Plant Lipids

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Plant Lipids: Generalities

- **Esters of fatty acids and alcohols or polyols**.
- Constituents of
  - cell structures such as **membrane phospho- and glycolipids**,
  - **coating elements** such as waxes or cutins, and
  - also reserve substances and **sources of energy** for the cell.
- **Lipids** = **„fats"**– are
  - **hydrophobic**, and **sometimes amphophilic** substances
  - **soluble** in apolar or barley polar organic solvents,
  - **non volatile**→referred to as „fixed" oils, as opposed to „essential oils"
- **Simple lipids,** esters of a fatty acid and of an alcohol that may be:
  - **glycerol**, constituent of triacylgycerols or triglycerides;
  - a high molecular-weight **aliphatic alcohol**, a constituent of waxy esters;
- Complex lipids: **phospholipids**, **glycolipids**.
  - They play a *fundamental role* in living organisms, particularly as **membrane constituent**s, but except for **lecithin**s, they have no pharmaceutical or industrial applications to date, therefore we shall no cover them here.

2. TRIACYLGLYCEROLS (TRIGLYCERIDES)

Natural Occurence

- **Triacylglycerols** are **practically nonexistent in vegetative organs** (leaves).
- They are **stored as** oily inclusions called **oleosomes**, which arise from the endoplasmic reticulum, and at times gather in large piles **in the cells of reserve tissues**;
- this is particularly true **in seeds** in which they **may represent over 50% of the dry weight**.
- The **triacylglycerol content** of seeds **increases during the maturation process** whereas in parallel, the phospholipids and glycolipids of young seminal tissues disappear.
- Exceptionally, **seeds may accumulate** not triacylglycerols, but **esters of fatty acids and of long-chain aliphatic alcohols** (see jojoba).
- Although this is less common, **some fruits concentrate triacylglycerols in their pericarp**: olive, avocado, bay berry.

2. TRACYLGLYCEROLS (TRIGLYCERIDES)

B. Structure ot Triacylgycerols

- They are **triester of a triol**, glycerol, **and of fatty acids**, in other words aliphatic carboxylic acids of variable length which normally have an **even number of carbon atoms.**

Nature of the Fatty Acids. The vast majority of vegetable fatty acids falls into two groups: **saturated fatty acids** and their **unsaturated homologs**. In both groups, 18 or 16 carbon atoms are most common.

Saturated Fatty Acids.

- Fatty acids with less than 12 carbon atoms are rare in plants: they occur, especially those in C_8 and C_{10}, in the triacylglycerols of palm seeds, mainly composed of lauric acid (C_{12}) and myristic acid C_{14}).
- Up to C_{14}, fatty acids are rarely present in substantial quantity: examples are bay butter (C_{12}) and nutmeg butter.
- Fatty acids with 20 or more carbon atoms are not common either: except in peanut oil, each normally represents less than 0.5% of the constituent fatty acids of oils.
- **Palmitic acid** (C_{16}) **is the major saturated constituent of vegetable oils**

Saturated Fatty Acids

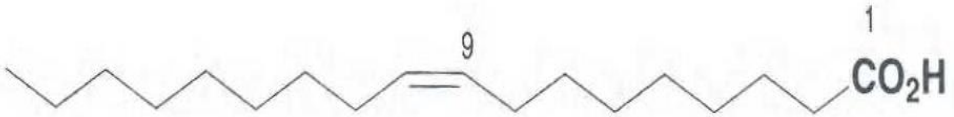
$C_{6:0}$:	hexanoic acid	=	caproic acid
$C_{8:0}$:	octanoic acid	=	caprylic acid
$C_{10:0}$:	decanoic acid	=	capric acid
$C_{12:0}$:	dodecanoic acid	=	lauric acid
$C_{14:0}$:	tetradecanoic acid	=	myristic acid
$C_{16:0}$:	hexadecanoic acid	=	palmitic acid
$C_{18:0}$:	octadecanoic acid	=	stearic acid
$C_{20:0}$:	eicosanoic acid	=	arachidic acid
$C_{22:0}$:	docosanoic acid	=	behenic acid
$C_{24:0}$:	tetracosanoic acid	=	lignoceric acid
$C_{26:0}$:	hexacosanoic acid	=	cerotic acid
$C_{28:0}$:	octacosanoic acid	=	montanic acid
$C_{30:0}$:	triacontanoic acid	=	melissic acid

Unsaturated Fatty Acids

- The most important ones are in the **C_{18} series**, the **configuration** of the unsaturation(s) is **Z** as a general rule, and in polyunsaturated molecules, the **double bonds occur in a 1,4-diene pattern.**

Examples (C18 series):

$C_{18:1}$:	9-octadecenoic acid	=	oleic acid
$C_{18:2}$:	9,12-octadecadienoic acid	=	linoleic acid
$C_{18:3}$:	9,12,15-octadecatrienoic acid	=	α-linolenic acid



Oleic acid

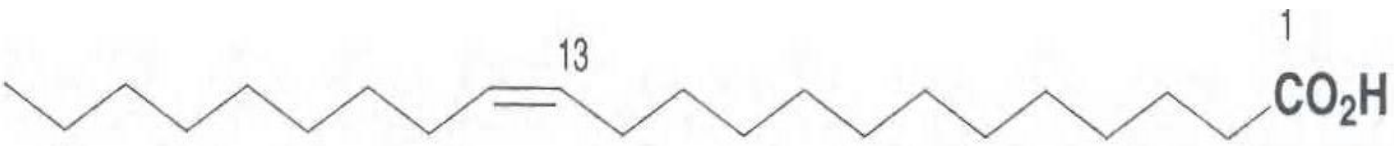
C18 : 1 (9)

- **Trans fatty acids** occur in milk, butter, and animal fats—they are formed during ruminal hydrogenation—and **arise, in vegetable fats, from isomerisation during hydrogenation (margarines).** The French diet is thought to contain 8 to 10 g/day and **questions have yet to be answered about their harmlessness**.

Unsaturated Fatty Acids

Unsaturated acids with short chains ($\leq C_{16}$) or with 20 or more carbons are less common:

C14:1 :	9-tetradecenoic acid	=	myristoleic acid
C16:1 :	9-hexadecenoic acid	=	palmitoleic acid
C20:1 :	9-eicosenoic acid	=	gadoleic acid
C22:1 :	13-docosenoic acid	=	erucic acid



Erucic acid

C22 : 1 (13)

Unsaturated Fatty Acids

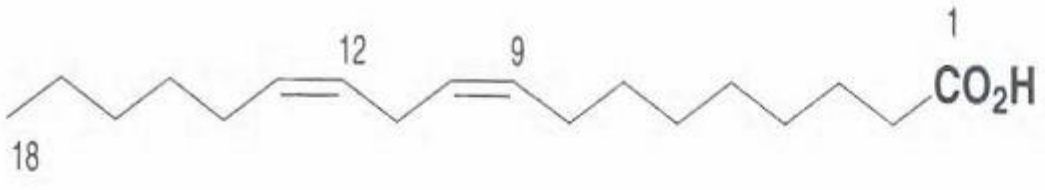
Positional isomers of these are also rare:

$C_{18:1}$:	6-octadecenoic acid	=	petroselinic acid
$C_{18:1}$:	11-octadecenoic acid	=	*cis*-vaccenic acid
$C_{18:3}$:	6,9,12-octadecatrienoic acid	=	γ-linolenic acid

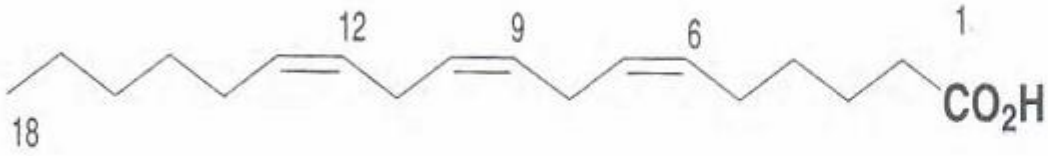
Some are exceptional:

$C_{20:4}$:	5,8,11,14-octadecatetraenoic acid	=	arachidonic acid

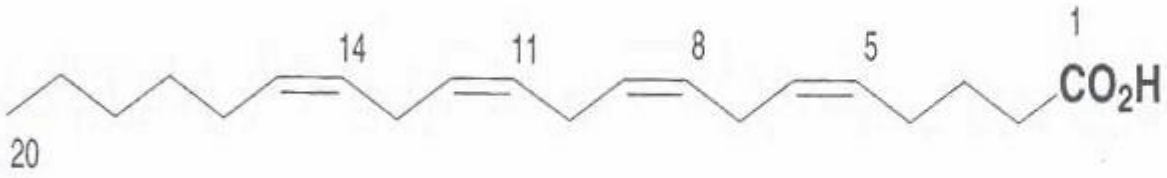
Unsaturated Fatty Acids



Linoleic acid
C18 : 2 (9, 12)

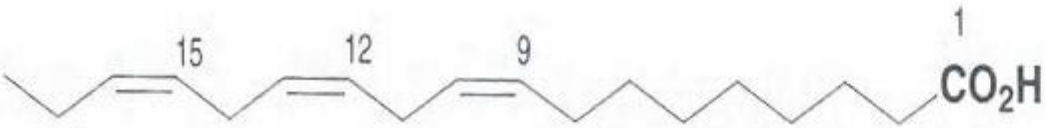


γ-Linolenic acid
C18 : 3 (6,9, 12)



Arachidonic acid
C20 : 4 (5, 8, 11, 14)

n-6 acids
= ω-6 family



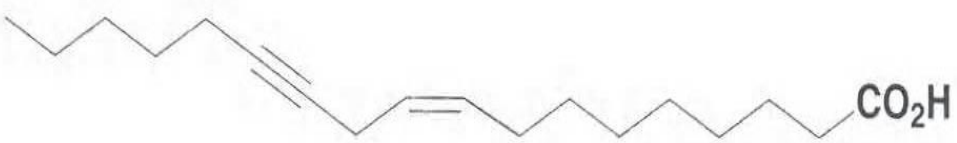
α-Linolenic acid
C18 : 3 (9, 12, 15)

n-3 acid
= ω-3 family

Unsaturated Fatty Acids

Other unsaturated fatty acids. They are **rare structures** generally **limited in distribution to a genus, a family, or a group of families**. For example,

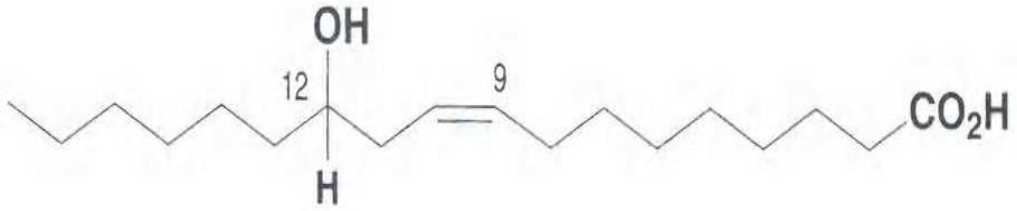
- **unsaturations** that are commonly *Z* **may be E** (e.g., **eleostearic acid**, C18:3 (9*Z*,11*E*,13*E*));
- one of the unsaturations may be **a triple bond** (**crepenynic acid**);
- there may be **up to six unsaturations** and they may be **conjugated** (**allene fatty acids**, e.g., **parinaric acid**, C18:4(9*E*11*E*13*E*15*E*)).



Crepenynic acid

Oxidized fatty acids.

- **ketonic fatty acids** such as **licanic acid** of the oils of Chrysobalanaceae (*Licania, Couepia),* particularly the oil of Brazil oiticica (4-oxo-9*E,*11*Z,*13*Z*- octadecatrienoic acid);
- **hydroxylated fatty acids** (e.g., **ricinoleic acid** = 12-hydroxy-9*Z*-octadecenoic, lesquerolic acid = 14-hydroxy-1 1*Z*-eicosenoic);
- **epoxy fatty acid** (e g., **vernolic acid** C18 1(9) (epoxy 12 13))



Ricinoleic acid

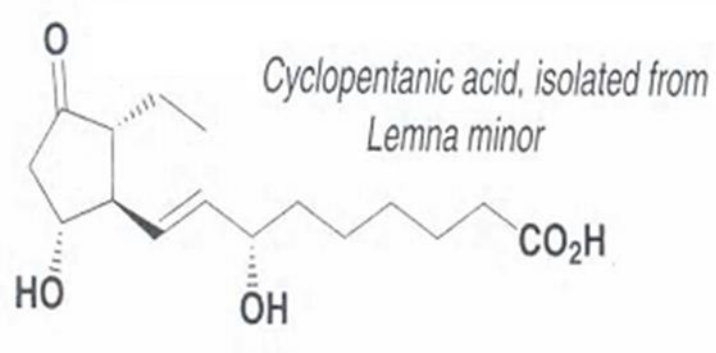
Unsaturated Fatty Acids

Cyclized fatty acids. In some cases the carbon chain is partially cyclized:

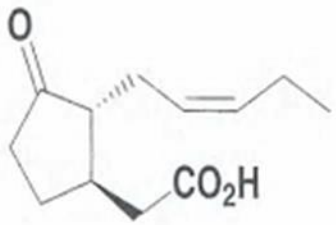
- **cyclopropanic acid** and **cyclopropenic fatty acids** of the Sterculiaceae (malvalic and sterculic acids), or of the oil from the seeds of litchi (*Litchi sinensis* Sonn., Sapindaceae),
- **cyclopentenic fatty** acids of the Flacourtiaceae.

Hydroxylated cyclopentane structures.

- molecules reminiscent of animal prostaglandins,
- plant growth regulators with hormonal properties (e.g. (—)—jasmonic acid and its derivatives).



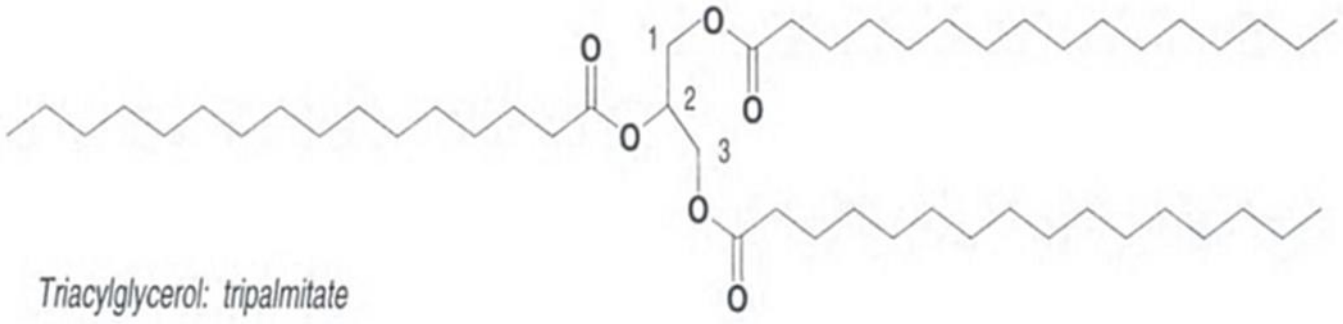
Cyclopentanic acid, isolated from Lemna minor



Jasmonic acid

Structures of Glycerol Esters

- A triglyceride may be **homogeneous** or **heterogeneous** depending on whether **the fatty acid moieties** that esterify the three alcohol functions of glycerol are **identical** or **different**.
- In general, **triacylglycerols are heterogeneous**, and a **vegetable oil** is **a complex mixture of triesters.**
- Note, however, that **saturated fatty acids** esterify preferentially the **primary alcohol functions** (α and α' positions) of glycerol and that unsaturated fatty acids esterify mainly its **secondary alcohol function** (β position).



