LIFESTYLES GROUP LTD.

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INTRODUCING.... R-LIPOIC ACID
The naturally occurring form of lipoic acid

Alpha-lipoic acid has been called the ideal antioxidant and is a key component in the antioxidant network. It has potent antioxidant actions in every cell of the body, protects membranes by boosting levels of other antioxidants (vitamin C, vitamin E, Coenzyme Q10 and glutathione) and reverses the cellular redox status (from a more oxidized to a more reduced state) which prevents inflammation, associated with all of the chronic degenerative diseases of aging.

Alpha-lipoic acid has been shown to be beneficial in a number of oxidative stress models such as ischemia-reperfusion injury, diabetes, cataract formation, HIV activation, neurodegeneration, and radiation injury.[1]

Does your lipoic acid supplement contain only the form found in nature?
Or does it also include a synthetic by-product that may interfere with the natural form's beneficial effects?

Alpha-lipoic acid occurs in three different forms

- **R-Lipoic Acid** (the **R (+)** enantiomer) is the pure form found in nature and the human body that is responsible for most of alpha-lipoic acid's beneficial effects.
- S-Lipoic acid (The S (-) enantiomer) is a by-product from chemical synthesis.
- Alpha-lipoic acid consists of 50/50 racemic mixture of the **R** and S enantiomers and is the normal commercially available form of lipoic acid.
- **R-Lipoic Acid** is the only naturally-occurring form of alpha-lipoic acid. Researchers at ASTA Medica claim that **R-Lipoic Acid** is 10 times stronger than the racemate alpha-lipoic acid for reducing inflammation.[2]
- The S-form can oppose the action of the **R**-form. In the aging rat heart, **R-Lipoic Acid** stimulated ATP production, whereas SLA inhibited it.[3]

The Benefits of R-Lipoic Acid

- **R-Lipoic Acid** significantly reduces inflammation, an underlying cause of the degenerative diseases of aging and is more potent by a factor of 10 over commercial ALA.[2]

- **R-Lipoic Acid** was more effective than the S form in a battery of metal chelation tests. One hypothesis of the cause of diabetic complications involves overloading by transition metals which could explain the stereospecific effect of the **R**-form.[4]

- **R-Lipoic Acid** is the only form of lipoic acid found in nature and therefore the only form recognized by the critical mitochondrial enzymes.[5]

- **R-Lipoic Acid** increases cellular and mitochondrial antioxidant activity and prevents mitochondrial decay. This effectively attenuates the reported increase in oxidative stress with aging.[6]

- **R-Lipoic Acid** improves memory, reverses cognitive dysfunction, and protects the brain from neurodegeneration associated with aging. [6] [7] [8]

- **R-Lipoic Acid** protects body fats against oxidative damage and reverses stress damage in the heart.[8]

- **R-Lipoic Acid** supplementation improves metabolic activity and lowers oxidative stress and damage evident in aging. [9]

- **R-Lipoic Acid** significantly increase insulin sensitivity, enhances glucose transport, increases metabolic rate and reduces the gain in body fat from aging.[10,11]

- **R-Lipoic Acid** has insulin-mimetic effects in glucose uptake in insulin resistant cells and may have therapeutic implications in restoring glucose availability in tissues such as the skeletal muscle.[12]

- **R-Lipoic Acid** significantly increases or maintains levels of other antioxidants including Coenzyme Q10, vitamin C, vitamin E and glutathione.[13,14,15]

- **R-Lipoic Acid** prevents depletion of the glutathione pool within the cytoplasm and mitochondria. Pre-treatment of PC12 cells with **RLA** leads to the preservation of mitochondrial complex I activity lost due to glutathione depletion.[14]

- The **R-(+)** enantiomer is much more effective than the S-(-) enantiomer at enhancing insulin-stimulated glucose transport and non-oxidative and oxidative glucose metabolism. [16]

- **R-Lipoic Acid**, through its positive effects on cellular energy metabolism, attenuates metabolic dysfunction associated with advanced glycation endproducts (AGEs). AGEs accumulate on long-lived proteins, including beta-amyloid plaques in Alzheimer's disease and contribute to neuronal dysfunction and cell death.[20]

- **R-Lipoic Acid**, a membrane permeable antioxidant, prevents the up-regulation of the AGE-induced gene expression responsible for regulating nitric oxide (NO) production. NO oxidizes and nitrates proteins which are markers of a chronic neuroinflammatory condition. This mechanism is relevant for Alzheimer's disease and for many chronic inflammatory conditions.[21]

About S Lipoic Acid

Until recently it was believed that S-Lipoic acid was physiologically inactive. Now there are a few reports from the patent literature suggesting this is not the case. There have been no human clinical trials to date that directly compare **RLA**, SLA and rac-ALA, although this will be forthcoming in the years ahead. In the meantime, we believe that enough evidence has been reported from in vitro and animal studies to warrant the use of pure **RLA** over the racemic ALA, when there is a choice.

