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Review Article

Contaminated Waters and Depleted Soils: Impact in Nutrition III from Medicinal Plants to Essentials oils I

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Abstract

Following the above intended title review series, this 3rd part deals with the status of more medicinal plants and essential oils being used in the human 3 phase process DETOX as well as their everyday use for maintenance and prevention of physical disfunctions.

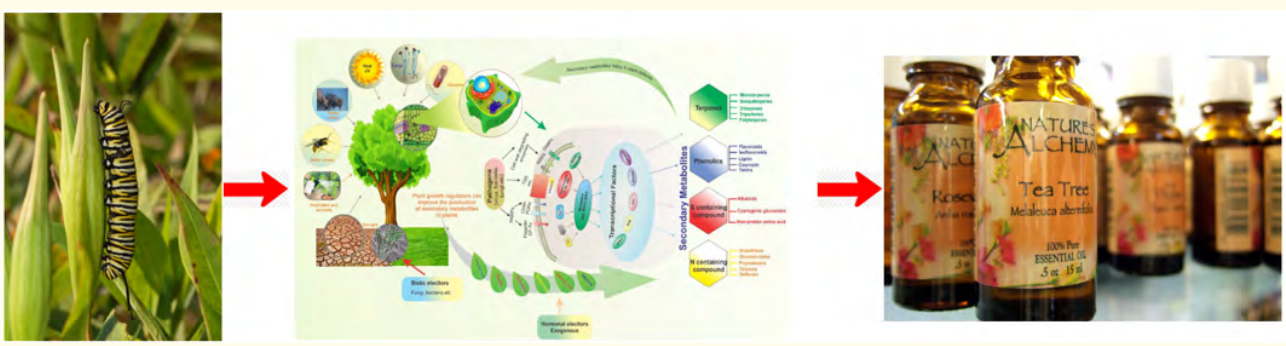
A brief introduction to the vegetal metabolic pathways generating the essential oils as well as the main chemical classes of their constituents are presented. The climate and soil conditions for the second metabolic vegetal production - the essential oils - are also addressed. The link between these chemical constituent classes and some human biochemical effects is discussed.

The highly importance of quality, entirety of volatile chemical components, and pesticide free grade essential oils is also highlighted.

For a thorough discussion of the 3 human DETOX phase process, please refer to [1].

Keywords: *Essential Oils; Mevalonic Acid Pathway; Shikimic Acid Pathway; Methyl Erythritol Pathway; Terpenes; Phenylpropanoids; Alkaloids; Flavonoids; Lignans; Alkaloids Toxicity; DETOX; Baccharis trimera - carqueja; Rhododendron groenlandicum - Labrador Tea; Cistus ladanifer - Rockrose or Labdanum; Daucus carota - Wild Carrot*

Graphical Abstract



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Introduction

Human body, as complex as it is, needs to be in a homeostasis state not only by proper nutrition but also through adequate elimination of undesirable metabolites arising from the processing of the digested nutrients. Many enzymes are intertwined and irreplaceable in the myriads of chemical compounds formation or degradation, in the absorption process of digestion of the whole nutrition process, and also in the completely excretion of useless metabolic products in the natural body DETOX process [1].

Nature has always been on the side of the animal kingdom. During the course of the centuries, we humans went far from only using the plants in their natural state [2]. Eons ago, essential oils, the devas of the vegetal kingdom, have been discovered and amply used not only to heal but also in performing religious celebrations, conserving the bodies of dead people, among many others [3,4].

Resins, here only the exudates of mainly gymnosperm and dicotyledon plants, have been used for thousands of years, as some of them are known all over the world. Some of their uses are from less important as food and perfumery industry, in ancient Egypt embalming ceremonies, to a higher degree of importance, in agriculture and medicine, presenting many bioactive compounds. Examples are myrrh (*Commiphora myrrha*), frankincense (*Boswellia sp.*), elemi (*Canarium luzonicum*), opoponax (*Opopanax chironium*), benjoin (*Styrax sp.*), galbanum (*Ferula sp.*), tolu balm (*Myroxylon balsamum* or *Myroxylon toluiferum*), breu branco (*Protium heptaphyllum*), copaíba (copahu) (*Copaifera sp.*), ciste (rock rose) (*Cistus ladanifer*), cedarwood (Atlas cedar) (*Cedrus atlantica*) [5,6].

Hydrodistillation of resins (distilled resin) and various possible parts of plants (yielding the essential oils) can present and be classified according to their chemical constituents into terpenoid/phenolic products. Terpenoid resins and their essential oils present terpenes, either monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), and/or triterpenes (C30), whilst phenolic resins and their essential oils present cinnamic acid derivatives, C-9 based phenolic compounds (phenylpropane), dimeric phenylpropanoids, lignans and flavonoids [7].

With the advent of Scientific Aromatherapy by Pierre Franchomme and Daniel Pénoël [8], many healing properties and ailment prevention have been further discovered since then and are still counting [9-11].

It is important to highlight here that the scientific aromatherapy, although a huge advance in the use of the essential oils, is not a synonym of “I am the only incontrovertible true knowledge, as I am the one truth” as some school of thoughts tend to impose on lay men. Thousands of years of making essential oils, resins or plants part of human’s everyday lives is a huge body of knowledge that nobody can deny or not take into serious consideration.

After reading even a single published study stating that this or that chemical compound in an essential oil can be harmful, one has to be aware that a single one or even a plentiful biased studies cannot erase all historic knowledge of that plant. One has to look carefully into the experimental conditions, and the conclusions must be taken into deep scrutiny. This is obvious a must in any scientific study performed in a laboratory. But considering the complexity of any vegetable extract, any essential oil, regarding the chemical composition, one has to consider that if a substance with a certain toxicity is present in a multitude of others, certainly in this natural vegetal synergy the antidote can be also present, even in ppm or ppb levels in the same plant extract. Not to mention the detection limit of the chromatography techniques employed in the chemical composition analysis - even coupled with mass spectrometry - sometimes cannot reach this concentration levels in a final essential oil extraction. Many toxicologic studies are carried out with only one chemical compound, the one suspected to be toxic, disconsidering in the experiments, the real synergy of a multitude of chemical compounds produced by a plant present in its extract, either as an essential oil or a resin. It is also a matter of concentration of the compound in the synergy to be considered a toxic one, and always the historic knowledge about those extracts. All directions for the use of essential oils, unless stated otherwise for a strong reasons, preconises the use of dilution into any edible vegetal oil carrier, before any human or animal using, in any of the 5 possible ways of administering these potent plant Devas.

Some plants do produce certain compounds inadequate to humans and some of them do not produce essential oils. Among these plants, some present toxic effects only after human manipulation, concentration, extraction or refining. Many of these substances, with various degrees of toxicity, were bring into the spotlight by Samuel Hahnemann when he had this genius insight and realized that poison is just a matter of concentration, as indeed it is. Homeopathy is normally a toxic substance when in a certain concentration, but a healing one when properly hyper diluted in water. This procedure makes the best of the memory capacity that water presents to retain the electromagnetic body of information of the substance(s) once in contact with it (them) [12-14].

To deprive humans of their historical body of knowledge by some disloyal competition, will never be considered in our best interest. In my point of view is a serious offence to the rights and liberty of human beings and I leave my opinion for your decision.

Let's take a look at the essential oils, here described with DETOX purposes, with open historical and scientific minds.

Discussion

Origins of essential oils

Vegetables are like no other evolving with the planetary evolution cycles. Being conceived as static beings, they must develop different, but nonetheless creative, manners to survive and to communicate. In other words, conceived and evolved to be in a strong interaction with the environment.

Biology and genomics were the intelligence, biochemistry was the tool, and their secondary metabolites, the produced agents. During millennia, plants had to cope with environmental biotic (flora and fauna) and abiotic (chemical and physical) factors causing stress in order to produce a healthier and stronger descendancy, like developing a climate-resiliency, deal with any other form of stress, insect and other animal attacks as the animal kingdom also evolved, pesticides, heat, extreme cold, water lack or excess. The most successful genomic arsenal capable plants, which developed an intricate biochemical reaction to produce the most efficient secondary metabolites, have seen the light of these present days. They provided the fittest species that could survive and pass on their better genes to their descendancy [15].

As generally static beings, vegetables must rely on their own biochemistry to produce metabolites to defend, communicate, and reproduce themselves efficiently. They did it by producing the essential oils - the consciousness of the Devas working in the vegetal kingdom.

Genomics and functional genomics (Transcriptomics, Proteomics and Metabolomics) are the fields of knowledge studying the genes responsible for the biosynthesis of the secondary metabolites in plants, the gene function and detection of possible novel pathways. Scientists know that the secondary metabolism of plants is a product of and controlled by genetics but most of all, by the environment. environment (Epigenetics). So, although there is much work still to be done, a body of knowledge concerning the essential oils, secondary metabolite products of some plants, has been constructed and is recognised and established by science [16].

Chemoecology is certainly the name of chemical and environmental body of knowledge of essential oils, as it encompasses the studies of chemical compounds in ecological interactions. Plants issuing essential oils are producers at the first trophic levels. They present intraspecific and interspecific communications by the possibility of using these same essential oils to sprinkle in the atmosphere and communicate with other plants. One example is the Blue Mountains in New South Wales, Australia, covered by a blue haze caused by the essential oil of the eucalyptus forest. The common name of the main compound giving the atmosphere this bluish color is the eucalyptol, chemically known as 1,8-cineol, a monoterpenoid (C10) oxide [17].

Previous chemistry knowledge of the chemical classes for the maximum composition of an essential oil an analytical instrument can provide, is crucial for determining not only the molecules responsible for its aroma, flavor but above all, its potential biological activities.

Many regions on the planet presenting severe weather are the ones more prone to provide stronger plants and, consequently, the most potent essential oils: As these substances are intended to defend the plants, the more aggressions they have to face, the stronger their essential oils will have to be. By the same reasoning, wild plants are stronger than cultivated ones, and indigenous plants are the ones producing the original chemical compounds present in their essential oils, as any additions to soil composition, artificial watering and absence of aggressions or stress in the environment, the less effort the plant has to put up to defend itself. The genes responsible for producing this or that chemical compound will not be activated by the lack of environment threats, thereby the standard chemical composition of the essential oil will be either incomplete and/or will greatly vary in concentrations. On the other hand, threats that is unknown to plants, if they can survive, will completely change their secondary metabolites and consequently, their essential oil chemical composition. These are pivotal concepts to fully understand the huge body of plant knowledge which is called Aromatherapy.

Mevalonic acid (MVA), shikimic acid and methyl erythritol (MEP) biosynthetic pathways of terpenes

Secondary metabolites

The secondary metabolites in a plant have also important roles in normal plant growth and development. The whole cycle of their production is where the biotic and abiotic stress act, producing changes that will impact the final products. Examples are genes, proteins and metabolites that work as a whole system.

