HERBAL ACTIVES

squalene

the originating triterpenoid

Lesson #3

squalene

Squalene is the foundational triterpene hydrocarbon found in both plants and animals.

From this thirty-carbon molecule, all other triterpenoids, the steroids, and sterols are synthesized in nature.

Squalene is a linear triterpene hydrocarbon composed of six isoprene units (30 carbon atoms), with a formula of $C_{30}H_{50}$.

It is found in plants, animals, fungi, and humans, and is the precursor to all cyclic triterpenoids, sterols, and steroids.

Squalene is abundant in amaranth seed oil

Terpenes & Terpenoids

- Both terpenes (CH) and terpenoids (CH+O2) are **present in ALL parts of the plant.**
- Built from repeating isoprene units consisting of five hydrocarbons (C5H8).
- Terpenes can be highly aromatic, the smaller volatile ones making up the essential oils while larger ones are found in the fixed oils.

Small volatile compounds:

Isoprene unit **1 isoprene unit** 5 carbon atoms basic unit 5C - (C5H8)

Monoterpenes **2 isoprene units** 10 carbon atoms essential oils, limonene, geraniol, thymoquinone, pinene, myrcene, linalool, camphene,

Sesquiterpenes **3 isoprene units** 15 carbon atoms essential oils, farnesol, bisabolol, caryophyllene, cedrene, zingiberene, farnesene

Larger non-volatile compounds:

Diterpenes **4 isoprene units** 20 carbon atoms (neutral color) Resins, Retinol (vitamin A_1), Retinal, Retinoic acid, Retinyl esters, Carnosic acid, Pine resin, Abietic acid, Phytol, Cafestol, Kahweol, Taxodione

Triterpenes **6 isoprene units** 30 carbon atoms (clear, waxy, or white) **Squalene**, Ursolic acid, Oleanolic acid, Betulin, Betulinic acid, Asiaticoside, Faradiol esters, Madecassoside, α & b-Amyrin, Taraxasterol, Shottenol, Spinasterol, Cycloartenol, Lupeol, Saponins, **Phytosterols**: Stigmasterol, β-Sitosterol, Campesterol, Brassicasterol, Δ5-Avenasterol, Δ7-Stigmastenol

Tetraterpenes **8 isoprene units** 40 carbon atoms (brightly pigmented, red, orange) **Carotenoids, β-Carotene, Lutein, Lycopene, Astaxanthin, (pro-vitamin A)** Tocotrienols, Abscisic acid (ABA), Strigolactones, Bixin and Norbixin, Crocetin, Corcins

foundations

As a precursor triterpene, squalene in humans converts to lanosterol, the first cyclic intermediate on the pathway to cholesterol, steroid hormones, and vitamin D.

In plants, the straight squalene terpene molecule cyclizes, meaning the molecule forms a ring, a closed circle, to create cycloartenol.

Cycloartenol is the starting point for the synthesis of almost all plant sterols, the phytosterols, such as stigmasterol and β-sitosterol, as well as triterpenoids like lupeol and ursolic acid.

