FACULTY OF VETERINARY MEDICINE

ECVCN RESIDENCY CLASS, TURIN 2019

Polyunsaturated fatty acids: n-3 and n-6 in nutrition and metabolism

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AIM OF THE REVIEW

- Address specific structure and metabolic pathways of n3 and n6 LCPUFA
- Comparative approach to n3 and n6 LCPUFA synthesis in living organisms
- Role in metabolism
- Role in nutrition - food chain abundance
- Use as nutraceutical?

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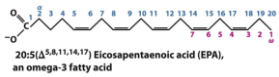
FATTY ACIDS

- Carboxylic acids with an aliphatic chain
- Chain-length
- Number of double bonds
- Nomenclature
- Fatty acid properties directly connected to the structure



20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

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STARTING POINT – ESSENTIAL FATTY ACIDS

Are they essential for all?

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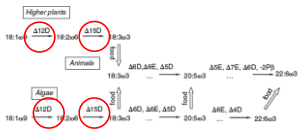
ARE ALA AND LA ESSENTIAL FOR ALL?

- Vertebrates (fish, birds, and mammals) -> cannot (lack of the genes Δ12 and Δ15 FAD)
- Bacteria, protozoa, higher plants and algae -> can
- Increasing number of studies have shown active LA synthesis in lower classes of animals: insects, nematodes and pulmonates (Malcicka, 2018.)



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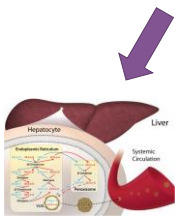
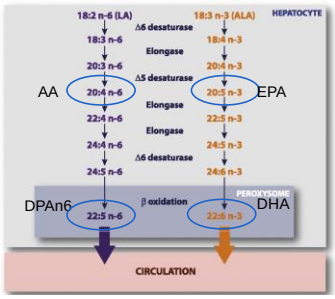
n-6 and n-3 pathway





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Layé et al, 2018.

DESATURASES ACTIVITY ACROSS ANIMAL KINGDOM

- The rate-limiting enzyme -> Δ-6-desaturase
- The biosynthesis of EPA and, particularly, DHA from ALA is very low in humans, cats and dogs
  - In men, conversion of ALA to EPA -> between 0.3 and 8%, and conversion to DHA <1%
  - in women up to 21% conversion to EPA and up to 9% conversion to DHA (Kidd, 2007; Plourde and Cunnane, 2007)
- Conversion rates in dogs, cats and horses are comparable to those of humans (Rivers, 1975; Dunbar and Bauer, 2002, Hansen et al., 2002; Heinemann et al 2005)

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DESATURASES ARE INFLUENCED BY:

- sex
- life stage
- dietary adaptations
- enzyme competition between substrates
- availability of several trace elements including zinc and iron
- gene FADS polymorphisms which control gene expression and enzyme activity
- epigenetic modification of *Fads* and *Elovl* genes, which will affect their expression

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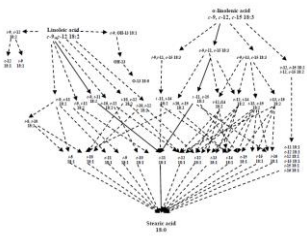
Childs et al 2008, Calder, 2016

RUMINANTS

- Microbial biohydrogenation (*Butyrivibrio fibrisolvens)*
- Substrates: vaccenic fatty acid and ~ 20 CLA isomers (rumenic acid – most abundant)



Vahmani et al 2013

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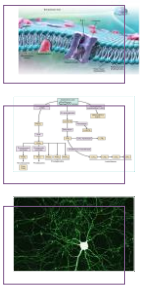
Role of n-6 and n-3 in metabolism

- Part of phospholipids which are the “building blocks” of cell membranes
  - (DHA-containing phospholipids are abundant in retina, testes, brain, heart, and skeletal muscle)
- Precursors of lipid inflammatory biomediators
- Regulators of transcription
- Modulators of functions in membrane protein
- Part of neutral lipids -> serve as storage materials in cells



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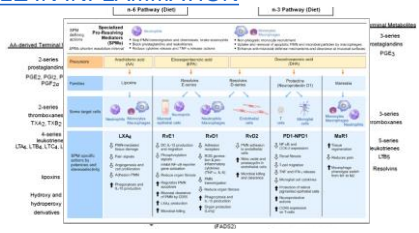
ROLE IN INFLAMMATION