- S-Lipoic acid produces different biological actions than R-Lipoic Acid that may be undesirable.[16-21, 25]
- S-Lipoic acid cannot bind with critical mitochondrial enzymes and inhibits ATP production.[19]
- S-Lipoic acid is less effective than R-Lipoic Acid as an antioxidant.[16]
- At high concentrations, S-Lipoic acid inhibits mitochondria metabolism.[22]
- S-Lipoic acid is metabolized in the outer cell membrane or cytoplasm. This may interfere with R-Lipoic Acid's ability to penetrate the inner mitochondrial membrane, thus limiting energy production.[22]

R-Lipoic Acid costs more per unit than alpha-lipoic acid, but it may be 10 times more effective than racemic alpha-lipoic acid at reducing inflammation; a primary cause of the diseases of aging.

References

1. Alpha-lipoic acid as a biological antioxidant. Packer L, Witt EH, et al. FreeRad Biol Med 1995;19:227-250.
2. Thioctic (lipoic) acid: a therapeutic metal-chelating antioxidant? Ou P, Tritschler HJ, Wolff SP. Biochem Pharmacol 1995; 50:123-126.
3. (R)-alpha-Lipoic acid-supplemented Old Rats Have Improved Mitochondrial Function, Decreased Oxidative Damage, and Increased Metabolic Rate. Hagen TM, Ingersoll RT, Lykkesfeldt J, Liu J, Wehr CM, Vinarsky V, Bartholomew JC, Ames AB. FASEB J 1999 13:411-418.
4. Influence of selegiline and lipoic acid on the life expectancy of immunosuppressed mice. Freisleben HJ, Neeb A, Lehr F, Ackermann H.Arzneimittelforschung 1997 Jun; 47(6): 776-80.
5. Pharmaceutical composition containing R-.alpha.-lipoic acid or S-.alpha.-lipoic acid as active ingredient. Ulrich H, Weischer CH, et al. US Patent 5,728,735, 1998.
6. Pre-treatment with R-lipoic acid alleviates the effects of GSH depletion in PC12 cells: implications for Parkinson's disease therapy. Bharat S, Cochran BC, et al. Neurotoxicology. 2002 Oct; 23 (4-5):479-86.
7. Oxidative stress in the aging rat heart is reversed by dietary supplementation with (R)-(alpha)-lipoic acid. Suh JH, Shigeno ET, et al. FASEB J 2001 Mar; 15(3): 700-6
8. Memory loss in old rats is associated with brain mitochondrial decay and RNA/DNA oxidation: partial reversal by feeding acetyl-L-carnitine and/or R-alpha -lipoic acid. Liu J, Head E, et al. Proc Natl Acad Sci U S A 2002 Feb 19; 99(4): 2356-61.
10. Oral administration of RAC-alpha-lipoic acid modulates insulin sensitivity in patients with type-2 diabetes mellitus: a placebo-controlled pilot trial. Jacob S, Ruus P, et al. Free Rad Biol Med 1999 Aug;27(3-4):309-14.
11. R-alpha-Lipoic Acid Action on Cell Redox Status, the Insulin Receptor, and Glucose Uptake in 3T3-L1 Adipocytes. Moines H, Trios O, et al. Arch Biochem Biophys 2002 Jan 15; 397(2): 384-91.
12. Oxidative stress in the aging rat heart is reversed by dietary supplementation with (R)-(alpha)-lipoic acid. Suh JH, Shigeno ET, et al. FASEB J 2001 Mar; 15(3): 700-6.
13. Cytokine-induced glucose uptake in skeletal muscle: redox regulation and the role of alpha-lipoic acid. Khanna S, Roy S, Packer L, Sen CK. Am J Physiol. 1999 May;276(5 Pt 2):R1327-33.
14. Oxidative stress in the aging rat heart is reversed by dietary supplementation with (R)-(alpha)-lipoic acid. Suh JH, Shigeno ET, et al. FASEB J, 2001 Mar; 15(3): 700-6.
15. Age-associated decline in ascorbic acid concentration, recycling, and biosynthesis in rat hepatocytes--reversal with (R)-alpha-lipoic acid supplementation. Lykkesfeldt J, Ames BN et al. FASEB J 1998 Sep; 12(12): 1183-9
16. Differential effects of lipoic acid stereoisomers on glucose metabolism in insulin-resistant skeletal muscle. Streeper RS, Henriksen EJ, et al. Tritschler HJ. Am J Physiol 1997 Jul; 273(1 Pt 1): E185-91.
17. Influence of selegiline and lipoic acid on the life expectancy of immunosuppressed mice Freisleben HJ, Neeb A, Lehr F, Ackermann H. Arzneimittelforschung 1997 Jun; 47(6): 776-80.
18. Cytosolic and mitochondrial systems for NADH- and NADPH-dependent reduction of alpha-lipoic acid Haramaki N, Han D, et al. Free Radic Biol Med 1997; 22(3): 535-42
19. Stereospecific effects of R-lipoic acid on buthionine sulfoximine-induced cataract formation in newborn rats. Maitra I, Serbinova E, et al. Biochem Biophys Res commun 1996; 221:422-429.
20. Stereospecific effects of lipoic acids on mammalian pyruvate dehydrogenase complex. Hong YS, Jacobia SJ, Packer L, Patel MS. Free Radic Biol Med. 1999 Mar;26(5-6):685-94.
21. Neuroprotection by the metabolic Antioxidant alpha Lipoic Acid. Packer, L; Tritschler, H; Wessel K, 1997 Free Rad Biol Med 22, Nos ½, 359-378.
22. Mitochondrial decay in the aging rat heart: evidence for improvement by dietary supplementation with acetyl-L-carnitine and/or lipoic acid. Hagen TM, Moreau R, Suh JH, Visioli F. Ann N Y Acad Sci. 2002 Apr;959:491-507.
23. Advanced glycation endproducts induce changes in glucose consumption, lactate production, and ATP levels in SH-SY5Y neuroblastoma cells by a redox-sensitive mechanism. de Arriba SG, Loske C,et al. Cereb Blood Flow Metab. 2003 Nov;23(11):1307-13.
24. Anti-inflammatory antioxidants attenuate the expression of inducible nitric oxide synthase mediated by advanced glycation endproducts in murine microglia. Wong A, Dukic-Stefanovic S, et al. Eur J Neurosci. 2001 Dec;14(12):1961-7.
25. Interaction of alpha-lipoic acid enantiomers and homologues with the enzyme components of the mammalian pyruvate dehydrogenase complex. Loffelhardt S, Bonaventura C, et al. Biochem Pharmacol. 1995 Aug 25;50(5):637-46.

