

Review

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Review

Pharmacy and Fragrances: Traditional and Current Use of Plants and Their Extracts

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Abstract: This paper aims to establish a current relationship between pharmaceutical sciences and the development of perfumes and fragrances, which bring significant economic benefits and whose added value is among other professionals, the one made by professionals in Pharmacy. For this purpose, historical data are used as a starting point and galenic, chemical and botanical aspects are discussed in a transversal way. In this sense, it must be taken into account that in the case of Spanish pharmacy, it is closely linked to the knowledge and use of plants. Sources such as Web of Science (WOS) and databases such as Scopus, monographs and various web pages (where scientific-technical documents appear) have been used. The results and discussion are based on the selection of the 50 plant species most commonly used in high quality fragrances. Therefore, this publication should be considered as an approach to this subject based on an analysis of a representative sample of data. Some characteristics of perfumes (classification according to the concentration of essential oils and combination of plant extracts) are presented beforehand. They also briefly compile the traditional and modern ways in the treatment of these extracts. The main focus of this work is the botanical and chemical analysis of these described plants, pointing out their common name, correct botanical name, geographical place of origin, used part of the plant and main molecules. The 50 botanical species belong to 27 families of angiosperms and are represented in a large part of the phylogenetic tree of botanical systematics. The most significant families are aromatic: Rutaceae (16.7%), Lamiaceae (16.7%) and Apiaceae (6.5%). The most represented genus is *Citrus* (with seven species or hybrids). However, it should be noted that natural extracts of good quality natural fragrances may be supplemented with chemically synthesized molecules. Of the 50 botanical species selected, 84% of the extracts have their origin in Tropical Asia, the Middle East and the Mediterranean region. This figure generally coincides with the percentage of medicinal plants (or their extracts) admitted by the European Pharmacopoeia. All parts of a plant (depending on which one it is) can be a source of molecules for the elaboration of these products. The most commonly used parts to obtain extracts are flowers (34%) and leaves (30%), a biological circumstance that is explained in this work. On the opposite side are the resins (10%), rhizomes and roots (8%). In this work, 110 molecules have been found that are part of the essences of perfumes and fragrances, the most frequent are: linalool, limonene, 1,8-cineole, eugenol and derivatives, geraniol, vanillin and derivatives, β -caryophyllene, p-cmene and farnesene and derivatives (3.64%). However, in order to elaborate a quality perfume, many other molecules must be taken into account, according to the creative experience of the perfumer, which is subject to confidentiality and chemical analysis according to current legislation, which would avoid fraud, allergy and dermatitis problems.

Keywords: cosmeceuticals; cosmetics; fragrances; history of pharmacy; pharmaceutical botany

1. Introduction

Human beings have considered it necessary to improve the appearance and visible properties of the body in order to increase their self-esteem, to be successful in love, war or social life. Hence, they have put their interest in the elaboration of cosmetics and fragrances. Different civilizations have used and continue to use plants for this purpose [1].

Smell is an essential tool for animals, as it is used to link chemical signals or substances of different origins with emotions and memories. It is understandable to think of perfumery as the art of composing fragrances using odorous substances from nature [2]. Following the Helicon considerations [3], the term perfume comes from the alliance of two Latin words: *per*, "by" and *fumare* "through smoke", since it was originally considered an odoriferous vapor. Further to this argument, the *International Fragrance Association* (IFRA) defines the concept of fragrance as a combination of chemical substances that possess aroma or odor, but it is much more, it encompasses cultural, historical, social, economic and emotional values". We must thus understand that fragrance is the very "soul" of perfume [4].

Economic reports from different countries show that the economic impact generated by the personal external care of the organism with the use of cosmetics and fragrances translates into millions of euros [5]. In addition, people are interested in the characteristics of the product they buy [1].

It is essential to highlight in the following pages the evolution of the use of perfume in different periods and civilizations. Perfume formulas have changed according to their uses and composition, requiring a high level of knowledge of botany, chemistry and pharmaceutical technology, as these sciences have been developed with new analytical and technical instruments.

If we go back in history, at the dawn of mankind there was a certain interest in the use of aromatic substances for hunting, to repel insects, and even in religious rites in the form of incense (*Boswellia sacra* Floeck.) [6].

The Sumerians began to manufacture the first perfumes for personal, medicinal and ceremonial use. The first chemical record of the history manufactured fragrances with flowers, oils, myrrh and balsams by boiling, enfloration, sublimation, filtration and pseudo-distillation can be attributed to Tapputi-Belatekallim (4th century BC) [7].