Triacylglycerol: tripalmitate

- In the **official nomenclature** of triacylglycerols, the classic α, α', and β are replaced by 1, 2, and 3, the number of the carbon atom of **D-glycerol in the Fischer projection**, with the secondary alcohol on the left, C-l at the top, and C-3 at the bottom.
- The **substituents** are **named using**, for convenience, **the common names** (e.g., 1 -palmityl-2-oleyl-3-sterylglycerol, 1 ,3-dipalmityl-2-linoleylglycerol). **Abbreviated symbols** are generally accepted: the above examples become POS and PLP.

Properties of Glycerides and Fatty Acids

Triacylglycerols are **soluble in organic solvents**, including acetone, and this differentiates them from phospholipids.

- **On treatment by an alkaline hydroxide**, they release **one** molecule of **glycerol** and **three** molecules of **fatty acid**: the **saponification value** determined by this method provides information on the **average chain length** (see below).
- **Unsaturated fatty acid-containing triacylglycerols become rancid**:
  - when exposed to air they develop foul smells more or less rapidly.
  - This phenomenon is linked to **peroxidation of unsaturated fatty acids**: the *resulting peroxides may polymerize*—the desired goal for paints based on flaxseed oil or other drying oils. They may also be cleaved yielding aldehydes, ketones, and acids of unpleasant odor.

At ordinary temperature, **fatty acids** are liquid if their **carbon chain** is **shorter than 10** carbon atoms; otherwise they are solid.

- They are all **insoluble in water** and **soluble in organic solvents**.
- **If unsaturated**, **they absorb UV light**, and this may be applied to their quantitation.
- As acids they **form salts**: this is the basis of the soap and detergent industry (alkaline salts, organic base salts).
- As acids they **may be esterified,** resulted methyl esters are suitable for GC analysis.

OIL PRODUCTION

- *From the description* of olive oil preparation by Pliny or that, more ancient, of the Assyrian sesame oil press *to the modern screw press*, **the principle of oil production has not changed: expression of the starting material yields the oil directly**.
- **Current procedures also use organic solvents**, and in both cases the crude oil undergoes various **refining steps**.

Required/Possible steps prior to oil extraction

- strict **quality control of the starting material** (e.g., absence of foreign matter and of deterioration) is in order and
- **preliminary procedures** are often required,
  - **general** (cleaning, drying),
  - **specific** (**washing** the olives; **delintering** cotton; **shelling** peanuts, soybeans, or sunflower seeds) linters=short fibers

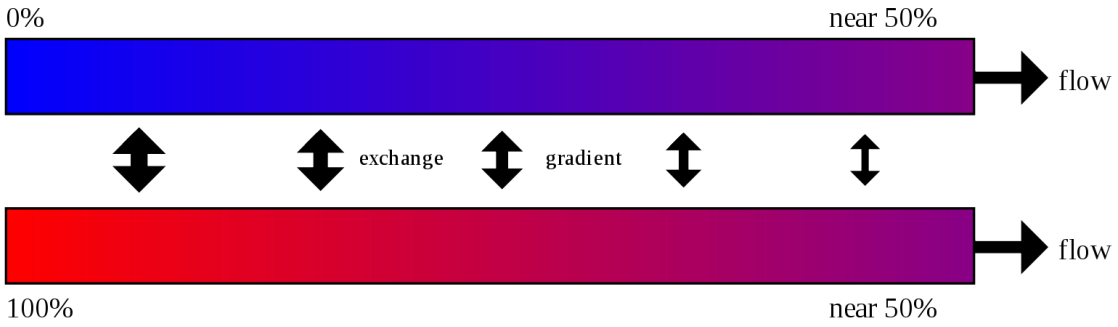
OIL EXTRACTION

Extraction by Expression

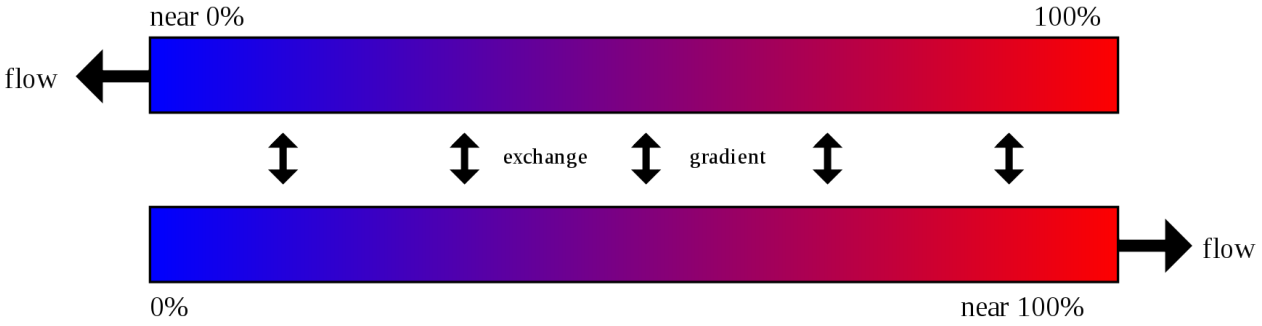
- Generally **screw presses** are used because they **afford a better yield than** the older **hydraulic presses**: they operate **at higher pressures** and **continuously**, not in batches, which is an added advantage.
- Prior to expression, **oilseeds rich in proteins undergo cooking** at around 90°C, which frees the oil by bursting cell structures, but also coagulates the proteins.
- Most often a **fast drying step** follows.

Extraction by Solvents

- It is *applicable to* **intact seeds** as well as *to* **seeds partially extracted** by expression.
- The solvent, generally **hexane** (bp 65°C), is added to the cleaned, hulled, and *rough-milled* seeds.
- An organic phase is recovered which is a **solution of the oil in the solvent** called **miscella**, and also a **solvent-soaked defatted meal**.
- **Industrial setups**: commonly have a **countercurrent design**. Oil recovery: 95 - 99%.



Concurrent Flow



Countercurrent Flow

Refining the Crude Oil

Crude oils obtained by distillation of the miscella may contain water, free fatty acids, lecithins, resins, pigments (carotenes, chlorophyll), sterols, waxes, substances with odors and tastes, and external contaminants (pesticides).

Refining includes the following sequence:

- **Degumming (**mucilage removal).
  - Its role is **to eliminate lecithins, proteins, and other constituents** present in the oil in colloidal suspension.
  - To accomplish this, **the hot oil is hydrated**, whereupon the **colloids form a dense gel which separates from the lighter oil**. The gel is discarded and the oil dried under vacuum.
  - In most cases, this treatment is replaced by an **injection of phosphoric acid into the hot oil**: the phospholipids then precipitate upon neutralization by sodium hydroxide;
- **Neutralization.**
  - The **free fatty acids**, always present in the crude oil, **are neutratized by dilute sodium hydroxide**.
  - *The soap* formed (soap stock) *adsorbs part of the impurities*: coloring matter, phenols, sterols, wax esters, traces of metals, and miscellaneous oxidation products.
  - The excess soap and sodium hydroxide are removed by washing with hot water

Refining the Crude Oil.

- **Bleaching.** This is done by **passing the oil through diatomaceous earths** or activated charcoal. The bleaching agent is removed by filtration.
- **Waxremoval.** From crude oils rich in waxes (sunflower, corn, cotton): **by cooling** (**winterization**): the crystallized waxes are removed by filtration.
- **Deodorizing.** The *aldehydes and ketones of unpleasant odor* are eliminated: **by injecting steam into the very hot oil** (200 °C) **under high vacuum**.

Subsequent treatments of the oils: mainly **in the food industry:** including **hydrogenation** and **interesterification** in the margarine industry

The **cattle cake** recovered is **treated** (solvents removed), and if needed **detoxified** and directed toward **animal feeding** (with some exception specific uses).

QUALITY CONTROL FOR LIPID-CONTAINING DRUGS: TESTS FOR FIXED OILS

- **Quality control for lipid-containing drugs** does not differ from that of other drugs: verification of **identity** and of the absence of **adulteration**, followed by the determination of the **fixed oil content**, are the main part of the assay, and are no major problem.
- **Quality control for the oil** itself is **more complex**: the purity check is required to include sophisticated analytical techniques to determine the **fatty acid composition**, the **glyceride structure**, and the **composition of the unsaponifiable fraction**.
- The principle behind the methodology is detailed and reviewed in specialized texts, **the methods themselves are standardized** (**by agencies** such as the *American Oil Chemist Society* = **AOCS**], or the *International Standardization Organization* [= **ISO**]), and they are applied mainly in the food industry.
- We shall cover here only a few basic concepts.

Determination of the fatty acid composition by GC

- It is *carried out on methyl esters* obtained by methylation subsequent to saponification or, more directly, by alkaline methanolysis.
- This method is by far the most often used for fat analysis.
- In *isothermal chromatography*, fatty acid esters are identified by their «**equivalent chain length**», i.e., the length of the **saturated fatty chain** that would have, in the same operating conditions, the same volume of retention as the fatty acid under study.
- This (non--integer) value is deduced from the relation between the **logarithm of** the **reduced retention volume** and the **number of carbon atoms** of the fatty acid (Rh. Eur. 5.0. 2.4.22.)

The *knowledge of the fatty acid composition* is not always sufficient to confirm the purity of the oil:

- **additional tests** are required, especially *the study of certain constituent*s of the **unsaponifiable fraction** which act as «**tracers**».

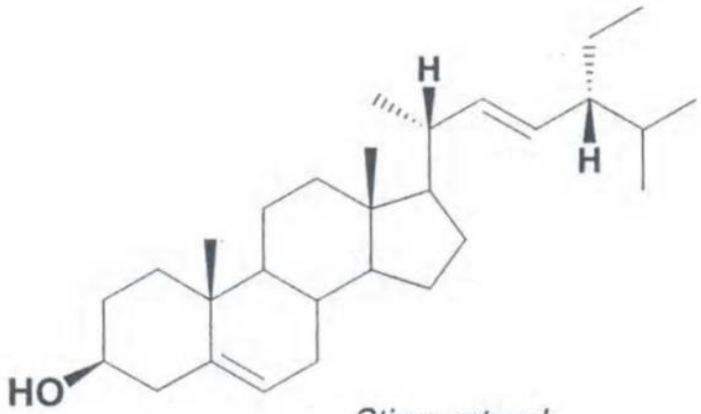
Test for unsaponifable matter

Unsaponifiable matter:

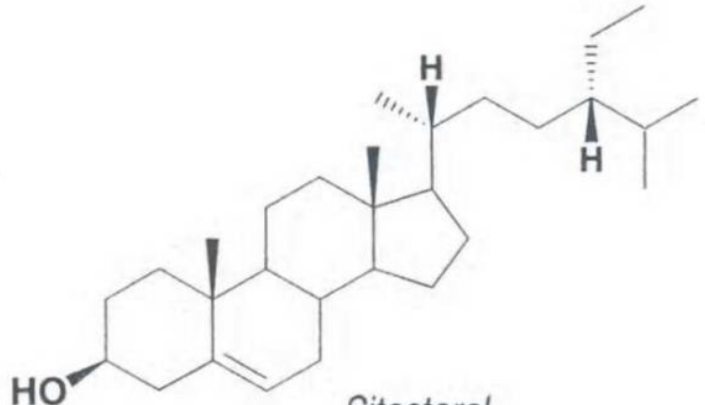
- **Main constituents:** saturated and unsaturated, aliphatic or tetraterpenoid **hydrocarbons** (carotenes), **sterols**, **triterpenoid alcohols**, **fatty alcohols**, **vitamins** (tocopherols, tocotrienols).

- **Sterols** are generally represented by two to five major sterols that are commonly Δ^5-sterols (sitosterol, campesterol, stigmasterol).
  - Their **composition** and their **ratios** are good **identity markers**: some sterols are specific (Brassicaceae **brassicasterol**) or their content is significant (**Δ^7-stigmasterol** in sunflower or safflower oil [Asteraceae]).
  - In most cases, sterol analysis allows the detection of illicit adulterations.
- Sterols are analyzed generally and tocopherols occasionally.
- In both cases, **preliminary extraction of the unsaponifiable matter** is necessary (with diethyl ether or hexane), and so is **separation**, which is straightforward **by preparative TLC**. The recovered **sterol fraction** is **analyzed** directly **by GC**.

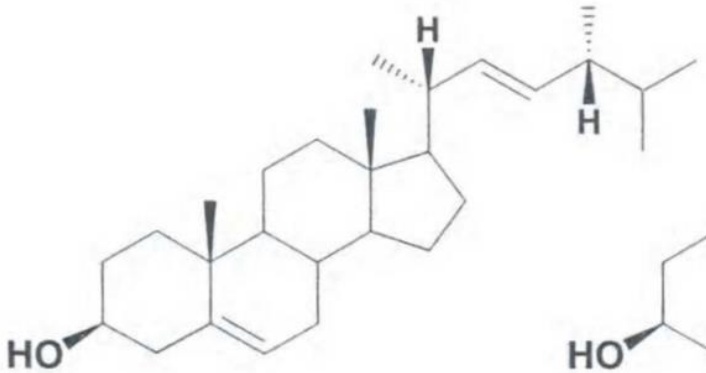
Major Sterols



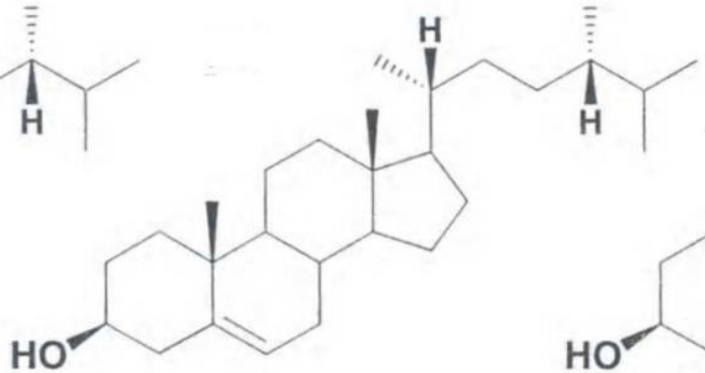
Stigmasterol



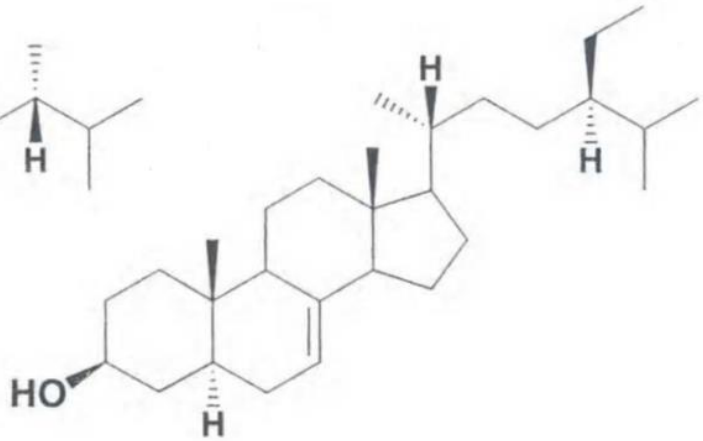
Sitosterol



Brassicasterol



Campesterol



Stigmastenol

Study of the glyceride structure

- It requires a **compromise between the complexity of the problem** (the number of possible combinations of glycerol and fatty acids) and **the need to do the work routinely.**
- This is accomplished by determining a simplified structure by classic chromatography:
  - **distribution of triacylglycerol molecular weights (GC);**
  - separation and **identification of the main triacylglycerols** by **Rp-HPLC**; separating triacylglycerols into groups as a function of their global unsaturation allows the detection of adulteration by other oils;
  - selective hydrolysis and **analysis of 2-monoglycerides**.