Olive oil is high in squalene

human and plant

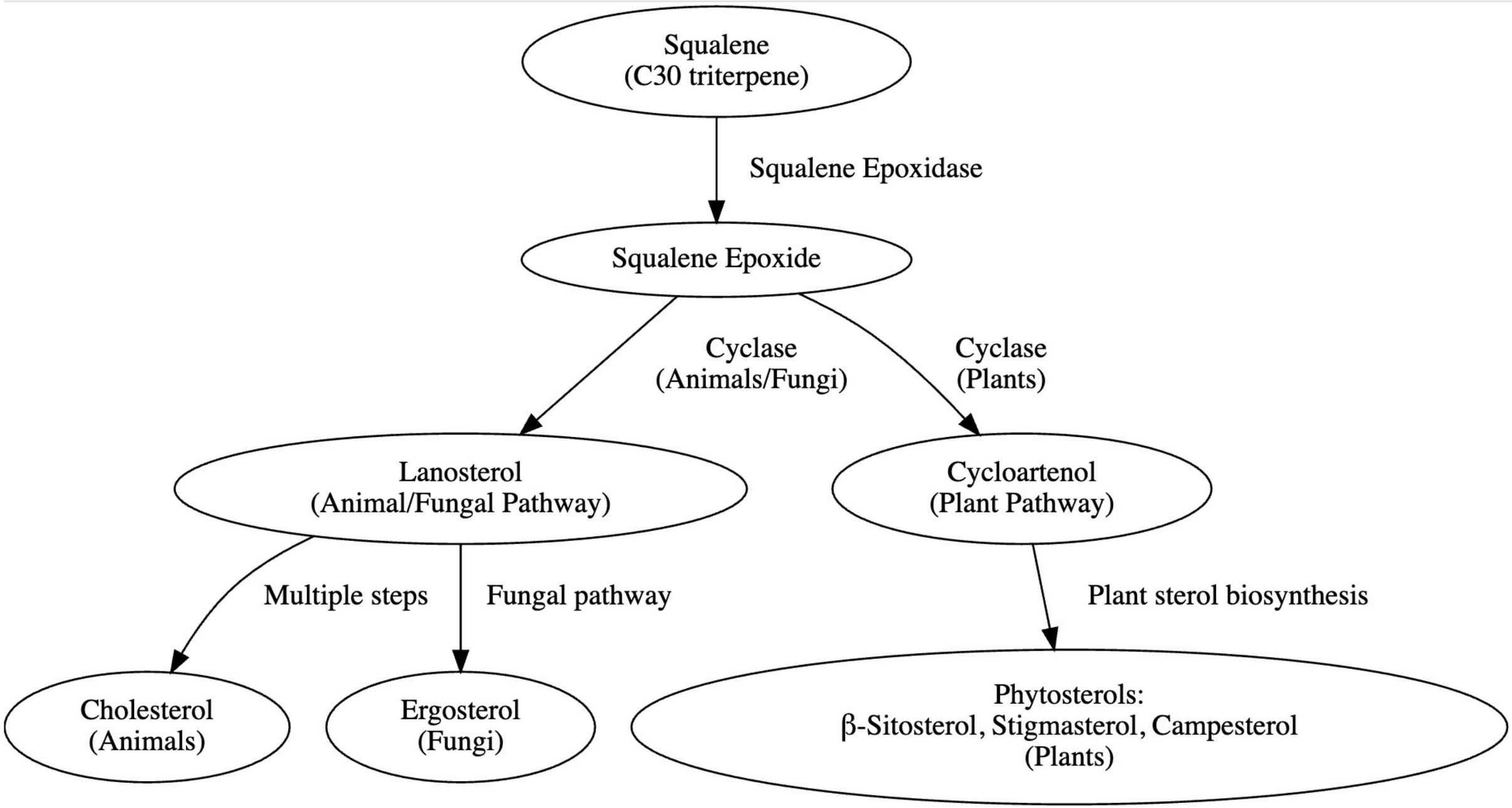
In human skin, squalene is found in the sebum, and is a lipid compound produced by the sebaceous glands, which forms part of the acid mantle.

In human skin, squalene accounts for approximately 10–15% of total skin lipids, occasionally up to 20%.

In the botanical world, squalene is not produced for hormonal purposes, as it is in humans. It accumulates as a protective lipid reserve.

Squalene is present in most plant oils, especially amaranth, olive, rice bran, and wheat germ.

squalene, plant & human



emollient

Squalene plays multiple roles as a necessary lipid compound in the skin and body, neutralizing oxidation and calming inflammation.

As both a structural lipid produced in the sebaceous glands and a signaling molecule, it supports the skin barrier and serves as a protective emollient layer.

Able to easily penetrate the skin, externally applied squalene integrates into the lipid layers and structures, smoothing and softening, and mimics the skin’s naturally produced squalene.