The importance of perfume reached high levels during Ancient Egypt, considered a significant status symbol and had its own deity, *Nefertum*. In the temples, substances were burned three times a day: frankincense in the morning, myrrh at noon and *Kyphi* in the evening. At this time, techniques such as maceration in animal fats and the pressing of aromatic plants were developed. Thus, fragrances based on rose (*Rosa* L.), violet (*Viola odorata* L.) and saffron (*Crocus sativus* L.) were elaborated, in which even Cleopatra bathed her skin [8].

According to Homer, the gods of Olympus taught mortals the manufacture and use of perfumes and deities such as Aphrodite, conferred scent and color to many aromatic plants. Greece and Rome borrowed from Egypt the numerous uses of perfumes, being a social stigma according to the quality and quantity used. It was common to use fragrances for personal hygiene, insect repellent, worship ceremonies and festivities. They did not skimp on containers, which were made of glass, alabaster or ivory. Authors such as Theophrastus, Pliny and Dioscorides wrote protocols for the manufacture of perfumes and descriptions of *romatis* scents [9]. During the expansion of the Roman Empire, perfume was a sign of social status, even Caligula wasted enormous quantities of perfume for his baths after intense orgies [10].

In Islamic times, there are records of the use of perfume by Arabs since the 6th century and its use was considered a religious duty according to the words of the prophet Mohammed. Its use was also popular for its medicinal properties according to Hippocrates' theory of humors. Physicians such as Avicenna used them for therapeutic purposes as a precursor of today's aromatherapy. It also included techniques such as filtration and distillation, and even highlighted side effects of essential oils. Fragrances, made up at that time of aromatic waters, oils and ointments, were manufactured on a small scale in small laboratories and apothecaries. Plants such as jasmine (*Jasminum officinale* L.),

clove [*Syzygium aromaticum* (L.) Merr & L.M.Perry)], camphor [*Cinnamomum camphora* (L.) J.Presl], narcissus (*Narcissus* L.), wallflower [*Erysimum cheiri* (L.) Crantz] and roses (*Rosa* L.) were used [11].

With the spread of Christianity, the relationship between aromas and worship was dissolved when perfumes were considered to stimulate “impure desires”. Reconciliation was to come later, always drawing an imaginary line between “permitted” and sensual scents. From then on, fragrances could be powders, pastes and resins, and their production fell to monasteries and apothecaries for their therapeutic use [12].

In the 14th century, Queen Elizabeth Piast of Hungary popularized the *Queen's Water* or *Eau de Hungary*, a fragrance with supposed rejuvenating and curative properties based on alcohol, rosemary water (*Rosmarinus officinalis* L.), rose water, orange blossom, cedar (*Cedra odorata* L.) and turpentine [1,13]. Also, as a consequence of plague epidemics and the idea that aromas avoid diseases, the custom of perfuming clothes and accessories appeared, causing a furor among the wealthy classes - Catalina de Medicis, for example- who, in addition to elaborating fragrances, were skilled in the art of poisoning [14,15].

During the 17th and 18th centuries, the manufacture of perfumes was in the hands of Italy and France. In these years the oldest “perfume” in the world reappeared, the aforementioned eau de Cologne or Eau de Toilette. At the court of Versailles (France), eau de cologne was a great success, originally prepared by Florentine nuns as *Aqua de Regina* - bergamot extracts - its formula was acquired by an Italian apothecary who manufactured the fragrance in Cologne in 1729. A breakthrough at the time was *Aqua Mirabilis*-by Gian Paolo Feminis-a citrus perfume with alcohol, bergamot (*Citrus × bergamia* Risso & Point.), lemon [*Citrus x limon* (L.) Osbeck] and orange (*Citrus aurantium* L.). His grandson, Giovanni Maria Farina, created the popular perfume *Aqua de Cologne* from essential oils and alcohol. At this time, laws appeared that regulated fragrances, differentiating them from medicines, making eau de cologne undrinkable [16].

The modern age coincided with the worldwide expansion of the perfume industry, making Grasse, in southeastern France, the perfume capital from the Renaissance to the mid-19th century. Advances in organic chemistry found their way into the world of perfumery, including synthetic molecules in perfumes at the hands of the Guerlain and Houbigant houses. The latter developed *Fougère Royale* in 1884, giving rise to the Fougère family of perfumes, which simulates the supposed scent of a fern [17]. In these years, pharmacists were the true experts in the elaboration of fragrances, since they were the experts in plant extracts for medicinal use, they possessed the necessary instruments, mainly distillers, they performed chemical mathematical calculations and they were already studying a science independent of medicine, at least in European countries [18]. It should be noted at this point that today's giant cosmetic companies were founded at the beginning of the 20th century by chemists and pharmacists in the United States of America and France. A well-known and current cosmetics company had its origin in the house-to-house sale of books, and along with the books also sold colognes manufactured by a pharmacist friend [19]. In the Spanish Pharmacopoeia of 1954 there are still 22 monographs for obtaining essences “Essentiae” and 6 monographs for obtaining waters, such as *Aqua destillata floris auriantii* (with freshly harvested petals of *Citrus aurantium*). All of them use steam distillation [20].