WHAT THE EXPERTS ARE SAYING ABOUT R LIPOIC ACID

"R-and S- enantiomers of the physiological compound alpha-lipoic acid have been synthesized. The S-enantiomer is not a naturally occurring compound. This part of the racemate , which is present as about a 50% impurity, needs to be eliminated.
Zimmer, G, ATP Synthesis and ATPase activities in Heart Mitoplasts Under Influence of R- and S- Enantiomers of Lipoic Acid. Methods in Enzymology vol.251 p.332-340. 1995

"In the case of the purely optical isomers of alpha-lipoic acid (R- and S- form, i.e. R-alpha-lipoic acid and S-alpha-lipoic acid), unlike the racemate, the R-enantiomer mainly has an anti-inflammatory activity..., being stronger by a factor of 10 than that of the racemate. The enantiomers therefore constitute very much more specific and stronger acting active substances than the racemate."
Ulrich H, Weischer CH, et al. Pharmaceutical composition containing R-alpha-lipoic acid or S-alpha-lipoic acid as active ingredient. US Patent 5,728,735,1998.

"... R-lipoic acid, a mitochondrial coenzyme, but not S-Lipoic acid, an unnatural isomer which is reduced in the cytoplasm, reverses the sensitivity of hepatocytes from old rats to an oxidative mutagen."
Progress Report: Mutagenesis and Carcinogenesis Core National Institute of Environmental Health Sciences Center. Univ of Cal at Berkeley. Allan H. Smith, Core Director, Bruce Ames, et al. 2001.