That being said, the three most important and well established pathways for the biosynthesis of the chemical compounds in the plant essential oils are the Mevalonic Acid (MVA), the Shikimic acid and methyl erythritol (MEP). Secondary metabolites are biosynthesized from primary metabolites (acetates, pyruvate derivatives, amino acids…) giving way to the terpenoids, the phenylpropanoids, and the alkaloids, mainly speaking.

Mevalonic pathway

In the mevalonic pathway, initially acetyl-CoA will end as isopentenyl phosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), both interconvertible (Refer to figure 2a). The condensation of both IPP and DMAPP, (in the presence of the enzyme geranyl pyrophosphate synthase), forms the geranyl diphosphate (GPP), a C_{10} skeleton, the precursor of isoprenoids. The isoprenoid $C_{10}H_{16}$ is the base chemical block for the monoterpenes. This geranyl diphosphate (GPP) added to an isopentenyl diphosphate (IPP), will originate a C_5 skeleton farnesyl pyrophosphate (FPP), the precursor of the sesquiterpenes ($C_{15}H_{24}$). One or more units of geranyl diphosphate (GPP) added to geranyl diphosphate (GPP) gives geranylgeranyl diphosphate (GGPP) with a C_{20} skeleton, originating the diterpenes ($C_{20}H_{32}$) [18-20].

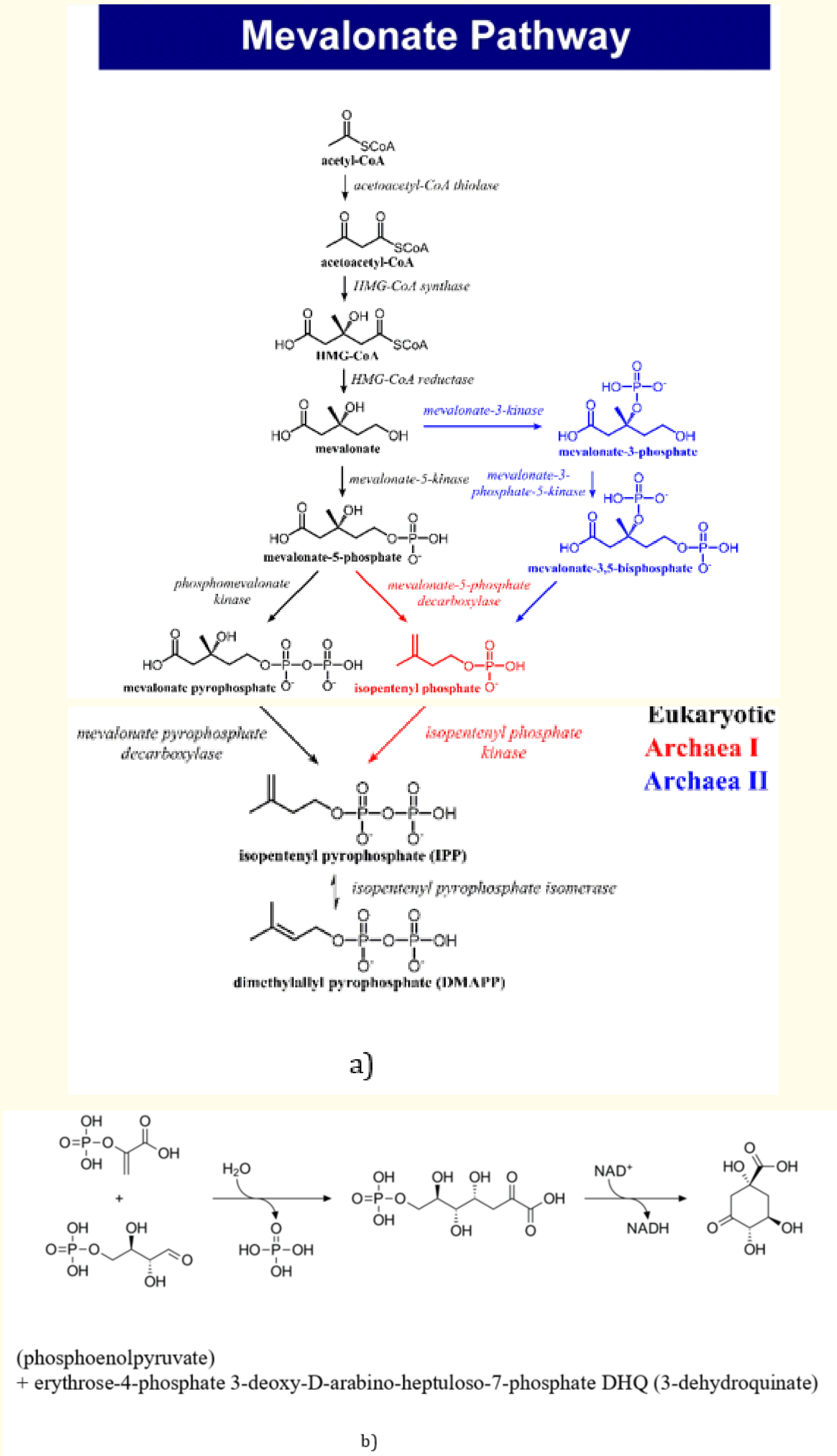
Shikimic acid pathway

Shikimic acid is formed, first step, from the condensation and cyclization of both precursors phosphoenolpyruvate plus D-erythro-4-phosphate, primary metabolites from glucose-6-phosphate (formed from a glucose molecule in a phosphorylation reaction in the early steps of photosynthesis). Second step, the product obtained (3-deoxy-D-arabino-heptulosonic acid-7-phosphate) is catalyzed (by 3-hidroquinate synthase) into a cyclic structure, 3-dehydroquinic acid. This enzymatic reaction needs cobalt (II) and NAD (nicotinamide adenine dinucleotide) as cofactors. Third step, the 3-hydroquinic acid can be converted in either 3-dehydroshikimic acid or to quinic acid. The 3-dehydroshikimic acid continues the pathway and the 4th step is the formation of the shikimic acid. Many steps and substrates after these initial steps, will give way to the phenylpropanoid derivatives (Refer to figure 2b) [21,22].

Methyl erythritol pathway

Methyl erythritol (MEP) (2-C-methyl-D-erythritol 4-phosphate or 1-deoxy-D-xylulose 5-phosphate (DXP)), the non mevalonate pathway (Refer to figure 2c), is another Nature’s resource to synthesize the 5C isoprene units from both DMAPP and IPP. Plants are the only living entities to employ 2 alternative pathways for their Biosynthesis (the mevalonate and the non mevalonate pathways of biosynthesis for secondary metabolites) [18,20,23].

Dimers of farnesyl pyrophosphate (FPP) produces triterpenes ($C_{30}H_{48}$) and dimers of geranylgeranyl diphosphate (GGPP) can produce tetraterpenes ($C_{40}H_{64}$). Normally present in the essential oils obtained by hydrodistillation are monoterpenes, sesquiterpenes, and diterpenes [18,24].



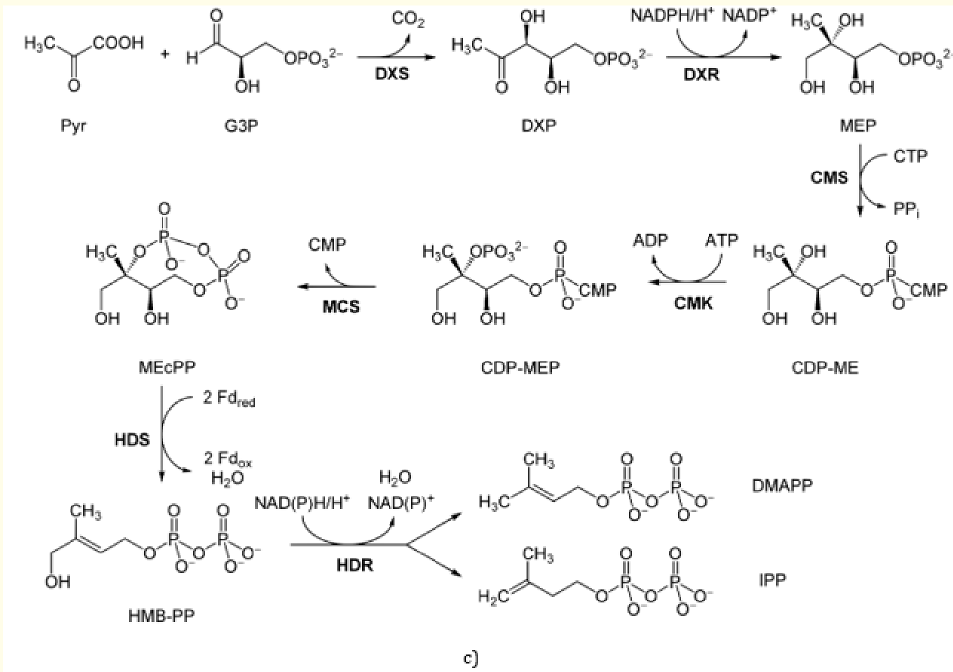


Figure 2: *a) Mevalonate pathway diagram showing the conversion of acetyl-CoA into isopentenyl pyrophosphate, the essential building block of all isoprenoids. The eukaryotic variant is shown in black. Archaeal variants are shown in red and blue. Courtesy of Uclasci1616, CC BY-SA 4.0; (<https://commons.wikimedia.org/w/index.php?search=mevalonate+pathway&title=Special:MediaSearch&type=image>, via Wikimedia Commons); the mevalonate pathway produces terpenes.*

b) Shikimate biosynthesis (for folates and aromatic amino acids): Step 1. PEP (phosphoenolpyruvate) + erythrose-4-phosphate + H2O → 3-deoxy-D-arabino-heptuloso-7-phosphate + orthophosphate; Step 2. 3-deoxy-D-arabino-heptuloso-7-phosphate + NAD+ → DHQ (3-dehydroquinate) + NADH; (<https://commons.wikimedia.org/w/index.php?search=Shikimate+biosynthesis&title=Special:MediaSearch&type=image>, via Wikimedia Commons); the shikimate pathway produces phenylpropanoids.

c) methyl erythritol (MEP) pathway, can produce monoterpenes and diterpenes. (Courtesy of Wikimedia Commons, public domain); Yikrazuul, Public domain, via Wikimedia Commons. < https://commons.wikimedia.org/w/index.php?search=methyl+erythritol+pathway+MEP&title=Special:MediaSearch&type=image> Accessed June 30th 2025.

Main chemical classes found in essential oils

Certain compounds produced in the secondary metabolic pathways as essential oils producing plants present ailment properties known for centuries - from the essenes to the Egyptians. Some of these plants and or their essential oils have been used in the kitchen, in the embalming of the dead, in the wellness, and in religious ceremonies.