Rice bran oil

antioxidant

Broadly antioxidant, squalene protects tissues from oxidative damage, shielding them from harm.

Squalene is also a highly effective singlet oxygen scavenger, targeting and neutralizing the reactive forms of oxygen, ROS, specifically singlet O2, which result from biological systems.

Protecting the skin from lipid peroxidation induced by UV exposure is another benefit of squalene.

In the skin, the polyunsaturated fatty acids that comprise parts of the lipid skin structures are more prone to oxidation and are specifically protected from oxidative damage.

UV exposure explained

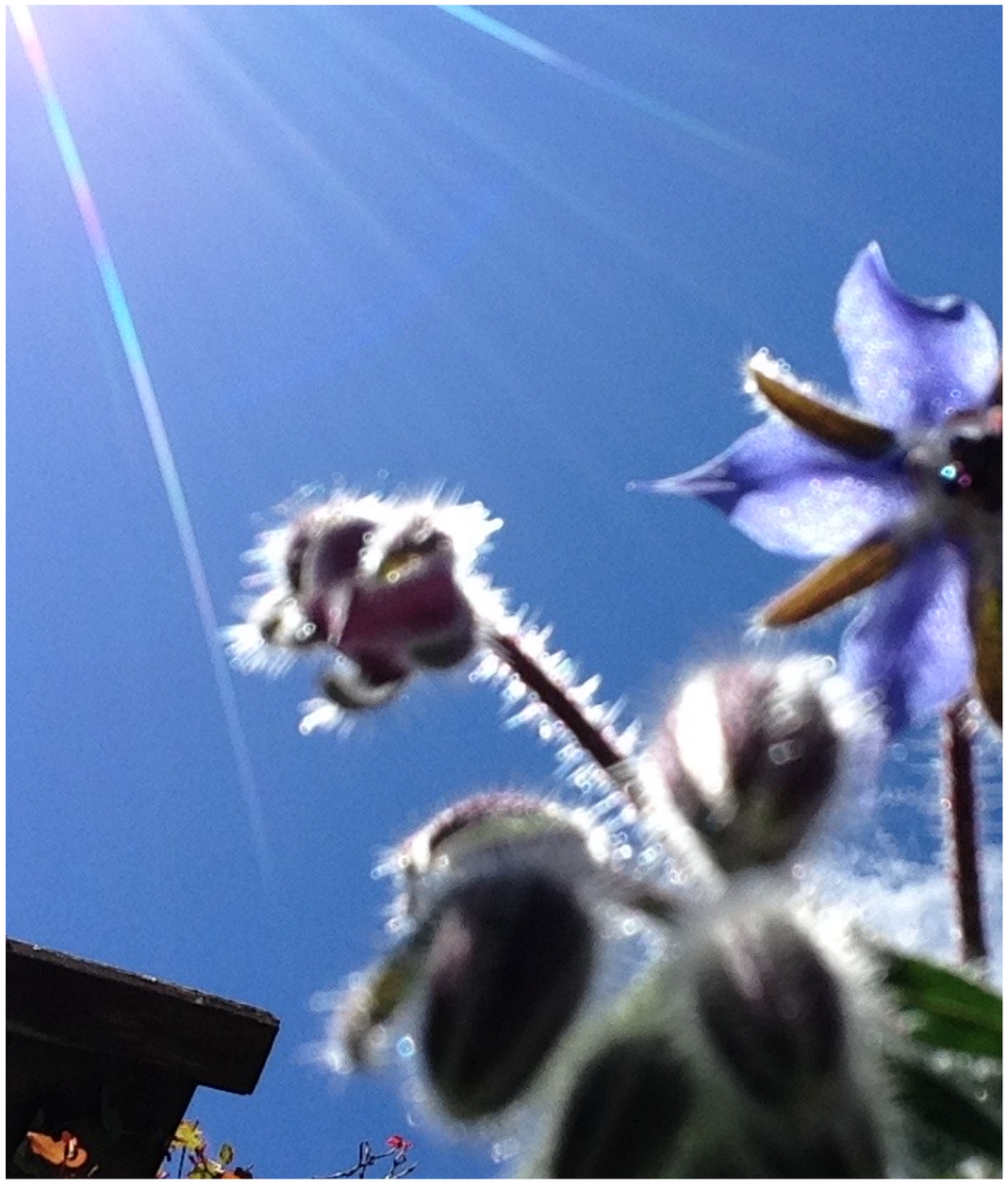
When UV rays, especially UV-A, penetrate the skin, they generate reactive oxygen species, ROS.