European Pharmacopoeia and Fixed Oils

Quality control of fixed oils listed in Ph. Eur. 5.0 includes **common assays** and, when relevant, **tests specific to the oil under consideration**.

Common assays

1. **Relative density** (2.2.5)

2. **Acid value** (2.5.1). This is the *number of milligrams of potassium hydroxide* needed *to neutralize the free acids* present **in 1 g** of substance. It is a **measure of the degree of alteration** of the oil or, if applicable, of the quality of the refining.

3. **Peroxide value** (2.5.5). This number expresses, in milli-equivalents of active oxygen, **the amount of peroxide** contained in 1000 g of substance.

4. **Unsaponifiable matter** (2.5.7).
   - This comprises the «substances that are not volatile at 100-105 °C and are obtained by extraction with an organic solvent of a solution of the substance of interest after saponification».
   - **In practice**, the saponification medium is diluted with water then extracted with diethyl ether; following washes and solvent elimination, the residue is weighed. The absence of significant amounts of fatty acids in this residue must be verified by acidimetry;

European Pharmacopoeia and Fixed Oils

5. **Foreign oils in fixed oils.**

- This test may be done by TLC (2.4.21), but the monographs that require it (all but that of castor oil) call for GC (2.4.22).
- **TLC** plates first developed in a petroleum ether solution of paraffin * are used.
  - **Sample solution** consists of the mixture of fatty acids from saponification, and the **reference standard solution** consists of the mixture of fatty acids from saponification of a 19:1 mixture of corn oil and rapeseed oil.
  - After TLC development, the **spots of fatty acids are visualized by iodine vapor.**
- **GC analysis** is not **applied to** the oil, but to the **methyl esters of its constituent fatty acids** (methylation by refluxing in anhydrous methanol under nitrogen, then pentane extraction of the fatty acid esters).
  - In parallel, on a reference standard solution of methyl esters is also analyzed. Evaluation: qualitative (equivaient chain length) and quantitative (integration, standard curve).
  - In each monograph, the Pharmacopoeia specifies the minimum and/or maximum levels of fatty acids normally contained in the fixed oil of interest.
  - A linear GC temperature program can also be used.

European Pharmacopoeia and Fixed Oils

6. **Most monographs** require, in addition, the determination of the following:

– **alkaline impurities** (2.4.19): neutralization of an acetone solution of the oil in the presence of bromothymol blue;

– **the refractive index** (2.2.6);

– **the saponification value** (2.5.6): this is the number of milligrams of potassium hydroxide needed to neutralize the free acids and saponify the esters present in 1 g of substance The shorter the fatty acid chains within the triacylglycerols, the higher the saponification value.

– **water** (2.5.12), when the oils are to be used in pharmaceutical formulations for parenteral administration. Water is determined by microquantitation and must be «not more than» a limit set for each monograph (0.05, 0.1, or 0.3%).

o In addition, the limits for the acid and peroxide values are lower in the case of oils for parenteral administration.

– **sterols** (2.4.23). After isolation of the unsaponifiable matter (2.5.7) and **separation** of the **sterol fraction by preparative** TLC (2.2.27), this fraction is **silylated for GC analysis** (2.2.28).

o Peaks identification: by **comparison with standards** (unsaponifiable matter of rapeseed and sunflower oils);

o **Betulin** (internal standard) is used **for quantitation** of the various constituents.

Almond Oil

Virgin almond oil (Ph. Eur. 5.0**):** is «the fatty oil obtained by cold expression from the ripe seeds of ***Prunus dulcis*** (Miller) D.A. Webb **var. dulcis** or ***Prunus dulcis*** (Miller) D.A. Webb **var. amara** (D.C.) Buchheim or a mixture of both varieties».

Refined almond oil (Ph.Eur.5.0). „obtained **by refining** of crude oil"

These Prunus varietas are very **widely cultivated around the Mediterranean**, but also in Iran and in the western U.S.

The **almond tree** is a Rosaceae with **white or pinkish flowers.**

Fruit : an **oblong drupe** with light green velvety epicarp;

Seed: oval, flattened, covered by **thin** and **wrinkly tegument**.

The seeds of the two varieties, **amara** and **dulcis**, are rich in oil (50-60%)

The **amara variety seeds** contain a cyanogenic glycosid, the gentiobioside of mandelonitrile: **amygdalin.**

Amygdalin hydrolysis yields two molecules of **glucose** and, by decomposition of mandelonitrile, **benzaldehyde** and **hydrocyanic acid**.

Amond Oil

Virgin almond oil

- **Fatty acid composition** (%): palmitic, 4-9; stearic, <3; **oleic, 62- 86; linoleic, 20-30**; linolenic, <0.4.
- **Unsaponifiable matter** (<0.7%):
  - Sterols: **sitosterol**, **Δ^5-avenasterol** (73-87% and >10% of total sterols, respectively); the cholesterol content is <0.7%, brassicasterol <0.3% (Eur. Ph.).
  - **α-Tocopherol** is dominant: 92-99% of total tocopherols.

Tests (Eur. Ph)**.**

- The common tests for oils.
- The composition of the sterol fraction and the fatty acid composition (and the absence of foreign fixed oils), determined by GC.

Uses

- **Almond oil**: **in cosmetology** and **dermatology.**
- **A fraction** of **low molecular-weight proteins associated with carbohydrates**: used in after-sun lotions, after-shaves, makeup removers, and so on.
- **Essential oil of bitter almonds :** used as a flavor (bezaldehyde), chiefly in food technology.
  - The **crude essential oil** obtained from the **cattle cake** by steam distillation is **treated with Fe_2SO_4** and **$CaCl_2$ to eliminate hydrocyanic acid**, then submitted to another steam distillation.

Refined peanut oil (Ph. Eur. 9.0)

Obtained from the shelled **seed** of a Fabaceae, ***Arachis hypogaea*** L., the peanut, also called arachis.

This species, **native to the South American tropics**, has been used since early times.

It is now one of the oilseed crops most cultivated on the planet, including in China, India, western Africa (e.g., Nigeria, Senegal, Sudan, Congo), the United States, and Indonesia.

This **annual herb** of modest size stands erect or lies down**.**

A curiosity is linked to its mode of **fructification**:

Flowers are produced aerially, fruit development occurs underground.

The gynophore, a support of the ovary, is capable of transporting the recently fertilized ovules into the soil.

Peanut: an **indehiscent pod** with bumps containing 1-3 seeds.

Seed: two oily cotyledons covered by a thin tegument of variable color.

The oil content of the kernel may exceed 50 %.

The cattle cake may be used as animal feed, as the protein content of the seed ranges from 20 to 50%.

Refined peanut oil

Refined peanut oil

- **Fatty acid composition** (%): *palmitic, 7-16; stearic, 1.3-6.5;* **oleic, 35-72**; **linoleic, 13-43**; arachidic, 0.5-3; eicosenoic, 0.5-2.1; behenic, 1-5; erucic, <0.5; lignoceric, 0.5-3.
- The wide ranges allowed by the Pharmacopoeia take into account the **variability** linked to the **geographical origin**: **African oils** contain far more **oleic acid (48-66%)** than the **South American oils**, which contain relatively more **linoleic acid (35-41%).**
- **Unsaponifiable matter** (<1%, Eur. Ph.1): **β-sitosterol** and **campesterol** (58-67% and 12-19% of total sterols, respectively), as well as **α-** and **γ-tocopherol** (42-65% and 30-52% of total tocopherols, respectively).
- **Oil for the preparation of parenteral formulations**: it must contain not more than 0.3% **water** and its **acid value** must be not more than 0.5%.

Hydrogenated peanut oil (Ph. Eur 9.0)used in pharmaceutical technology

- Fatty acids (%): **palmitic, 7-16**; **stearic, 3- 19**; **oleic and isomers, 54-78**; **linoleic and isomers, < 10**; arachidic, 1-3; eicosenoic, <2.1; behenic, 1-5; erucic and isomers, <0.5; lignoceric, 0.5-3.

Peanuts and derived products (meal, oil, butter) are among the most common **allergy-causing foods**.

Sometimes fatal (cardiac arrest, anaphylaxis), **peanut allergy is most often severe**: respiratory difficulties, edema of the larynx, eczema, and gastrointestinal symptoms.

Corn Oil

- During the starch preparation process, the steeped grains are separated from the germs prior to fine milling: **the germs** are recovered, and **may contain up to 20% lipids** (dried germs).
- **Virgin wheat-germ oil, Ph. Eur. 5.0:** „The fixed oil obtained from the germ of the grain of *Triticum aestivum* L. **by cold expression** or **by other suitable mechanical means**."
- **Fatty acid composition** (%): *palmitic, 14- 19; stearic, <2*; **oleic, 12-23; linoleic, 52-59; linolenic, 3-10**; eicosenoic, < 2.
- **Tests**:
  - **general tests** for oils
  - GC determination of the **brassicasterol level** in the sterol fraction. It must be **not more than 0.3%.**

Olive Oil

- **Virgine olive oil** (Eur. Ph. 5.0): „obtained by cold expression or other suitable mechanical means **from the ripe drupes** of ***Olea europea*** L.
- **Refined olive oil** (Eur. Ph. 5.0): „obtained **by refining** of crude oil”
- **Olive tree:** cultivated for its **edible fruits**, and secondarly for its **leaves** (Oleae folium, Eur. Ph. 5.0).
- Olives are ellipsoid **drupes** (1-3 x 1-1.5 cm) and their thin and smooth epicarp gradually turns from green to blackish-purple during ripening.
- This **epicarp** sorrounds a fleshy and **oily mesocarp**, which in turn sorrounds a **hard kernel** with sclerified endocarp.
- The fruit produced in the entire Mediterranean region are harvested either green (for the canning industry) or at a more advanced states of maturity (for the food and oil industry, generally small fruit varieties)
- **Fresh fruit:** water (40-45%), carbohydrates (10-20%), and **lipids (~ 30%).**

Production of Olive Oil

- The **sorted and quality-controlled olives** must be terated as expeditiously as possible to limit **hydrolysis**, and **enzymatic and microbial lipolysis** phenomena that are detrimental to the quality of the final product.
- Following a **wash**, the **olives are cruched** by millstone grinders or in disc mills, and **worked around 25-30 °C** in order for the oil to garther into large drops or into pockets of continuous lipidic phase.
- The **olive paste** then undergoes a **first expression** (disc press, continuous screw press, or continuous roller press).
  - Instead of expressing, it is possible **to fluidize the paste moderately with lukewarm water** and **to centrifugate** in order to separate the **oil**, the **aqueous phase** and the **solids** (the «foots»).
  - **The crude oil** – a mixture of oil and water – is **sieved,** then **clarified** by decantation or centrifugation **resulting virgin oil.**
- The **residual paste** may undergo a **second expression** and yield an oil that will require **refining** before becoming edible.
- The **solvent extraction** of the residual oi**l** gives a product which may only be used industrially.

Olive Oil

Fatty acid composition (% Eur. Ph. 5.0):
palmitic, *7.5-20*; *palmitoleic*, *<3.5*; *stearic, 0.5-5;* **oleic, 56-85; linoleic, 3.5-20**.

Unsaponifiable matter of virgine olive oil (<1.5%):
sterols, **tocopherols** (α-, 52-87%, β-, 10-25%, γ-, 7-23%), **triterpenes**, and **pigments** (carotenes, chlorophylls).

Tests

- The **Eur Ph. 5.0 monograph** specifies **limit percentages for five sterols**: β-sitosterol >93%, cholesterol and Δ^7-stigmasterol <0.5%, stigmasterol <campesterol <4%.
- The **absence of foreign oils** must be verified **by GC.**

Uses

- **Virgine olive oil** (Eur. Ph. 5.0): **:**
  - as a **choleretic or cholagogue**,
  - as a **mild laxative** (traditional uses);
  - as a **demulcent and emollient,**
  - as a **solvent for drugs (externally)**.
- **Refined olive oil** (Eur. Ph. 5.0)**:** solvent **for parenteral preparations**.

Castor Oil, Virgin

„Fatty oil obtaine by **cold expression** from the seeds of *Ricinus communis* L.” (Ph. Eur. 5.0)

- Castor is **a herbaceous or arborescent Euphorbiaceae** which is annual or perennial, depending on the climatic conditions.
- Probably **native to Ethiopia,** castor is a species that spread very rapidly: it has adapted wherever the climatic condions were favorable, from Africa to the south of the former USSR, and from the Mediterranean to eastern Asia. The same naturalization phenomenon took place in the New World after its introduction, probably by African slaves.
- Wherever it is cultivated (India, China, Brazil), the dwarf varieties are exploited for the purpose of of oil production.

Castor Oil, *Ricinus communis* L.

- The **stem** is branchy and bears large **palmitolobate leaves** (5-12 lobes), the petiole and underside of which are, in some varieties, purple.

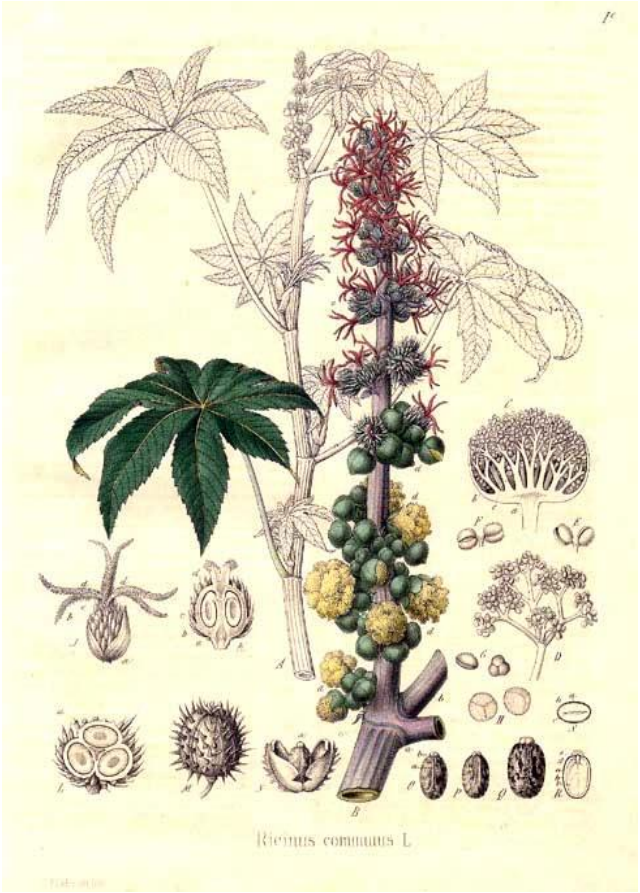
Flowers are grouped in racemes of cymes;

- the **male flowers** have noumerous stamens with branched filaments;
- the **female flowers** have a carpellate ovary and long reddish styles.

The fruit is a tricoccous capsule with multiple types of dehiscence, armed with spikes (although there are inerm varieties).

The seed, „castor bean" (8-12 [18] x 4-9 [12] mm), generally has a smooth and shiny tegument, most often gray marbled with red, black, or brown.

- A fleshy prominence, the caruncule, prolongs the top extremit;
- the raphe forms a very visible ridge on the ventral face.



