Greenwood, Wilson, & Almada, 2002; Lowery, Appicelli, & Lemon, 1998; Thom, Wadstein, & Gudmundsen, 2001).

As mentioned, the prevalence of obesity is increasing among Iranians, and losing fat for a healthy body composition through diet, exercising, and supplementation helps this population to keep themselves away from the consequences of obesity and high levels of BFM. As studies has shown that CLA supplementation has a beneficial effect on human body composition, there is a need to investigate the effect of this supplementation (c-9, t-11 CLA and the trans-10, cis-12 CLA) on the body fat mass of the overweight Iranians who used to be obese and have marginal body fat percentages and simultaneously compare the combination of exercise with supplementation to determine changes in the anthropometric measurements and biochemical analysis. Unfortunately, there is lack of research in this matter on the aforementioned population.

It has been assumed that supplementation with CLA with the combination of a controlled weight loss diet and exercising would lower the body fat mass percentages, and this procedure might be elevated among who were exercising regularly. It also has been theorized that the exercising participants' situations, anthropometric measurements, and blood tests will come out even more balanced especially in case of the free fatty acid content of blood and inflammatory biomarkers.

1.2 Problem Statement

According to the information provided in the previous section, the current research attempts to address three existing research problems in the area. Firstly, contradictory findings exist in previous research pertaining to the effect of CLA on Body Weight (BW), Body Mass Index (BMI), waist circumference, Waist to Hip Ratio (WHR), Body Fat Mass percentage (BFM), and blood lipid profiles including triglyceride (TG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), and Free Fatty Acid content of blood (FFA), inflammatory profiles including Tumor Necrosis Factor alpha (TNF-α), C-reactive protein (CRP), and interluekin-6 (IL-6), and lastly Fasting Blood Sugar (FBS) (L. D. Whigham, Watras, & Schoeller, 2007; Dilzer & Park, 2012).

Secondly, there is less attention paid to combinatorial effect of CLA and exercise on BW, BMI, WHR, BFM, and blood profiles (Kennedy et al., 2010; Kreider, Ferreira, Greenwood, Wilson, & Almada, 2002; Lowery, Appicelli, & Lemon, 1998; Thom, Wadstein, & Gudmundsen, 2001).

Finally, there is a lack of previous research on CLA supplementation among overweight Iranians who used to be obese. We verified lack of research in this matter on the aforementioned population by searching for related publications with different combination of keywords pertaining to it in well-stablished scholarly research web search engines such as Google Scholar and PubMed.

1.3 Significance of Study

In this study we are providing more data about the effects of CLA on healthy exercising and non-exercising overweight Iranians who used to be obese. These effects are assessed according to the anthropometric measurements and biochemical analysis. Additionally, this research contributes to knowledge on the control of obesity by supplementation which nowadays is an important and interesting topic.

1.4 Study Objective

The general objective was to determine effects of CLA supplementation and its combination with exercising on anthropometric measurements and biochemical analysis among overweight Iranians after weight loss during 12 weeks. Objectives in detail are as below:

- To determine and compare the effects of CLA and combination of CLA and exercising on body weight (BW), body mass index (BMI), waist circumference (Wargent et al.), waist to hip ratio (WHR), and body fat mass percentage (BFM) among three groups named Control, CLA, CLA+E.

- To determine and compare the effects of CLA and combination of CLA and exercising on blood lipid profiles including triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), and free fatty acid content of blood (FFA), inflammatory profiles including tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), and interluekin-6 (IL-6), and lastly blood sugar (FBS) among three groups named Control, CLA, CLA+E.

- To analyze the collected data to find the strongest parameters for the prediction of body fat mass changes which is the main factor of the current study using linear regression. Hence, we aim to predict BFM changes using predictors such as age, gender, all the anthropometrics, and biochemical analysis (changes in anthropometrics, and biochemical analysis). The linear regression model will be designed for the all three groups.

1.5 Null Hypothesis

I. There is no significant difference between the anthropometric measurements including body weight (BW), height (H), body mass index (BMI), waist to hip ratio (WHR), and body fat mass percentage (BFM) measurements of the Control and intervention (CLA and CLA+E) groups.

