LIPIDS

Introduction
- simple lipids

Marek Vecka

LIPIDS

DEFINITION OF LIPIDS

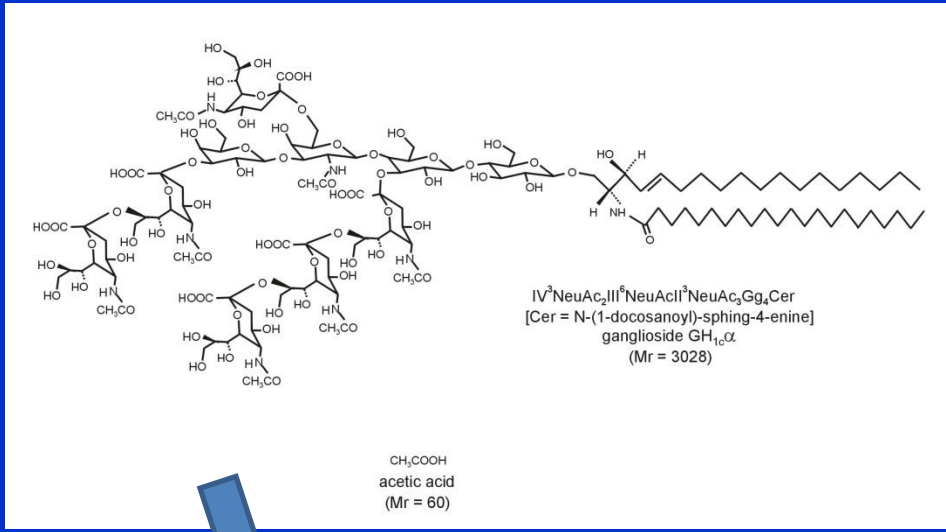
(no precise definition exists…)

I. Based on physicochemical properties

The term "lipid" defines substances as oils, fats and waxes which can be only characterized by a large array of properties:

insoluble or immiscible with water but soluble in organic solvents such as chloroform, ether, benzene, acetone,…

(i.e. hydrophobic/amphipatic structures)



coming from animals and plants living or fossilized, but they can also be produced by chemical synthesis

LIPIDS

DEFINITION OF LIPIDS

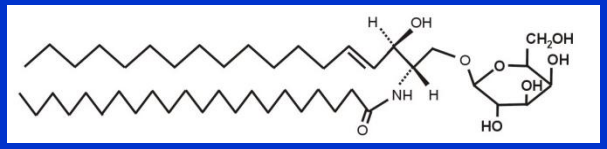
(no precise definition exists…)

II. Based on molecular structure

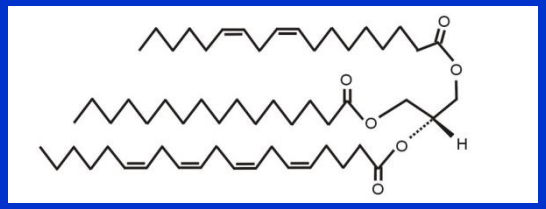
- formed of long-chain hydrocarbon groups (carbon and hydrogen) but may also contain oxygen, phosphorus, nitrogen and sulfur.

Lipids are fatty acids and their derivatives, and substances related biosynthetically or functionally to these compounds.

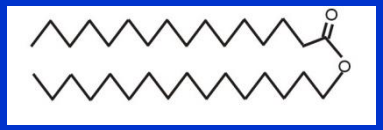
cerebroside



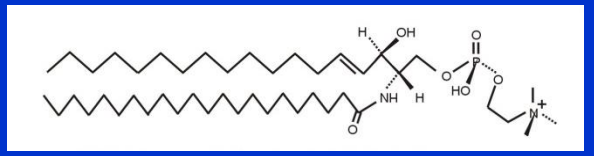
oil (= liquid fat)



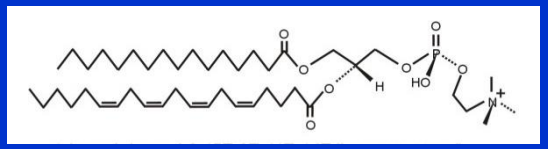
wax



sphingomyeline



lecithin



?? CHOLESTEROL ??

LIPIDS

DEFINITION OF LIPIDS

(no precise definition exists…)

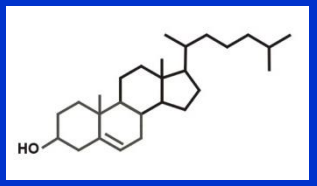
II. Based on molecular structure

- formed of long-chain hydrocarbon groups (carbon and hydrogen) but may also contain oxygen, phosphorus, nitrogen and sulfur.

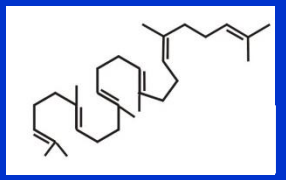
Lipids are fatty acids and their derivatives, and substances related biosynthetically or functionally to these compounds.

Lipids are hydrophobic or amphipathic small molecules that may originate entirely or in part by carbanion-based condensations of thioesters (fatty acids, polyketides, etc.) and/or by carbocation-based condensations of isoprene units (prenols, sterols, etc.).

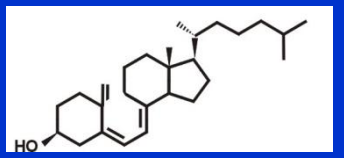
cholesterol



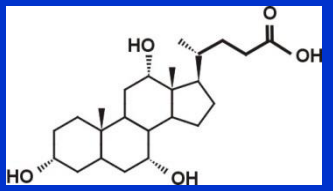
squalene



vitamin D_3

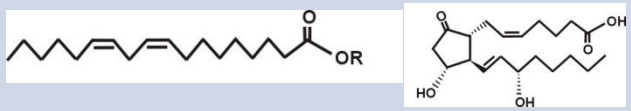
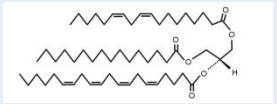
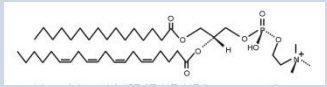
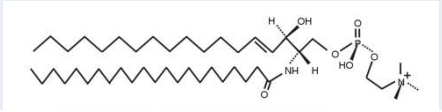
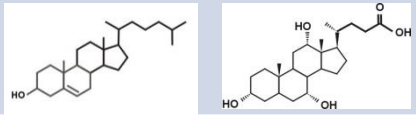


bile acid



CLASSIFICATION OF LIPIDS I

- molecular structure

Lipid class	Abbreviation	N of known structures
Fatty acyls 	FA	5869
Glycerolipids 	GL	7541
Glycerophospholipids 	GP	8002
Sphingolipids 	SP	4338
Sterol lipids 	ST	2715
Prenol lipids 	PL	1259
Other – saccharolipids, polyketides	SL, PK	1293+6742

