Setting the Case Study Framework – An Introduction to PHOs

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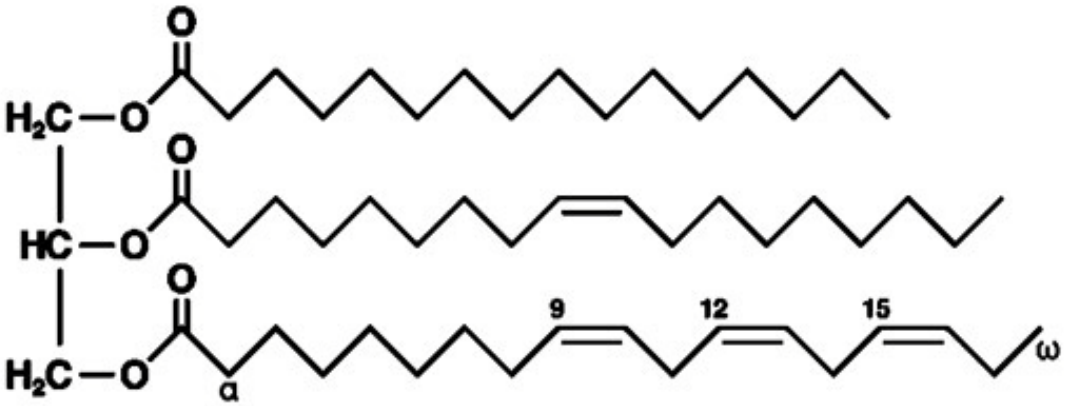
Dr. RONIS HAS
NO CONFLICTS OF INTEREST

Chemical Structure of Fats and Oils

Triglyceride Molecule



Saturated Fatty Acid

Monounsaturated Fatty Acid

Polyunsaturated Fatty Acid

Glycerol

Fatty Acid

Physical Properties of Fats

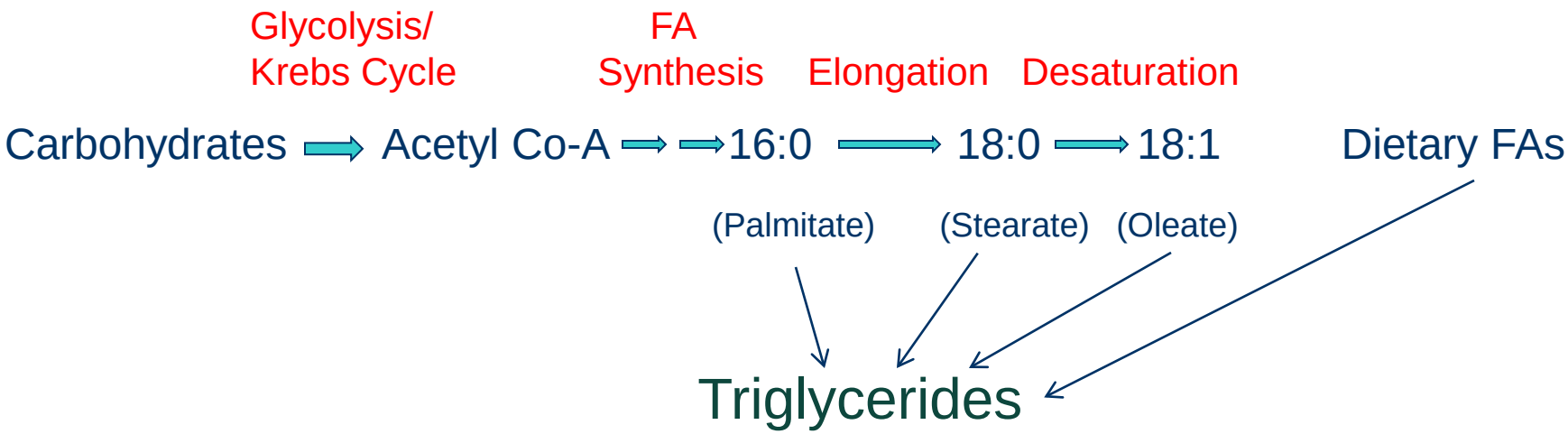
- Melting point (solid vs. liquid at room temperature) determined by:

  a) Carbon Chain length

  b) Saturation

  c) Unsaturated bond geometry:
  cis vs. trans

Endogenous Fat Synthesis in Animals



Animal Fats: Lard (pork fat); beef tallow; dairy products are rich in 16:0/18:0 are solid at room temperature.