The ROS then oxidize the skin lipids, especially those that are poly-unsaturated in cell membranes and sebum.

This exposure leads to a chain reaction of lipid peroxidation, which damages the ceramides, fatty acids, and cholesterol of the stratum corneum, as well as sebum and cell membranes of keratinocytes.

The result is the disruption of the skin barrier, inflammation, changes in skin pigmentation, DNA damage, and conditions that promote premature aging.

Squalene is one of the few lipid-based molecules that can directly neutralize singlet oxygen, generated by ROS.



communicating cytokines

Interactions between immune cells, keratinocytes, and macrophages, influence cytokine activity—the group of small proteins that act as signals and mediators of communication between cells.

Communication between skin layers and functions helps regulate the skin's natural processes, maintaining hydration, barrier recovery, and collagen production, among others.

Squalene can modulate the cytokine activity through specific signaling pathways.

The influence of cytokines helps regulate excessive inflammation during the repair process and promotes skin homeostasis, while early detection of injury or pathogens can speed the repair process.

transport

As a lipid compound, complementary and compatible with the skin, squalene, when included in formulations, protects the skin barrier function and hydration, preventing TEWL, the loss of moisture from the skin’s surface.

Due to squalene’s molecular fluidity and solubility, it **helps transport other lipophilic, oil-soluble compounds** and bio-actives into the skin, where they remain as reserves.

The antioxidant carotenoids, tocopherols, and tocotrienols, as well as the anti-inflammatory phytosterols, and a wide range of terpenoid compounds found in the plants, are transported into the skin’s functioning matrix with the aid of squalene.