"(R)-form of lipoic...is the naturally occurring enantiomer in mammalian cells. Only the (R)-form is used by mitochondrial - keto acid dehydrogenases and specifically reduced to dihydrolipoic acid, a powerful antioxidant... (R)-lipoic acid supplementation may be more potent than either the racemic mixture (the form sold commercially as - lipoic acid) or (S)- enantiomer... (R)-lipoic acid increases ATP synthesis and aortic blood flow during reoxygenation after hypoxia... The (S)-enantiomer had no effect on ATP synthesis and improved blood flow at only 10-fold the effective dose of (R)-lipoic acid.... (R)-lipoic acid supplementation may be a safe and effective means to improve general metabolic activity and increase antioxidant status, affording increased protection against external oxidative and xenobiotic insults with age."
Tory Hagen, Russell Ingersoll, et al. (R)--Lipoic acid-supplemented old rats have improved mitochondrial function, decreased oxidative damage, and increased metabolic rate. FASEB 13:411-418, 1999.

"...R-(+) alpha lipoic acid is suitable for the treatment of diabetes and insulin resistance... the S-(-) alpha lipoic acid practically is not usable for this... Our own investigations studies have shown ... the key enzyme, pyruvate dehydrogenase, surprisingly was inhibited by the S-(-) alpha lipoic acid... preferably R-(+)-.alpha.-lipoic acid proves to be suitable for the treatment of diabetes mellitus types I and II and its sequelae and late complications and for the treatment of sub clinically and clinically manifest insulin resistance and its sequelae."
Use of R-(+)-alpha.-lipoic acid, R-(-)-dihydrolipoic acid and metabolites in the form of the free acid or as salts or esters or amides for the preparation of drugs for the treatment of diabetes mellitus as well as its sequelae. United States Patent 6,117, 889. September 2000. Klaus Wessel, Harald Borde, et al.

"The racemate of lipoic acid at high dosage (350 mg/kg body weight) reduced the life span significantly. The S (-)-enantiomer of lipoic acid (75 mg/kg body weight) increased the 50% survival rate, whereas the physiologic R (+)-enantiomer (9 mg/kg body weight) expanded the total life span of its group."
Freisleben HJ, Neeb A, et al. Influence of selegiline and lipoic acid on the life expectancy of immunosuppressed mice. Arzneimittelforschung. Jun; 47 (6):776-80. 1997.

"Cells from old animals were incubated with either (R) - or (S)-lipoic acid... The physiologically relevant (R)-form, a coenzyme in mitochondria, as opposed to the (S)-form significantly protected hepatocytes against t-BuOOH toxicity. Dietary supplementation of (R)-lipoic acid [0.5% (wt/wt)] for 2 weeks also completely reversed the age-related decline in hepatocellular GSH levels and the increased vulnerability to t-BuOOH as well... cells from old animals are more susceptible to oxidant insult and (R)-lipoic acid, after reduction to an antioxidant in the mitochondria, effectively reverses this age-related increase in oxidant vulnerability."
Bruce Ames, et al. Delaying Aging with Mitochondrial Micronutrients and Antioxidants. Miami Nature Biotechnology Short Reports. The Scientific World, 2001.

"...(R)-lipoic acid may be a more potent supplement than the racemic mixture (which contains both (R) and (S) forms) sold commercially as alpha-lipoic acid... (R)-lipoic acid increased glucose uptake and the number of glucose transporters in muscle tissue much more effectively than (S)-lipoic acid and that the (R)-form more effectively chelated copper and prevented copper-induced lipid peroxidation... (R)-lipoic acid increased ATP synthesis and aortic blood flow during reoxygenation after hypoxia in a

working heart model, but (S)-lipoic acid had no effect on ATP synthesis and only improved blood flow at ten times the effective concentration of (R)-lipoic acid.''
The Durk Pearson & Sandy Shaw® Life Extension News. Volume II, Issue #3, April 1999.

"R-alpha-Lipoic acid is found naturally occurring as a prosthetic group in alpha-keto acid dehydrogenase complexes of the mitochondria, and as such plays a fundamental role in metabolism…. it has the ability to alter the redox status of cells and interact with thiols and other antioxidants. …that this compound has important therapeutic potential in conditions where oxidative stress is involved."
Bustamante J, Lodge JK, et al. Alpha-lipoic acid in liver metabolism and disease. Free Radic Biol Med. Apr 24 (6): 1023-39, 1998.