Bioactive compounds, secondary metabolites

For instance, the phenolics (shikimate pathways) are almost ubiquitous in medicinal plants due to its essentiality in the promotion of plant growth and reproduction, apart from its strong performance in defense mechanisms. Generally, phenolics are chemical substances with an aromatic ring with -OH substituents: phenolic acids, flavonoids, tannins, isoflavonoids, anthocyanins, quinones, stilbenes (e.g. *trans*-resveratrol).

The terpenes (mevalonic acid pathways) are ubiquitous and the most extensive compounds in Nature, being sub-divided in hemiterpenes (a single isoprene unit - C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30), and tetraterpenes (C40).

The scientific explanations of all those bioactive capabilities now have their say after the 20^{th} century myriads of scientific studies published, and those studies could help clarify the chemical compounds produced by the plants for those positive effects [25].

The main involved explanation for their special capabilities is given by the chemistry and biochemistry as well as chemoecology sciences, which will be discussed briefly.

Eryngium campestre L.

As an example, the Apiaceæ plant *Eryngium campestre* L. ("field eryngo" or "cardo corredor" - a thistle - figure 3) has been studied by many scientists in order to explain its ancient use as a medicinal plant. Like any thistle plant, it has thorns and thrive in dry areas. It can be largely found and used as food in Turkey, Spain, Kosovo and Italy. It has been long known as presenting many ethnomedicinal uses like: " … whooping cough and kidney and urinary tract inflammation; the aerial and root parts are known as antispasmodic, aromatic, diaphoretic, diuretic, expectorant, galactagogue and stimulant, antitussive, diuretic, and appetizer…" [26].

Different parts of the plants normally give different essential oil compositions. Different plant habitats also give different composition of the essential oils as well as different seasons when the plant were collected, even the time of the day, shall give different chemical compound essential oils.

That is why is so important to take into account, first the 100% pureness of the essential oil and then the Latin name as well as their chemotype (main chemical composition), and to know the basics of the essential oil chemistry body of knowledge.

For one to have a better idea, concerning *E. campestre* essential oils, studied from different countries, from different years, one obtained in the extraction of aerial parts, spathulenol (figure 4a) as its major component, in the root extract essential oil, nonanoic acid, 2,3,4-trimethylbenzaldehyde and octanoic acid as the major components [27]. Spathulenol is a tricyclic terpene alcohol, while trimethyl benzaldehyde (figure 4b) is an aromatic aldehyde, and both nonanoic and octanoic acids, are carboxylic acids (figure 4c), all of these molecules also found in the same study. (Refer to figure 5 for the chemical classes).

Figure 3: *Eryngium campestre L. Photograph taken in Tauberland, Germany, 31/07/2005. (Courtesy of Bernd Haynold, CC BY-SA 2.5 <https://creativecommons.org/licenses/by-sa/2.5>, via Wikimedia Commons) accessed June 5th 2025.*

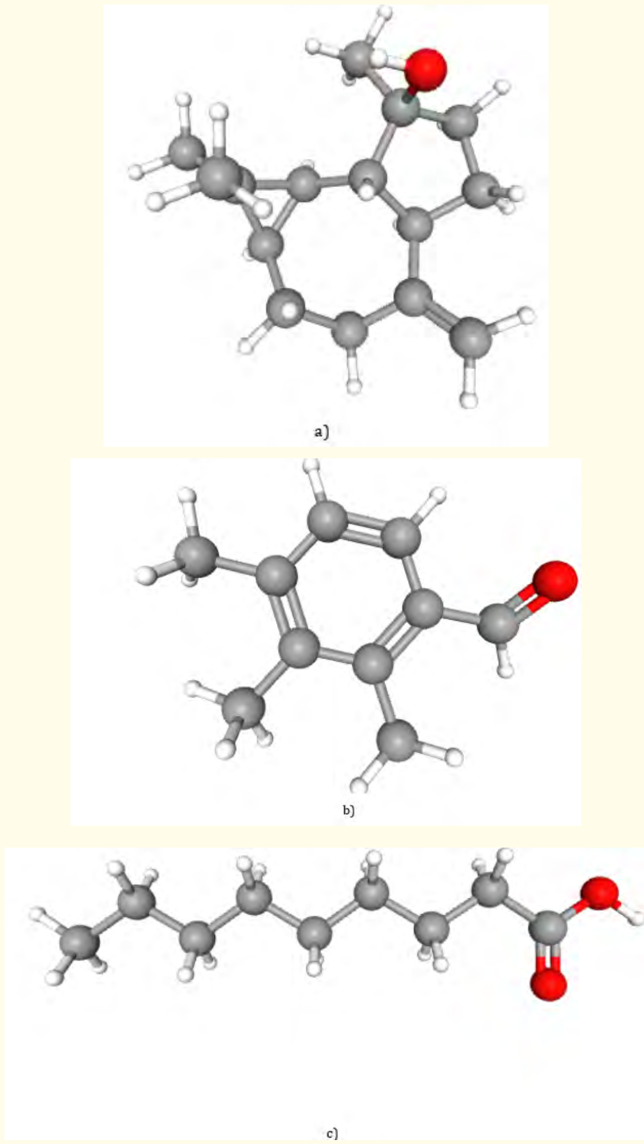


Figure 4: *3-D representation of some major chemical compounds present in Eryngium campestre L.: a) Spathulenol, one of the 5,10-cycloaromadendrane sesquiterpenoids, 4-methylidenedecahydro-1H-cyclopropa[e]azulene carrying three methyl substituents at positions 1, 1 and 7 as well as a hydroxy substituent at position 7 (SQTol = alcohol sesquiterpene); b) 2,3,4 trimethyl benzaldehyde, an aromatic aldehyde; c) nonanoic acid (octanoic acid with 1 C atom less), are carboxylic acids.*

Carbon atoms = grey balls; Oxygen atoms red balls; Hydrogen atoms white balls. Courtesy of PubChem @ <https://pubchem.ncbi.nlm.nih.gov/> Accessed June 1st 2025.

In other study [28] addressing the different chemical composition of *E. campestre* in first inflorescences, and then, in the leaves and stems essential oils, according to different pH soils, sampled in the southwest of Spain, around Cádiz area, the results showed as follows. Germacrene D (sesquiterpene - SQT), β-curcumene (SQT), β-myrcene (monoterpene - MNT) and (*E*)-β-farnesene (SQT) as the main constituents in the inflorescences with the remark that the constituent myrcene were the highest percentage in populations growing in acidic soils, while in more alkaline soil populations, this concentration was the lowest. On the other hand, β-curcumene concentration was higher in plants growing in alkaline soils, whilst practically absent in acidic soils. The stem and leaves obtained essential oils, germacrene D and β-myrcene were the main constituents, not being affected by soil pHs. As could also be seen in this study, terpenoid compounds were highly influenced by the soil pH in some cases, with monoterpenes being higher in concentration in plants growing in alkaline soils.

In a work where extraction of the aerial parts of *E. campestre* from Italy was reported [29], the results also showed essential oils rich in sesquiterpenes with germacrene D (SQT) as the major compound, and also alloaromadendrene (SQT), β-elemene (SQT), spathulenol (Refer to figure 4a) - SQTol), and ledol (SQTol).

In a work with the same *E. campestre* but this time from 37 different locations of harvesting in the western Algeria [30], in soils with low organic matter and low water resources, the main highlighted chemical compounds obtained in the essential oils from hydrodistillation extraction of the aerial parts showed mainly the components: germacrene D (SQT), campestrolide (17-membered ring lactone), spathulenol (refer to figure 4a) - SQTol) and α-cadinol (a cadinane sesquiterpenoid that is cadin-4-ene carrying a hydroxy substituent at position 10, therefore also a sesquiterpenol - SQTol).

In other works in the literature, in other oil extracted from different plants where spathulenol were found as one of the major compounds, many important bioactivity were reported. Some of them are anticholinesterase, anti-nociceptive, anti-hyperalgesic, anti-mycobacterial, antioxidant, anti-proliferative, anti-œdematogenic, among others. [31]

Bioeletronic referencial for essential oils

According to the Bioelectronic referential first established by Pierre Franchomme and Daniel Pénöel [8] (Refer to figure 5 for an adaptation and for some examples), what one can expect from the actions of sesquiterpenes (SQT), non polar molecules, are a major anti-inflammatory, soothing, hypotensive, antiallergic and venolymphatic decongestant, among many others. The last described effect is one of the major actions also for sesquiterpenols (SQTols), which reinforces the probability of *E. campestre* essential oil to be a good choice for these ailments and in DETOX protocols. There is however, a certain path of regularity in the production of the chemical compounds in all vegetal kingdom, but the whole range of them can be very large.

Considering that even the plants studied in these works, described above, being naturally native grown in those countries where the soil conditions are very similar, dry and poor in organic matter, the concentration of the major constituents varied considerably. Notwithstanding, apart from an unpublished chemical compound (the described lactone) the work has unveiled, some of the others found were constantly present in many of the previous studies. In the overall, abiotic conditions do influence the Epigenetics of the vegetal realm [26-30].

Other works reported in the scientific literature have shown many therapeutic values presented by the medicinal plants producing essential oils and some examples will follow.

According to two reviews published in 2014, [32,33], going back as far as published in 1970, grouped and systematized below, the main terpenes found in the essential oils as well as their main therapeutic properties are in the general highlights for many plants, as follows.

Concerning the acyclic monoterpenes (MNT)

β-myrcene (MNT); β-ocimene (MNT); (-)-linalool (MNT alcohol); (-)-citronellol (MNT alcohol); (+)-citronellyl acetate (acetate ester of citronellol - MNT ester); linalyl acetate (acetate ester of linalool - MNT ester); geraniol (MNT alcohol); citral (*Z*-isomer = neural; *E* isomer = geranial - both MNT aldehydes) [32,33].

Main therapeutic properties:

a. Strong antibacterial activity (both gram-positive bacteria and gram-negative bacteria) - being increased by the presence of an oxygen-containing functional group (alcohol, aldehyde, ester).

b. Anti-inflammatory and anti-œdematous activity

c. Cytotoxic, antitumor and chemopreventive properties of acyclic monoterpenes.

(To be highlighted here is the ability of unsaturated terpenes of "trapping activated oxygen species *in vivo* to yield intermediate epoxides, which can alkylate DNA, proteins, and other biomolecules"...) [32 and references 33 - 38 therein] [33].