Castor Oil

Chemical Composition

- **Castor seed**
  - little water, 15-20% **proteins**, and 40-60% **lipids**.
  - **ricin**: a toxic glycoproteinic lectin; **ricinine:** a cyano derivative of pyridone.
- **Castor oil** has a very peculiar composition, in that its **major constituents** (90%) are **triacylglycerols containing ricinoleic acid**→ an unsaturated and hydroxylated C_{18} fatty acid: (R)-(+)-12-hydroxy-Z-octadec-9-enoic acid. The other castor oil fatty acids are also C_{18} compounds: oleic (3%) and linoleic (3-4%).
- Castor oil is a dense, viscous, and non-drying oil.

Uses

- **Virgin castor oil**: as a **laxative** (it is a drastic cathartic)
- **in pharmaceutical technology**
  - **Polyethoxylated castor oil** (Macroglycerol hydroxystearate, Ph. Eur. 5.0.): a vehicle for parenteral preparations, it can induce anaphylactic-like reactions !
  - **Hydrogenated polyethoxylated castor oil** (Macroglycerol ricinoelate, Ph. Eur. 5.0.).

Castor Oil

Uses (cotinued)

- It is above all **an industrial product**: it is used directly **to manufacture resins** and it **can** also **be converted**.
- **Its hydrogenation product** is a major constituent of **lubricating greases** (lithium 12-hydroxystearate).
- The **«dehydrated» oil** (dehydrated by acidic catalysis) is **used to make resins**.
- Oil **cracking products**: **undecylenic acid** and **heptanal** (a starting material for textile polyamides Rilsan ®} and **polyol esters** [aviation turbine oils]).
- In addition, it is used to obtain surfactants, waxes, varnishes, inks, resins, and electrical insulation coatings, as well as for the preparation of various synthetic intermediates.
- **Undecylenic acid** has been used as **an antifungal agent** and may be used as a **preservative in cosmetic formulations**.

Castor: a Toxic Plant

Ricin is an **extremely dangerous toxin**. It is **a glycoprotein consisting of two subunits, A and B.**

First, subunit B links the toxin to cell membranes sites that have galactosyl residues, then the A chain, an enzyme, can enter the cell by endocytosis and **inactivate the 28S subunit of ribosomes**, thereby **blocking protein synthesis**.

Parenteral administration of a few tens of micrograms of **ricin** can kill (**LD5O** [mouse, IP] = **0.1 µg**).

Although ricin seems **far less toxic per os**, the ingestion of seeds **can cause gastrointestinal symptoms**, the severity of which varies mainly as a function of the number of seeds ingested and whether or not they were chewed (in two of the three case reports published in 1997 about adult patients, 10 to 15 seeds were chewed).

Persisting **digestive troubles** (vomiting, diarrhea) can lead to **dehydration** with subsequent onset of **neurological symptoms**.

Intoxication by castor beans, especially in young children, **makes hospitalization absolutely necessary** (toxin removal, control of electrolytes). **Death is exceptiona**l.

In industrial settings, it is **important to clean up**, **at every procedural step**, the dusts that are carriers of the allergenic principles.

Sesame oil, refined; Sesami oleum raffinatum (Eur. Ph., 5.0)

«Obtained **from the ripe seeds of *Sesamum indicum*** L. by **expression** or **extraction** and subsequent **refining**, (it) may contain a suitable antioxidant» (Eur. Ph., 5.0)

Sesame is **a very rugged Pedaliaceae**

- dispersed very early on from Africa to India and Asia.
- **An annual herb** of modest size (0.6-1 m),
- flowers with a **white or pinkish bilabiate corolla**,
- **bilocular ovary** leads to **a capsule with four locules** containing
- numerous **small oval seeds** (<3 mm) which escape spontaneously at maturity.

A largely exploited oil crop but its consumption remains local (the exportation non-existent).

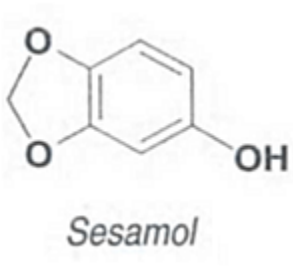
Major producers are **Asian** (China, India, Mynamar), **African** (Sudan), or **American** (Mexico). The world production is **2.7 million metric tons** of seeds [1997])

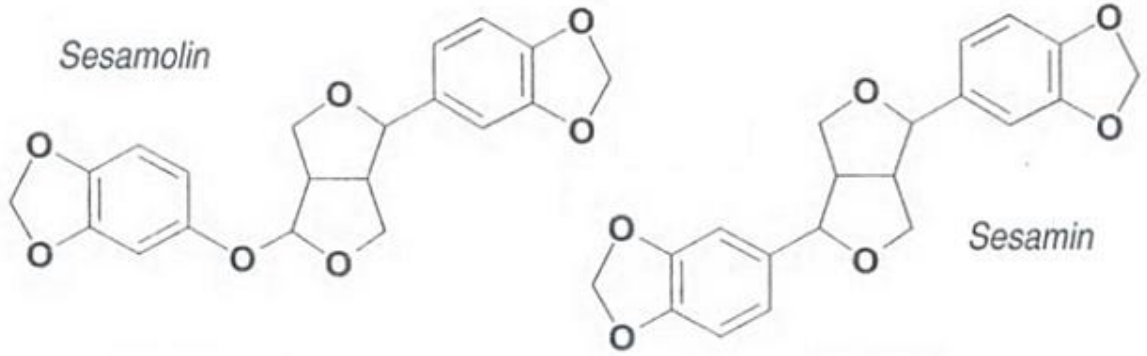
Sesame seeds: 40-50% **lipids**, 20% carbohydrates, and 20-25% proteins.

Sesame Oil, Refined; Chemical Composition

- **Fatty acid composition** (%): *palmitic, 7-12; stearic, 3.5-6*; **oleic, 35-50**; **linoleic, 35-50**.
- **Unsaponifiable matter** (**<2%** [Eur. Ph., 1998]) contains:
  - **sterols** (campesterol [18-19%], stigmasterol [6-7%], **β-sitosterol** [59-62%], Δ^5-avenasterol [10-11%]),
  - **tocopherols** (**γ**- and **δ**-tocopherol [83% and 11% of total tocopherols, respectively])
  - diarylfuranofuranic **lignans**, including **sesamin** and **sesamolin** (up to 0.5% of each)
  - **sesamol**, sesamolinol: **antioxidant phenols** formed from sesamolin during industrial refining

Sesamol allows the detection of sesame oil in other oils: it **gives a color reaction with furfural in acidic medium**.





Uses

- **Sesame oil, refined:** as a mild laxative**;** as a drug solvent
- **An extract enriched in unsaponifiable matter** (lignans): as an **antioxidant** and radical scavenger in cosmetics industry.

SOYBEAN OIL

The refined fatty oil obtained from seeds of ***Glycine soja*** Sieb. Zucc. and ***Glycine max*** (L.) Merr. (G. hispida (Moench) Maxim)».

- Soybean, ***Glycine max*** (L.) Merr., is a **Fabaceae** which **only** exists **in culture**;
- it is very close to ***G. soja*** Siebold & Zucc. which is probably its **wild ancestor**.
- It is a **small herbaceous annual plant**, with
- **trifoliolate leaves**, with oval and pubescent folioles.
- The **fruit is a pod**; brown, bumpy, and very fuzzy,
- it contains 1-4 **ovoid to spherical seeds** of variable color.

Soybean: origin, penetration and production

- It is originate possibly from the Australian continent from where migratory birds introduced it into China.
- It has undoubtedly been used for a long time in Asia, especially
  - as **«milk» (t*onyu*)** obtained by steeping and grinding the seeds, followed by boiling and sieving, and
  - as **tofu**, a kind of «cheese» arising from the coagulation, draining, and pressing of *tonyu* (traditionally; the industrial preparation entails ultrafiltration and in-line coagulation).
  - Tofu is consumed fresh, cooked (fried), or fermented (*sufu*); it can be sterilized (UHT or ultra high temperature) or pasteurized.
  - The Orientals also consume **fermentation products** obtained by inoculating pounded seeds (*tempeh, miso, natto*) as well as **«sauces»** such as *shoyu*, which are protein hydrolysates rich in glutamic acid.
- Soybean became known rather late in Europe and its culture in the United States started at the beginning of the twentieth century.
- The market for this oil crop—the most important one in the world—is largely dominated by the United States (74 million t in 1997); Brazil, China, and Argentina are also major producers, far ahead of India and Canada.

Soybean Seed and Oil

Soybean seed contains:

- 15-35% **carbohydrates** (mainly insoluble fibers),
- 35- 40% **proteins** containing a fair amount of **essential amino acids**, and
- 15-20% **lipids** (2-3% phospholipids).
- **Saponin glycosides** with a triterpenoid aglycone, thermolabile **antitrypsic factors**, and **phytic acid** at a high concentration.

Fatty acid composition of the oil (major fatty acids, %, Eur. Ph., 3rd Ed.): *palmitic, 9-13; stearic, 3-5;* **oleic, 17-30; linoleic, 48-58; linolenic, 5-11**; arachidic, gadoleic and behenic, <1.

Usaponifiable matter

- **sterols**: β–sitosterol (47-59%), stigmasterol (17-19%), campesterol (19-23%), Δ^5-avenasterol (2-4%), Δ^7-sterols (2-4%)
- **tocopherols**: y- (44-60%), δ- (30-43%), α- (5-10%), β- (2-3%).

Tests. Determination of the customary values, unsaponifiable matter (<1.5%), and **brassicasterol by GC** (<0.3%).

SOYBEAN OIL, USES

Soybean oil, refined (Eur. Ph., 5.0) is used in pharmacy **for parenteral feeding** (for caloric intake and essential fatty acid intake).

- The formulation is a 10 or 20% 0/W emulsion which provides 1,100 or 2,000 kcal/L;
- the administration must be by slow infusion under medical observation; the **adult posology** is **1-3 g/kg/day**.

Soybean oil, hydrogenated (Eur. Ph., 5.0) , it is **a white mass** (MP 66-72 °C) mostly composed of triglycerides of **saturated fatty acids**: stearic acid (79-89%) and palmitic acid (9-16%).

The main use of soybean oil is, of course, **dietary.**

Soybean Proteins

Soybean is an important source of proteins:

- the **cattle cake** is used **for animal feeding**,
- **meals** (protein content = 45 to 65%), **concentrates** (65 to 90%), and **isolates (**over 90%) are becoming more common **as meat substitutes** (vegetable protein hamburgers).
- This use of soybean proteins has **healthful benefits**: it has long been known—a meta-analysis published in 1995 clearly demonstrated it—that **substituting soybean proteins for animal proteins** (average consumption 47 g/day) induces a decrease in triglycerides (—10.5%), total cholesterol (—9.3%), and LDL-cholesterol (—12.9%), without altering HDL-cholesterol.
- Because of a **good biological value** and because the **absence of toxicity** has been documented by secular use of soybean products in Asia, many experts recommend blending these proteins into **diets designed to control hypercholesterolemia**.
- This advice is well accepted because **proteins incorporated in «classic» foods do not have the peculiar taste and bitterness** that are hard for western consumers to accept.

Soybean Lecithins

Soybean is currently the chief source of lecithins used in food technology.

Since **crude lecithin** from degumming generally **contains 60-70% lecithins and 30-40% soybean oil**, products are preferred that have undergone one or several **treatments**:

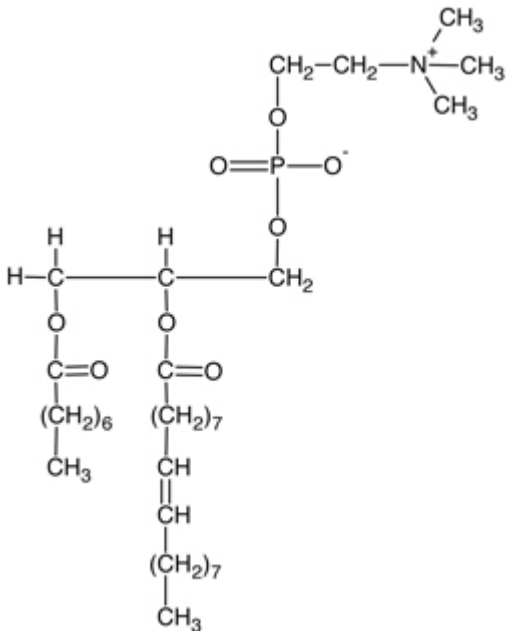
purification, **defatting** (low viscosity products), **modifications** (to obtain more hydrophilic products), **fractionation** or **hydrogenation.**

In pharmacy, **lecithin yields liposomes** and can help formulate stable emulsions.

Its **main outlet is food technology** (Eur. id. code E322), including the industry of margarine (20 g/kg), chocolate, cooked cereals, and instant products (a **lecithin film** allows rapid and lump-free reconstitution of a dehydrated product rich in lipids); it is also a **good lubricating agent** (facilitates removal of food from a mold).

Some countries authorize the use of **artificial lecithin obtained by glyceride hydrolysis of hydrogenated rapeseed oil** and subsequent phosphorylation and neutralization by ammonia**.**

- The diacyl ester of glycerol 3-phosphate is also known as a **phosphatidic acid**, and is the basis of **phospholipid structures**.
- In these structures, the phosphate is also esterified with an alcohol, which is usually choline, ethanolamine, serine, or *myo*-inositol, e.g. **phosphatidyl choline.**
- **Phospholipids** are important structural components of cell membranes, and because of the polar and non-polar regions in their structure, they have detergent-like properties.



Soybean, Other Emulsifiers

Monoglycerides. These amphophilic compounds arc prepared by transesterification between a triacylglycerol and glycerol at 200-250°C in the presence of sodium hydroxide. The starting materials are cottonseed oil and sunfiower oil, as weil as hydrogenated animal fats. Distillation of the reaction mixture under vacuum separates the more volatile monoglycerides.

Fatty acid mono- and diglycerides are used directly (Eur. id. code E471), or as esters (acetate, iactate, citrate, and so on: E472a-f), as ester sugars (E473), as glyceride sugars (E474), as polyglyceric esters (E4'is), and so forth.

Also used are monostearates and the monooleate of **sorbitan** (**Spans**®), as well as their polyethoxylated derivatives (**Tweens** ®).

Highly esterified ester sugars (hexa- to octaesters) are a possible substitute for fats in low-fat foods (Oiestra®).

Rapeseed Oil

Rapeseed, ***Brassica napus*** L., var. oleifera (Brassicaceae) is the natural (amphidiploid) hybrid of two cabbages *(B. campestris* x *B. oleracea* L.);

- it is a herbaceous annual plant with
- **ramified stems**, **waxy leaves**,
- racemes of **tetramerous yellow flowers**,
- **dehiscent siliques**.

Essentially all cultivated varieties are winter forms with long rosette phase (cycle from September to July).

Rapeseed Oil

- Normally, **the oil** obtained from the seeds **contains about 45% of** a C_{22} unsaturated fatty acid, **erucic acid ($C_{22.1(13)}$).**
- Since animal experiments have indicated a potential for **myocardial toxicity for this acid**,
- breeders have **optimized varieties devoid of erucic acid**, and also devoid **of glucosinolate**s—these impart to cattle cake some undesirable properties for non-ruminants—or, more precisely, fulfilling European standards.
- Effective in 1990, European standards set the **maximum erucic acid concentration in the oil at 2%** and the **maximum giucosinolate concentration in the defatted cattle cake at 35 µM/g**; the latter limit was later lowered.
- The **oil** is extracted **by expression after hulling and cooking**. The **residual cattle cake oi**l is recovered by hexane extraction.
- Solvent removal from the cattle cake (by steam) eliminates the volatile products of glucosinolate decomposition.
- The yield is approximateiy 40 kg of crude oil/100 kg of seeds. Major producers: China, India, Canada, France, Germany, United Kingdom.