CLASSIFICATION OF LIPIDS II

- susceptibility to hydrolysis

Nonhydrolyzable lipids – group not reacting with H_2O:

- fatty acids
- sterols
- eicosanoids (oxylipins)
- vitamins (*fat soluble*)

Hydrolyzable lipids – group reacting with H_2O:

- glycerophospholipids
- glycerosphingolipids
- triacylglycerols
- diacylglycerols
- monoacylglycerols

CLASSIFICATION OF LIPIDS III

- yield of hydrolysis

Simple lipids – at most 2 types of products:

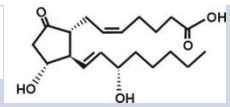
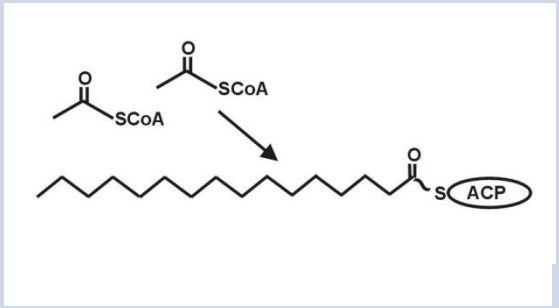
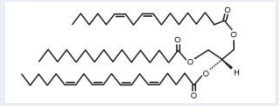
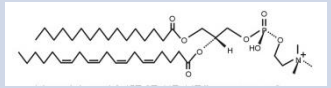
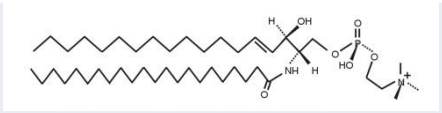
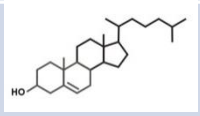
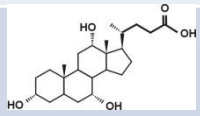
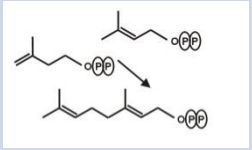
- fatty acids
- waxes
- sterols
- triacylglycerols
- diacylglycerols
- monoacylglycerols

Complex lipids – at least 3 types of products:

- glycerophospholipids
- glycerosphingolipids

CLASSIFICATION OF LIPIDS IV

- biosynthetic route

Lipid class	Biosynthetic route
Fatty acyls  	condensation of thioesters 
Glycerolipids 	
Glycerophospholipids 	
Sphingolipids 	
Sterol lipids  	condensation of activated isoprene units 
Prenol lipids 	
Other – saccharolipids, polyketides	other types

CLASSIFICATION OF LIPIDS V

- polarity

neutral lipids – no polar group

hydrocarbons/prenols/waxes
steryl esters
triacylglycerols
sterols
diacylglycerols/monoacylglycerols

free fatty acids
glycerophospholipids
glycerosphingolipids

polar lipids – polar group within molecule

FUNCTION OF LIPIDS

I. Energy storage and utilization

Triacylglycerols (TAG)

1 g TAG ~ 38 kJ (best E source, very long chain fatty acids)

nonpolar lipid = lipid droplets in adipocytes etc.

II. Specialized lipid microenvironment

bile acids – ingestion of lipids

lipoproteins – transport of lipids/lipid soluble vitamins

FUNCTION OF LIPIDS

III. Insulation

Thermal insulation

- TAGs in subcutaneous fat (loss of heat)
- TAGs in visceral fat (thermal stability)

Mechanical/electrical insulation

- sphingomyelins, cholesteryl esters, TAG (myeline sheaths)
- layers preventing from impact shock (sole)

Water loss prevention

- ceramides in skin, TAG/cholesteryl esters in sweat

Pulmonary surfactant - air-liquid tension reduction

IV. Intrinsic part of membranes

- compartment „insulation“

FUNCTION OF LIPIDS

V. Metabolites of lipids

Signalling molecules

eicosanoids oxysterols

fatty acid amides

Ligands for nuclear receptors

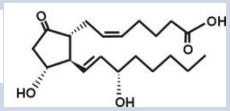
oxysterols/oxylipins - PPARs, LXR, FXR

VI. Modification of proteins, saccharides

anchoring in membranes

antigenic determinants

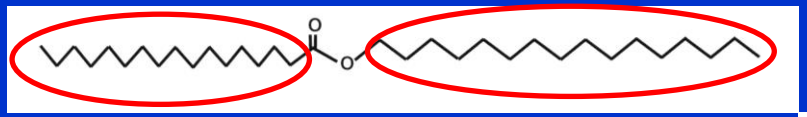
CLASSIFICATION OF LIPIDS

Lipid class	Abbreviation
Fatty acyls  	FA
Glycerolipids	GL
Glycerophospholipids	GP
Sphingolipids	SP
Sterol lipids	ST
Prenol lipids	PL
Other – saccharolipids, polyketides	SL, PK

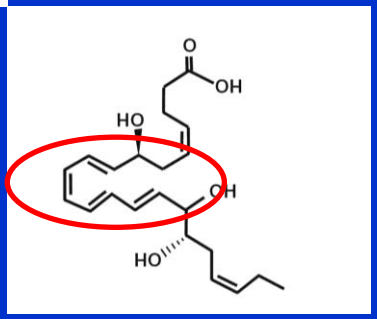
FATTY ACYLS

(Free) fatty acids

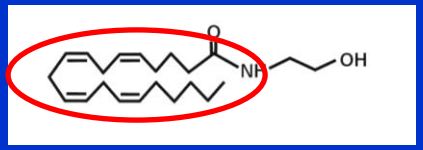
Waxes



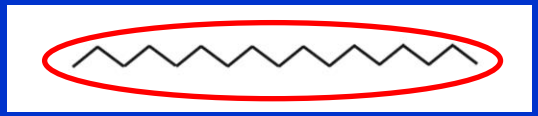
Eicosanoids/Docosanoids



Fatty acid amides



Hydrocarbons



1. Hydrophobic

2. Simple = part of complex lipids, ubiquitous

FATTY ACIDS (FA)