Vegetable Oils and Fish Oil

- Coconut and palm oil: Medium chain saturated FA, 16:0

- Vegetable Oils:

  Olive Oil: Mainly 18:1 MUFA, with 18:2 PUFA

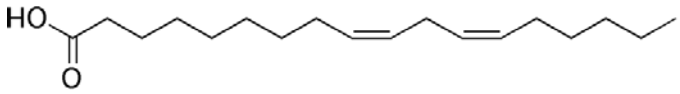
  Soy Oil: Mainly 18:2, some 18:3 PUFA

  Canola Oil: 18:1, 18:2, some 18:3 PUFA

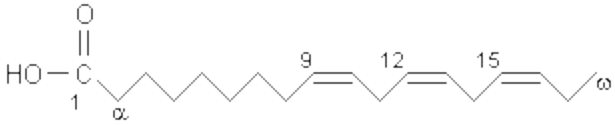
  Corn/Sunflower/Safflower: Mainly 18:2

- Fish Oils: EPA (20:5n-3) and DHA (22:6n-3) PUFA

Essential Fatty Acids



Linoleic Acid (18:2n6)



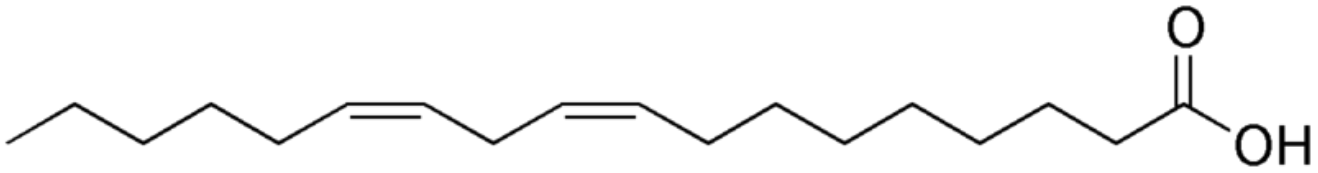
α–Linolenic Acid (18:3n3)

Arachidonic Acid (20:4n6)

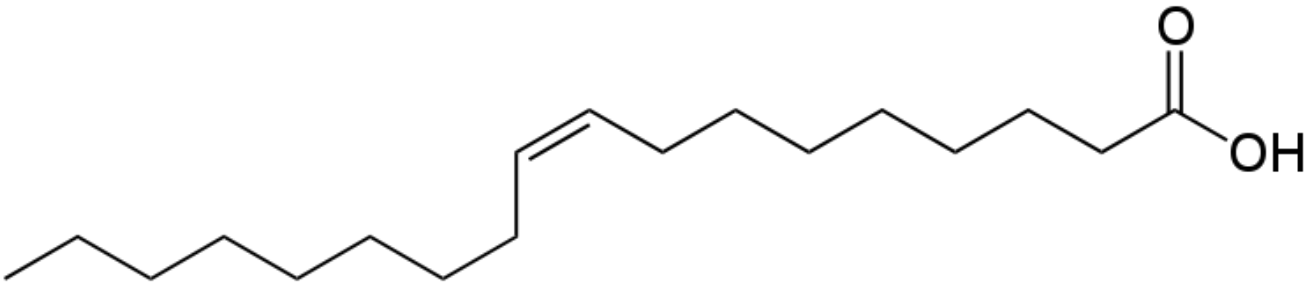
Eicosapentaenoic Acid (20:5n3)

Prostaglandins, Thromboxanes, Leukotrienes, Resolvins HETES, HODES etc.