Rapeseed Oil

Refined Rapeseed Oil (Eur. Ph. 5.0)

- Obtained from the **seeds** of ***Brassica napus*** L. and ***B. campestris*** L. by mechanical expression or by extraction. It is then refined".
- ***Fatty acid composition*** (%): palmitic, 2.5-6; stearic, <3.0; **oleic, 50-67; linoleic,16-30; linolenic, 6-14**; **erucic, <2.0**.
- **Unsaponifiable matter: rich in sterols** (530-790 mg/100 g, in major part β-sitosterol and campesterol) and **in tocopherols** (up to 90 mg/100 g, γ- and α-tocopherol, 2/3-1/3).

High Erucic (Acid) Rapeseed

- Rapeseed varieties rich in erucic acid (50% of the oil).
- This oil and erucic acid are used **to prepare additives** (plastics industry), **detergents, lubricants** stable at high temperature, and more.
- Other Brassicaceae seed sources: ***Crambe abyssinica*** Hochst. Ex R.E. F (erucic acid, 55% of the oil). **Nasturtium.**

Rapeseed and Diester

Treating rapeseed oil with methanol yields a product, the diester, which may be incorporated in fuel oil industry products.

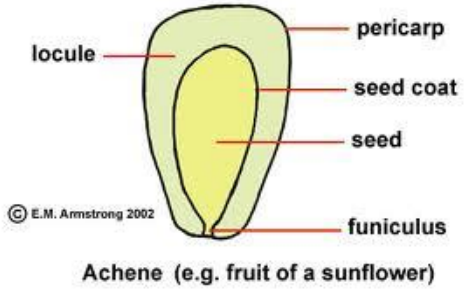
SUNFLOWER OIL

The sunflower, *Helianthus annuus* L., is an Asteraceae from North America.

It is characterized by its **large capitulums**, whose **receptacle** may bear 2,000 tubular flowers, by its large **cordate leaves**, and by its **angular akenes**.

It has continually been optimized: **oil** content **reaches 50%** / **single-stalk plants** (wild sunflower is ramified)/ **akenes with a thin hull**.

Chief world producers: the United States, far behind Argentina, Russia, Ukraine, and France [1996 world production: 25 million t].



Achene (e.g. fruit of a sunflower)

Fatty acid composition (main fatty acids , %):

Palmitic, 3-10; stearic, 1-10; **oleic, 14-35**; **linoleic**, **55-75**; linolenic, <0.3.

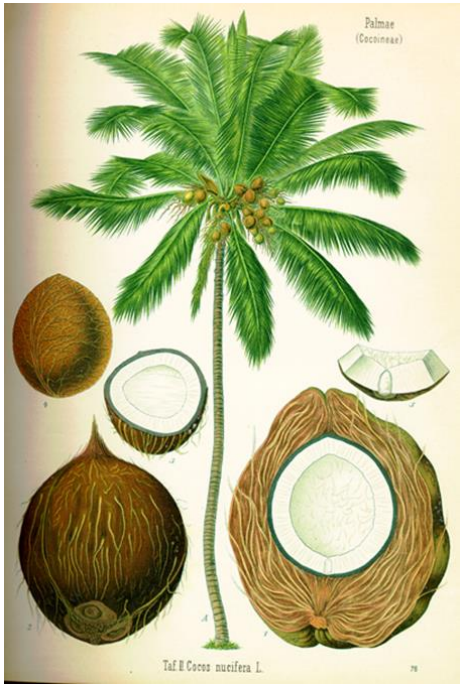
Trilinoleate (LLL) and oleodilinolein (OLL) each represent about 1/3 of the triacylglycerols.

Unsaponifiable matter:

Sterols: **β-sitosterol** (60%), alongside Δ^7-stigmasterol (7-14%) and Δ^5-avenasterol (4-6%). Tocopherols: **α-tocopherol** almost exclusively.

Uses : Seed in the oil industry; Defatted (aleurone) meal in dietetic products.

Coconut palm, *Cocos nucifera* L.



- The coconut palm is **a lignified plant** with the habit of a tree:
- its **straight stipe** bears **a spiral rosette of leaves** that only appear compound (they are in fact divided into segments through tearing).
- The **fruit** is a **large drupe** with **hard endocarp** and **fibrous pericarp**.
- The **seed and its endocarp** are the commercial **«coconut».**
- The **seed albumen** is in part **liquid**—hence its name, **coconut milk**—and in part **solid**—this is **copra.**
- **Dry copra** contains **about 65% lipids**.
- In temperate regions, **copra oil** is a **«concrete oil»**: **below 25-27 °C** it forms a white, tasteless, and odorless mass.

Coconut palm, Uses

Copra

- to obtain **semisynthetic glycerides** (in pharmacy),
- as a **dietary product** (Végétaline ® in France)
- to produce **detergents of the lauryl-sulfate type** (an industrial product).
- In countries where coconut palms are cultivated (Africa, southeast Asia) they yield many other products: cattle cake, palm wine, vegetable charcoal, and the fibrous pericarp called coir made into brooms, brushes, rugs, ropes, and more.

Medium-chain Triglycerides (Ph. Eur. 5.0).

- They are «obtained from the oil extracted from the **hard**, dried **fraction of the endosperm** *of* ***Cocos nucifera*** L. or from the **dried endosperm** of ***Elaeis guineensis*** Jacq.
- They consist of ***a mixture of triglycerides of*** *saturated fatty acids* (> 95% of C8 and C10 fatty acids).
- **Fatty acid composition:** caproic acid (C6), <2%; **caprylic acid** (**C8**), **50-80%; capric acid** (**C10**)**, 20-50%;** lauric acid (C12), <3%; myristic acid (C14), <1%.

OIL PALM, *Elaeis guineensis* Jacq., E.oleifera (Kunth) Cortés

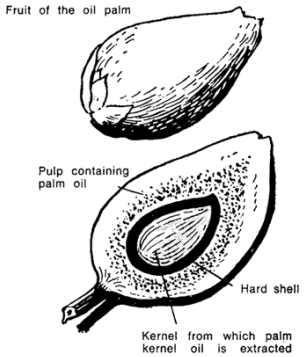
This species is a **tall palm** (15-30 m) with **reddish fruits** gathered into ovoid «bunches» of 1,000 to 2,000 **plum-size drupes**;

It is **cultivated in** southeast Asia (**Indonesia, Malaysia**), as well as in Africa (**Nigeria, Zaire, Cameroon**), and in South America (**Brazil**).

Palm oil. The **ripe fruits** are expressed (the mesocarp contains 65 to 70% lipids).

Palm kernel oil. The **nut** = **the seed surrounded by the endocarp**, is pressed or extracted with solvents.

These oils, like copra, **are solid in temperate climates; with a deep color due to carotenoids**; sometimes are called **«red oil».**



OIL PALM

Chemical composition (major fatty acids, %):

1- *copra*					
caprylic :	5-10	capric :	4.5-8	lauric :	43-51
myristic :	16-21	palmitic :	7.5-10	oleic :	5-10
2- *palm kernel oil*					
caprylic :	2.4-6.2	capric :	2.6-5	lauric :	41-55
myristic :	14-18	palmitic :	6.5-10	oleic :	12-19
3- *palm oil*					
myristic :	0.5-2	palmitic :	41-47	oleic :	36-44
linoleic :	6.5-12	stearic :	5.5-6		

- The **unsaponifiable matter** of palm oil is high in **carotenes** (0.5-0.7 g/kg of oil) and its tocopherol fraction contains over 80% **tocotrienols**. These tocotrienols are also characteristic of the unsaponifiable matter of copra oil.
- The main **uses of paim oil** are **in the margarine and soap industries**.

PUMPKIN, *Cucurbita pepo* L., Cucurbitaceae

- Pumpkin seeds were official until the beginning of the twentieth century.
- They have long been used for their vermifuge properties (a taenicide proprietary product based on pumpkin seeds used to be marketed in France until the early 1980s).
- For a few years now, some European countries have been marketing the oil of **pumpkin seeds** as a drug **treatment for benign prostate hypertrophy**.

- This large **annual plant** with procumbent stems is characterized by
- **large leaves** covered with stiff hairs, ramnified tendrils,
- large (5-10 cm), pentamerous, unisexual (two pairs of fused stamens + one; three-carpellate ovary), gamopetalous, **yellow flowers**, and by a
- **humongous berry** containing a large number of **seeds within a spongy pulp**.
- The **seed** is flattened (15-20 x 8-10 x 2-3 mm) and whitish. It is tapered at one end and has a rounded rim.

PUMPKIN

- Pumpkin seeds are rich (**30-50%**) in **unsaturated oil** (43-55**% linoleic acid**).
- The **vermifuge** properties of the seed are attributed to a cyclic amino acid: 3-amino-3- carboxypyrrolidine (0.4-0.8%).
- It is the **sterol composition of the unsaponifiable matter** that has retained the attention of chemists.
- **Chief constituents**

– **Δ^7-sterols and their glycosides**: spinasterol glucoside, 24β-ethyl-5α-cholesta-7,25(27)-dien-3β -ol 3-*O*-(β -D-glucopyranoside), and the corresponding 7,22*E*,25(27)-trien-3β -ol; they occur alongside

– **Δ^5-sterols** (cierosterol, isofucosterol, stigmasterol, campesterol), **squalene**, and others.

- **The activity of pumpkin seeds** on the symptoms linked to benign prostate hypertrophy is **attributed to the 7-sterols**, but its mechanism is not known and there are few published clinical studies.
- **The use of pumpkin oil** is an ancient and current practice **in Germany**, and in other **countries of central Europe**, and Commission E approves the use of the seed, while specifying that is merely **a symptomatic remedy**.
- Pumpkin seed extract is sometimes combined with *Serenoa repens* extract.

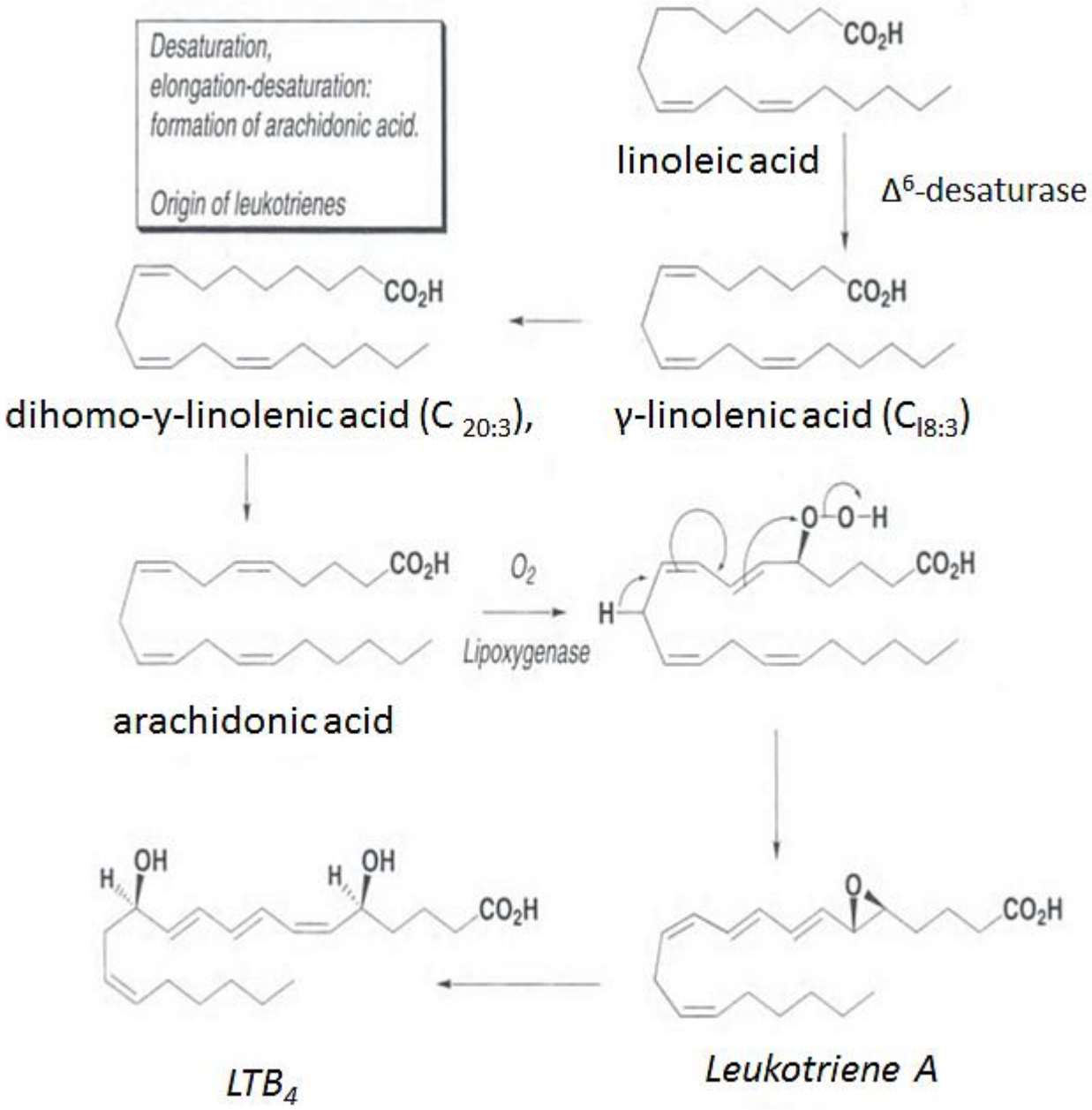
MISCELLANEOUS OILS,
A. Oils with y-Linolenic Acid