In 1921 *Chanel n° 5* was born, a perfume that included five types of aldehydes, jasmine, orange blossom, rose, sandalwood (*Santalum alum* L.) and vetiver [*Crysopogon zizanioides* (L.) Roberty] that bring a unique freshness that has survived to this day. The second half of the 20th century would be marked by the use of patchouli (*Pogostemon cablin* Benth), fresh waters and masculine perfumes in men's daily routine [13]. In recent years, the production of fragrances prioritized quantity and marketing over quality, investing especially in advertising by famous faces who founded their own lines such as Justin Bieber, Kim Kardashian, David Beckham or Lady Gaga among others [21].

With these considerations in mind, it seems interesting to recall the World Health Organization's definition of health, which may in part be related to perfumes and fragrances: Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Proper care of the external appearance of the body contributes to achieving this complete state of well-being. Hence the growing demand for information on this subject [1]. One of the main objectives

of this publication is to provide the chemist-pharmacist with useful and current references for the elaboration of fragrances. This information is traditionally known, but it is dispersed and very atomized in publications from different areas of knowledge. For these reasons we have carried out this transversal, integrative and synthetic work, product of our experience as professors of the Faculty of Pharmacy of Seville. For this purpose, we have chosen applied botany as a source of natural products, one of the basic fundamentals that form part of fragrances and on which part of the content of this work is based.

2. Methodology

A search for printed bibliographic material was carried out at the CRAI (Resource Center for Learning and Research) of the University of Seville, where books were found (with difficult access) on the history of perfume, as well as its cultural and social relevance in different civilizations around the world. The Web of Science and the Scopus database were consulted on the Internet. When the keyword "Fragrance" was entered in the search engine, the number of documents found was very high, so the search had to be narrowed down with the term Review. The initial results were 12,114 documents vs. 88 (WOS) and 33,984 vs. 3,548 (Scopus). Given this number of documents, the most recent articles were analyzed. When this prospection was carried out, it could be seen that most of the documents were monographs of specific molecules on perfumes and fragrances dealing with chemical synthesis, chemical analysis, toxicity and allergenic character, hence only the documents necessary to meet our objective were taken into account.

In this case, the criterion chosen was to gather a representative sample of 50 plants relevant to the production of perfumes and fragrances, following the information provided on their websites by different commercial companies that produce these products, such as Calvin Klein, Gucci, Chanel, Christian Dior and Guerlain [17,22,23]. However, these websites may change and may not last over time.

The scientific names of the species and plant families were reviewed in the *WFO Theplantlist* [24], *eFloras* [25] and *Mobot* [26]. Each species also details its geographical origin, part used in perfumery and its main composition of its essential oil supported by bibliography such as *Fitoterapia.net* [27] (a professional page where complete monographs of plants with therapeutic action appear, related to the Spanish Pharmacopoeia and Theplantlist).

3. Results and discussion

3.1. Previous considerations on perfume and fragrances

Perfume is a product intended to provide a pleasant odor on the body mainly, and is a combination of natural essential oils and/or with synthetic molecules, dissolved in alcohol (sometimes with a part of water) [28].

There is no homogeneous classification of these products. This is based on the type of notes that remain over time (Figure 1), concentration of essences [29,30] and the composition of the olfactory note wheel [31]. Top notes or top notes are due to more volatile molecules of lower molecular weight (they last 15-20 minutes after application). Their effect usually lasts a few minutes and attributes to citrus (*Citrus*) and fruity notes such as strawberry (*Fragaria* L.), mango (*Mangifera indica* L.), cherry or peach (*Prunus* L.). The middle notes, lasting up to one hour, are provided by extracts of lavender (*Lavandula angustifolia* Mill), geranium (*Pelargonium graveolens* L'Her.), rosemary (*Rosmarinus officinalis* L.), laurel (*Laurus nobilis* L.), basil (*Ocimum basilicum* L.), rose (*Rosa*) and cucumber (*Cucumis sativus* L.). The base notes have a "soporific and aphrodisiac" character. They last several hours and it is difficult not to perceive their perfume. Their components are usually extracted from sap, roots or wood. Some notes in this category come from sandalwood (*Santalum album*), cananga or ylang-ylang [*Cananga odorata* (Lam.) Hook.f. & Thomson], *Fragaria*, patchouli (*Pogostemon cablin* Benth.), vanilla (*Vanilla planifolia*), chocolate (*Theobroma cacao* L.), tonka bean [*Dipteryx odorata* (Aubl.) orsyth f.).