II. There is no significant difference between biochemical analysis including triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), fasting blood Glucose (FBG), tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), interluekin-6 (IL-6), and free fatty acid content of blood (FFA) between the Control and intervention (CLA and CLA+E) groups.

1.6 Conceptual Framework

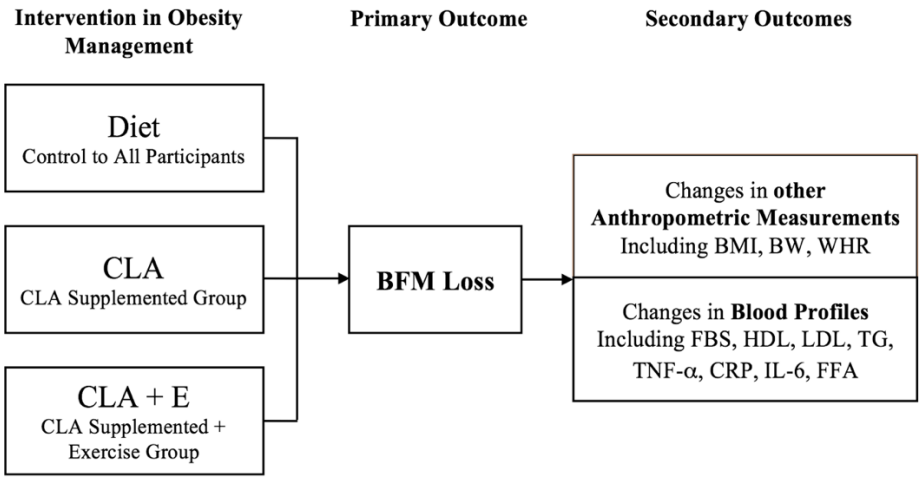

Figure 1.1. Conceptual Framework Based on the CONSORT Statement (Schulz, Altman, & Moher, 2010).

Comparison of the data in each group and the analyses of them (week 0, 6 and 12) will be done by within subject ANOVA, and after the whole data collection (end of week 12) data will be tested through MANOVA; a significance level of 0.05 will be used in all tests, and all tests are two-tailed. For all these analyses, SPSS (version19) software will be used.

9. Operational Aspects

All electronic data files will be stored on password protected computers which is accessible only to members of the research team. Archived electronic data files and any hard copies of data, consent forms, questionnaires or other papers containing data will be stored in locked filing cabinets in locked research rooms at each Clinic. Participants' name will just appear on the Consent Form, and all the other Hard Copies and even Samples would be labeled by their ID number, so at the end of the study it is applicable to inform them about the results.

References

1. Bhattacharya A, Banu J, Rahman M, Causey J, Fernandes G: Biological effects of conjugated linoleic acids in health and disease. J Nutr Biochem 2006, 17:789-810.

2. Wahle KW, Heys SD, Rotondo D: Conjugated linoleic acids: are they beneficial or detrimental to health?. Prog Lipid Res 2004, 43:553-587.

3. Cheng WL, Lii CK, Chen HW, Lin TH, Liu KL: Contribution of conjugated linoleic acid to the suppression of inflammatory responses through the regulation of the NF-kappaB pathway. J Agric Food Chem 2004, 52:71-78.

4. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr: Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest 2003, 112:1796-1808.

5. Xu H, Barnes GT, Yang Q, Tan G, Yang D, Chou CJ, Sole J, Nichols A, Ross JS, Tartaglia LA, Chen H: Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest 2003, 112:1821-1830.

6. Park Y, Albright KJ, Liu W, Storkson JM, Cook ME, Pariza MW. Effect of conjugated linoleic acid on body composition in mice. *Lipids*. 1997;32:853–8.

7. DeLany JP, Blohm F, Truett AA, Scimeca JA, West DB. Conjugated linoleic acid rapidly reduces body fat content in mice without affecting energy intake. *Am J Physiol*. 1999;276: R1172–9.