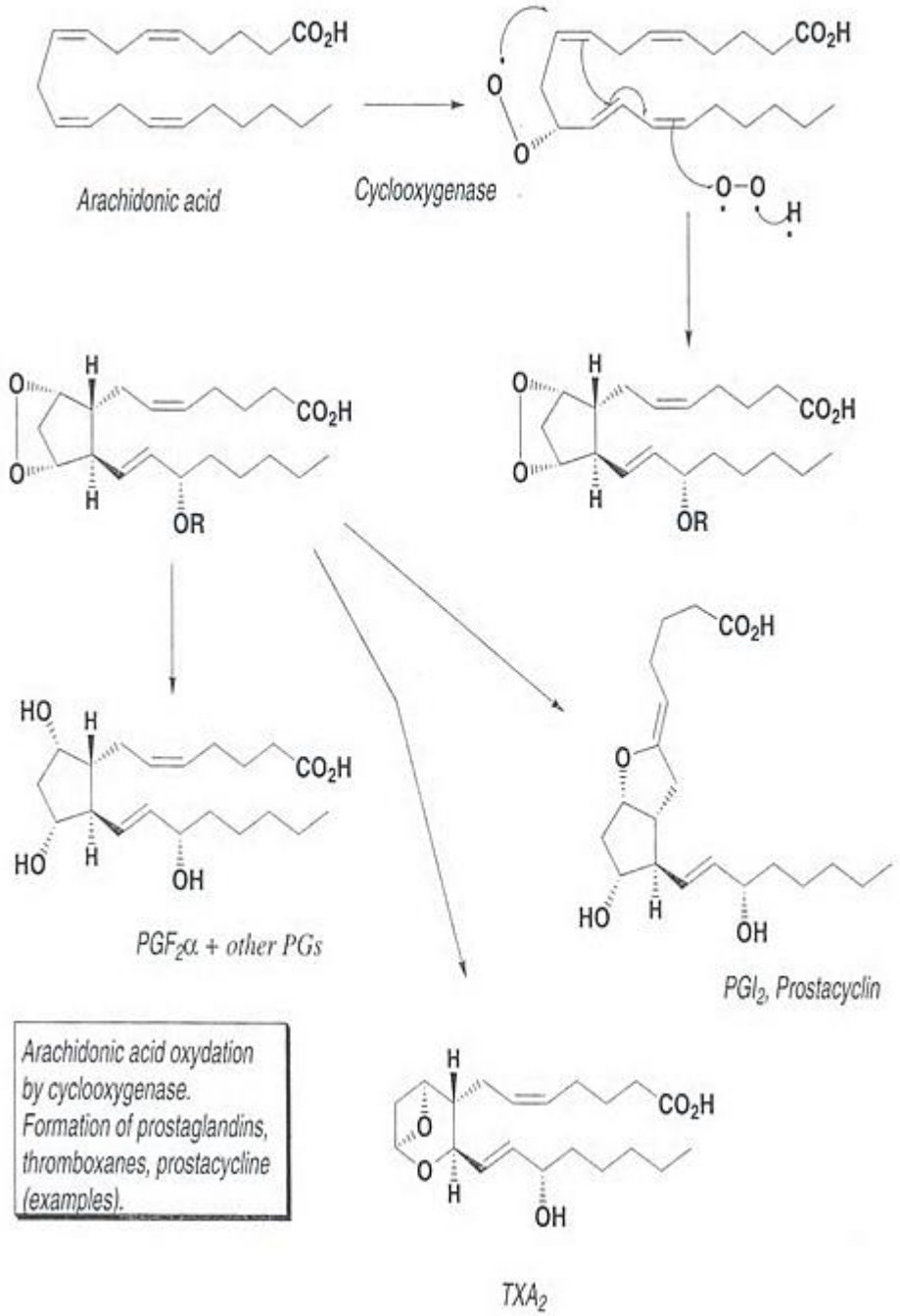
MISCELLANEOUS OILS, A. Oils with y-Linolenic Acid

- Fats are required nutrients, and it is generally accepted that they must constitute 30 to 35% of the daily caloric intake in a normal diet. Although fats provide a substantial amount of energy in a small volume, it must be noted that all the fatty acids that constitute them do not have the same role or the same worth.

Essential Fatty Acids (**= EFA**s)

- Some polyunsaturated fatty acids, indispensable
  - they are **not synthesized** by the human body (e. g. *linolenic acid*), or
  - are **synthesized in sufficient amounts** only by the young and healthy body (*arachidonic acid*).
- **EFAs have an important biological role:**
  - as **constituents of the phospholipids of cell membranes**, they may contribute to ensuring membrane fluidity;
  - they are also the **precursors of eicosanoids** (prostaglandins, leukotrienes, and thromboxanes),
  - eicosanoids have multiple known functions as **intra- and intercellular mediators**, and as **agents in platelet aggregation** or **in the inflammatory process**.
- The biosynthesis of these compounds involves arachidonic acid, which normally arises from the desaturation of linoleic acid to γ-linolenic acid ($C_{18:3}$) under the influence of a Δ^6-desaturase, followed by an elongation (dihomo-γ-linolenic acid [$C_{20:3}$]), and by a new desaturation leading to arachidonic acid ($C_{20:4}$). It is this acid which is the substrate upon which cyclooxygenase and lipoxygenase will act to form eicosanoids.


Desaturation,
elongation-desaturation:
formation of arachidonic acid.
Origin of leukotrienes
CO2H
linoleic acid
Δ6-desaturase
CO2H
γ-linolenic acid (C18:3)
CO2H
dihomo-γ-linolenic acid (C 20:3),
CO2H
arachidonic acid
O2
Lipoxygenase
O-O-H
H
CO2H
OH
H
OH
H
CO2H
LTB4
O
CO2H
Leukotriene A



Arachidonic acid oxydation by cyclooxygenase. Formation of prostaglandins, thromboxanes, prostacycline (examples).

Oils with y-Linolenic Acid

- Thus, **linoleic acid** is necessary regardless of age or health status, and the **need is estimated at about 6-8% of the caloric ration** and is satisfied by the consumption of vegetable fats.
- The same applies to the 0.5-1% of the caloric ration in α-linolenic acid indispensable for a balanced diet .
- **Linolenic acid deficiency** manifests itself by
  - **dermatological signs** (such as eczema lesions, impetigo, and erythema),
  - **delayed growth, hypertension**, and **poor platelet aggregation.**
- Certain factors may lead to a marked **decrease in Δ^6-desaturase activity**:
  - stress, aging, alcoholism, nicotine addiction, hepatic insufficiency, and diabetes mellitus, among others.
- **Diet** must then fulfill the **needs in polyunsaturated fatty acids**, especially
  - in **arachidonic acid**, present in **eggs** and **livers**, but absent in vegetable oils.
  - **α-Linolenic acid** is present in most vegetable oils, but
  - **y-linolenic acid** is much more **rare**. The most interesting **sources** appear to be **the seeds of black/red currant, evening primrose, and borage .**

EVENING PRIMROSE, *Œnothera biennis* L., Onagraceae

- The evening primrose is easy to identify by its **large ephemeral flowers** with
- **four yellow emarginate petals**,
- which **bloom at night**, hence the name (*Nachtkerze* in German).
- Originated **from North America**, this species **common in Mediterranean and Atlantic coastal regions**.
- **Cultivated in the United Kingdom for seed production.**
- The **seed**, **small** (1-2 x 0.5-1 mm) and **angular.**

EVENING PRIMROSE OIL

Evening primrose oil

- extracted **by cold expression** (25% of the seed)
- rich in unsaturated fatty acids:
  - **γ-linolenic acid (8-14%),** linoleic acid (65-80%), and oleic acid (6-11%).
- very **difficult to preserve**.

Uses.

- **in cosmetic products and toiletries**
- with the aim of **preserving skin elasticity and preventing wrinkle formation**.
- Modest results may justify its use **for cyclic breast pains**,
- Other proposed uses relying on contradictory and fragmented data (oral route).
  - breast pain, premenstrual syndrome, **hypercholesterolemia**, eczema, cirrhosis, rheumatoid arthritis, psoriasis, and more.

BORAGE, Starflower, *Borago officinalis* L., Boraginaceae

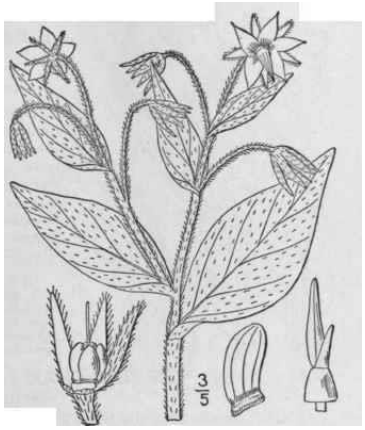
Borago officinalis oleum raffinatum (Eur. Ph. 5.0). Fatty oil **obtained from the seeds by extraction and/or expression**. It is **than refined**.

The **oil yield is uncertain**: *unsynchronized blooming / seed maturation* leading to loss of ripe seeds (nutlets!) before and during harvest.

The **oil content** varies **from 13 to 33%** depending on the mode of extraction and the degree of ripeness.

This is an unsaturated fatty acid-containing oil, with **linoleic acid** (30-40%), **oleic acid** (15-19%), and **γ-linolenic acid (18-25%)** dominating.

The **uses** of this *unstable oil* are **the same as those of evening primrose oil**; its efficacy in the indications that are claimed are just as controversial.



FLAX, *Linum usitatissimum* L., Linaceac
Lini oleum virginale Ph. Eur. 5.0

Flax is an **annual erect herb** with simple leaves that are alternate and lanceolate.

The **pentamerous blue flowers** stand solitary on slender ramifications of the stem.

The fruit is a **capsule** with ten 1-seeded locules.

“Fiber” flax varieties have been cultivated in Europe since ancient times.

Nowadays the so-called **“seed” varieties** are exploited (Canada, China, India).

They have multiple flowers on ramified stems.

They are shorter plants, therefore they are less vulnerable to being beaten down by the wind.

FLAX

Flaxseed or linseed, dried and ripe (Eur. Ph., 3rd Ed.)

- It is elongated, ovoid, flattened (4-6 x 2-3 x 1.5-2 mm), and rounded at one end.
- Its tegument is dark reddish-brown, smooth, shiny, and its surface finely punctuated (as seen through a magnifier).
- The external walls of the epidermis are mucilaginous.
- Swelling index: seed > 4, powdered >4.5.

Chemical Composition

Linseed

- **oi**l (35-45%), **protein**s (20-25%), and **mucilage** (6-10%);
- **cyanogenic glycosides** (linustatin, neolinustatin, traces of linamarin),
- **a glycoside of secoisolariciresinol**, and phenylpropanic glycosides.
- The **mucilage** can be fractionated into a neutral fraction—a ramified arabinoxylan composed of D-xylose, L-arabinose, D-glucose, and D-galactose—and an acidic fraction mainly composed of L-rhamnose and D-galactose.

Linseed oil is a highly unsaturated oil, therefore the ground seeds spoil in storage (oleic acid, 10-18%; linoleic acid, 23-24%; **α-linolenic acid**, 35-50%).

FLAX, Proprties and Uses.

The occurrence of mucilage justifies the use of linseed **as a bulk laxative.** The seeds must be taken with a sufficient quantity of fluids to avoid any risk of obstruction of the digestive tract.

Folk medicine traditionally mixes **linseed powder** and mustard seed powder to **manufacture cataplasms**.

The German Commission E monograph acknowledges that the drug is **capable of increasing the volume of the bowel contents**, therefore it **stimulates peristalsis**, and it **protects the mucous membrane in case of inflammation** (colitis).

The oil, a source of calories (1 g of seeds = 4.7 kcal).

The occurrence of **cyanogenic glycosides does not preclude the consumption of the seeds**. Although these are not food, they are approved in France, **as long as their level does not exceed 5%,** for incorporation in specialty breads and crackers.

The **hormonal symptoms** observed in women who consume linseed daily have been **attributed to phyto-estrogens**, namely enterodiol and enterolactone.

These compounds are thought to **arise from the degradation of secoisolariciresinol glycoside** by the flora of the colon**.**

They are lignans which exert an **antitumor effect** *in animals* (e.g., decrease in tumor induction by benzanthracene).

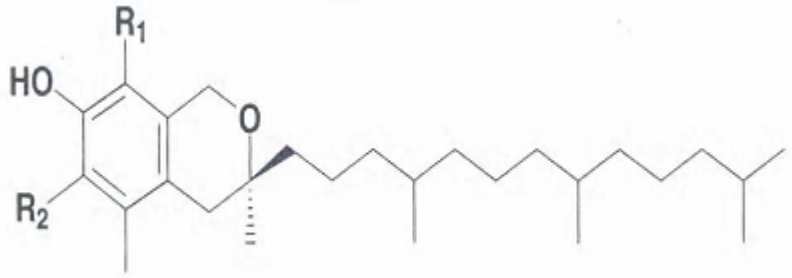
Tocopherols

$R_1 = R_2 = CH_3$: α-*Tocopherol*

$R_1 = CH_3$, $R_2 = H$: β-*Tocopherol*

$R_1 = H$, $R_2 = CH_3$: γ-*Tocopherol*

$R_1 = R_2 = H$: δ-*Tocopherol*



Tocopherols = Prenylated benzodihydropyrans

Tocopherols and **tocotrienols** are distinguished by their lateral chain saturated or unsaturated, respectively;

in either series the position and the nature of the substituents define **four different compounds** (α, β, γ, δ).

Homogentisic acid is their **biosynthetic precursor**

The tocopherols = vitamin E, a **natural antioxidant**, especially for fatty acids, are **highly oxidizable**: form an epoxide first, then by opening and dehydration, a p-quinone. Oxidized vitamin E is then reduced by ascorbic acid.

The normal consumption of oils, margarines, and cereals easily fulfill the daily needs (10-12 mg/day). A maximum safe dose is 40 mg/day.

Tocopherols

Thouhg lipoprotein oxidation might play a role in atherogenesis, studies fail to show a significant correlation between vitamin E intake and the risk of coronary disease.

Vitamin E might have a protective effect during the early phases of carcinogenesis induction (digestive tract, lungs).

Tocopherol acetate indications

- **vitamin E deficiency** (treatment, prevention)
- proposed by some authors:
- **urinary incontinence in women** and **progressive myopia**;
- **patients with high blood lipoproteins** who are not eligible for treatment to lower blood lipids (as an adjunct; debateble)

Tocopherol acetate, further uses

in small doses: in dozens of proprietary drugs, overthe-counter drugs, and **dietary supplements**, in combination with other vitamins, flavonoids, fish oil, minerals, and more.

Tocopherols

As authorized antioxidants **in food technology**: natural extracts (Eur. id. code E306) or synthetic tocopherols (α, β, γ, δ, E307—9).

as antioxidant often combined (for synergy) with ascorbic acid: **in pharmaceutical technology**

PRUNUS AFRICANA, Kalkm., Rosaceac

This *African forest species* grows mostly in mountain areas with heavy rainfall.

It is a tall ever green tree, which may reach 30 m,

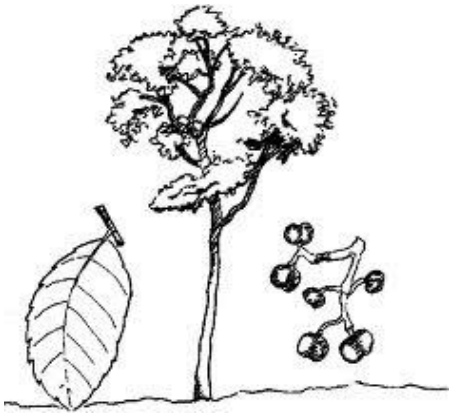
with elliptic, weakly acuminate, thick, and coriaceous leaves.

Flowers: small, white, and pentamerous.

Fruit: tough red akene with a depression at the top

The drug consists of the bark: red or dark brown, it smells weakly of hydrocyanic acid.

The product most commonly used is **a lipid and sterol extract obtained by organic solvent extraction**.



PRUNUS AFRICANA, Cheimical Composition

The lipid and sterol extract obtained by organic solvent extraction

- It contains a **lipid fraction** (C_{12-24} fatty acids),
- **phytosterols** (free and conjugated β-sitosterol, campesterol),
- **triterpenoid pentacyclic acids** (ursolic, oleanolic, and their homologs di- or trihydroxylated at C-2, C-3, and/or C-24, sometimes acylated by ferulic acid), and
- **linear aliphatic alcohols**: n-tetracosanol and n-docosanol, which seem to occur in the extract **as ferulic acid esters**.

PRUNUS AFRICANA, Pharmacological Activity

The mechanism of action of **the extract of *P. africana*** has not been elucidated completely.

There may be several factors, particularly the **inhibition of 5-lipoxygenase** in the polymorphonuclear leucocytes that infiltrate prostatic tissue (t**he extract is an anti-inflammatory**).

Interaction with testosterone metabolism is excluded by most published studies, although a 1996 publication showed, in vitro, a partial inhibition of 5α-reductase and of aromatase, therefore the possibility of an action on tissues whose growth is hormone-dependent.

The extract regenerates the prostatic epithelium in rats and dogs.