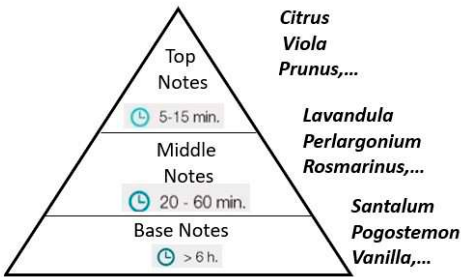


Figure 1. Olfactory pyramid. Own elaboration from citations 29,30.

The denomination of the type of perfume or derivatives can be established according to the amount of pure fragrance concentration (although there are no exact amounts) and the time in which the formulation is perpetuated in the body odor. According to the above, this type of products would be divided into five classes: Agua fresca, Eau de cologne, Eau de toilette, Eau de parfum and Perfume (Figure 2).

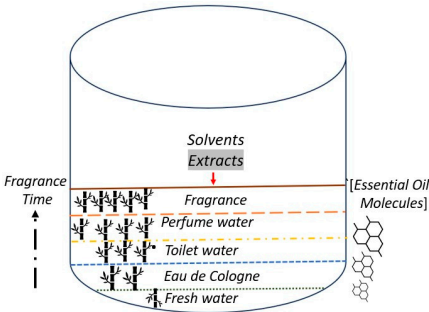


Figure 2. Types of fragrances according to their concentration of essences and duration of effect. Own elaboration based on citations 29,30.

As will be seen below, the list of raw materials of plant origin is very broad and it is complex to establish a classification of perfumes according to their plant composition, since extracts can often be combined with each other to obtain different characteristics and notes [31]. This complexity is illustrated in Figure 3, in which a whole architecture of floral notes and fragrances is superimposed from concentric circles. Figure 3 is a simplification that is taken into account to produce a whole catalog of plant-based fragrances, starting from four basic floral notes (Floral, Fresh, Woody and Oriental), which in turn are subdivided into smaller categories. This figure, as an example, shows some of the plant associations that are scientifically responsible for the properties of the fragrance wheel used to demonstrate the complexity of a perfume and derivatives, and perhaps for marketing purposes.

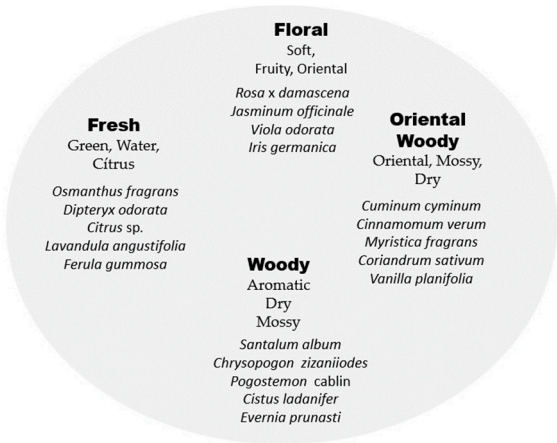


Figure 3. Classification of perfumes and fragrances according to the combination of notes provided by the different plant extracts. Own elaboration based on citation 31.

3.2. Methods of obtaining essences

Natural extracts used by the fragrance and cosmetic industries, namely essential oils, concretes, resinoids and absolutes, are produced from natural raw materials. The most commonly used methods are summarized below [29,32,33] (Figure 4):

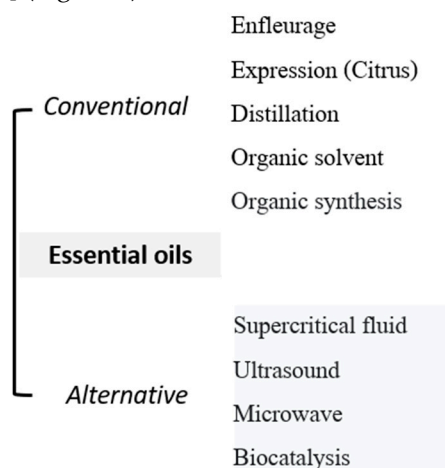


Figure 4. Summary of methods for obtaining essences. Own elaboration.

Enfleurage. The flowers are put in contact with refined and odorless animal fats for several days to extract the essences, until an ointment is obtained from which the absolute is extracted (the most concentrated fragrance and most appreciated in perfumery). It is a manual and expensive method.