Hydrogenation of PUFA



18:2

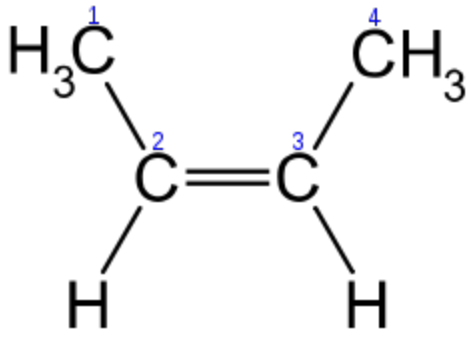


18:1

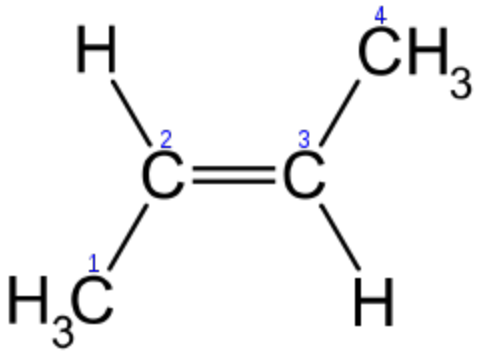
18:0

Heat
+
H_2
+
Catalyst

Cis vs. Trans Carbon Double Bonds

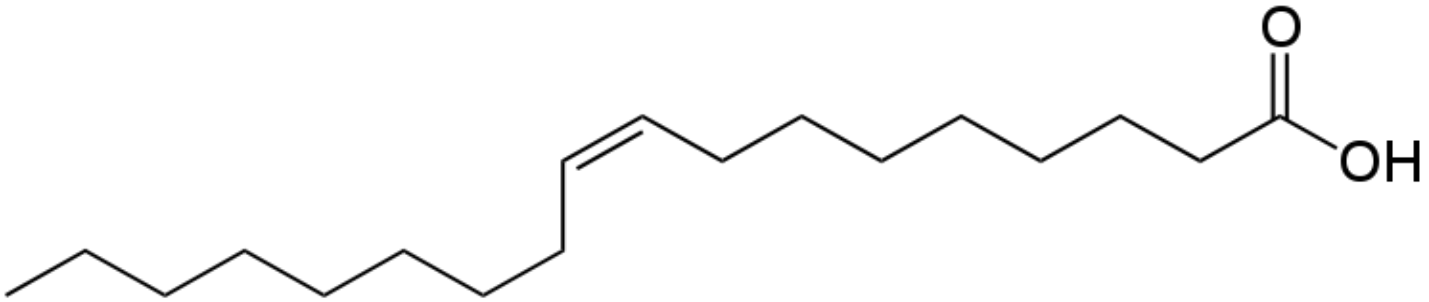


cis-but-2-ene

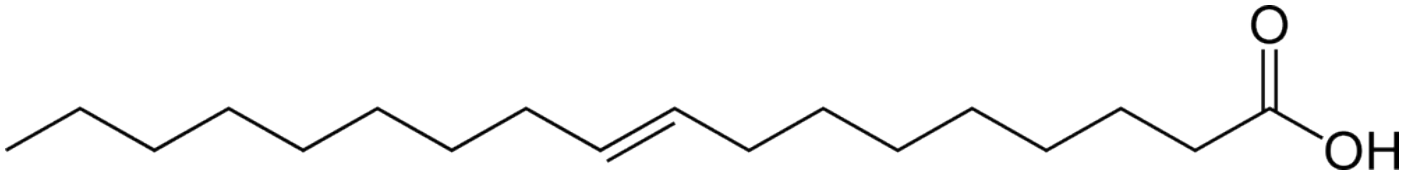


trans-but-2-ene

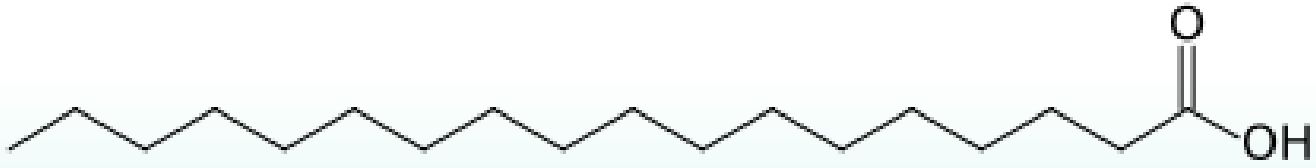
Trans Fat Formed During Manufacture of PHOs



Oleic Acid (9 cis-18:1)



Elaidic Acid (9 trans-18:1)



Stearic Acid (18:0)

PHO Uses in the Food Industry

- Intermediate melting point of trans fats (13-44^{o}C) results in PHO products immediately spreadable eg. margarines.
- Increased shelf life due to greater stability than PUFA to oxidation (rancidity).
- Superior baking properties.
- “Mouth feel”. Melts in mouth with no waxy after taste.