The extract **inhibits the cell proliferation**

- **induced by the main growth factors** (EGF, bFGF, IGF-1) responsible for the normal and pathological development of prostatic tissue (*cell cultures of rat prostatic fibroblasts)*
- of cultured cells in the absence of stimulation, and
- of cultured cells stimulated by a protein kinase C activator, TPA.

No cytotoxicity is associated with *the P. africana* extract.

Studies in rabbits (at high doses)

- The extract prevents the functional problems with bladder contractility and metabolism that are induced by a partial obstruction of the urethra, but
- does not decrease the compensatory bladder hypertrophy (a consequence of the increase in bFGF).

PRUNUS AFRICANA

Clinical trials

- state a *significant difference from a placebo* for nocturnal pollakiuria and other symptoms of benign prostatic hyperplasia (post-voiding residual volume, maximum urinary flow rate) as well as for subjective symptoms;
- it has no action on the volume of the adenoma.
- Other trials show that the activity is, in similar conditions, comparable to that of *Serenoa repens* fruit extracts.

Uses

***P. africana* extract**

- It is used orally (100 mg/day in 6-8-week cycles)
- to treat moderate bladder outlet obstruction symptoms due to benign prostatic hyperpiasia (BPH).
- The treatment is no dispensation from having a physician monitor the BPH.

SAW PALMETTO, Serenoa repens (Bartr.) Small = Sabal serrulata Rohm. & Schult., Palmae

Dwarf American palm is **a palm with «fan-shaped leaves»** with a fairly short single stipe (0.5-2 m).

Leaves: bluish-green, deeply split, borne by a petiole lined on the edge by small sharp needles.

Flowers: small, gathered into a spadix (raceme-like panicle).

The fruit

- **constitutes the drug,**
- is globose (2-3 x 1.5 cm), monoseeded, and bluish to black at maturity.

The species **grows wild in** sandy soils of **the southern United States.**

SAW PALMETTO, Chemical Composition

Fruits and seeds

- are rich in **a triacylglycerol-containing oil**, with nearly 50% of the **fatty acids containing 14 or fewer carbon atoms**.

Commercial lipid and sterol hexane extract

- the **above mentioned fatty acids**, especially **lauric acid**,
- **linear alkanes** (C9-C28), **aliphatic alcohols** (hexacosanol [C_{26}], octacosanol [C_{28}], triacontanoi [C_{30}], and **their esters**) and monounsaturated **alkenes** (C_{12}, C_{13}, and C_{24}),
- **phytosterols** (sitosterol, campesterol, cycloartenol, and *sitosterol derivatives*: 3-O-glycoside, 3-O-palmitate, 3—O-myristate, 6' -O-acyl-3-O- glucosyl, and others),
- **polyprenols**.

SAW PALMETTO, Pharmacological Activity

The hexan extract (studied extensively)

- In the mouse and the castrated rat, it exerts a **peripheral antiandrogenic effect**, a consequence of its complex **interaction with the metabolism and the mode of action of testosterone in the prostate**.
  - It **inhibits steroid 5α-reductase and 3α-reductase**; (*in vitro*, cell culture)
  - It **decreases the binding between dihydrotestosterone (DHT) and** cytosolic and nuclear **androgen receptors** (*in vitro,* and in vivo (rat),
  - Contradictory data from other studies:
    - **use of very high doses**, **therefore the mechanism would be nonspecific**
    - distinguishing the effects on both type 1 and type 2 isoforms of 5α-reductase
    - anti-androgen activity /prostate volume→ results seem contradictory

The acidic lipophilic fraction of a supercritical carbon dioxide extract

- **inhibits cyclooxygenase and lipoxygenase in vitro**, an effect which **might explain the antiinflammatory and antiedema activi**ty attributed to saw palmetto extracts.
- A **spasmolytic activity** and **inhibitory effects on** growth factor-induced prostatic **cell proliferation** have also been considered.

SAW PALMETTO, Clinical trials

- The daily, short- or long-term administration of saw palmetto lipidosterolic extract (320 mg/day) does not significantly alter **plasma levels of DHT**; it also has no effect on plasma levels **of prostate-specific antigen (PSA**).
- Long-term use apparently results in a decrease in hormonal receptors in the prostate.
- **Controlled clinical trials**, not using normalized inciusion criteria:
- Convergent results show that 1 to 3 months of treatment (320-480 mg/day) lead to an **increase in urinary flow rate**, a marked **decrease in post-voiding residual urine**, and more generaily, to an **improvement of the symptoms**.
- Problems: the lack of usual placebo effects and rispons for simple monitoring.
- Only one study—recent, but not placebo-controlled—quantitates the symptoms with a normalized questionnaire (I-PSS); it reveals a decrease of 35% of the initial score after 3 months of treatment.
- Another study, controlled and including a large number of patients, showed an efficacy similar to that of finasteride, at least in terms of I-PSS score and quality of life score.

SAW PALMETTO, Uses

- The lipidosterolic extract of the saw palmetto is marketed with the following indication (320 mg/day, per os):
- treatment of moderate bladder outlet obstruction symptoms linked to benign prostatic hyperplasia.
- The product is very well tolerated in the vast majority of cases (administration on an empty stomach can cause nausea).

Lipid Related Compounds: Alkanes, Alcanols and Esters

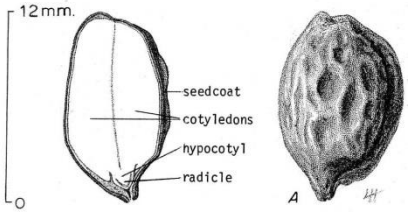
- **Waxes** commonly occur on the surface of leaves and fruits where they **form, with cutin, the very hydrophobic cuticle**
- Cuticule: limits water losses, controls gaseous exchanges, and participates in the protection against pathogenic agents.
- Chemically, **waxes are mixtures** comprising **hydrocarbons**, free and hydroxylated **aliphatic acids**, aliphatic **alcohols**, aliphatic **aldehydes**, and aliphatic **ketones**, β-**diketones**, and **esters**. They may also contain **terpenoids** and **flavonoids**.
  - The **saturated aliphatic hydrocarbon chains** have an **odd number of carbon atoms**, often **between 17 and 37**, most often equal to 29 or 31. In some cases the homolog iso-C_{27}-C_{33} and anteiso-C_{28}-C_{34} series occur.
  - Common **esters** are derived from 1-alkanols, and may have up to 72 carbon atoms; the most widespread correspond to C_{18}-C_{22} acids and to C_{26}-C_{28} alcohols. Some diesters of diacids are known (e.g., estolides).
  - **Terpenoids** are frequent and are alcohols, ketones, or acids **with** a triterpenoid **pentacyclic skeleton** (oleanane, ursane, lupane, glutinan). Triterpenoid alcohols **may be esterified by fatty acids**.
- Waxes: extractible by organic solvents (hexane, chloroform), amenable to GC analysis.
- Except for phytochemical or physiological considerations, **waxes** and their constituents **are of very limited interest**.

BAZIILIAN WAX PALM = CARNAUBA PALM, *Copernicia prunifera* (Miller) H.Moore, Palmae

- **Carnauba wax** (Ph. Eur. 5.0) is obtained from the leaves of this palm tree from the Brazilian northeast.
- **Occurs** as a powder, or flakes, or solid lumps.
- It is **a mixture of esters of long-chain aliphatic alcohols and aliphatic acids** (e.g., C_{30}).
- **Identification** by TLC of the wax dissolved in chloroform (visualized by phosphomolybdic acid).
- **Assays:** melting temperature (80-88 °C), acid value, saponification value, and total ashes (<0.25%).
- The wax is **used as a pharmaceutical aid to polish coated tablets** and **in food techonology** (E903).

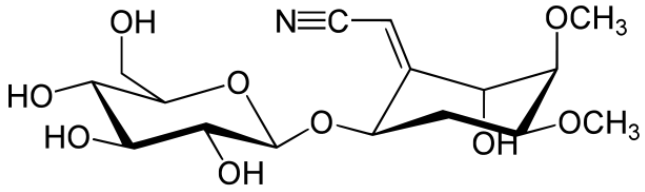
JOJOBA OIL,
Simmondsia sinensis (Link.) C. Schneider, Buxaceae

- The jojoba is a **dioecious bushy shrub** widespread in the **low-rainfall deserts** of the **USA** (from Tucson and Phoenix to San Diego) and of the north of **Mexico** (Baja California, Sonora).
- It is characterized by **blue-green leaves**, the color of which is due to the **thick cuticle** that covers them and drastically **limits water losses.**
- Cultivated: in **South America**, in **Israel**, and experimentally in some arid regions of the African continent.
- Typically only female plants are grown since **the drug consists of the seeds**.



JOJOBA OIL

- **The seed** contains up to **60% of an «oil»** that is in fact **a mixture of wax esters**.
- **Constituents** of this «oil»
  - **esters** involving **eicosenoic** (C20) and **docosenoic** (C22) **acids** on the one hand, and **eicosenol** and **docosenol** on the other hand.
  - **simmondsin** and analogs (**glycosides** with a cyanomethylenecyclohexyl-substituted aglycone).
- **A liquid below 10 °C**, jojoba oil is **barely oxidizable**, and its behavior permits its use in place of preparations traditionaly obtained from cetaceans (spermaceti).
- **Jojoba production is currently limited** in spite of numerous possible applications for the product, and in spite of the potential of this species as a means to enhance the productivity and value of arid regions.
- *In rats fed jojoba oil*, **changes are observed in the histological and enzymatic activity of the small intestine**, which probably preclude any dietary use.
- **Cosmetology** uses jojoba oil after hydrogenation (it is then a solid up to 65 °C): in the formulation of creams, lotions, soaps, lipsticks, and other preparations designed to be spread onto the skin or the hair;
- It is **a good**, **non-greasy lubricant**.



simmondsin

Alkyne derivatives, Generalities

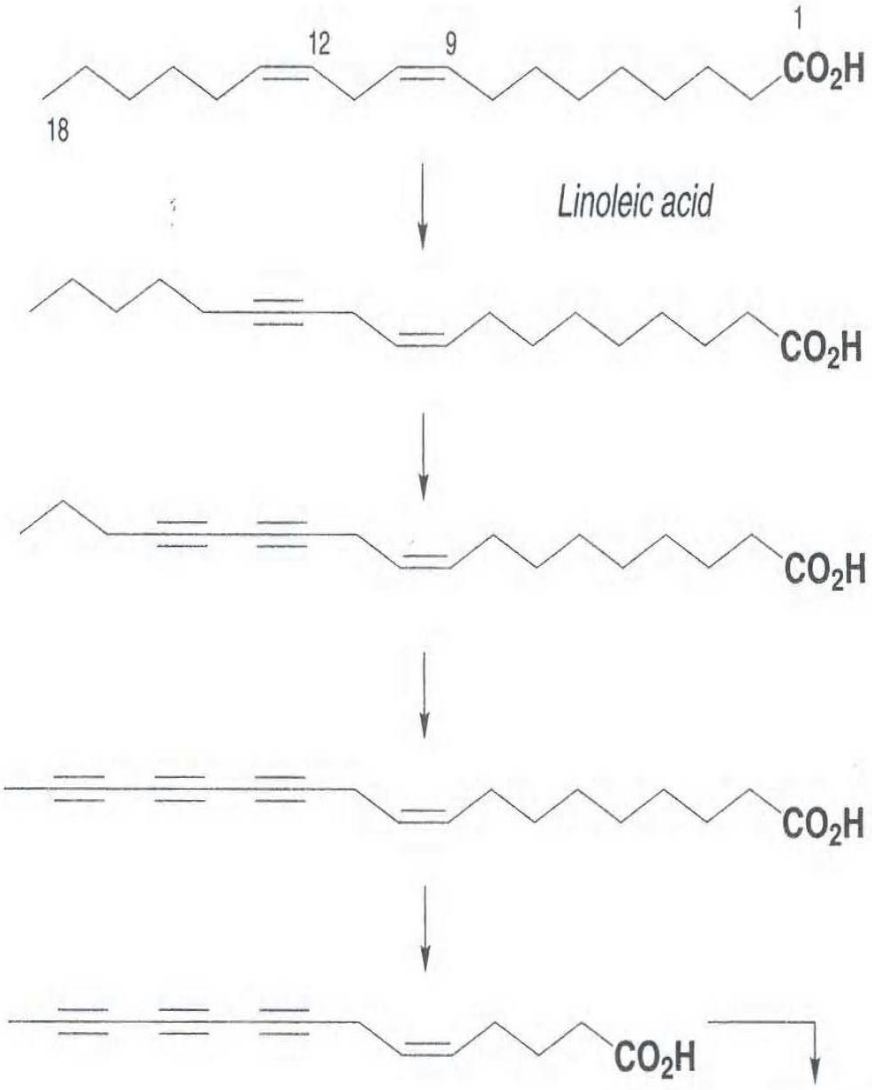
Substances (>1000) **containing one or several triple bonds** ,

- occuring **in the Asteraceae**, but also in the **Apiaceae, Araliaceae**, and **Campanulaceae**.
- Their **limited distribution** and **structural variety** make them good **chemotaxonomic markers**, especially to distinguish tribes among Asteraceae.
- **In some species they** are *not* normally present, but **develop after fungal attack**, for example in certain Fabaceae and Solanaceae (e.g., falcarindiol production by *Cladosporium*-infected tomatoes).
- **Alkynes or polyalkynes** , often **linear**, sometimes **partially cyclized**.
- They may **contain** one or several **double bonds** and **heteroatoms** (oxygen, sulfur, chlorine) **frequently included in a heterocycle**: furan, dihydrofuranone, thiophene, thietanone, or dithiacyclohexadiene.
- **Biosynthetically** are **related to fatty acids** (all of these compounds)

Origin of polyalkenes, I.

Most **arise from linoleic acid** through a series of **desaturation reactions** which lead, via **crepenynic acid**, to a **C18 triyne acid**.

