Health Effects of CLA

- Anti-carcinogenic
- Anti-atherogenic
- Anti-diabetogenic
- Decreases body fat
- Increases lean body mass
- Improves immune response
<table>
<thead>
<tr>
<th>Author</th>
<th>Sps</th>
<th>Fat</th>
<th>LBM</th>
<th>Risks</th>
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<tbody>
<tr>
<td>Pariza, 97</td>
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<tr>
<td>Delany, 99</td>
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<td>NE</td>
<td>Liver, Spleen, Insulin, Leptin</td>
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<td>Pigs</td>
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<td>NE</td>
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<tr>
<td>Ostrowaska, 99</td>
<td>Pigs (A)</td>
<td>↓</td>
<td>↑</td>
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<td>Stangl, 00</td>
<td>Rats</td>
<td>↓</td>
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Study Design

- Diet With Placebo (N=17)
- Diet With CLA (N=10)
- Diet With Placebo (N=7)

STUDY DAYS

0 15 30 45 60 75 90

BLOOD DRAWS

INFLUENZA VACCINATION
Effect of CLA on Resting Energy Expenditure

kcal/day, adjusted for FFM

Placebo  CLA

Study Week

0 2 4 6 8
Effect of CLA on Fat Oxidation at Rest

Study Week

mg/min

Placebo  CLA

0  2  4  6  8

Effect of CLA on Fat Oxidation at Rest
CLA & Rate of Glycerol Appearance

- µmol/min x kg

Week 0 vs Week 4:
- Resting: Lower values in Week 4 compared to Week 0.
- Walking: Higher values in Week 4 compared to Week 0.
CLA & Fatty Acid Re-esterification

![Graph showing re-esterification rates for Resting and Walking conditions across weeks 0 and 4. The graph indicates a decrease in re-esterification rates from week 0 to week 4 for both conditions.]
Effect of CLA on Weight and Body Composition

<table>
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<tr>
<th></th>
<th>Weight</th>
<th>FFM</th>
<th>Fat Mass</th>
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<tr>
<td></td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Change</td>
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<tr>
<td>kg</td>
<td>-1</td>
<td>0</td>
<td>-1</td>
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Diagram showing the change in weight, FFM (Fat Free Mass), and fat mass with CLA vs. placebo (P). The diagram indicates a decrease in weight and fat mass with CLA compared to placebo.
Summary of Results

After 4-8 wks of supplementation, no effect of CLA on:

- Energy expenditure
- Respiratory quotient, fat oxidation
- Lipolysis
- FFA re-esterification
- Body weight, body composition
CLA Has No Effect on Body Fat Change in Obese Humans During Weight Reduction

Subjects:
- 80 obese adults
- CLA (2.7 g/d) or placebo for 6 months
- All decreased caloric intake and increased exercise
- Body fat decreased by 1 kg in both groups

CLA Reduces Body Fat in Humans

- **Subjects:**
  - Mean age = 45 years
  - 53 healthy adults

- CLA (4.2 g/d) or placebo for 3 months

- % body fat decreased by -1.2% (p<0.0001)
  (determined by BIA & skin fold thickness)

CLA Affects Body Composition of Overweight and Obese Subjects

Adapted from Blankson et al. J. Nutr 2000;130:2943-8.
Summary of Human Studies

- In contrast to the results from animal models, supplementation with a mixture of CLA isomers failed to reduce body fat, except in the Norwegian study.
- In most studies food intake and activity levels were not controlled.
- Generally safe but some undesirable effects found in several studies.
Contrasting Results:
CLA and Body Composition

- Sensitivity and error in body composition measures, prediction errors 1.5-2 Kg fat
- Amount and type of food & activity level
- CLA dose and isomer composition
- Duration of supplementation period
- Type subjects, age, BMI (obese vs normal)
- Other confounding variables
Discrepancies Between Animal and Human Studies

- CLA dose per Kg body weight
- Species differences
- CLA isomer composition
- Growing animals vs adult humans
- Methods to determine body composition and their prediction errors
- Composition, amount and storage of the diets
- Other confounding variables
CLA Alteration of Immune Response in Animals

- Splenocyte or lymphocyte proliferation (mitogen) ↑ or no effect
- CD4+/CD8+ ↑ or did not change
- IL-2 ↑ or did not change
- DTH ↑ or did not change
- Listeria resistance, NK activity & lymphocyte cytotoxicity no effect
- IL-6, TNFα ↓
- IgA, IgG, IgM ↑
- IgE ↓

Conclusion: Modest and variable effects only
Summary of WHNRC Study

- 8-Fold increase in PBMC CLA concentration; no significant changes in other fatty acids.
- No change in lymphocyte proliferation & phenotypes, DTH, antibody production, secreted PGE$_2$, LTB$_4$, IL-1$\beta$, TNF$\alpha$, or IL-2.
- No change in intracellular concentration of IL-2, IFN$\gamma$, TNF$\alpha$, and % of cells producing them.
- No change in platelet activation, serum lipids.
## Effect of Dietary CLA on Serum Influenza Antibody Titers

<table>
<thead>
<tr>
<th>Viral strain</th>
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<th>CLA</th>
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<tr>
<td>B/Habrin</td>
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<tr>
<td></td>
<td>92</td>
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</table>
CLA Stimulates Antigen Specific Antibody

Unilever study, supplemented CLA 1.7 g/d for 84 d to healthy men (30-70 yr, 25/group); two different mixtures of CLA, containing the c9,t11 and t10,c12 isomers in a ratios of 50:50 or 80:20, were used

DTH and other indices did not change

Serum antibody against Hep B and PBMC proliferation not different, however twice the number of subjects in 50:50 group attained antibody titers > 10 IU/L

Authors suggest that t10, c12 isomer of CLA enhanced humoral response

Mohede et al 2001, AOCS Annual Meeting Absts
Summary Human Studies Re Effects of CLA on Immune Fx

- Most indices of immune fx (DTH, number circulating WBC & their sub-sets, lymphocyte proliferation and phenotypes, secretion of cytokines & eicosanoids, etc) not changed

- Serum antibody titer against influenza not altered but increased against Hep B?
Safety Issues Regarding CLA

- Animals: increased liver and spleen weights, decreased leptin & increased insulin
- Humans: Benefits are questionable
- Some adverse effects noted in human stds WHNRC std elevated insulin decreased leptin
- Sweden std decreased glucose disposal, insulin sensitivity & serum HDL
- Norwegian std decreased HDL
- Other side effects in individual subjects
Safety Issues Continued

- Individuals taking CLA on their own:
  - Subj 1 taking adderall for ADHD, developed nausea, insomnia, rapid heart beat, hungry even after a full meal
  - Subj 2 MS patient, developed optic neuritis and loss of balance
- Symptoms disappeared in both within a week of discontinuation
Areas for Future Research

- Safety vs benefits; relevance to improve human health
- Isomer specific effects on body composition, immune fx, lipid and CHO metabolism, minimum amount needed
- What is the best model to study health effects of CLA, Primates vs humans, obese, dislipidemic, immune compromised, other disease conditions, normal
- Long-term studies with controlled food intake and activity level at more than one labs; the effects should be greater than the prediction errors.
- Mechanisms by which CLA isomers alter physiologic fx