Concerning the monocyclic terpenes

Carvone (MNT ketone), (+)-limonene (MNT), thymol (MNT phenol), (–)-carveol (MNT alcohol), (–)-perillyl alcohol (MNT alcohol, limonene precursor), terpinen-4-ol (MNT alcohol), (+)-α-terpineol (MNT alcohol), 1,8-cineol (MNT bicyclic ether, epoxy), *p*-cymene (MNT), carvacrol (MNT phenol), eugenol (phenylpropanoid derived - PPN - MNT phenolic), γ-terpinene (MNT) and menthol (MNT alcohol) [32 and references 33 - 38 therein] [33].

Main therapeutic properties:

a. Antimicrobial (antibacterial, antifungal).

b. Vasorelaxant and hypotensive activities.

c. Anti-Inflammatory, antioxidant (some MNT possess both anti-inflammatory and antioxidant properties), local anesthetic, analgesic, antiseptic and choleretic properties.

(To be highlighted also here is the capacity of a studied synergy comprising these MNT above to present a bactericidal effect against methicillin-resistant *Staphylococcus aureus* MRSA). Eugenol alone was responsible for an antibacterial effect against MRSA and MSSA (methicillin-susceptible *Staphylococcus aureus*), and the inhibition of 30 *Helicobacter pylori* strains *in vitro* at low pH level. The bicyclic ether 1,8-cineol showed *in vitro* anticancer and antibacterial properties [32 and references 17, 71 and 72 therein] [33].

Concerning the bicyclic monoterpenes

(+3)-3-carene (MNT), (+)-α-pinene (MNT) and (+)-β-pinene (MNT), (+)-isoborneol (MNT alcohol), (+)-*cis*-verbenol (MNT alcohol) [32,33].

Main therapeutic properties:

a. Local anesthetic and antimicrobial (antifungal, antibacterial, antiviral).

b. Hypotensive and antioxidant activity.

c. Antioxidant and anti-inflammatory.

(Pinenes in plants are antifungal compounds; (+)-*cis*-verbenol showed anti-ischemic activity, antioxidant and anti-inflammatory properties) [32].

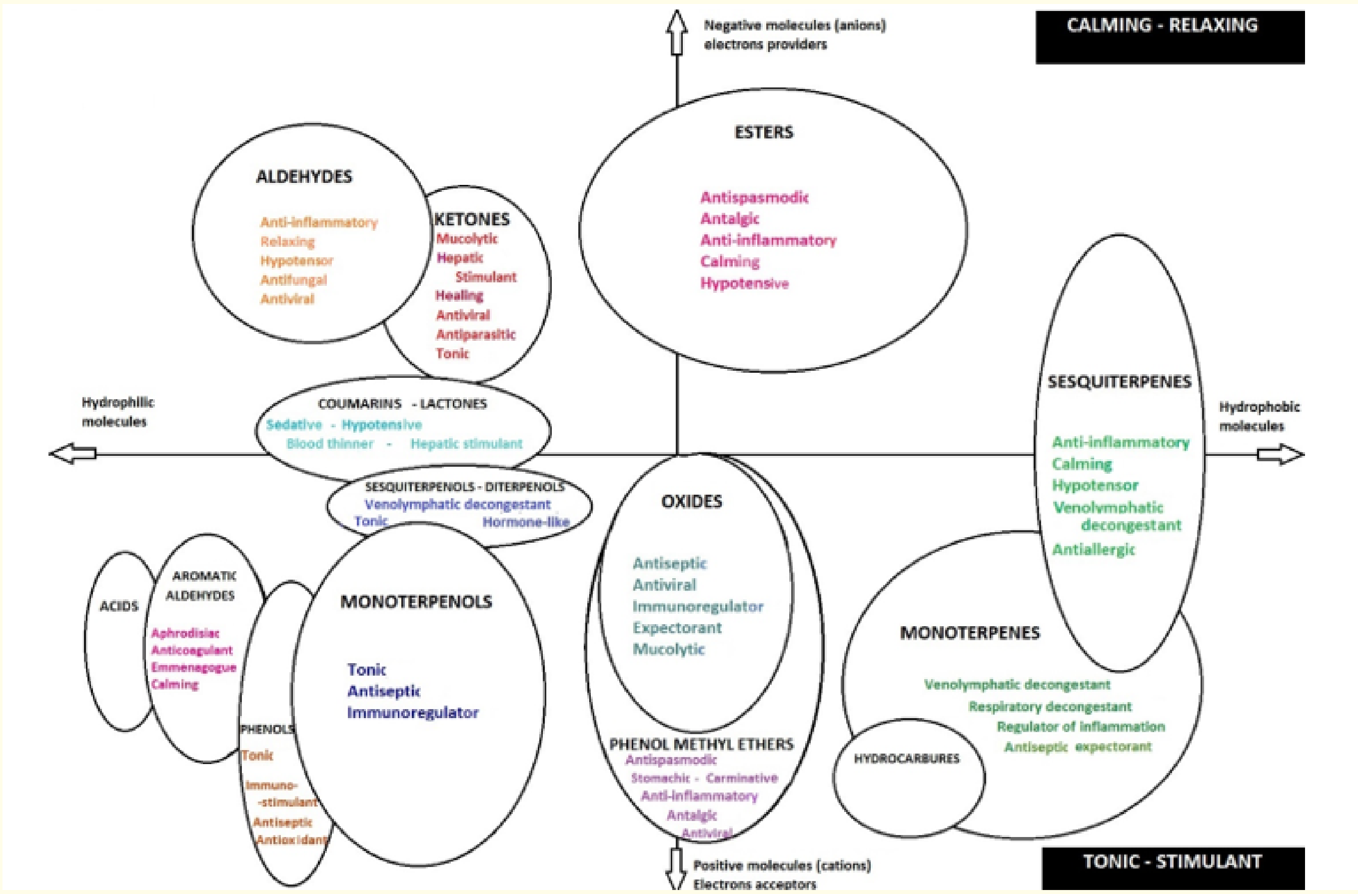


Figure 5: *Bioelectronic diagram of the main chemical classes of essential oils compounds and some of their therapeutic properties stated in some herein cited references as well as in reference [8]. Adapted from [8].*

Some main important therapeutic properties of oxygenated terpenes as acids are antiseptic/anti-infectious action, the most potent being in decreasing order: phenols > acids > alcohols.

Biological activities of essential oils - toxic or not toxic?

Biological systems are primarily composed of chiral compounds and the vegetal kingdom is not an exception. The stereochemistry of chemical compounds that Nature can produce are unparalleled and most of the times very difficult to reproduce in laboratories.

Plant secondary metabolism (Refer to figure 2), apart from being a complex biosynthesis reinforced by the interaction with the environment, has many functions, also being their role to ensure normal plant growth. The complexity here means that, in their biosynthesis, genes, proteins and metabolites (catalyst, elicitor, gene, signal transduction, transcription factor, and transporter) are all working as a one system. Modifications in one or more compounds will induce adjustments, and consequently variations in the others, in the Biosynthesis pathways [16].

That is why same species grown in different weather and soil conditions, produce, sometimes, completely different secondary metabolites and their concentrations. The medicinal plants are not exceptions [34]. The same reasons will affect their produced and consequently extracted essential oils [35-37].

The production of secondary metabolism has as another goal to stop plants from being predated by animals, insects, and mold… and also to become fitter to face the inclemencies of the weather during the ages. So, in the light of that, some chemical compounds can be toxic to the biochemistry of animals and insects, to different degrees. For the sake of simplicity in this section, we shall put these secondary metabolites in three main groups: terpenes (from mevalonic acid), phenylpropanoids (shikimic acid) (Refer to figure 2), and N-containing compounds (alkaloids) [38], and eventually S-containing compounds also (glucosinolates) [39].

The traditional and more widespread way of extracting essential oils are through hydrodistillation, which leaves almost no room to carry large molecules, like triterpenoids, tetraterpenoids, flavonoids and alkaloids. For reaching to their medicine power, as options, one has to use the plants, mother tincture or sometimes teas, and associate them with essential oils or use supercritical CO_2 extraction essential oils, the *totum* of the plant extraction [1,40].

Coumarins

Coumarin (1,2-benzopyrone) [41] derived compounds present in the zests of citrus fruits, among other plants, are phototoxic to human skin. Coumarins inhibit synthesis of vitamin K, a key component in blood clotting in humans.

On the other hand, in plants, these same coumarins and furocoumarins (e.g. 5-geranyloxy-7-methoxycoumarin; 5,7-dimethoxycoumarin (syn. limettin); 5,8-dimethoxypsoralen (syn. isopimpinellin); 5-methoxypsoralen (syn. bergaptene); 5-geranoxypsoralen (syn. bergamottin)), are produced by the citrus fruit peels in order to catch more sunlight to produce more sugar in the juices, along with having an antifungal activity. This production provides the fruits to be more attractive for animals and their seeds to be amply dispersed and be further sprouted up [42].

The smallest coumarin unit is 2*H*-1-benzopyran-2-one (or 1-benzopyran-2-one, a lactone) (Refer to figure 6a), which by gaining an extra -OH group, becomes umbelliferone (Refer to figure 6b) to finally be transformed by multiple steps into psoralen (Refer to figure 6c), the precursor (by other multiple steps) of the furanocoumarins - the group from xanthotoxin cluster and the other group, from bergapten cluster.

Umbelliferone also gives the coumarin osthol in only one biosynthetic step (figure 6d). All previous examples have their source in the smallest coumarin unit 2*H*-1-benzopyran-2-one (or 1-benzopyran-2-one; figure 6a) (lactone).

The continuous, rapid and efficient evolution of plants, had been possible because of the presence of certain enzymes in their metabolism that are capable of producing different results anytime these enzymes are at work. Some enzymes are proteins and some are RNA molecules functioning as enzymes (ribozymes). These RNA derived ribozymes are called promiscuous enzymes, having the ability to recognize and hydrolyze different substrates, presenting then a catalytic promiscuity and not an specific catalytic action. Catalytic promiscuity is defined as the ability of an enzyme to catalyze additional reactions besides the main intended one. The objective for an enzyme to lose its primary activity and being reduced to a promiscuous activity is gene evolution [15,43,44].

As an advantage to the organisms, keeping the capacity to generate high chemical diversity, the promiscuous enzymes enhances their chances of biosynthesize some useful molecule, and the collateral products, as not energy consumed, can find some usefulness in the future [15]. This is the Universe intelligence evolving. In figure 6, one can see the evolution of a single coumarin representation molecule, the smallest one (a) into others in the biosynthesis pathway of some vegetables (b-d).