Expression. A mechanical method usually used on citrus fruits, the oils of which are found in the pericarp (mesocarp) of the fruit. Water and oil are separated by centrifugation.

Steam distillation. Distillation is the most frequent method used in the industry to extract essences, whether simple, fractionated or by steam distillation, depending on the boiling points and volatility of the products to be separated. In the collecting flask, aqueous and oily faces are easy to separate. The “perfumed” waters can be used to make rose water or orange water.

Solvent extraction. Large quantities of plants macerated in hexane or acetates are used. It is based on the different solubility of the mixture in the solvent and the soluble part is obtained in the organic solvent (concrete), not very soluble in alcohol. In this sense, absolutes are much nobler, richer and easier to use in perfumery.

Tinctures and resinoids. They are the result of the maceration of raw materials with alcohol. They are then heated and tinctures are obtained, which are similar to absolutes.

As mentioned in the introduction, the use of fragrances is increasingly in demand, and this has forced synthetic organic chemistry to obtain molecules similar to those found in nature without resorting to plants [33]. This is the case of the best known synthetic fragrance in history: Iso E Super®.

If we go into the concept of the so-called “green chemistry”, new techniques for the extraction of essential oils are currently being developed. These new alternative methods aim at a more efficient extraction. We can mention the use of supercritical fluids, microwave-assisted extraction and ultrasound. They are recognized as efficient extraction methods and can significantly reduce the amount of solvents and extraction times, improve yields and the quality of the essential oil. Although these methods are predominantly exploited at the laboratory scale [34,35].

Another alternative to produce some fragrance base molecules is the use of biocatalysis in which from plant cell cultures, immobilized enzymes or metabolic products of some microorganisms (bacteria, yeasts and other fungi) [36]. For example, several strains of *Pseudomonas putida*, *Aspergillus niger*, *Corynebacterium sp.*, *Arthrobacter globiformis* and *Serratia sp.* produce vanillin as an intermediate compound in the microbial degradation of various substrates such as ferulic acid, stilbenes, phenolic acids, lignin, eugenol and isoeugenol [37].

3.3. Botanical considerations on perfumes and fragrances

As can be deduced from what has been developed up to this point, “Botanical Science” is an inexcusable factor to elaborate or at least fully understand the significance of products with a good quality odor, whether of the body or of the rest of the things to suppress unpleasant aromas. This *desideratum* is within the reach of a pharmaceutical botanist. For this reason we dedicate this epigraph to make botanical considerations on this subject, in which we will take into account, as already mentioned, a reasonable and representative quantity of plants (50), which are presented in alphabetical order (Table 1) by their common name in English, followed by their correct and complete scientific name (so defective in many occasions in labels and leaflets), The first geographical origin (although many of these plants can be cultivated far from their initial cradle), botanical family according to the current systematics and part or organ used. With the new analytical detection techniques (one of the most used is Gas Chromatography/Mass Spectrometry -GC/MS), the number of molecules found in the extracts is increasing, although many of them with a smaller quantitative minority participation.

Table 1. Botanical characteristics of plants [24–26] and their essential oils as a source of extracts and fragrances.

COMMON NAME	SCIENTIFICAL NAME BOTANICAL FAMILY GEOGRAPHICAL ORIGIN USED PARTS	ESSENTIAL OIL	REF.
ACID LIME	<i>Citrus x aurantiifolia</i> (Christm.) Swingle Rutaceae. Asia. Pericarp.	Limonene, mircene, geraniol, linalool, citronellol.	[38]
ANISSED	<i>Pimpinella anisum</i> L. Apiaceae. SE Mediterranean.	<i>trans</i> -anethole.	[27]
BAY	<i>Laurus nobilis</i> L. Lauraceae. Mediterranean. Leaf.	1,8-cineole, metil-eugenol, terpinen-4-ol, linalool, eugenol.	[27]
BEARDER IRIS	<i>Citrus x limon</i> (L.) Osbeck Rutaceae. Asia. Pericarp.	Irone	[27]
BERGAMOT ORANGE	<i>Citrus bergamia</i> (Risso) Risso et Poit. Rutaceae. Italy. Flower, Pericarp.	Limonene, linalyl acetate, quercetin, hesperidin.	[27]
BIRCH	<i>Betula pendula</i> Roth Betulaceae. Europe. Bark.	Betulinic acid, lupane, dammarane	[27]
BITTER ORANGE	<i>Citrus aurantium</i> L. Rutaceae. Asia. Flower, Pericarp	Limonene, 1,8-cineole β -pinene, p-cymene.	[39]
BLACK PEPPER	<i>Piper nigrum</i> L. Piperaceae. India. Fruit.	Sabinene, limonene, β - cariophyllene, β pinene.	[27]