squalene
squalane

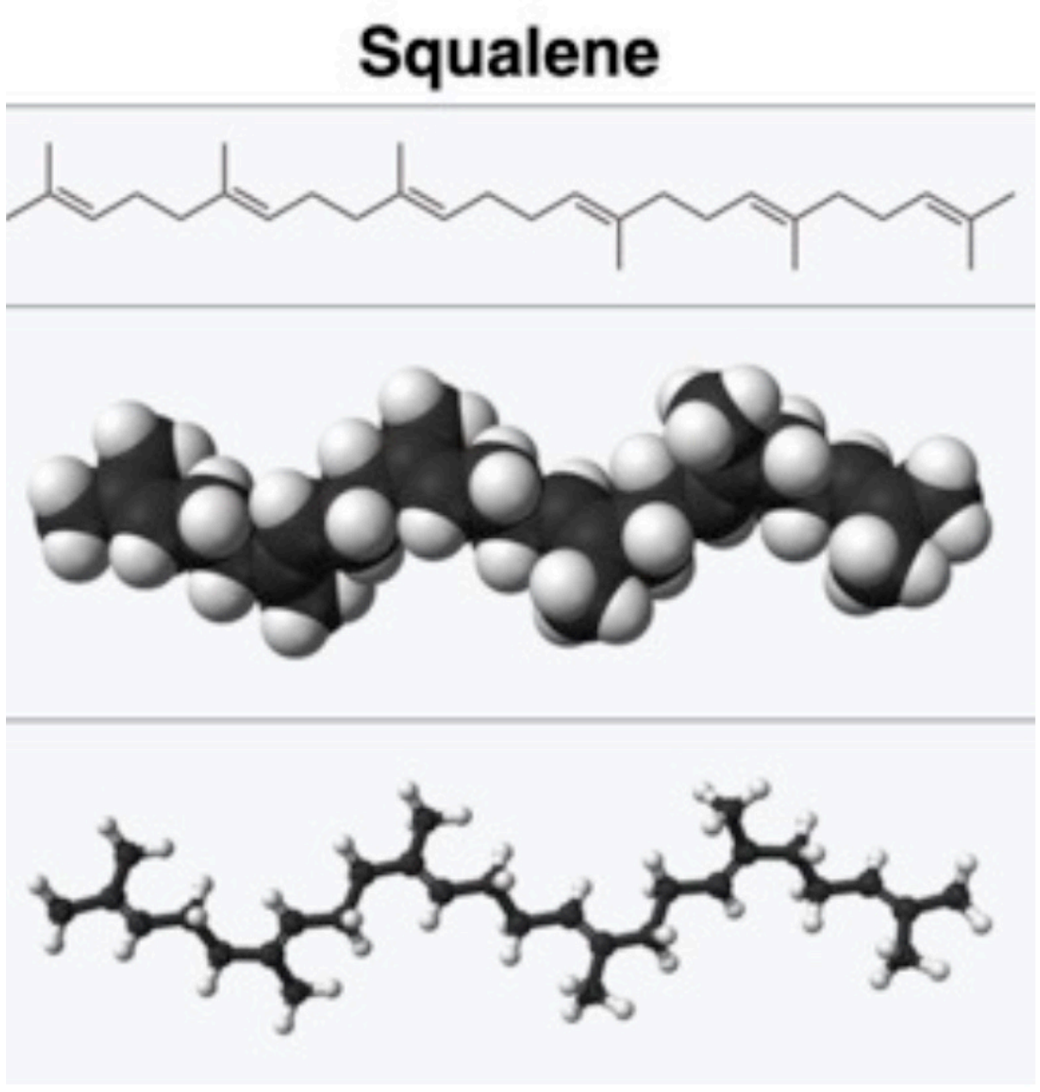
Squalene and squalane are not the same despite their similar names.

Squalene is the active, and very unsaturated lipid compound we have explored in this lesson.

And so prone to oxidation if stored for an extended period, it is also sensitive to light and air.

Squalane is a modified version of squalene, obtained through hydrogenation, where the unsaturated natural form is converted into a saturated form, resulting in a wide range of uses in cosmetics due to its increased stability and emollient properties.

The modification of squalene to a saturated form as, squalane, increases shelf stability, but it lacks the active antioxidant functions of the natural compound squalene.

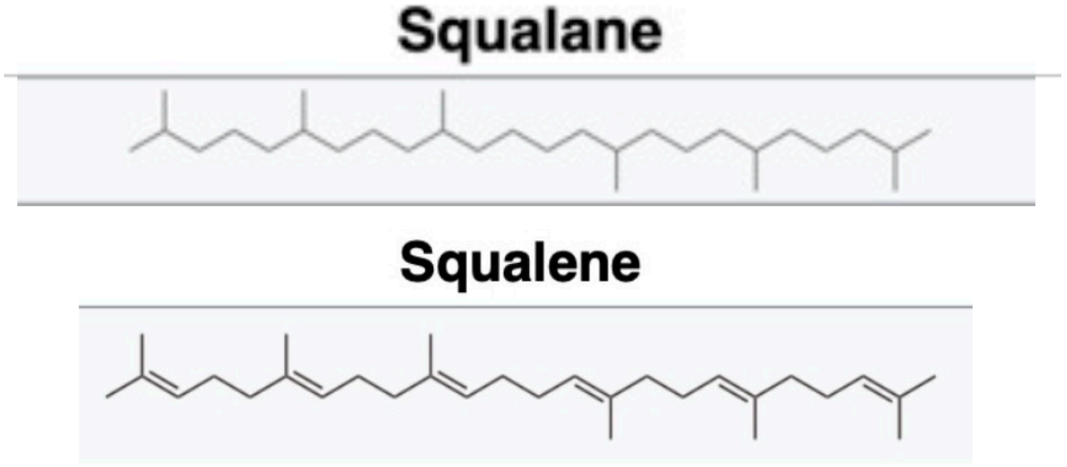


squalane

Squalane has no antioxidant function.