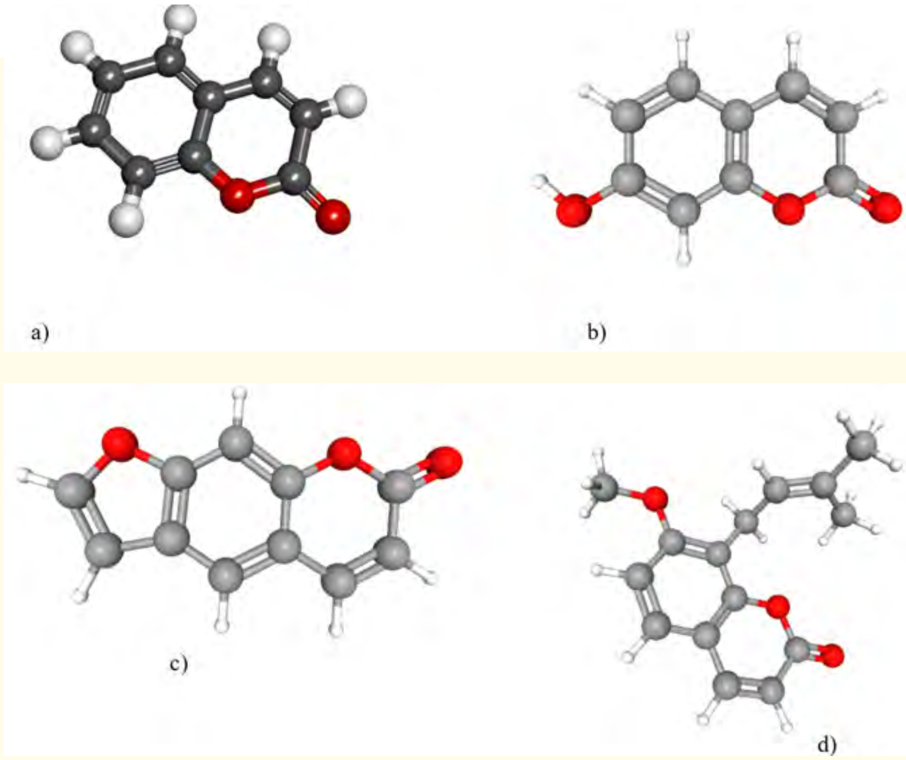


Figure 6: *3-D representation of a) smallest coumarin unit 2H-1-Benzopyran-2-one (or 1-Benzopyran-2-one); b) coumarin umbelliferone (added by one -OH from the coumarin smallest unit) (7-Hydroxy-2H-1-benzopyran-2-one) c) psoralen - precursor of all furanocoumarins (7H-Furo[3,2-g][1]benzopyran-7-one); d) coumarin osthol (7-Methoxy-8-(3-methylbut-2-en-1-yl)-2H-1-benzopyran-2-one).*

Carbon atoms = grey balls; O atoms red balls; H atoms white balls. Courtesy of PubChem @ <https://pubchem.ncbi.nlm.nih.gov/>.

Flavonoids

Nature ingenuity is far beyond our imagination. These Nature Devas are certainly capable of myriads of chemical and biochemical processes. Concerning the complexation of metals by plants secondary metabolic compounds, many studies can be found in the scientific literature.

A work published in a book in 2008 [45], showed the antioxidant and the complexation properties of flavonoids with some biologically relevant metal ions (there are plenty of them). Quercetin in figure 7 in a 2-D (a) and a 3-D (b) representations, has 5 -OH groups that are capable of chelating metal ions (metal ions = deficient in electrons). Quercetin and luteolin (flavonoids) are natural metal chelators [46].

The flavonoids are obtained by the phenylpropanoid biosynthetic pathway, and are present in fruits and vegetables. Complexation studies of flavonoids were done with the main essential metal ions: Mg^{2+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Mn^{2+}, Fe^{2+}, Fe^{3+} [45,47,48] and also with Cr^{3+}, Co^{2+} and Ni^{2+} [46].

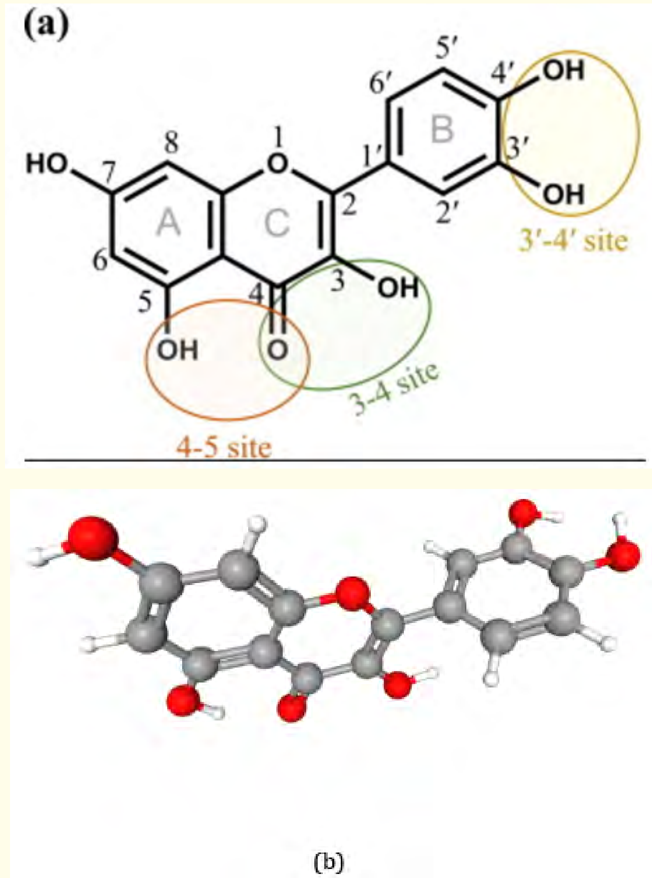


Figure 7: *(a) 2-D representation of Quercetin showing the binding possible sites in the molecule. (b) 3D representation of Quercetin, a flavonoid structure present in many plants; flavonoids present a flavane 2-phenyl-benzo-γ-piran nucleus (composed of 2 benzene rings and linked by an heterocyclic pyran ring). Carbon atoms = grey balls; Oxygen atoms = red balls; Hydrogen atoms = white balls. Courtesy of PubChem @ <https://pubchem.ncbi.nlm.nih.gov/> Accessed June 2nd 2025; Adapted from reference [46].*

The results showed the formation of stable complexes of the studied flavonoids and these metal ions in a 1:1 ligand to metal experimental ratio. All metal ions studied formed stable enough complex to be measured by Potentiometric Titrations [49-53] and other complexed species were also found starting around and before neutral pH, specially Zn^{2+}, Cu^{2+}, Fe^{3+}, Mn^{2+}. They all presented antioxidant activities, specially for the ligand to metal ratio of 1:1 complexes. The proposed structure is the complexation being through the oxygens atoms of carbon number 3 and number 4 (ring letter C in figure 7a). However other two sites are possible to form complexes with metal ions: Through the Oxygen atom: a) 3’ and 4’ in ring B present -OH groups (ring letter B in figure 7a), (e.g. flavanone eriodictyol - 5,7,3’,4’-tetrahydroxyflavanone; flavone luteolin 5,7,3’,4’-tetrahydroflavone; quercetin 3,5,7,3’,4’,5’-pentahydroxyflavone…); b) Oxygen atom 4 (ring letter C figure 7a) and 5 (ring letter A figure 7a) (e.g. flavonol quercetin - 3,5,7,3’,4’-pentahydroxyflavone…). In fact, 1 mol of quercetin can hold (complex, bind) 3 mols of metal ions given the right pH and concentration conditions [45-48].

Flavonoids have been studied in metabolic diseases, prevention and treatment [54,55]. Many forms of cancer are caused by metabolic triggered origins [56-58] and many other studies showed positive results in consuming bioflavonoids [59,60] and in avoiding certain foods, mainly glucose containing ones [61,62]. These kind of studies attempt is a clear evidence of how promising a healthy diet, in which flavonoids are privileged, as well as maintaining healthy habits can prevent many ailments.

The flavonoid-Fe^{2+} complexes showed unique properties like DNA targeting and nitration of Heme and confirmed the alternation of redox potential (antioxidant activity); membrane transport and lipophilicity, and heme enzymes and Fe(II) /Fe(III) dependent enzymes (enzyme inhibition). So, some of the flavonoids biological effects can be enhanced or due to their complexing ability towards transition metal ions [48,59].

Other studied flavonoid metal complexes displayed antiproliferative activity against cancerous cell lines. When the complexes of quercetin with rare earth metal ions were studied, DNA transcription and inhibition of tumor cell growth through chelation to DNA were clearly shown, with the activity of the complexes being superior to that of the flavonoid alone [59].

Complexes of flavonoids and many metal ions were studied in various works presenting all of them, different pharmacological activities. Those are from anti-diabetic to anti-microbial, anti-inflammatory, anti-tumor to anti-oxidant. One remarkable finding was that lanthanide-quercetin complex inhibited cancer cell proliferation better than that of free quercetin on human cervical carcinoma cells [46,63,64].

An example of a study showing the crucial importance of Zn^{2+} in the diet to boost the immune system can be found in reference [65]. A recent review on natural products and immunity can be found in [66].

Alkaloids

Alkaloids are derived from amino acids and can be synthesized also as secondary metabolites specially in plants. Because of their origins, they all present Nitrogen atoms in their structure. Because of the presence of N these substances exhibit a basic character when reacting and normally are considered as amine and therefore, Lewis bases [67,68]. Alkaloids, in one systematic way to put them, can be divided into classes according to their backbone structure into indoles, isoquinolines, pyrrolidines, pyridines, pyrrolizidines, quinolines, tropanes, and steroids.

Alkaloids, either natural or synthesized, present strong pharmacologic activity and are part of the plant arsenal to cope with the environment.

In general, many researches showed their anti-inflammatory, anticancer, analgesics, local anesthetic and pain relief, neuropharmacologic, antimicrobial, antifungal, antibacterial, antimitotic, anti-inflammatory, analgesic, local anesthetic, hypnotic, psychotropic, and antitumor activities… for some of them [69-72].

Some examples of alkaloids are morphine, strychnine, quinine, atropine, caffeine, ephedrine, and nicotine… Speaking of quinine - a well known anti-malarial agent [73], a 2012 publication stated: "…Quinine was first recognized as a potent antimalarial agent hundreds of years ago. Since then, the beneficial effects of quinine and its more advanced synthetic forms, chloroquine and hydroxychloroquine, have been increasingly recognized in a myriad of other diseases in addition to malaria. In recent years, antimalarials were shown to have various immunomodulatory effects…" [69,74].

These properties of either quinine and hydroxychloroquine, although from different origins (quinine figure 8a), natural, from plants - chloroquine [75] (figure 8b) and hydroxychloroquine (figure 8c) - synthetic), both present Nitrogen atoms, represented as blue balls in their 3-D structure representations, which eventually may explain their similar biological effects to the natural alkaloid quinine.