8. West DB, DeLany JP, Camet PM, Blohm F, Truett AA, Scimeca J. Effects of conjugated linoleic acid on body fat and energy metabolism in the mouse. *Am J Physiol*. 1998;275:R667–72

9. Azain MJ, Hausman DB, Sisk MB, Flatt WP, Jewell DE. Dietary conjugated linoleic acid reduces rat adipose tissue cell size rather than cell number. *J Nutr*. 2000;130:1548–54.
10. Yamasaki M, Mansho K, Mishima H, et al. Dietary effect of conjugated linoleic acid on lipid levels in white adipose tissue of Sprague-Dawley rats. *Biosci Biotechnol Biochem*. 1999;63:1104–6.
11. Dugan MER, Aalhus JL, Schaefer, AL, Kramer JKG. The effect of conjugated linoleic acid on fat to lean repartitioning and feed conversion in pigs. *Can J Anim Sci*. 1997;77:723–5.
12. Wiegand BR, Swan JE, Larsen ST, Parrish FC, Baas TJ.Conjugated linoleic acid improves feed efficiency, decreases backfat and improves pork quality attributes. *J Anim Sci*. 2000;78:45 (abst).
13. Mougios V, Matsakas A, Petridou A, et al. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. *J Nutr Biochem*. 2001;12:585–94.
14. Riserus U, Berglund L, Vessby B. Conjugated linoleic acid (CLA) reduced abdominal adipose tissue in obese middleaged men with signs of the metabolic syndrome: a randomized controlled trial. *Int J Obes*. 2001;25:1129–
15. Ostrowska E, Muralitharan M, Cross RF, Bauman DE, Dunshea FR. Dietary conjugated linoleic acids increase lean tissue and decrease fat deposition in growing pigs. *J Nutr*. 1999;129:2037–42.
16. Parra, Pilar, Andreu Palou, and Francisca Serra. "Moderate doses of conjugated linoleic acid reduce fat gain, maintain insulin sensitivity without impairing inflammatory adipose tissue status in mice fed a high-fat diet." *Nutr Metab (Lond)*7.5 (2010).
17. Whigham, Leah D., Abigail C. Watras, and Dale A. Schoeller. "Efficacy of conjugated linoleic acid for reducing fat mass: a meta-analysis in humans." *The American journal of clinical nutrition* 85.5 (2007): 1203-1211.
18. Terpstra, Antonius HM. "Effect of conjugated linoleic acid on body composition and plasma lipids in humans: an overview of the literature." *The American journal of clinical nutrition* 79.3 (2004): 352-361.
19. Kennedy, Arion, et al. "Antiobesity mechanisms of action of conjugated linoleic acid." *The Journal of nutritional biochemistry* 21.3 (2010): 171-179.
20. Lowery LM, Appicelli PA, Lemon PWR. Conjugated linoleic acid enhances muscle size and strength gains in novice bodybuilders. *Med Sci Sports Exerc*. 1998;30.5:S182
21. Thom E, Wadstein J, Gudmundsen O. Conjugated linoleic acid reduces body fat in healthy exercising humans. *J Int Med Res*. 2001;29:392–6.
22. Kreider R, Ferreira M, Greenwood M, Wilson M, Almanda A. Effects of conjugated linoleic acid supplementation during resistance training on body composition; bone density, strength, and selected hematological markers. *J Strength Conditioning Res*. 2002;16:325–34.
23. Ritzenthaler KL, McGuire MK, Falen R, et al. Estimation of conjugated linoleic acid intake by written dietary assessment methodologies

underestimates actual intake evaluated by food duplicate methodology. J Nutr 2001; 131(5):1548–1554.
24. Mougios V, Matsakas A, Petridou A, et al. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. J Nutr Biochem 2001; 12(10):585–594.
25. Petridou A, Mougios V, Sagredos A. Supplementation with CLA: Isomer incorporation into serum lipids and effect on body fat of women. Lipids 2003; 38(8):805–811.
26. Chen, Shu-Chiun, et al. "Effect of conjugated linoleic acid supplementation on weight loss and body fat composition in a Chinese population." *Nutrition* 28.5 (2012): 559-565.
27. Onakpoya, Igho J., et al. "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." *European journal of nutrition* 51.2 (2012): 127-134.
28. Dilzer, Allison, and Yeonhwa Park. "Implication of conjugated linoleic acid (CLA) in human health." *Critical reviews in food science and nutrition* 52.6 (2012): 488-513.
29. Blankson, Henrietta, et al. "Conjugated linoleic acid reduces body fat mass in overweight and obese humans." *The Journal of nutrition* 130.12 (2000): 2943-2948.