When the double bonds of squalene transform into the saturated form of squalane, the molecule loses its ability as an antioxidant to neutralize ROS, including singlet oxygen, which can lead to a chain reaction of lipid peroxidation.

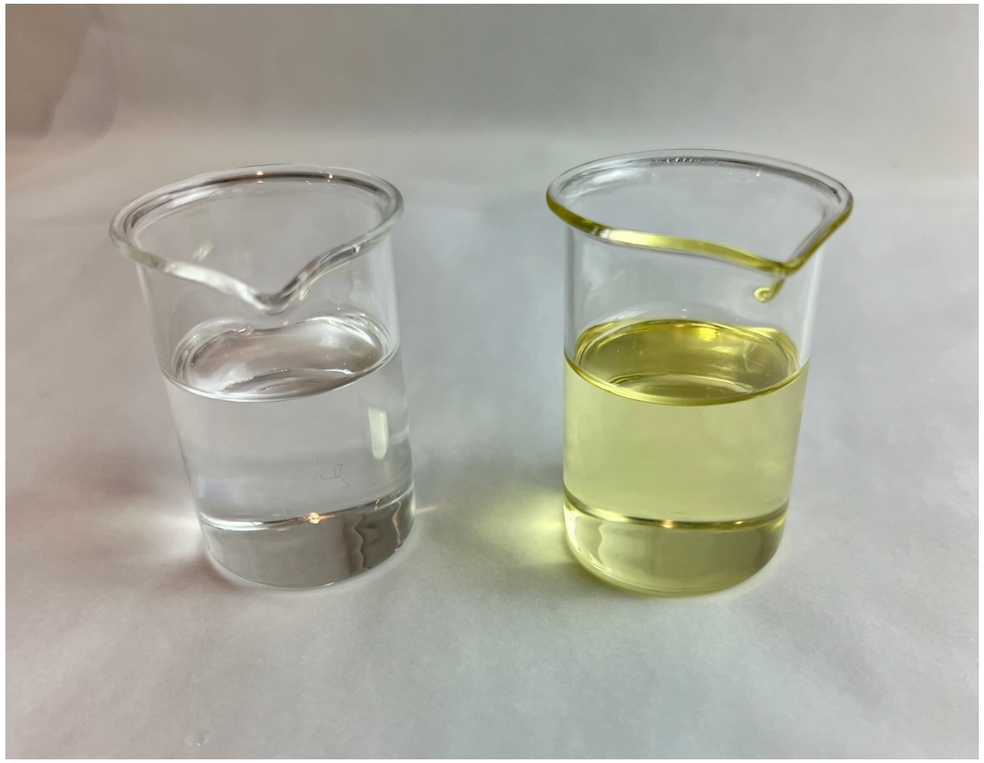
It appears that the double bonds of carbon compounds neutralize reactive oxygen species, thereby protecting tissues from oxidative damage.



Without double bonds in the molecule, it cannot neutralize damaging oxygen, nor perform signaling and communication functions as squalene does.

It is, however, emollient, able to protect the barrier function through its lipid film.

Squalane is bio-inert, making it suitable for sensitive skin because it doesn’t provoke or interact with cellular signaling.



Squalus spp. squalene

Squalene is a remarkably impressive natural compound, and the discovery that it serves as the foundation for all triterpenes, including our steroids, sterols, and ultimately, cholesterol, reinforces its impressiveness.

First discovered in 1916 in Japan, the name squalene comes from *Squalus spp.*, the Latin name for shark.

Up to 80% of shark liver oil is composed of squalene, making the extraction of the compound from sharks the most economical source.

Our livers also produce squalene, which is then transported to our skin and other tissues.

The sebaceous glands secrete squalene at a rate of between 10 to 15% and protect the skin's outer layers.