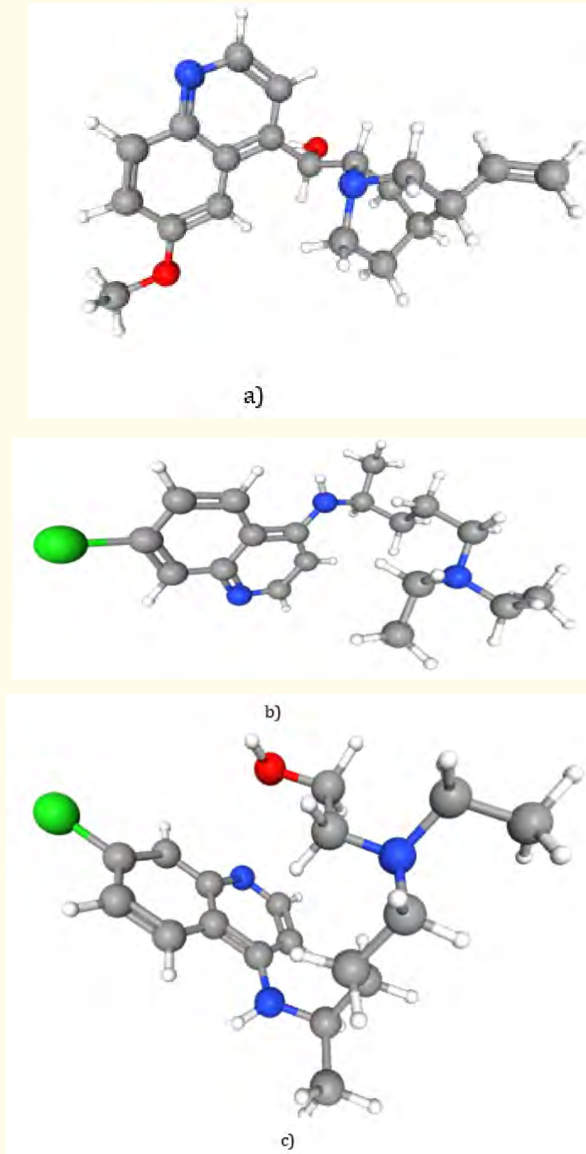


Figure 8: *3-D representation of the structures: a) quinine - b) chloroquine - c) hydroxychloroquine - Carbon atoms = grey balls; Oxygen atoms = red balls; Hydrogen atoms = white balls; Cl atom = green ball and Nitrogen atoms = blue balls. Courtesy of PubChem @ <https://pubchem.ncbi.nlm.nih.gov/> Accessed June 6th 2025.*

Certain alkaloids however, present toxicity even at very low concentrations. This is also a matter of individual sensitivity, some being more susceptible than others to their toxic effects and concentration (dosage). Also a proper identification of plants is crucial to avoid accidental ingestion of these toxic alkaloids. The toxic alkaloids can be present in seeds, flowers or weeds. The toxic effects can appear by ingestion or from harvesting the plants without proper body protection. Some of them that are toxic at low doses are tropane alkaloids (atropine, hyoscyamine, scopolamine…), coniine, aconitine and cytisine. The toxic effects can vary from as potent neurotoxins, as responsible for severe cardiovascular effects to causing liver, kidneys and gastrointestinal tract disorders [76,77].

Some alkaloids biosynthesized that are addictive and toxic must be avoided in an intended DETOX session. Examples are strychnine (from *Strychnos* species), curare (*Chondrodendron tomentosum*), coniine (*Conium maculatum*); and others with psychedelic activity, mescaline (*Anhalonium species*), psilocybin from the fungi *Psilocybe mexicana,* and the main alkaloids present in the vine *Banisteriopsis caapi*, which main ingredients are used for the ayahuasca rituals, the alkaloids harmaline, harmine and tetrahydroharmine [78]. Those, and others not cited herein but toxic in any way, must be avoided in any circumstance [1,79].

Alkaloids can be found in seeds, roots, stems and leaves of higher plants, such as those in the Solanaceæ, Annonaceæ, Ranunculaceæ, Loganiaceæ, Menispermaceæ, Amaryllidaceæ, Lamiaceæ and Papaveraceæ families.

Examples of this important alkaloid group of phytochemicals

The plant *Hydrastis canadensis* L. (Goldenseal - Ranunculaceæ), presenting isoquinoline alkaloids (hydrastine, berberine, berberastine, (-)-hydrastinine, tetrahydroberberine, canadine, and canalidine), has been used for ages as medicinal in Ayurvedic and Chinese Medicines [80,81].

The family Annonaceæ encompasses many species with proven anticancer properties. These plants are very welcome in a DETOX session because of that prevention effect they have.

The genus *Duguetia (*Annonaceæ), mainly from South America for instance, present isoquinoline alkaloids, as well as in the *Guatteria* genus (Annonaceæ). The isoquinoline-derived rare copyrine alkaloids were present in the *Duguetia* species studies [82,83].

Sampangine (a copyrine alkaloid) found in the cananga tree, has been investigated and found antimicrobial action and antitumor potential [83]. Other species from *Duguetia*, *D. hadrantha* studied [84] showed 2 new alkaloids at that time, 4,5-dioxo-1-azaaporphinoids, hadranthine A and hadranthine B among others, that showed specificity towards antimalarial activity, cytotoxicity to selected human cell lines and to human malignant melanoma. A few unusual groups of alkaloids appear to be specific to this genus [82].

Paw paw, *Asimina triloba* and Brazilian paw paw (*Annona muricata* L., (graviola)), Annonaceæ, twig extracts have been known and used for its anticancer properties. These anticancer properties are mainly due to the acetogenin alkaloids present in this plant: 10-hydroxyglaucanetin, annonacin, and annonacin A. The induction of secreted VEGF protein represents a key event in hypoxia-induced tumor angiogenesis. These acetogenins are only found in Annonaceæ species [85,86].

Leaves of *Moringa oleifera* Lam. (Moringaceæ) contain active components like polyphenols, flavonoids, phenylpropanoids, terpenoids, fatty acids, alkanes, sterols, carotenoids, alkaloids, glucosinolates, isothiocyanates, folates, tannins, saponins, and minerals, vitamins and fatty acids. Polyphenols and flavonoids, the main bioactive constituents, present antioxidant activity and anticancer properties; are anti-epilepsy, antisepsis, anti-inflammatory, antifungal, anti-hypertension, anti-diabetes, anti-spasm, anti-hyperthyroidism; reduce metal toxicity and plasma and liver lipids and affects obesity-related reproductive diseases, among many others. The alkaloids presented by *M. oleifera* are responsible for cardiac stimulation, stabilizing blood pressure, decrease of fat and cholesterol thus preventing hyperlipidemia. Isothiocyanates contained in *M. oleifera* seeds are anti-inflammatory, antioxidant, antibacterial and anticancer; its essential oil has coagulant effect that can accelerate wound healing [84,87].

Some alkaloids have a preventive role in neurodegenerative disorders, by attenuating their development either by inhibiting the activity of acetylcholinesterase, by increasing the level of gamma-aminobutyric acid (GABA), as an antagonist of N-methyl-D-aspartate (NMDA) receptors, which become severely disordered in Alzheimer' disease, among other functions. Among the isoquinoline alkaloids Berberine (*Berberis vulgaris* - barberry), piperidine alkaloids, piperidine (*Piper nigrum*, *Piper longum*, black pepper and long pepper), vinca alkaloids, vinpocetine (*Vinca minor* - lesser periwinkle), are some examples [88].

A plant known as "Boldo do Brasil" - *Plectranthus barbatus* Andrews. Engl. - has medicinal popular use in Brazil, in tropical Africa, India, and China. Phytochemical screening confirmed the presence mainly in the leaves of saponins, tannins, alkaloids, terpenoids and essential oils [89].

In the roots, the analysis of the extracts found at least 15 polyphenolic (some flavonoids) and their derivatives as quinic acid, protocatechuic acid, 4-hydroxybenzoic acid, 2-hydroxybenzoic acid, protocatechuic aldehyde, gentisic acid, 4-hydroxybenzoic acid *O*-hexoside, vanillic acid, caffeic acid, syringic acid, *p*-coumaric acid, ferulic acid, ellagic acid, hydroxygallic acid and rosmarinic acid (around 1mg/g extracted root mass) were identified, thus presenting a high antioxidant potential [90].

Plectranthus barbatus (Boldo do Brasil) essential oils, thanks to their antibacterial properties, can also be useful in the treatment of dermatological diseases, inhibits the growth of *Staphylococcus aureus*, better than the popular tea tree (*Melaleuca alternifolia*) essential oil used for the care of acne-prone skin, the former being effective against *Staphylococcus epidermidis*. Additionally, the oil reduces the growth of *Candida albican*s yeasts responsible for candidiasis of the skin and mucous membranes [91,92]. Also in the roots of Boldo do Brasil it was found forskolin (one of the 67 diterpenes [92], this one of the labdane family - main biologically active compound) which is an adenylate cyclase activator (raises the cyclic adenosine monophosphate level in cells). By activating adenylate cyclase and thus increasing the level of cyclic adenosine monophosphate, forskolin prevents platelet aggregation and lowers blood and intraocular pressure, among others [90].

Boldo do Brasil - *Plectranthus barbatus* - also presents 0.4 to 0.5% of the benzoquinolinic alkaloids which boldine (figure 9a) is the main toxic one but only in a much higher concentration than the one presented by the plant. Notwithstanding, boldine seems to present more cytotoxicity to cancer cells and strongly suppresses their telomerase activity than other counterparts. As DNA polymerase (ribonucleoprotein complex, whose enzymatic core contains the telomerase reverse transcriptase (TERT) and the non-coding human telomerase RNA (hTR) acting as a template), in the addition of telomer repeats to chromosome ends, is not capable to completely copy DNA at the very ends of chromosomes, thus some nucleotides (around 50) are lost during each cell cycle [93]. This process will produce gradual telomere length shortening. There is a critical point to this shortening, when then these shorter telomeres will cause senescence and eventually cell death. However, tumor cells have the ability to activate the maintenance of telomere length process, therefore this telomerase expression which is restricted and tightly controlled during homeostasis, presents increased activity and levels in most human cancers [94]. Although the search for eternity is among us humans, the telomerases have a lot to teach. The damages that DNA can suffer are legion and if all DNA are supposed to be "immortal", one or more harmful mutation could then replicate indefinitely, like the hallmarks of cancer. Although telomeres are non-coding DNA, in being shortened, do produce overall health impacts on the body, mainly in cellular function.

Boldine is a benzoquinolinic alkaloid that is found in many other "boldos" (e.g. *Peumus boldus* Molina - "boldo do Chile") [95] presenting as well isoquinolinic alkaloids as laurotetanine (figure 9b), and coclaurine (figure 9c).