- carboxylic acids (organic acids)
- hydrocarbon chain + carboxyl group

- many types of FA in nature
  - human plasma – more than 60 different FAs

  - usually bound in lipids as esters
  - most have even carbon number
    (biosynthesis from 2C units)

FATTY ACIDS (FA)

have variable chain length:

short chain fatty acids (SCFA)

FA with < 6C

medium chain fatty acids (MCFA)

FA with 6-12C

long chain fatty acids (LCFA)

FA with 13-20C

very long chain fatty acids (VLCFA)

FA with > 21C

FATTY ACIDS (FA)

can have various chain modifications:

double (triple) bonds

one C=C, more C=C, (C≡C rarely) = ***unsaturated FA***

side methyl groups

iso-, anteiso- branched FA = ***branched FA***

hydroxy groups

hydroxy FA = ***hydroxy FA***

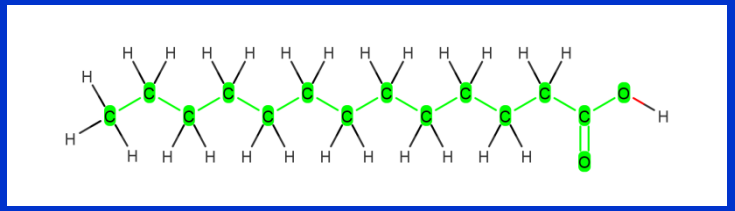
other modifications

oxy-, thia-, cyclo-, dicarboxylic- …

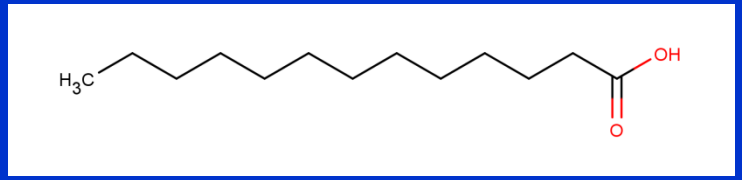
FATTY ACIDS

structure of fatty acids:

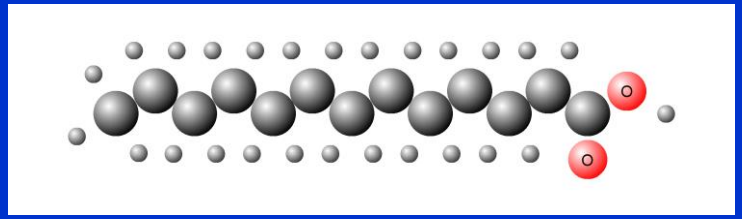
simple structural formula



reduced structural representation



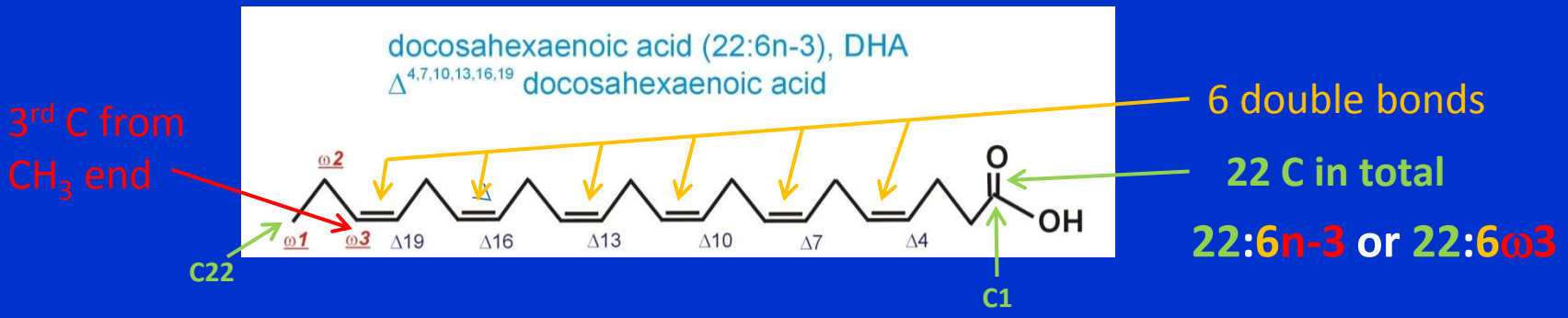
real position of atoms



FATTY ACIDS

shorthand notation for fatty acids

C:N-x or C:Nωx notation is the most common



C:N-x notation

C … number of carbon atoms in the molecule

N … number of double bonds in the molecule

x … position of the first double bond from the methyl end

C:N ωx notation

ω … the same as x above

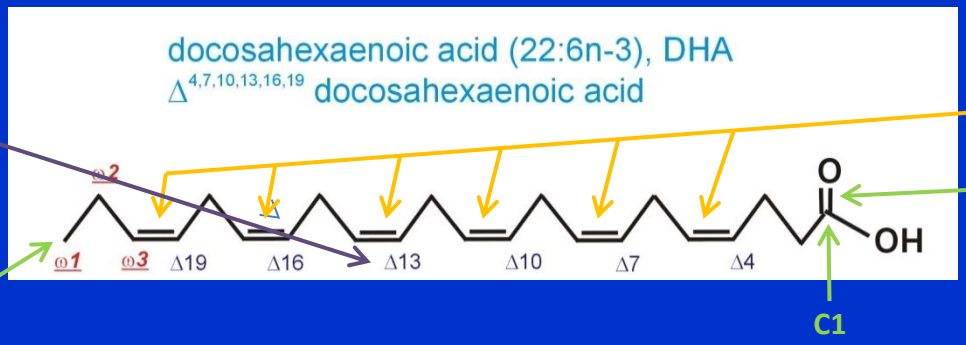
NOTE: ASSUMES THAT ALL DOUBLE BONDS ARE IN PENTADIENIC CONFIGURATION!