Thus, the interaction of omega-3 and omega-6 fatty acids and their lipid mediators in the context of inflammation is complex and still not properly understood (Innes and Calder, 2018)

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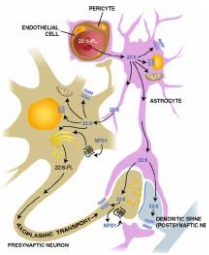
n-3 and n-6 fatty acids in neural tissue

- Retina -> the cells of the rod outer segment have an exceptionally high content of DHA in their membranes (50–70% of fatty acids)
- Brain ->More than 50% of the dry weight of the brain is lipid, most abundant PUFA in phospholipids: DHA and AA
- The precise mechanisms by which DHA-containing phospholipids contribute to brain functions are largely unknown



Bazinet and Layé, 2014, Calder, 2016

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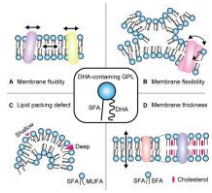
COULD OTHER FATTY ACIDS SUBSTITUTE DHA?

- Because of its highly unsaturated nature, DHA adopts a three-dimensional shape that is different from that of other common membrane fatty acids
- This shape strongly influences membrane order and has an impact on membrane protein function and on the assembly of lipid rafts



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NEONATAL DEVELOPEMENT

Maternal diet alpha-linolenic acid during gestation and lactatio does not increase docosahexaenoic acid in canine milk (Bauer al, 2004)

- Supplementation of gestation and lactation diets with LA or AL does not appear to be an effective method of increasing milk-f LCPUFAs in developing canines
- Similar study on developing felines by Pawloski et al 1997 -> supplementation of maternal diets by corn oil -> low accumula... of DHA in 8 wk old kittens in retina, sufficient accumulation of AA

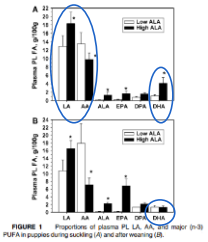

FIGURE 1 Proportions of plasma PL LA, AA, and major (n-3) PUFA in puppies during suckling (A) and after weaning (B).

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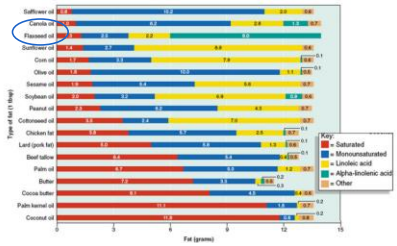
LCPUFAS IN FOOD CHAIN

- Animal derived product - sources od LCPUFA
- Higher plants (plant oils) - sources of ALA and LA



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Boyle and Anderson, 2010.

ALGAE AS SUSTAINABLE SOURCE FOR LCPUFA

Whole cell Schizochytrium sp. algae DHA content: minimum of 17% DHA (total fat content ≥ 40%)

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N3 PUFA AS NEUTRACEUTICALS

Table 1—Approximate dosages of EPA and DHA recommended as adjunctive dietary treatment for various clinical disorders in dogs.

Clinical disorder	Dosage (mg/kg$^{0.75}$)*	Approximate EPA and DHA dose for a 10-kg (22-lb) dog (mg)†
Idiopathic hyperlipidemia	120	675
Kidney disease	140‡	790
Cardiovascular disorders	115	645
Osteoarthritis	310‡	1,745
Inflammatory or immunologic (atopy or IBD)	125	700
NRC recommended allowance[22]	30	170
NRC safe upper limit	370	2,080

*Calculated on a metabolic BW basis; if BW is recorded in pounds, it must first be divided by 2.2 to convert it to kilograms for use in this equation. †Values have been rounded to the nearest 5 mg. ‡Dosage may be increased (depending on the severity and chronicity of the disorder) up to the NRC safe upper limit.

Bauer 2011.

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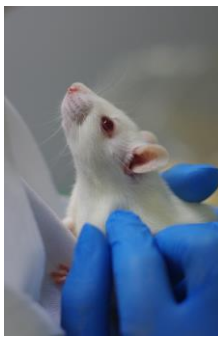
LIPIDOMICS

- Lipidomics has been defined as “the full characterization of lipid molecular species and of their biological roles including gene regulation”
- FA have diverse roles in cellular signaling and cell–cell interactions
- The interest in lipidomics has also been driven by the widening role of lipid species in the cell



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Thank you for attention!

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