The chemical constituents of any plant can vary according to biotic and abiotic conditions, as explained above. These chemical constituents can vary also according to the plant parts, like wood, leaves, root and bark. "Boldos" are not exception, and boldine can be found in the same plant species (*Peumus boldus*) ranging from (relative abundance) wood as 12.8%, root as 8.5%, and leaves as 57.7%. In the same assay, coclaurine can be found from 0.0% in wood, 6.1% in roots, 17.6% in leaves to 8.8% in bark. Laurotetanine, on the other hand, was found from 2.4% in wood, 1.2% in roots, 31.7% in leaves to 0.0% in bark [96]. The "boldo do Chile" - *Peumus boldus* Molina - presents apart from alkaloids in their leaves, catechin, epicatechin, gallic acid, caffeic acid, rutin, quercetin glycosides, Kæmpferol derivatives, among others, all antioxidant, anticancer and anti-inflammatory compounds most searched in a DETOX program [1,95].

The main desired features presented by the alkaloids found in "boldos" in a DETOX program are (also for other chemical compounds): to significantly reduce inflammatory cells, including eosinophils, neutrophils, lymphocytes, and macrophages [97]; the great antioxidant power with main action in the liver cells [98,99]; to regulate the digestive system their diuretic and expectorant powers [99,100].

The infusion of leaves and of wood of "boldo do Chile" in [95,99,100] showed the presence of the following alkaloids:

a. Infusions obtained from the leaves:

- Boldine 0.38 ± 0.11 μg/mL
- Coclaurine 3.64 ± 1.91 μg/mL
- Laurotetanine 1.45 ± 0.58 μg/mL

b. Infusions obtained from the wood:

- Boldine 1.95 ± 0.25 μg/mL
- Coclaurine 5.98 ± 1.73 μg/mL
- Laurotetanine 1.20 ± 0.53 μg/mL

Boldine has long been recognised as an antioxidant compound [101] and hepatoprotective, but not only. In 2024 [35] and in 2025 [102] two articles published a list of the beneficial effects in humans of boldine. It is a nootropic agent (improves mental performance), has anti-cancer activity [103], has kidney protective, cytoprotective and neuroprotective activities, is anti-Alzheimer's and anti-osteoporotic properties, and is capable of modulating many biological networks. These are main important ones required in a DETOX program [1]. Boldine is also found in *Lindera aggregate*, *Actinodaphne pruinosa*, *Litsea cubeba* and *Phoebe grandis* [103,104].

Laurotetanine is also found in *Litsea cubeba (*Lour.) Pers. plant. It was found that this alkaloid decreases inflammatory cytokines, serum IgE and histamine in asthma studies [97].

The rosmarinic acid is a phenolic compound (Refer to figure 5) with a high antioxidant action. This compound is present in other plants known to have a great antibacterial action, as well in their essential oils, like in *Rosmarinus officinalis* 1,33 mg/g of extracted root mass and *Origanum vulgare,* 12.4 mg/g [105].

Coclaurine is a nicotinic acetylcholine receptor (nAChRs) antagonist with antineoplastic properties [106]. Coclaurine is also found in *Cissampelos pareira* L., used in Ayurvedic and Chinese medicine [107]; in *Annona muricata* L. [108]; *Asimina triloba* L. Dunal [109]; *Annona squamosa* L. [106,110], among others.

Aromatherapy - Promoting DETOX

Main properties of chemical compounds present in essential oils and their possibilities of ailments

In figure 5, a general overview of some of the possible biological and pharmacological effects of essential oils is depicted. Although not exhaustive, because of the myriads of possibilities when one considers the synergies among two or more essential oils, it is however a good summary of their therapeutic activities.

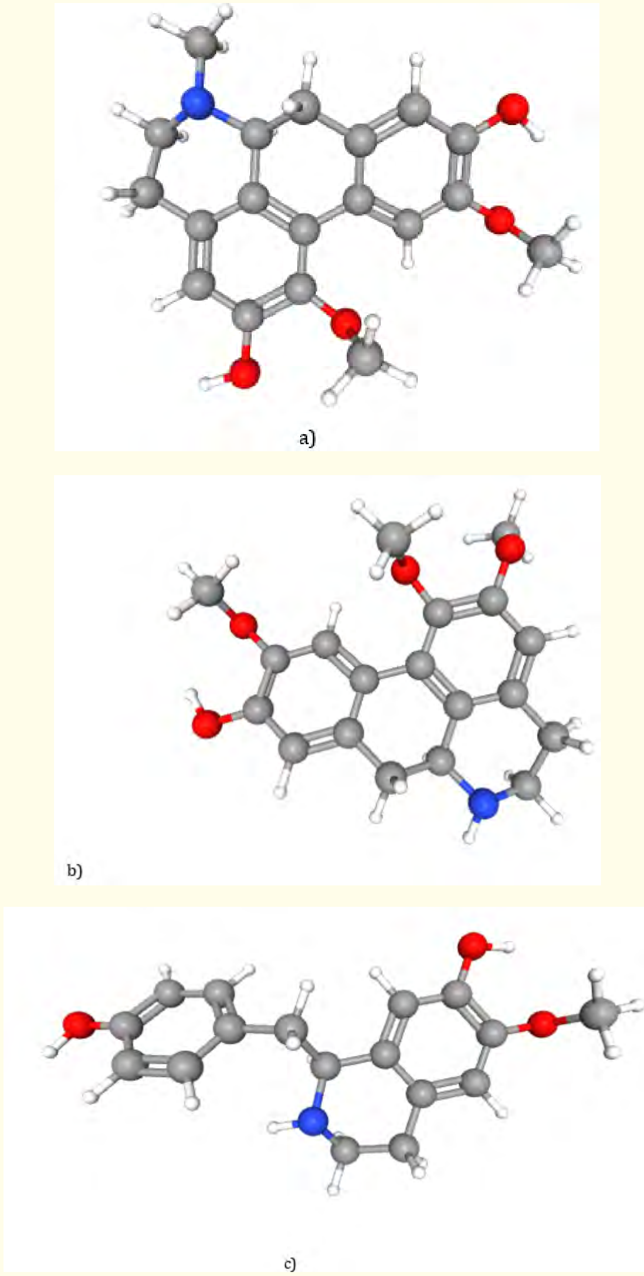


Figure 9: *3-D representation of the molecules a) boldine ((6aS)-1,10-dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinoline-2,9-diol); b) laurotetanine ((6aS)-1,2,10-trimethoxy-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolin-9-ol); c) coclaurine ((1S)-1-[(4-hydroxyphenyl)methyl]-6-methoxy-1,2,3,4-tetrahydroisoquinolin-7-ol).*

Carbon atoms = grey balls; Oxygen atoms = red balls; Hydrogen atoms = white balls, and Nitrogen atoms = blue balls. Courtesy of PubChem @ <https://pubchem.ncbi.nlm.nih.gov/> Accessed June 25th 2025.

Specific properties many times are found in the trace or minor compounds in the essential oils, as it can be seen in many of them, either in synergy or in each one of them, including almost all chemical class compounds studied and characterised so far in the scientific literature.

Essential oils (EOs) are concentrates from a plant, normally extracted from steam distillation of one or various parts of it. The parts can be leaves, flowers, stems, barks, aerial part, roots… and EOs have been used for ages.

There is a huge panoply of plants producing essential oils. So, in this work we will review some not that popular but nonetheless some of the most powerful combination of chemical compounds issued by genetic expression of plants living in very harsh conditions. These harsh conditions can be related to soil, weather, rainy and/or drought and/or freezing conditions, and those capable of living and thriving in sand, near the coast lines. For more detailed informations on essential oils, please refer to google scholar for thousands of scientific articles on many essential oils known to present.

It is important to enphasize that the original site where the plant was originally developed is the one and only place for acquiring the essential oil. In their original habitat, not only the indigenous plants will provide the original oils, but also the plants will be the most potent and efficient producers of the essential oils bearing their names.

The essential oils that are described in this work (more to follow on a future publication) are as follows:

- *Baccharis trimera* (Less.) DC. or *Baccharis genistelloides* subsp. *crispa* (Spreng.) Joch.Müll. - common name, carqueja.
- *Rhododendron groenlandicum* (Oeder) Kron and Judd - common name, labrador tea;
- *Cistus ladanifer* L. - common names, gum rockrose or Labdanum;
- *Daucus carota* L. (wild species) - common name, wild carrot.

Essential oil studies with carqueja (*Baccharis trimera*)

Plant natively found in the south and southwest of Brazil [67], in dry areas with very occasional rain, nonetheless present in Amazonian Forest, also is found in Argentina, Chile, Bolivia, Peru, Paraguay and Uruguay. It is a Latin American plant.

In [111] it was shown carqueja's pharmacological action against enterotoxigenic *Escherichia coli*. Enterotoxigenic *E. coli* is responsible for producing major virulence factors including colonization factors and producing enterotoxins, the latter inducing diarrhea in the host.

In [112] and many references therein and in [113], it was shown the main constituents of the EO as: the unusual o-menthane skeleton compounds carquejyl acetate ([(1S,6R)-5-methylidene-6-prop-1-en-2-ylcyclohex-2-en-1-yl] acetate or *(2R,3S)-ortho*-mentha-1(7),4,8-trien-3-ol acetate), and carquejol (5-methylidene-6-prop-1-en-2-ylcyclohex-2-en-1-ol); and several sesquiterpenic alcohols: palustrol, ledol, spathulenol, viridiflorol, β-eudesmol; sesquiterpenes: α-pinene and β-pinene, germacrene D, myrcene, *trans*-caryophyllene, bicyclogermacrene; and a sesquiterpenic oxide: caryophyllene oxide. Also carqueja's essential oil showed anti-helminthic and antimicrobial actions and counting. In [112], a total of 150 volatile compounds were identified.

In [114] it was shown an antiulcer activity by decreasing the expression of COX-1, increasing the expression of VEGF and by decreasing the activity of pro-MMP-2. In [115] it was shown antioxidant activity *in vitro,* as well as anti-inflammatory, antidiabetic, analgesic, antihepatotoxic, and antimutagenic properties among myriads of others.

In summary, the carqueja EO is very adequate to a DETOX process, where the emunctories are clean and aseptic and dewormed.

Essential oil studies with labrador tea or greenland moss or ledum (*Rhododendron groenlandicum*)

Commonly found in subarctic and boreal ecosystems, has adapted well to the far north regions of the northern hemisphere.

In 1993 [116], a study in Québec with labrador tea showed already, considering the then analytical tools limitations compared to today, 75 chemical compounds, with the majority of them, chemically elucidated. This can give an idea of how rich Ledum species are in secondary metabolites production.

Among some of the flavonoids, phenolic acids and terpenoids, which are ledum major components, the ones identified in [117] are as follows.