FATTY ACIDS

shorthand notation for fatty acids

IUPAC notation also used

positions of C=C from COOH end



6 double bonds

22 C in total

22:6$\Delta^{4,7,10,13,16,19}$

or

22:6 (4,7,10,13,16,19)

C:N $\Delta^{x,y,z}$ notation

C … number of carbon atoms in the molecule

N … number of double bonds in the molecule

x,y,z … positions of the double bond(s) from the carboxyl end

C:N (x,y,z) notation

x,y,z … the same as above

NOTE: NO ASSUMPTION FOR MUTUAL DOUBLE BOND CONFIGURATION!

SATURATED FATTY ACIDS (SFA)

- straight chain or branched
- even or odd number of C
- SCFA, MCFA, LCFA, VLCFA

SATURATED FATTY ACIDS

Short chain fatty acids (SCFA)

acetic acid (2:0)

propionic acid (3:0)

butyric acid (4:0)

- in humans formed in proximal colon during fibre fermentation
- quickly absorbed, used in liver for synthesis (Glc, FA) (~10% REE)
- used in metabolism, proliferation and restoration (cell replication) of colonocytes
- cause limited reproduction of saprophytic bacteria due to decreased acidity

SATURATED FATTY ACIDS

Medium chain fatty acids (MCFA)

caproic acid (6:0) caprylic acid (8:0) pelargonic acid (9:0)

capric acid (10:0) lauric acid (12:0) undecylic acid (11:0)

- 6-10:0 characteristic odors (*caper*, goat), in milk
- not in membrane lipids
- quickly absorbed, as TAG used in enteral nutrition
- liquid

SATURATED FATTY ACIDS

Long chain fatty acids (LCFA)

lauric acid (12:0)

myristic acid (14:0)

palmitic acid (16:0)

stearic acid (18:0)

arachidic acid (20:0)

- in animal and vegetable oils
- not readily absorbed
- **atherogenic and thrombogenic effects**
- solid (plastic)

SATURATED FATTY ACIDS

Fats rich in SFA

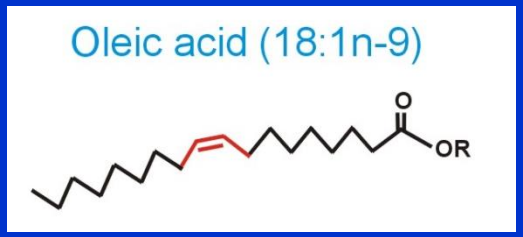
	animal sources	vegetable sources
4:0, 6:0	butter	
8:0	butter	coconut oil
10:0	butter	coconut oil
12:0	butter	coconut oil
14:0	butter, tallow	coconut oil
16:0	lard, tallow	coconut oil, palm oil
18:0	lard	palm oil
20:0		shea butter

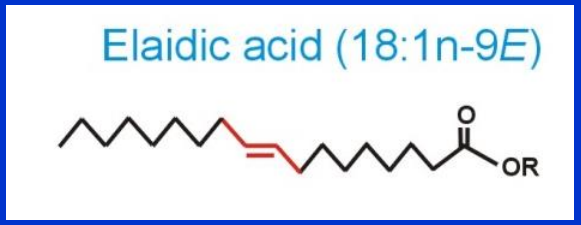
UNSATURATED FATTY ACIDS

Monounsaturated fatty acids (MUFA)

- only one double bond in the chain

configuration *cis* *trans*





Polyunsaturated fatty acids (PUFA)

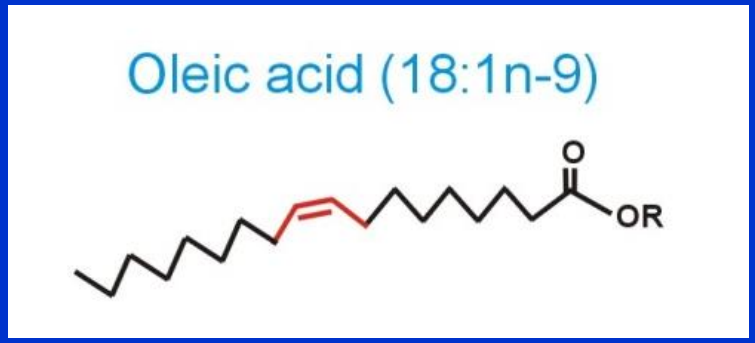
- two or more double bonds in the molecule
- usually in *cis,cis*-pentadienic structure

n-3 family n-6 family CLAs

MONOUNSATURATED FATTY ACIDS

Double bond in *cis* configuration

- most of MUFA
- the chain is slightly bonded
- lower melting point vs. *trans*- isomer

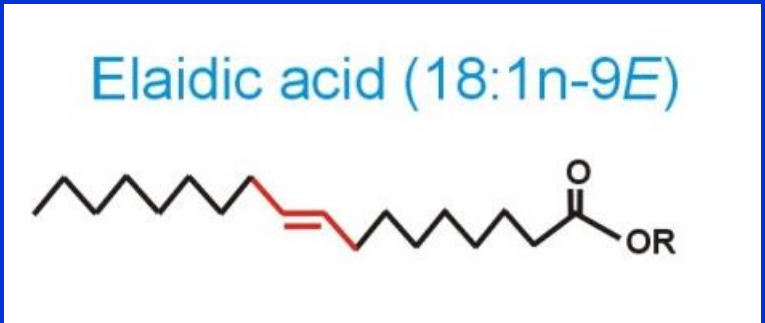


- sometimes referred to as *Z* (*cf. German zusamenn*) isomer

MONOUNSATURATED FATTY ACIDS

Double bond in *trans* configuration

- minority of MUFA
- the chain is nearly straight
- higher melting point vs. *cis*- isomer



- sometimes referred to as *E* (*cf. German entgegen*) isomer

MONOUNSATURATED FATTY ACIDS

melting point

Stearic acid (18:0)

68 °C

easily packed

Oleic acid (18:1n-9)

16 °C

Elaidic acid (18:1n-9*E*)

45 °C

Linoleic acid (18:2n-6)