8 billion lb of soybean oil (50% production) hydrogenated in 2006.

Trans Fat Isomers in PHOs

- 16:1 t isomers: t-16:1n9, t-16:1n7
- 18:1 (elaidic acid + large range of isomers)
- 18:2 t isomers: 5 t isomers at 9, 12 or 15.
- Smaller amounts of 18:3 t isomers derived from longer chain PUFA.

Trans fat content up to 45% in manufactured PHOs

Trans-FA Composition of Foods (% Total Fat)

FA	Soybean Oil	Hydrogenated Oil	Baked Goods	Margarines	Shortening
Linoleic	53	17	17	35	27
Linolenic	8	1	1	5	2
18:1 cis	1	9	9	5	8
18:1 trans	0	24	25	16	13
18:2 trans	0	6	2	1	2

Modified from Kummerow FA, Atherosclerosis 205: 458-465, 2009.

Consumption of PHO-Trans Fats

Overall: 5-10 g/d (2-4% energy in a 2000 kcal/diet)

By Country:

North America: 3 - 10 g/d
Greece, Italy, Portugal, Spain: 1.2 - 2.1 g/d
UK, France, Germany, Sweden: 2.4 - 3.0 g/d
Iceland: 6.7 g/d
Asian countries: 0.1 - 0.6 g/d
Australia: 3 - 8 g/d