CAMARU (TOKAN BEAN)	<i>Dipteryx odorata</i> (Aubl.) Forsyth f. Fabaceae. South America. Seed.	Coumarin (2H-1-benzopyran-2-one).	[40]
CANANGA TREE (YLANG-YLANG)	<i>Cananga odorata</i> (Lam.) Hook. f. & Thomson. Anonoaceae. Flower.	Linalool, geraniol, α -farnesene, farnesol, β -cariophyllene.	[27]
CARDAMON	<i>Elettaria cardamomum</i> L. Maton Zingiberaceae. Tropical Asia. Seed.	1,8-Cineole, α -terpinyl acetate, sabinene.	[41]
CEDAR	<i>Cedrela odorata</i> L. Meliaceae. South America. Leaf.	Catechins, luteolins, tocopherol, α -pinene, limonene.	[42]
CINAMMOMUM BARK	<i>Elettaria cardamomum</i> L. Maton Zingiberaceae. Tropical Asia. Seed.	1,8-Cineole, linalool, β - cariophyllene, safrol, <i>trans</i> - cinamic aldehyde, eugenol.	[27]
CITRONELLA	<i>Cymbopogon nardus</i> L. Poaceae. Asia. Stem, Leaf.	Citronellol, δ -cadinene, geraniol, 4- eugenol.	[43,44]
CLOVE	<i>Syzygium aromaticum</i> L. Merr. & L. M. Perry. Myrtaceae. Indonesia. Flower bud.	eugenol, β -caryophyllene.	[27]
COMMON BASIL	<i>Ocimum basilicum</i> L, Lamiaceae, Africa, Asia. Leaf, Stem.	Estragole, fenchole, linalool, metil-eugenol.	[27]
COMMON MYRTLE	<i>Myrtus communis</i> L. Myrtaceae. Mediterranean. Leaf, Flower.	α -pinene, myrtenol, cineole, metil-eugenol.	[45]
CORIANDER	<i>Coriandrum sativum</i> L. Apiaceae. Mediterranean. Leaf, Seed.	Linalool, pinene, limonene, geraniol, borneol.	[27]
DAMASK ROSE	<i>Rosa \times damascena</i> Mill. Rosaceae. Asia. Flower.	Citronellol, geraniol, linalool, eugenol, nerol	[27,46]
EUCALYT	<i>Eucalyptus globulus</i> Labill. Myrtaceae. Australia. Leaf.	1,8-Cineole, α -terpineol, cimene, α and β -pinene.	[27]
GALBANUM	<i>Ferula gummosa</i> Boiss. Apiaceae. SE Mediterranean. Resin.	α and β - pinene, δ -caren	[47]

GARDENIA	<i>Gardenia jasminoides</i> J. Ellis Rubiaceae. SE Asia. Leaf.	Iridoid glycosides	[48]
GERANIUM	<i>Pelargonium graveolens</i> L'Hér Geraniaceae, South Africa. Leaf, Flower.	Linalool, isomentone, terpineol, citral, geraniol.	[49]
GINGER	<i>Zingiber officinale</i> Roscoe Zingiberaceae. Tropical Asia. Rhizome.	Zingiberene, sesquiphellandrene farnesene, geranial, bisabolene, curcumene.	[50]
GRAPEFRUIT	<i>Citrus x paradisi</i> Macfad Rutaceae. Caribe. Fruit.	β -pinene, linalool, α -terpinene.	[27]
JASMINE	<i>Jasminum officinale</i> L. Oleaceae. Asia. Flower.	Linalool, benzyl acetate, indol.	[49]
LABDANUM	<i>Cistus ladanifer</i> Stokes Cistaceae. Mediterranean. Resin.	Linalool, indol.	[51]
LAVANDER	<i>Lavandula angustifolia</i> Mill. Lamiaceae. Europe. Inflorescence.	Limonene, nerol, cineole, linalool, geraniol, borneol, lavandulol.	[27]
LEMON	<i>Citrus x limon</i> (L.) Osbeck Rutaceae. Asia. Fruit.	Limonene, β -pinene, terpineol.	[27]
MIMOSA	<i>Acacia dealbata</i> Link. Fabaceae. Australia. Flower.	Ethyl propionate, ethyl butanoate.	[52]
MINT	<i>Mentha x piperita</i> L. Lamiaceae. Europe. Leaf.	L-Mentol, menthone, isomenthone, cineole, Menthyl acetate (neomenthol, isomenthol).	[27]
MYRRH	<i>Commiphora myrrha</i> T. (Nees) Engl. Burseraceae. Asia. Resin.	α -thujene, α -pinene p-cymene, 1,8-cineole, cypere β - caryophyllene (Z)- β -farnesene.	[53]
NAGRIS	<i>Narcissus poeticus</i> L. Amaryllidaceae. Asia, Mediterranean. Flower.	Limonene, heneicosanol, dihydroactinidiolide, 4,8,12,16- tetramethyl heptadecan-4-olide, heptanal, nonanal, (2E,4E)- decadienal	[54]
NUTMEG	<i>Myristica fragrans</i> Houtt. Myristicaceae. Tropical Asia. Seed.	Sabinene, α , β -pinene, limonene, g-terpinene, α - phellandrene	[27]