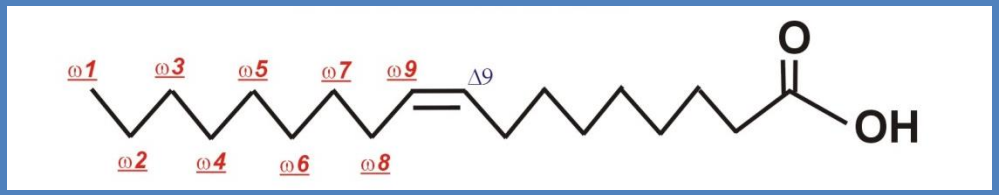
-7 °C

not easily packed

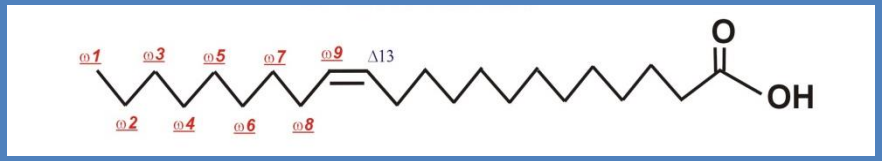
MONOUNSATURATED FATTY ACIDS

oleic acid (OA, 18:1n-9)

- most common
- olive, rapeseed, peanut oils
- **antithrombotic, antiatherogenic properties** (oxidation resistant)

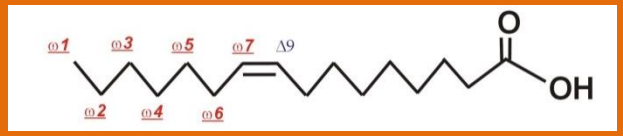


erucic acid (22:1n-9)
- cardiotoxic, now low erucic rapeseed oils

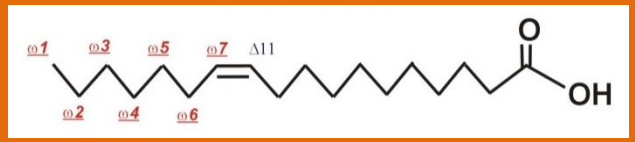


n-9 MUFA

palmitoleic acid (16:1n-7)
- in lard, other fats



vaccenic acid (18:1n-7)



n-7 MUFA

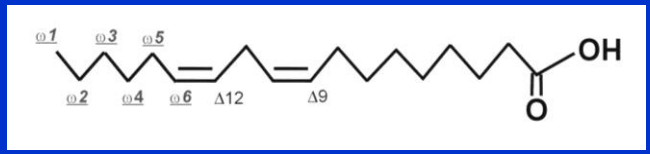
POLYUNSATURATED FATTY ACIDS

n-6 PUFA family

double bonds are on 6th C from CH_3 end

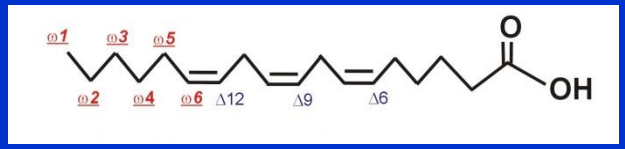
linoleic acid (LA, 18:2n-6)

- synthesized only in plants (EFA)
- in soya, corn, sunflower oils
- animals use for ARA synthesis



γ-linolenic acid (GLA, 18:3n-6)

- in borage oil
- **antiinflammatory effects**

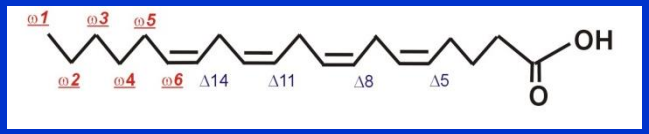


POLYUNSATURATED FATTY ACIDS

n-6 PUFA family

double bonds are on 6th C from CH_3 end

arachidonic acid (ARA, 20:4n-6)



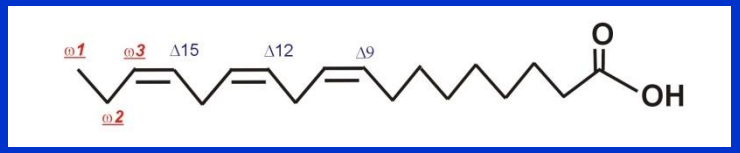
- most important FA of n-6 PUFA
- major constituents in membrane phospholipids (…meat)
- precursor for eicosanoids with inflammatory and thrombogenic effects
- important for angiogenesis (placenta)

POLYUNSATURATED FATTY ACIDS

n-3 PUFA fami***ly***

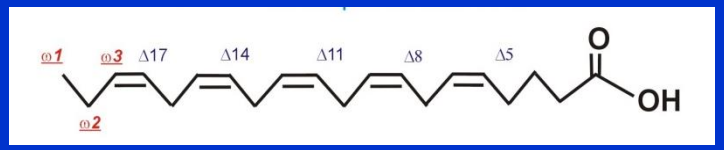
double bonds are on 3rd C from CH_3 end

α-linolenic acid (ALA, 18:3n-3)

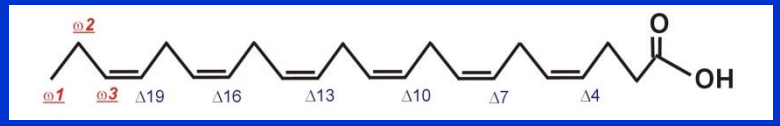


- in linseed oil
- synthesized only in plants (EFA)

eicosapentaenoic acid (EPA, 20:5n-3)



docosahexaenoic acid (DHA, 22:6n-3)