Linoleic acid

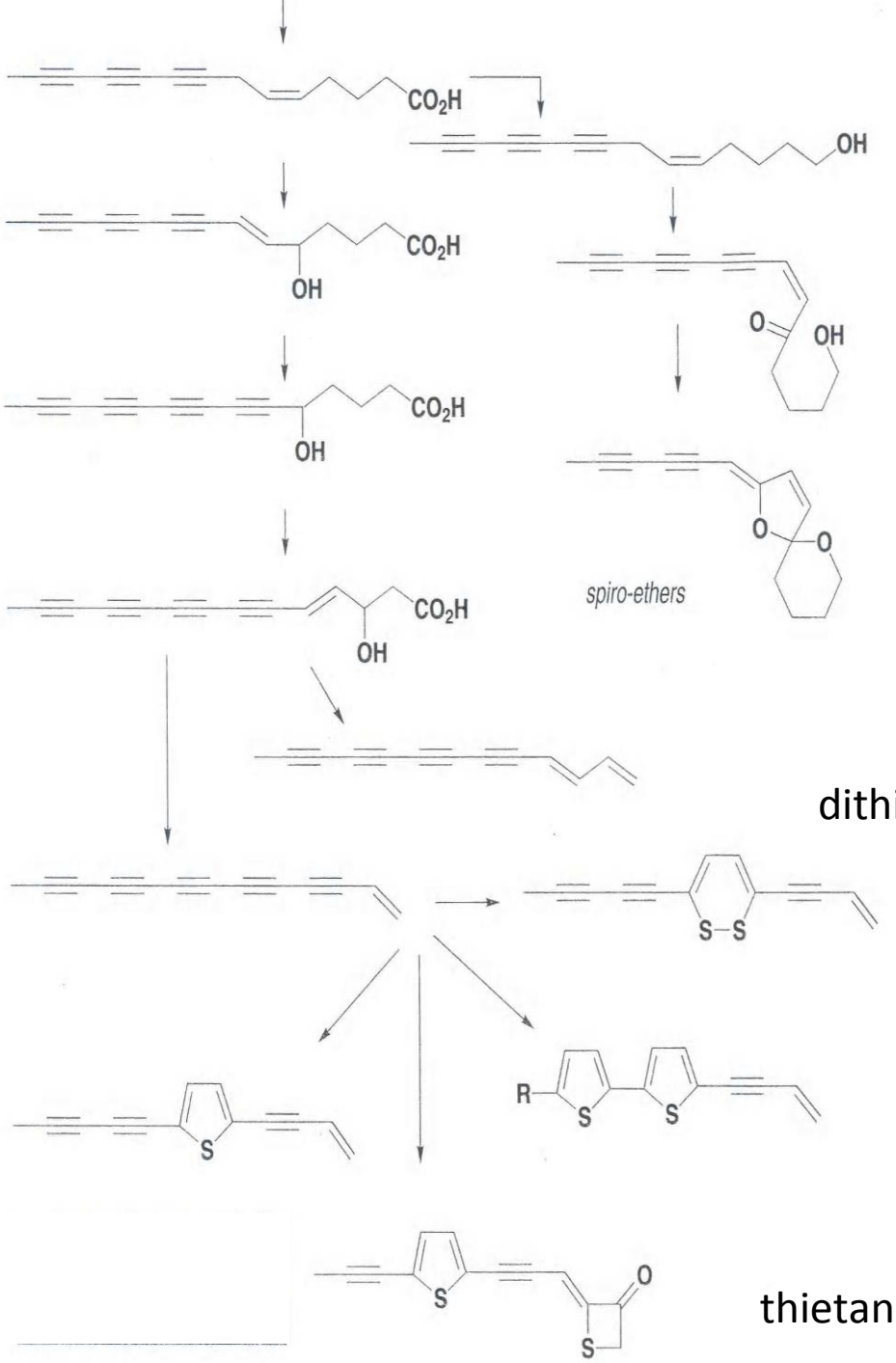


Crepenynic acid

C_{18} triyne acid

C18 triyne acid leads to compounds of various lengths.

Enepentyne precursor of the sulfur-containing heterocycles of the Asteraceae.



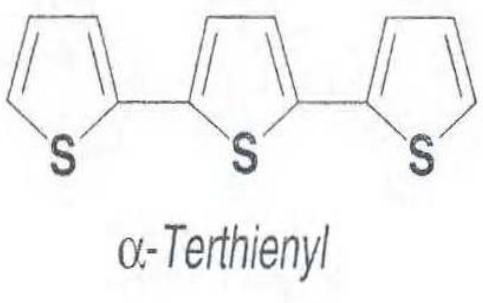
Origin of polyalkynes: examples and the specific case of sulfur-containing compounds

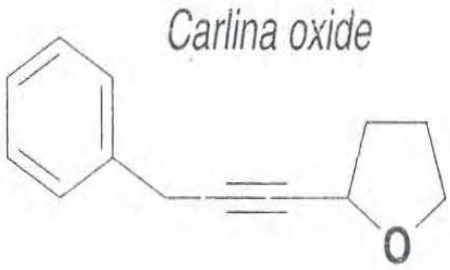
Alkyne derivatives, Biological Properties

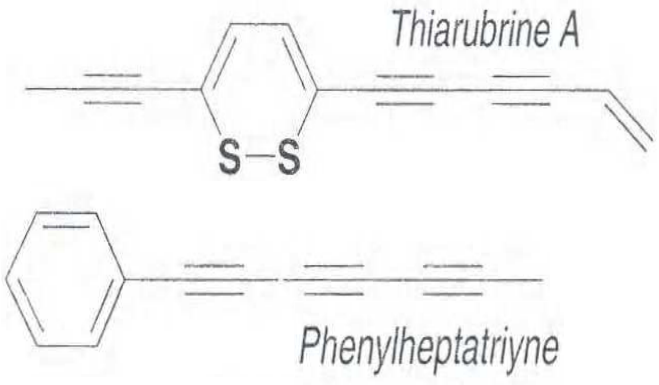
- **Phototoxic activity**: **UV A-dependent**, particularly pronounced against nematodes, insect larvae, certain fungi (for example Candida), some bacteria, and some viruses.

Note the remarkable coincidence between the use, in most traditional medicines, of **Asteraceae for the treatment of skin diseases**, and the presence in the plants of **polyunsaturated or thiophene-type compounds**:

- ***Aspilia*** of east Africa**:** its activity due to their **thiarubrines** which is comparable to that of fungizone **on *Candida albicans* or *Aspergillus fumigatus***, and is greater than that of amphotericin.
- **Phenylheptatriyne** containing ***Bidens***, used in China (*B.* ***parviflora*** L., *B.* ***tripartita*** L.) for the treatment of eczema, wounds and ulcers, and also in South and Central America (*B.* ***pilosa*** L.) **for candidiasis**.
- The **thiophenes** of Tagetes (China) or of Porophylum (Colombia).
- In Europe, the reputation of the root of stemless carlina (***Carlina acaulis*** L.) for the treatment of **skin disorders** is to be related to **carlina oxide** with **antistaphylococci activity** demonstrated *in vivo*.







BURDOCK,
Arctium lappa L. (*Arctium majus* Bernh.), Asteraceae

- **The dried root** of this Asteraceae is the sole part of the plant listed in the 10th edition of the French Pharmacopoeia.

- A hardy, **biennial plant** .
- Very **common in** almost all of **Europe**.

It is easy to identify:

- very **large cordate leaves** (50 x 30 cm),
- **capitulums** of **purple tubular flowers** surrounded by
- **green bracts ending in hooks**.

BURDOCK, Chemical Composition

- **Root** (the drug)

– may contain over **50% inulin**, **2-3% phenolic acids**;

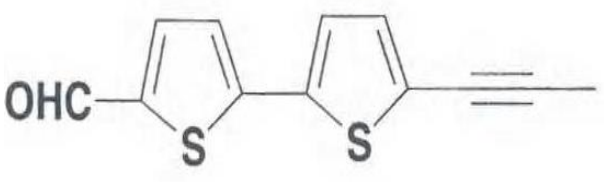
– rich in **polyunsaturated compounds:** *polyalkenes, and polyalkynes*.

– **polyalkynes:**

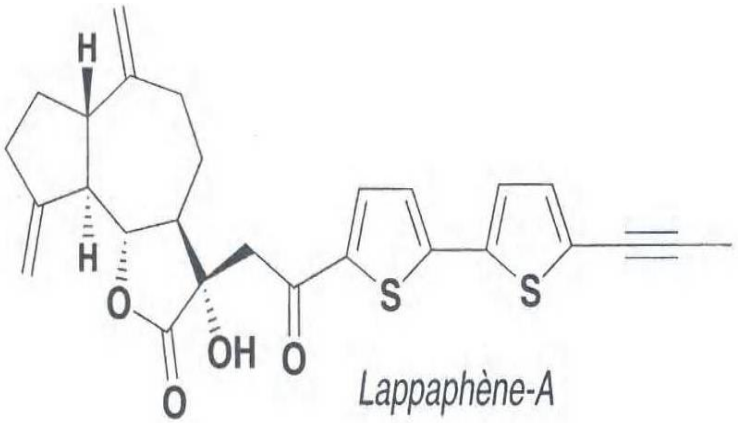
  – **linear compounds** (trideca-1,11-diene- 3,5,7,9-tetrayne),

  – derivatives of 5'-(1-**propynyl**)-2,2'-**bisthien**-5-**yl** (arctinones, arctinols, **arctinal**, arctic acid),

  – **Lappaphens**: complex molecules that probably result from the addition of **arctinal** onto an exomethylene-substituted sesquiterpenoid lactone of **guaianolide** type



Arctinal



Lappaphène-A

BURDOCK Root, Uses

- Traditionally used **for the treatment of dermatosis** and **furunculosis**.
- This application is **in part justified** by the presence of **polyunsaturated compounds** with **antimicrobial** and **antifungal** properties demonstrated *in vitro*.
- The **German Commission E monograph** states that the applications that are claimed (gastrointestinal pain, arthritis, rheumatism, skin disorders) have not been substantiated, therefore the **therapeutic use of burdock** root **cannot be approved**.
- Still recommend by some plant therapist:
  to treat furuncles, whitlows, varicose wounds, pilo-sebaceous infections, and acne.

ECHINACEA or CONEFLOWER, *Echinacea* spp., Asteraceae

- **Different species** of this genus **of North American origin** are used in phytotherapy and homeopathy, according to which the **subterranean parts** possess **immunostimulatory properties**.
- ***E. angustifolia*** DC., ***E. purpurea*** (L.) Moench (= Rudbeckia purpurea L.), and ***E. pallida*** (Nutt.) Nutt.

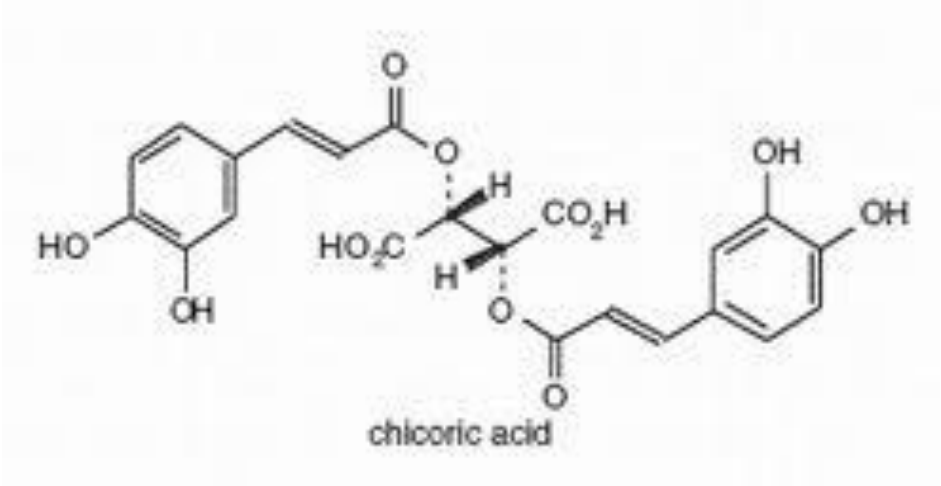
- Echinacea are hardy plants with **oval or lanceolate leaves**, entire or more or less **pinnate** (purpurea).
- The **large-size capitulums** comprise **purplish tubular flowers** gathered into **a sphere** and **large ligulate dangling**, generally **pink** (or purplish, or very pale) flowers.

- The **drug consists of the root**, and
- its microscopic examination is required to identify the species and verify the absence of a common **falsification by** another Asteraceae: ***Parthenium integrifolium*** L.

E. angustifolia

ECHINACEA, Chemical Constituents

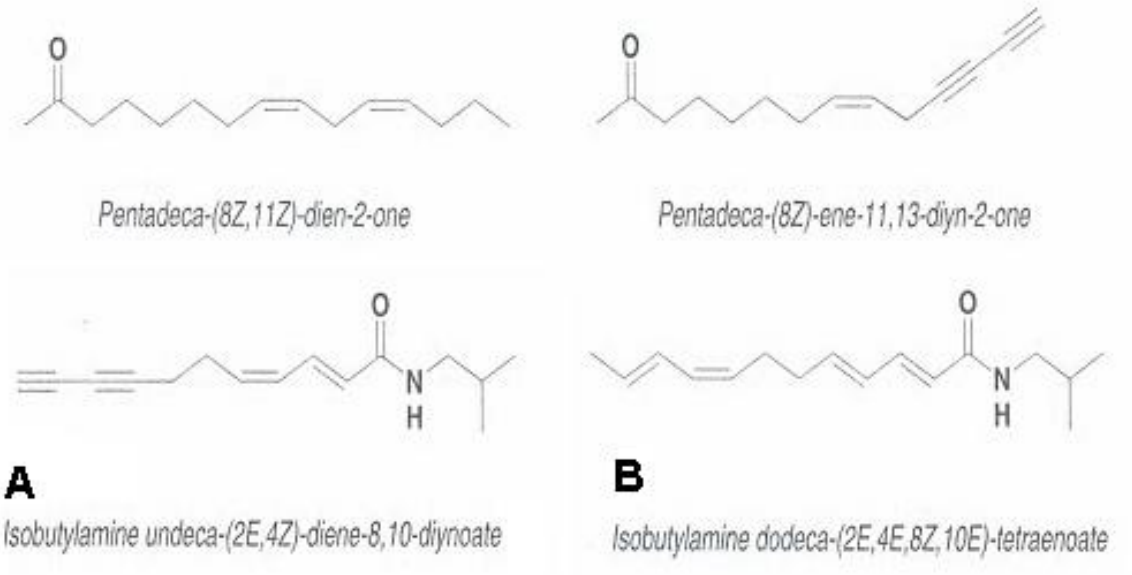
- An **essential oil**, **pyrrolizidine alkaloids**.
- **Phenolic compounds** derived **from caffeic acid**.
  - caffeic acid, chlorogenic acid, and dicaffeoylquinic acids (**cynarin** is specific to *E. angustfolia*);
  - the monocaffeate, dicaffeate, and ferulate of **tartaric acid** (the dicaffeate {= **cichoric acid** is abundant in *E. purpurea* (0.6-2.1%), but practically absent in *E. angustifolia*);
  - sugar esters of caffeic acid (**echinacoside**: 0.3-1.7% [except in *E. purpurea*]).



chicoric acid

ECHINACEA, Chemical Composition

- **long-chain fatty acids and alkanes** in all species in the genus.
- **unsaturated aliphatic compounds**
  - aliphatic amides, isobutylamides of polyenyne acids (A) and of polyene acids (B).
  - ketoalkynes and keto-alkenes especially in *E. pallida*



- **Polysaccharides:** glucuronoarabinoxylan in the roots of, fucogalactoxyloglucans, arabinogalactan in cell cultures of *E. purpurea*.

ECHINACEA, Pharmacological Activity and Uses

- **Native American Indians**: used externally **as wound-healing agents**, as well as internally **for headaches, stomach aches**, or **as antitussives**.

Pharmacology presents echinacea-based preparations as **immunostimulatory**, based on various experiments:

- carbon clearance test in the mouse (detects an **increased phagocytosis**)
- phagocytosis test for granulocytes and macrophages,, **induction challenge for mediators** (interferon, interleukins).
- The **polysaccharides** are active, but, in many tests, **the lipophilic fraction** is also active, and sometimes more so.
- In 1994, a critical analysis of **clinical data** obtained in humans showed that these data were **not sufficient to make therapeutic recommendations**.

Uses

- **The root of Echinaceae species** or **the plant of *E. purpurea*** , as a tincture, used for the supportive treatment of common cold.
- The drug and its preparations seem devoid of toxicity.

ECHINACEA, Uses

- The **root of Echinaceae species** and also the **plant of *E. purpusea*** can be used as tincture for the supportive treatment of common cold.
- Many **German practitioners**, **on the basis of possible immunostimulating effects** of Echinacea, **recommend its use as a tincture**, mother tincture, or extract, alone or in combination (e.g., Baptisia, Thuja) **to stimulate defense mechanisms**:
- **for the prevention and treatment of** *colds*, of the *flu*, and of various *respiratory disorders*,
- **as adjunctive therapy to** *chemotherapy for common ailments*
- as **a prophylactic treatment against** *opportunistic infections in high-risk patients*.
- The drug and its preparations seem devoid of toxicity.