OAKMOSS	<i>Evernia prunastri</i> L. Parmeliaceae. Europe. North America. Thallus.	β -Elemene, linalool, α -coanene myrtenal, β -gurjunene, myrtenol, α -cedrene, Terpinolene, β -caryophyllene.	[55]
PATCHOULI	<i>Pogostemon cablin</i> Benth. Lamiaceae. India. Leaf.	α and δ -guaiene, Patchulol.	[56]
PERU BALSAM	<i>Myroxylon balsamum</i> L. Fabaceae. South America. Resin.	Cinamein, vainillin.	[27]
ROSEMARY	<i>Rosmarinus officinalis</i> L. Lamiaceae. Mediterranean. Stem. Leaf.	1,8-cineole, camphor α and β pinene, Borneol, limonene, p- cymene,	[57]
SAGE	<i>Salvia officinalis</i> L. Lamiaceae. Mediterranean. Leaf.	α , β thuyone, camphor.	[27]
SANDALWOOD	<i>Santalum album</i> L. Santalaceae. Asia. Stem.	Z- α -santalol, z- β -Santalol, bergamotol, lanceol, santalene.	[58]
SPIKENARD	<i>Nardostachys jatamansi</i> (D. Don) DC. Caprifoliaceae. Asia. Flower.	Seychellene, β caryophyllene, rogoistol	[59]
SWEET ORANGE	<i>Citrus sinensis</i> L. Rutaceae. Asia. Flower, Fruit.	Citral, n-decicilaldehyde, Limonene, 1,8-Cineole, β - Pinene, p-Cymene.	[39]
TANGERIN TREE	<i>Citrus reticulata</i> Blanco Rutaceae. China. Pericarp.	Citral, n-decylaldehyde, limonene, 1,8-cineole, β -pinene, p-cymene	[39]
TARRAGON	<i>Artemisia dracuncululus</i> L. Asteraceae, Central Asia. Stem, Leaf.	estragole, Metileugenol, cis- trans ocimeno limonene.	[27]
THYME	<i>Thymus vulgaris</i> L. Lamiaceae. Europe. Leaf.	Linalool, borneol, geraniol, sabinene, thymol.	[60]
TOLU BALSAM	<i>Myroxylon toluiferum</i> Harms Fabaceae. South America. Resin.	Benzoates and cinnamates of triterpene alcohols, free benzoic and cinnamic acids.	[27]
TUBEROSE	<i>Polianthes tuberosa</i> L. Asparagaceae. South Africa. Flower.	Methyl 2-aminobenzoate, Methyl iso-eugenol, trans- Farnesol.	[61]
VANILLA	<i>Vanilla planifolia</i> Andrews Orchidaceae. Central America. Fruit.	Vanillin, vanillic acid, p- hydroxybenzaldehyde ethersides: Vanilloside or	[62]

		glucovanilla glucovanillic alcohol.	
VETIVER	Chrysopogon zizanioides (L.) Roberty Poaceae. India. Root.	Mucilages, mainly from kaempferol), salicylic acid, anthocyanosides (violamine), β caryophyllene, khusimene, α humulene.	[63]
VIOLET	<i>Viola odorata</i> L. Violaceae. Europe. Asia. Flower.	1-Phenylbutanone, linalool, benzyl alcohol. -	[64]

In the following paragraphs, botanical and chemical aspects will be highlighted to make the context in which perfumes and fragrances are elaborated more comprehensible. It should be noted first of all that the data presented here come, as already indicated, from the choice of the 50 most frequent plants, although this list could be more extensive. For example, minority species that are also used in the formulation of these products have not been considered according to the search criteria: jojoba seed oil [*Simmondsia chinensis*, (Link) C.K.Schneid] sunflower seed oil (*Helianthus annuus* L.), sampaguita leaf extract [*Jasminum sambac* (L.) Aiton], red camellia flower extract (*Camellia japonica* L.), tobacco leaf extract (*Nicotiana tabacum* L.), etc. On the other hand, 27 families of Angiosperms (less than 10% of the total number of families) [26], one species of lichen (*Evernia prunasti*) and no species of “gymnosperms” were found.