"…R-(+)-ALA increased insulin-mediated 2-DG-uptake by 64% (P < 0.05), whereas S-(-)-ALA had no significant effect. Although chronic R-(+)-ALA treatment significantly reduced plasma insulin (17%) and free fatty acids (FFA; 35%) relative to vehicle-treated obese animals, S-(-)-ALA treatment further increased insulin (15%) and had no effect on FFA".
Streeper RS, Henriksen EJ, et al. Differential effects of lipoic acid stereoisomers on glucose metabolism in insulin-resistant skeletal muscle. Am J Physiol 1997 Jul: 273(1)1,1997.

"An intact organ, the isolated perfused rat heart, reduced R-Lipoate six to eight times more rapidly than S-lipoate, consistent with high mitochondrial dihydrolipoamide dehydrogenase activity and results with isolated cardiac mitochondria."
Haramaki N, Han D, et al. Cytosolic and mitochondrial systems for NADH- and NADPH-dependent reduction of alpha-lipoic acid. Free Radic Biol Med. 7;22(3):535-42, 1997.

"Addition of 1 mM racemic lipoic acid reduces these damaging effects to the lens by one-half, while S-lipoic acid potentiated LDH leakage. Therefore, stereospecific protection against this opacity is consistent with specific reduction of R-lipoic acid in mitochondria of the vulnerable cells at the lens equator…"
Kilic F, Handelman GJ, et al. Modeling cortical cataractogenesis 17: in vitro effect of a-lipoic acid on glucose-induced lens membrane damage, a model of diabetic cataractogenesis. Biochem Mol Biol Int. 37(2): 361-70,1995.

"Overall, the results indicate a greater effect of R-thioctic compared to the S isomer. This finding is consistent with the results of previous studies on the ability of the isomers of thioctic acid to alter glucose uptake in both in vitro and ex vivo paradigms. Thus, in vivo administration of R-thioctic acid stimulates the subsequent in vitro transport of glucose into skeletal muscle to a greater extent than the S isomer. Similarly, in vitro R-thioctic acid stimulates glucose transport into isolated muscle cells to a greater extent than the S isomer. The R isomer has an additive effect on insulin stimulated glucose transport, but S thioctic acid inhibits insulin's action. In addition, R-thioctic acid promoted the translocation of GLUT-1 and GLUT-4 to the plasma membrane, where the S isomer does not." Peter Jenner, T.A. Seaton, and C.D. Marsden. Chapter 16 in Lipoic Acid in Health and Disease; Altered C-Deoxyglucose Incorporation in Rat Brain Follwing Treatment with Alpha-Lipoic Acid; ed. Fuchs J, Packer L, Zimmer G Marcel Dekker, Inc New York, Basel, Hong Kong (1997) pp259-268

"At a concentration of 0.05-0.1 mumol of the R-enantiomer, aortic flow rises precipitously during reoxygenation, reaching over 70% of normoxic values compared to 50% of the controls. By contrast, with the S-enantiomer a value of about 60% is attained at 1 mumol, only. Accordingly, ATPase activity in mitochondria isolated from rat hearts previously treated with 0.05-0.1 mumol of the R- or S-enantiomer was significantly decreased or increased respectively. Consequently, whereas mitochondrial ATP synthesis was increased when the R-enantiomer was previously added to the working heart at 0.05-0.1 mumol concentration, with the S-enantiomer ATP synthesis remained within the control range. Mitochondrial membrane fluidity, measured with diphenylhexatriene, revealed a trend towards increase with the R- and decrease with the S-enantiomer."
Zimmer G, Beikler TK, Schneider M, Ibel J, Tritschler H, Ulrich H. Dose/response curves of lipoic acid R-and S-forms in the working rat heart during reoxygenation: superiority of the R-enantiomer in enhancement of aortic flow. J Mol Cell Cardiol. 1995 Sep;27(9):1895-903.

Conjugated linoleic acid, CLA

Chemical background, occurrence in foods

Conjugated linoleic acid (CLA), a derivative of ω-6 linoleic acid, refers to a group of polyunsaturated fatty acids (PUFA) that exist as geometric and positional isomers of conjugated dienoic octadecadienoate (18:2). At least 9 different isomers have been identified in foods. The predominant isomer in foods is the cis9trans11-CLA isomer (also called "rumenic acid"), followed by 7,9-CLA (cis/trans), 11,13-CLA (cis/trans), 8,10-CLA (cis/trans), and trans10cis12-CLA isomer.