- marine unicellular algae → in seafish
- important for neuronal structures (pregnancy)
- precursors of eicosanoids (EPA) or docosanoids (DHA) with

beneficial effects on cardiac, cognitive functions

inflammation

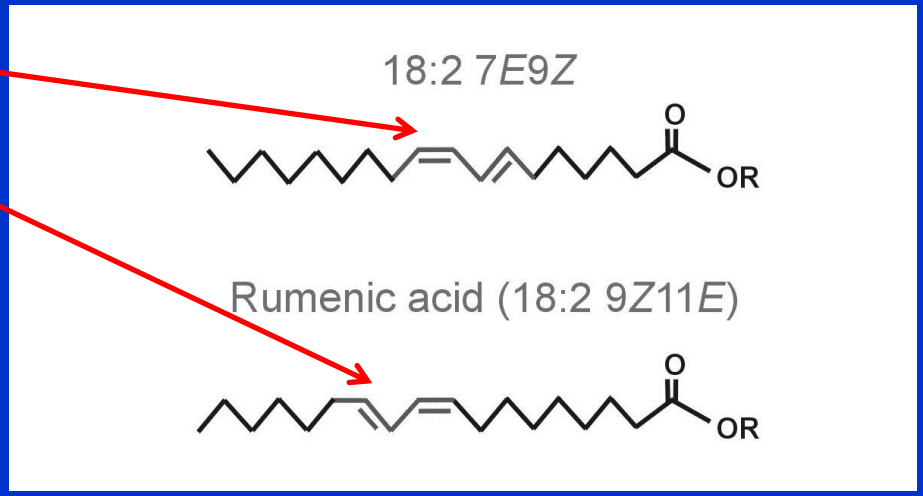
POLYUNSATURATED FATTY ACIDS

Symptoms of PUFA deficiency

Clinical feature	PUFA n-6	PUFA n-3
liver function	steatosis	
growth/reproduction	disturbed	normal
retina/brain	normal	abnormal electro-retinogram, neurological disturbances
skin	skin lesions	normal skin
water balance	polydipsia	polydipsia

CONJUGATED LINOLEIC ACIDS

double bonds are not in pentadiene form, but are conjugated



conjugated forms of linoleic acid (CLAs)

- the double bonds are in *cis, trans*- or *trans, cis*- configuration
- the positions are 7,9 or 9,11 or 10,12

CONJUGATED LINOLEIC ACIDS

sources of CLA

- *in vivo* as intermediates of hydrogenation of LA in the rumen by several bacterias (*Butyrvibrio ssp*.)
- *in vivo* as intermediates of hydrogenation of tVA in the mammary milk gland

→ meat, milk of ruminants

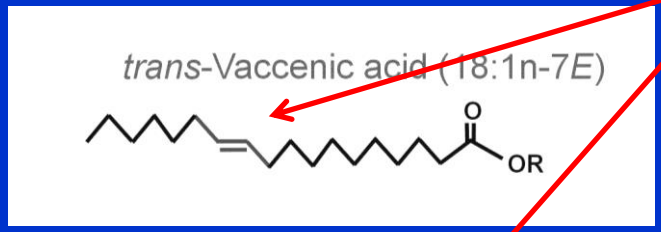
- *endogenously* by thermal procession of milk/dairy products

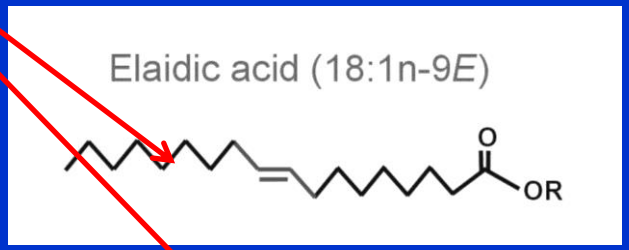
effects of CLA

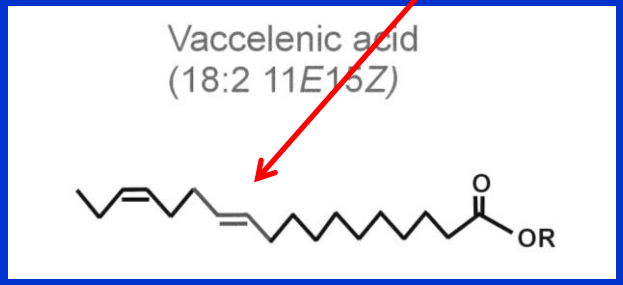
- promising data on animal models (body weight/hypertension)
- in human, the results are contradictory
- can be isomer specific?

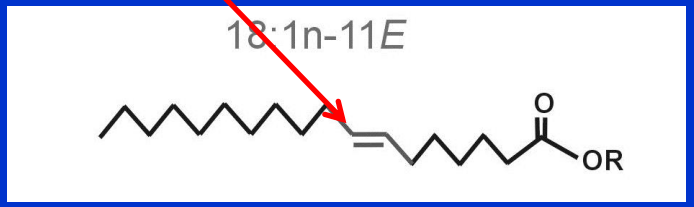
TRANS ISOMERS OF FATTY ACIDS

at least one double bond is in trans configuration









the chain structure is nearly linear (~SFA)

TRANS ISOMERS OF FATTY ACIDS

at least one double bond is in trans configuration

sources of trans fatty acids (TFA)

in vivo as intermediates of hydrogenation of LA in the rumen by several bacterias (*Butyrvibrio ssp*.)

→ meat, milk, butter, cheese of ruminants (app. 2-8% trans fatty acids by weight)

by hydrogenation (oil hardening)/heating (frying) of vegetable fats (almost TFA free)

effects of trans fatty acids (TFA)

- **similar to SFA (risk factor for ATH: LDL-C↑)**

BRANCHED FATTY ACIDS

various aliphatic substituents are attached to the chain

sources of branched FA

- products of microbial metabolism (tuberculostearic acid)
- microbial degradation of substrates in ruminants, marine organisms

  → can be in the diet

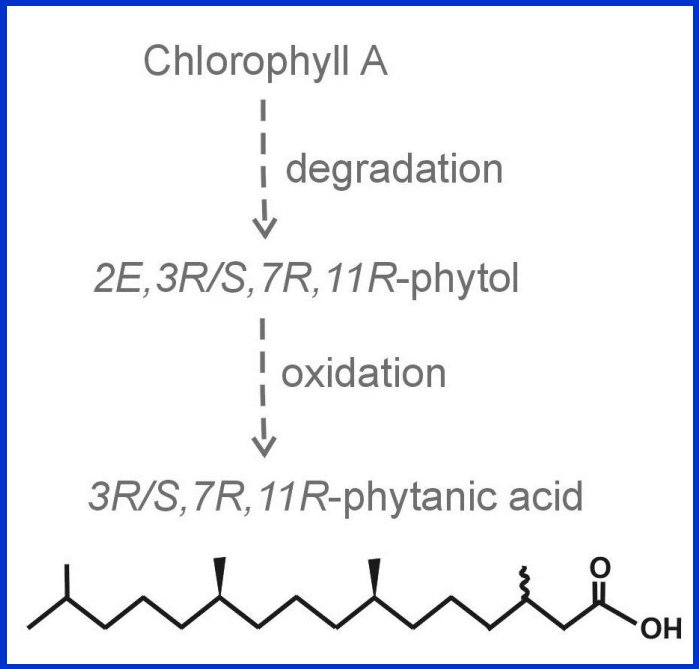
- in animals rarely (sebum, *vernix caseosa* – biofilm covering fetus)