Teegala et al. J. AOAC Int. 92: 1250-1257, 2009

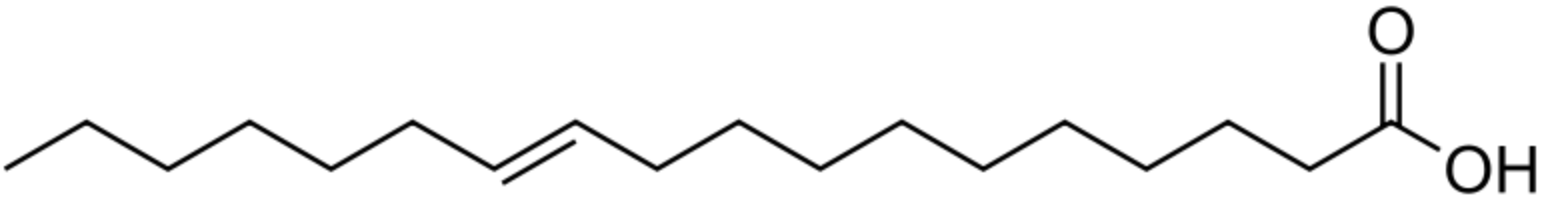
“Natural” Ruminant trans Fatty Acids

Linoleic Acid
Linolenic Acid

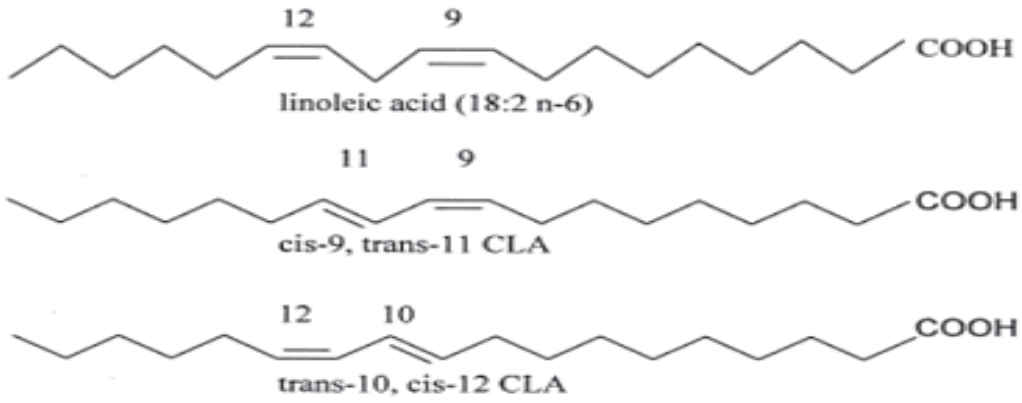
Anaerobic Bacteria

Vaccenic Acid, Conjugated Linoleic Acid (CLA)
Total rTFAs: ~5% of diary product fat, 4% beef fat
CLA 4.5 mg/g dairy product fat, 4.3 mg/g beef
Average rTFA intake 1 - 1.7 g/d
(Gebauer et al. Adv. Nutr. 2: 332-354, 2011)

rTFA Chemistry



Vacennic Acid (trans-11,18:1)



Rumenic Acid
90% CLA intake

CLA Capsules (supplement) are usually 50:50 9,11 and 10,12 CLA

Potential Toxic Effects of PHOs

Cardiovascular toxicity:

Lipid Dysregulation

- Increased LDL/HDL Ratio
- Changes in lipoprotein particle size
- Increased plasma triglycerides
- Inhibition of cycloxygenase, prostaglandins

- Evidence for increased inflammation: IL6, TNFα
- Increased cellular adhesion

Increased abdominal obesity, insulin resistance, metabolic syndrome

Increased cancer risk

Infertility

Alzheimer's Disease

Challenges to Toxicological Assessment of PHOs and Other Food Ingredients

Epidemiological/Observational Studies of Diet Effects

Complexity of diet composition: what do we measure, when and how?

Food frequency questionaires
Chemical composition of foods, fluids
Extrapolation of indicators eg. LDL/HDL

Potential confounders:

a) Other diet components
b) Weight, body composition, age, sex
c) Healthy worker effects
d) SES, Lifestyle, Smoking, Drinking
e) Independent risk factors eg. blood pressure
f) Accuracy of intake data

Challenges to Toxicological Assessment of PHOs and Other Food Ingredients

Clinical Trials on Health Effects of Dietary Components

How many meet the gold standard of placebo controlled, double blind?

Statistical limitations: small numbers of subjects

Short duration studies with surrogate endpoints

With macronutrients what is the appropriate control diet?

Dietary control: Did subjects eat what they were supposed to?

Is there enough data to determine dose-response slope and shape?

Is there a threshold for health effects?

Challenges to Toxicological Assessment of PHOs and Other Food Ingredients

Studies on Food Ingredients in Animal Models and Cell Culture

Advantages: Cheap, easy to generate mechanistic data.

BUT

Can they be extrapolated to people???

Species differences in lipid metabolism and development of diabetes

Do mechanisms identified in rodent models or in culture using individual dietary components apply to humans eating diverse food sources and diets?

Is the reductionist approach even possible in relation to the toxicological assessment of food ingredients?

Manufactured tFAs vs. Ruminant tFAs

Man-made bad, natural good?

Suggested health beneficial effects of ruminant tFAs:

Improved body composition
Cancer prevention

Are there differences in the biological properties and molecular mechanisms underlying effects of different tFAs – in PHOs or ruminant tFAs especially CLA?

Are the reported differences only related to dose?

SOT FDA Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety

Health Effects of PHOs and Trans Fatty Acids: Data from Clinical Trials – Dr. Martijn Katan, VU University, Amsterdam, The Netherlands

Epidemiological Studies on Health Effects of PHO: Strengths and Limitations of the Available Human Data – Dr. Ingeborg Brouwer, VU University, Amsterdam, The Netherlands

Dose-Response Assessment Approaches to the Analysis of Non-cancer Health Effects: Current Practices, Advice from the National Academies, and 2014 WHO/IPCS Guidance – Dr. Weihsueh Chiu, EPA ORD, Washington, DC

Mode of Action and Dose-Response Evaluation of the Effect of Partially Hydrogenated Oils on LDL-Cholesterol- Dr. Michael Dourson, TERA, Cincinnati, OH