Phenolic acids and flavonoids: quercetin, kæmpferol, and myricetin derivatives; phenolic acids gallic acid, ellagic acid, and caffeic acid derivatives, chlorogenic acid, (+)-catechin, (-)-epicatechin, B-type proanthocyanidins, quercetin-3-*O*-galactoside, quercetin-3-*O*-glucoside, quercetin-glycoside, quercetin-3-*O*-arabinoside; myricetin, hyperoside, rutin, myricetin.

Terpenoids: Terpenoids, monoterpenes (terpinen-4-ol-monoterpene alcohol present in the essential oil of tea tree), sesquiterpenes (ledol, palustrol, *trans*-nerolidol, viridiflorol, α-pinene, α- and β-selinene, α-copaene, limonene, α-gurjunene, β-caryophyllene, *p*-cymene, *cis*- and *trans*-*p*-mentha-1,7(8)-diene, elemene, cubebene, sabinene, germacrene, germacrone, germacrene A and germacrene B,…) and triterpenes (taxerol, uvaol, ursolic acid).

Coumarins: Coumarins (fraxetin, fraxin, esculin…) knowing that all their percentages can greatly vary depending on which part of the plant is analysed. According to ethnopharmacological studies, the essential oil of *R. groenlandicum* is less toxic than *R. tomentosum* due to less Ledol concentration in the former and sterols.

The plant is historically known in Canada as presenting anti-inflammatory activities towards the liver, kidney, lung, and digestive system diseases [117].

The essential oil of *R. groenlandicum* obtained in this study [117] showed 160 different compounds, all elucidated. This researchers also studied other species of *Rhododendron* capable of producing essential oils.

According to [118] of 2015, 166 compounds were found in the essential oil of *R. groenlandicum* and 158 chemically identified. In these 158 chemical compounds identified, also aldehydes were detected (nonanal, myrtenal, *trans*-2-decenal), and ketones (sabina ketone, *trans*-4-caranone and *cis*-4-caranone, carvotan acetone…).

Considering the scheme in figure 5, the essential oil of Ledum produces chemical compounds almost classified in all possible chemical classes found in the vegetal kingdom. This essential oil can help human biochemistry in numerous ways, but unfortunately, there are few studies concerning its biological and pharmacological effects in the scientific literature. This essential oil is one of my favorites because of its broad-spectrum pharmacological action in any possible way a plant or its essential oil can give to us humans.

Essential oil studies with rockrose (*Cistus ladanifer*)

Originally from the western Mediterranean lands, comprising Iberian Peninsula, southern France, Marocco and Algeria, the rockrose is very adapted to fires (are pyrophile plants) and can thrive in very poor soils. The plant from whom labdanum is also produced by its leaves, *Cistus* genus has many species present all over the Mediterranean sea. According to common knowledge in eastern Marocco, *Cistus ladanifer* and *C. libanotis* are used as an anti-diarrheic, antiacid and antispasmodic by simple decoction of their leaves. According to [119 and references cited therein] a number of compounds with bioactivity can be found in *Cistus ladanifer* such as: antihypertensive, antimicrobial, antioxidant, antifungal.

In a 2013 [119] and in a 2024 [120] studies, the main chemical constituents found in the essential oil of *C. ladanifer* was: Terpenes: camphene, α-pinene, α-cubebene, δ-cadinene, γ-terpinene, aromadendrene; alcohol terpenes (terpenols): borneol, viridiflorol, ledol, 1,10-di-*epi*-cubenol, carvacrol, *trans*-pinocarveol, *trans*-carveol, *p*-mentha-1,4-dien-7-ol, *p*-cymen-8-ol, terpinen-4-ol, myrtenol, palustrol, spathulenol; ketones (terpenones): (*Z*)-β-damascone, cyclohexanone-2,2,6-trimethyl, sabina ketone, verbenone; terpene aldehyde (terpenals): myrtenal, α-campholene aldehyde; ester terpene: bornyl acetate, myrtenyl acetate; terpene oxide as caryophyllene oxide.

Its bioactivity is very wide due to a broad-spectrum of its chemical class compounds. From [120] antibacterial activity (*Staphylococcus aureus, Salmonella typhi, Escherichia coli, Acinetobacter, Candida glabrata, Candida tropicalis, Candida dubliniensis*…), antifungal activity (*Aspergillus niger*…) were found; and from [121] a powerful antimicrobial activity was seen (against *Staphylococcus aureus*, *Escherichia coli*, *Acinetobacter baumannii* - full antibiotic resistants), *Salmonella Typhi)*, as well as antifungal activity - *Candida tropicalis* and *Cryptococcus neoformans* appeared to be the most sensitive strains to the essential oil, followed by *Rhodotorula rubra* and *Penicillium* sp., then *Candida dubliniensis* and *Candida glabrata*.

Essential oil studies with wild carrot (*Daucus carota subsp carota*)

The main difference between the wild and the cultivated carrot are obviously the chemical composition the plant produces as secondary metabolites. While the wild species florishes in a poor and dry soil, and thus develop a very small root system (the carrot), the cultivated one (*Daucus carota* subsp *sativus*) is intended to produce a developed root - the carrot). So, the environmental conditions must be the opposite to produce either the one or the other species. The essential oil of the wild or the cultivated are obtained by hydrodistillation of the flowering tops with mature umbels with developed seeds, giving a very small yield of essential oils if the plant is almost dried.

Therefore, one is tempted to buy the essential oil from the cultivated one, because the price has no parallel to the wild one. But do not let yourself be deceived, as the potency and variety of the essential oil chemical compounds issued by the seeds of a wild plant surpasses by far the one obtained by the cultivated plant ones.

In 2009 a group of researches leaded by Lígia Salgueiro in Portugal [122], studied and characterized the essential oils obtained by wild plants from Sardinia, Italy (Mediterranean sea), and Portugal (Atlantic coast), and compared both. The results showed remarkable differences in the major constituents of the 2 essential oils. EO from Portugal showed major components being geranyl acetate (ester monoterpene) and α-pinene (monoterpene), while EO from Sardinia, β-bisabolene (sesquiterpene) and 11-α-(H)-himachal-4e-en-1-β-ol (diterpene alcohol). Both EOs presented antifungal activities, with the EO from Sardinia showing the highest power in this biological activity.

This is clearly a proof that soil composition (proximity from the sea, salty lands, dry areas, rocky land…), extreme weather condition, and plant stress, make a group of genes to express in one set of the same plants (Sardinia), while being silenced in another set in very different conditions (Portugal), for instance. Also, what one can observe from the results is that the Portuguese plants biosynthesized monoterpenes only, while the Sardinian plants, went far in the biosynthetic capabilities, producing sesquiterpenes and diterpenes. This shows the importance of knowing the chemotype of the essential oil to be acquired.

Another study [123] from 2010, compared essential oils from wild carrot from 2 different sites in Tunisia. The first one in Sejnane, presenting as major components, terpenes: sabinene, α-selinene; terpene alcohol: eudesm-7(11)-en-4-ol, carotol and 11-alpha-(H)-himachal-4-en-1-beta-ol. The second study in [123], the sample was taken in Tunis, with the major components being, the phenylpropanoid elemicin and the terpene alcohol, carotol.

The discovery of the huge importance of the essential oil of wild carrot in DETOX, was published in 2015 [124] when then the results showed an striking ability of this essential oil to be hepatoprotective and antioxidant. Once again, in this work, it was shown that the percentage of the chemical compounds vary greatly with different geographical origins and weather and soil conditions. The oil extract in this study showed the mainly chemical compounds as phenols, flavonoids, monoterpenes, sesquiterpenes, and phenylpropanoids. Specifically: sesquiterpenes, mainly, α-humulene, β-caryophyllene, α-longipinene, α-selinene, γ-selinene, β-selinene, and β-himachalene; sesquiterpene alcohol: 2-himachalen-6-ol; phenylpropanoids: elemicin, (*E*)-methyl isoeugenol, and methyl eugenol.

Elemicin is also a very striking chemical element, which name came from *Canarium luzonicum* (Elemi), having properties ranging from antibacterial, antifungal, anti-allergic, anti-proliferative (and antitumor effect [125]) to anti-cholinergic, among others.

In two recent published reviews on wild carrot, one in 2024 [126] and the second in 2025 [127], it is stated: "Traditionally, the wild carrot has been recognized for its antilithic, diuretic, carminative, antiseptic, and anti-inflammatory properties and has been employed in the treatment of urinary calculus, cystitis, gout, prostatitis, and cancer".

More on anti-proliferative and other pharmacological and biological actions of other essential oils will appear in a future review publication.

Conclusion

It is a huge bonus to have the knowledge to use nature's not transformed compounds or parts of plants in many forms - teas, mother tincture, powder, essential oils… - daily as many of these substances have therapeutic effects even in the management of cancer - prevention, treatment, and also in remission. Those are the case of some alkaloids.

In a complete DETOX program, one should foresee plants or essential oils for the stopping of uncontrolled cell proliferation, the promotion of apoptosis of abnormal cells, the elimination of advanced ROS production, to provide wide access of nutrients to cells as well as to the mitochondria, and the protection of the genetic cell materials. Natural alkaloids and terpenes can have anticancer, antifungal, analgesic, insecticidal, antidiabetic and antimalarial properties for instance, among plenty of others [106,125].

Our cells are producing energy 24/7. Along with these biochemical processes, many wastes are produced. It is necessary for a good health and maintaining of the homeostasis not only a good and organic grown source of plant based diet, but equally also, a good and clean source of water and a good source of oxygen in the air, free from pollutants to accomplish all required chemical human biochemical reactions. A good source of antioxidants is also a recommendation, every single day. Many medicinal plants and their derivatives (essential oils for instance) present lots of them.

The metabolic wastes generated in one single cell, can block the entering of nutrients and the leaving of wastes, if the cell cannot get rid of the waste produced in the first place. In this situation, ROS and other free radicals are constantly bombarding it and neither oxygen, nor water can reach to it. This vicious cycle either due to a disfunction or to a very bad diet habits, combined with chemical, licit, and illicit drugs, can be a clock bomb. That is why the knowledge of a natural diet and an efficient natural DETOX, on a regular basis, must be employed, now more than never, considering our 21st century high stress and surreal competitivity lifestyle. No wonder metabolic diseases are among the most deadly in the world nowadays. The wastes produced by our body must get out, and one way of taking care of them is fully described in [1] with a proposed DETOX program.

Depending on the work environment, on the place one inhabits, it is highly plausible to exist contaminations with either radioactive or heavy metals. A clear mind, psyche and body are the key to homeostasis - body and spirit [67].

In the final article of this series, to appear in the future, more essential oils will be presented and synergies will be presented and explained.

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