BRANCHED FATTY ACIDS

various aliphatic substituents are attached to the chain

Phytanic acid

- product of degradation of chlorophyll
- in bovine milk lipids (~0.1%)
- must be metabolized in peroxisomes (accumulation in brain/blood)



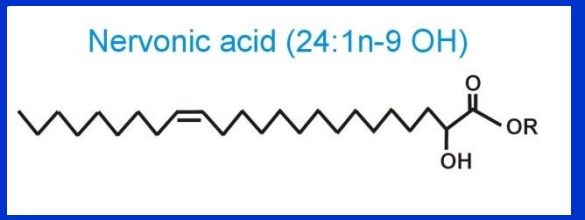
18:0 3,7,11,15m

Refsum´s disease

- inherited neurological disorder
- the catabolism of phytanic acid ineffective
- the sources of phytanic acid must be avoided

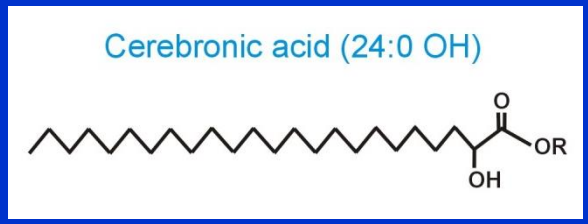
HYDROXY FATTY ACIDS

hydroxy substituents are attached to the chain



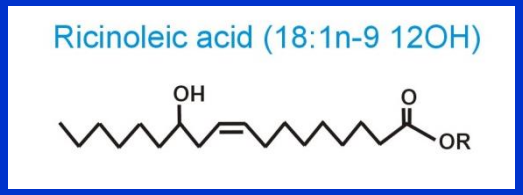
Glycoshingolipid biosynthesis

- mainly cerebronic and hydroxynervonic acids
- in neuronal tissues, other - role in reproduction



Plant sources

ricinoleic acid – castor oil (purgative, defoamer…)



Oxylipins

- OH FA derived from LA, ALA, EPA, DHA …
- precursors for octadecanoids/eicosanoids/ /docosanoids (*see lecture on eicosanoids*)

FATTY ACID AMIDES

amino group derivative - carboxyl of FA changed

FA amides

- not in vegetable oils/fats
- in neuronal tissues, blood
- ligands for cannabinoid receptors

Anandamide

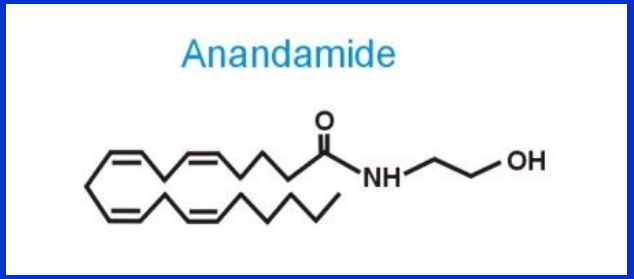
- *N*-arachidonoylethanolamide

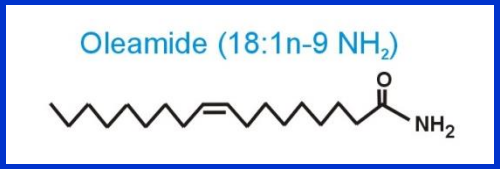
Oleamide

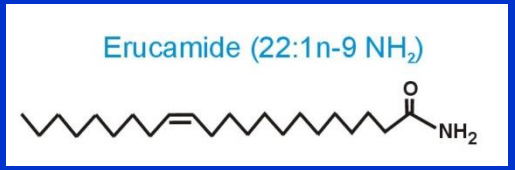
- sleep inductor in mammals

Erucamide

- angiogenic factor in the mesentery





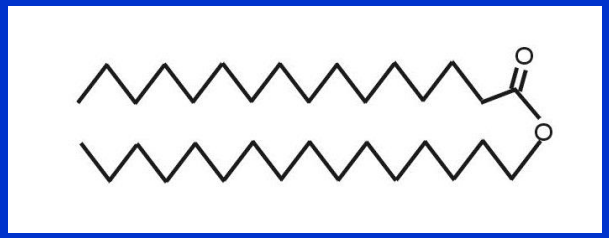


WAXES

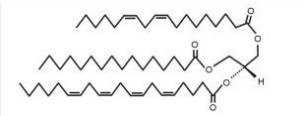
esters of long-chain fatty alcohols with long-chain fatty acids

Sources of waxes

- commercial: beeswax, lanoline, jojoba
- plant surface: leafs, fruits
- skin: sebaceous glands
- sperm whale oil (76% waxes)



CLASSIFICATION OF LIPIDS

Lipid class	Abbreviation
Fatty acyls	**FA**
Glycerolipids 	**GL**
Glycerophospholipids	**GP**
Sphingolipids	**SP**
Sterol lipids	**ST**
Prenol lipids	**PL**
Other – saccharolipids, polyketides	**SL, PK**

GLYCEROLIPIDS

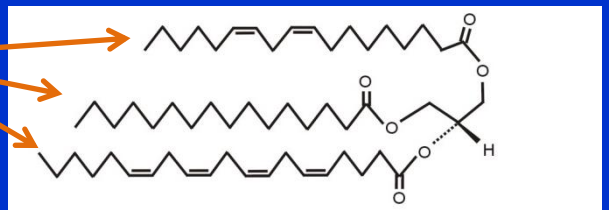
esters of glycerol with fatty acids

triacylglycerols (TAG)
- very hydrophobic
- used as E source/depo – oils/fats

diacylglycerols (DAG)
- rare in oils/fats
- intermediates in TAG biosynthesis
- signalling function