CLA is found in foods such as beef (3.7 mg/g fat), lamb (5.2 mg/g fat), milk (4.49 mg/ g fat) and other dairy products. The average CLA intake in the U.S. is in the range of 151-212 mg/day. CLA is commercially produced through processing sunflower or safflower. A mixture of CLA isomers found in nutritional supplements is composed primarily of the cis9trans11-CLA and the trans10cis12-CLA isomers. Biological activities of these isomers may be different.

Major biological activities and mechanisms of action

- **Effects on body composition**

Numerous animal studies have demonstrated that CLA reduces body fat to varying degrees in mice, chicks, rats, and pigs. There is evidence to suggest that CLA stimulates energy expenditure, increases lipolysis, and inhibits the deposition of fat in adipocytes. In animal experiments, CLA supplementation delayed onset of type 2 diabetes, reduced plasma leptin. In type 2 diabetic patients CLA reduced fasting glucose level. CLA may improve fasting blood glucose via improved insulin sensitivity, body composition and/or leptin levels (Belury et al., 2003).

It is believed that CLA inhibits lipoprotein lipase and stimulates lipolysis. Mechanism of CLA action is not clear; some authors suggest that CLA may act through steroid hormone receptors PPARs (peroxisome proliferator-activated receptors-γ).

CLA is metabolized into desaturated and chain elongated products. It remains unclear whether these conjugated metabolites may be involved in the effects of CLA on fatty acid metabolism (Bretillon et al., 2003).

Biological activities of CLA are isomer specific. Available experimental data suggest that the trans10-cis12 isomer is the active isomer associated with the antiobesity and insulin-sensitizing properties of CLA, whereas cis9,t11-CLA has weaker inverse correlation with body weight and leptin level than the total CLA (Belury et al., 2003).

- **Anticarcinogenic**

Preliminary data suggest that CLA may contribute to preventing certain human cancers (Hunter, 2000). Cis9trans11-CLA isomer is believed to be responsible for antitumorogenic effects of CLA observed in model studies. This action may be related to antioxidant properties of CLA.

- **Antiatherogenic**

Animal studies indicate that supplementation with CLA may favorably affect blood lipid profile and restrain atherosclerosis development (Hunter, 2000).

Applications

- Weight management

Results of most human studies indicate that CLA supplementation may decrease body weight and adipose tissue mass, particularly abdominal fat, while increasing lean body mass (Riserus et al., 2003; Smedman and Vessby, 2001; Thom et al., 2001; Blankson et al., 2000).

In a randomized, double-blind study 60 overweight or obese volunteers received placebo (9 g olive oil), 1.7, 3.4, 5.1 or 6.8 g conjugated linoleic acid per day for 12 weeks. A significantly higher reduction in body fat mass was found in the CLA groups compared with the placebo group. The reduction of body fat within the groups was significant for the 3.4 and 6.8 g CLA groups (with no significant differences between them) (Blakson et al., 2000).

In a recent double-blind, placebo-controlled randomized clinical study overweight subjects (26 men and 28 women) received either 1.8 g/day CLA or 3.6 g/day CLA or placebo per for 13 weeks. Subjects were first submitted to a very-low-calorie diet (2.1 MJ/d) for 3 weeks after which they started with the 13-week intervention period. The regain of fat-free mass was favorably, dose-independently affected by CLA supplementation. Increased resting metabolic rate was observed (Kamphuis et al., 2003).

The results of the first long-term study of CLA supplementation to 180 overweight subjects were presented in May 2003 at the Meeting of American Oil Chemists' Society. After 12 months of supplementation with 3.4 g of CLA daily, body fat mass was reduced by 9% and lean body mass increased by 2% (Gaullier et al., 2003).

Some studies, however, failed to demonstrate positive effect of CLA on body composition (Mougios et al., 2000; Zambell et al., 2000). It is likely that dose, duration (short- vs. long-term) and the isomeric composition of CLA will each impact the ability of CLA to affect obesity and various metabolic parameters in humans. The distribution of adipose tissue (e.g., intra-abdominal vs. subcutaneous fat) is also a factor. In addition, it is not clear how age- and sex-specific effects of various isomers of CLA influence adipose tissue accumulation. Further research is needed to clarify these issues.