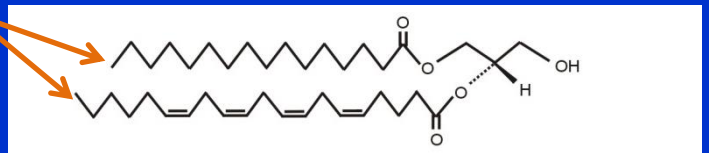
monoacylglycerols (MAG)
- end products of TAG digestion
- 2ARA glycerol (resembles anandamide)

3 FA



1-hexadecanoyl-2-(*5Z*,*8Z*,*11Z*,*14Z*-icosatetraenoyl)-
-3-(*9Z*,*12Z*-octadecadienoyl)-*sn*-glycerol
(triacylglycerol)
TAG

2 FA



1-hexadecanoyl-2-(*5Z*,*8Z*,*11Z*,*14Z*-icosatetraenoyl)-*sn*-glycerol
(diacylglycerol)
DAG

1 FA

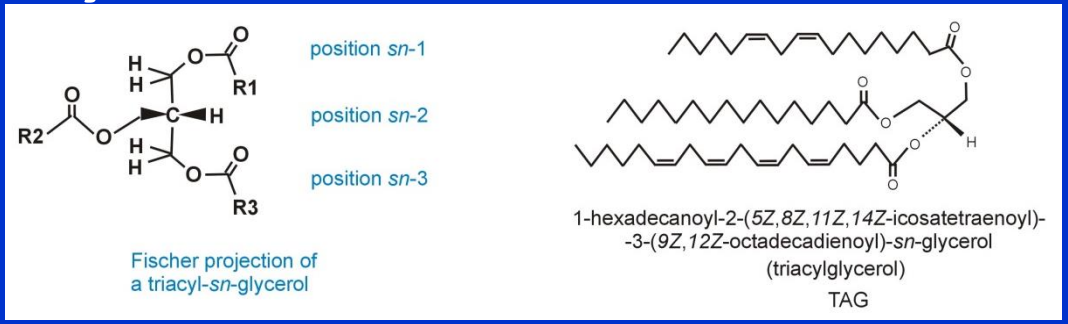
1-hexadecanoyl-*sn*-glycerol
(monoacylglycerol)
MAG

GLYCEROLIPIDS

esters of glycerol with fatty acids

triacylglycerols (TAG)

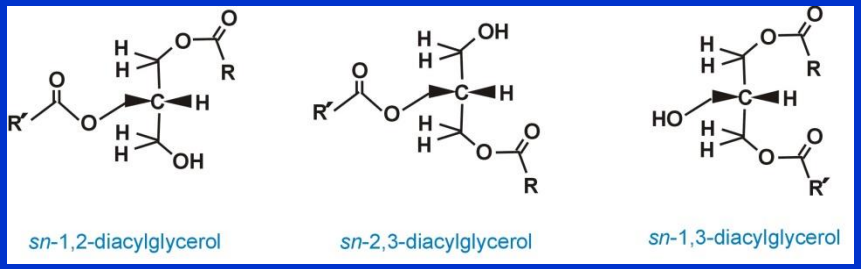
- *sn* nomenclature
- no charge → **neutral**



diacylglycerols (DAG)

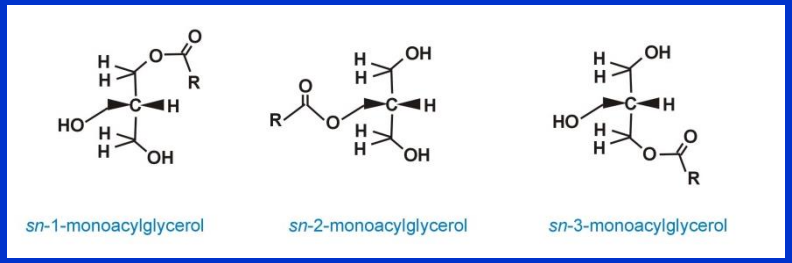
- possible isomers:

sn-1,2-DAG, *sn*-2,3-DAG, *sn*-1,3-DAG



monoacylglycerols (MAG)

- 3 possible isomers: *sn*-1-MAG, *sn*-2-MAG, *sn*-3-MAG

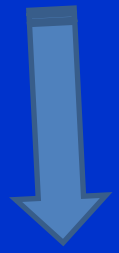


Analysis of lipids

LIPIDOME

= all lipids in the organism

- some organisms have only limited number of lipidic molecules
- humans: human plasma lipidome > 1000 different lipidic molecules



Lipidomics: area of bioanalytical CH describing the lipidomes (structure, function, content, compartmentalization …)

Further reading

Textbooks, monographs

Biochemistry of Lipids, Lipoproteins and Membranes (5th Ed); Vance DE, Vance Je (Eds.), Elsevier, Amsterodam (The Netherlands) 2008

Lehninger Principles of Biochemistry (6th Ed); Nelson DL, Cox MM (Eds.), Susan Winslow, New York (U.S.A.) 2013

Harper´s Illustrated Biochemistry (28th Ed); Murray RK, Bender DA, Botham KM, Kennely PJ, Rodwell VW, Weil PA (Eds.), McGraw-Hill, New York (U.S.A.) 2009

Articles

Fahy E, Subramaniam S, Brown HA, Glass CK, Merrill Jr. AH, Murphy RC, Raetz CRH, Russell DW, Seyama Y, Shaw W, Shimizu T, Spener F, van Meer G,Van Nieuwenhze MS, White SH, Witztum JL, Dennis EA: A comprehensive classification system for lipids. *J Lipid Res* 2005; **46**: 839–861.

Fahy E, Subramaniam S, Murphy RC, Nishijima M, Raetz CHR, Shimizu T,Spener F, van Meer G, Wakelam MJO, Dennis EA: Update of the LIPID MAPS comprehensive classification system for lipids. *J Lipid Res* 2009; **50**: S9–S14.

Ratnayake WMN, Galli C: Fat and Fatty Acid Terminology, Methods of Analysis and Fat Digestion and Metabolism: A Background Review Paper. *Ann Nutr Metab* 2009; **55**: 8–43.

Das UN: Essential Fatty Acids - A Review. *Curr Pharm Biotechnol* 2006; **7**: 467-482.

Web sources

http://www.cyberlipid.org

http://lipidlibrary.aocs.org

http://www.lipidmaps.org