Figure 5 shows that this sample of plants (which at first can be considered “reduced”) is present in almost all the current large groups in which plants are classified from the point of view of molecular genetics in the form of a phylogenetic tree. In the first place, the group of primitive angiosperms appears, with families of Asian origin, rich in spices and whose interest led to the discovery of the American continent and later the first round-the-world voyage by sea [65]. Figure 5 also shows (in green) that only three botanical families are the source of almost 40% of plant extracts in the manufacture of perfumes: Rutaceae and Lamiaceae (16.7% each), Apiaceae (6%). These figures are not correlated with the quantitative importance according to number of species that these families have in the angiosperms as a whole (Asteraceae, Orchidaceae, Fabaceae, etc.) [66]. It is also important to note that 58% of the plants named here were studied by Linnaeus. As is well known in the scientific world, Linnaeus was a physician and naturalist who was dedicated to naming and describing many of the plants known since classical-Cracero-Roman antiquity (and other new ones) to which he had access, starting in many cases from descriptions that previous botanists had made with Arabic translations of plants already described by Dioscorides (1st century BC) [67]. It must be taken into account that for hundreds of years the plants that were studied were for their economic, medicinal and agricultural importance.

Figure 5 below shows that the plants most commonly used in perfumes and fragrances are at the lower end of the phylogenetic tree (*Core Angiosperms*), characterized by smaller flowers that tend to have calyx and corolla with sepals and petals welded together, which trap insects once they are pollinating the flower.

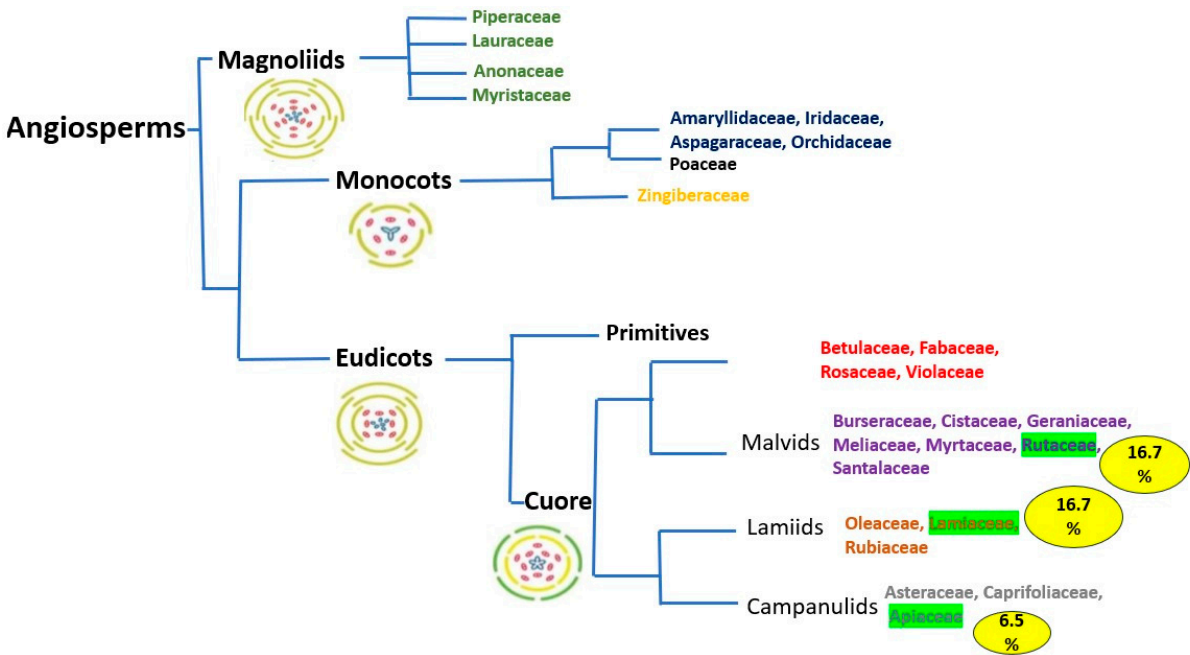


Figure 5. Botanical systematics in the form of a phylogenetic tree of the families that form part of the fragrances according to this work. Floral diagrams. Own elaboration from (APGIV) [26].

If we analyze the initial geographic origins of these plants (Figure 6), we observe an asymmetry in their origin, since a large majority are native to central and tropical Asia and the region where the Mediterranean Sea is located (84%).

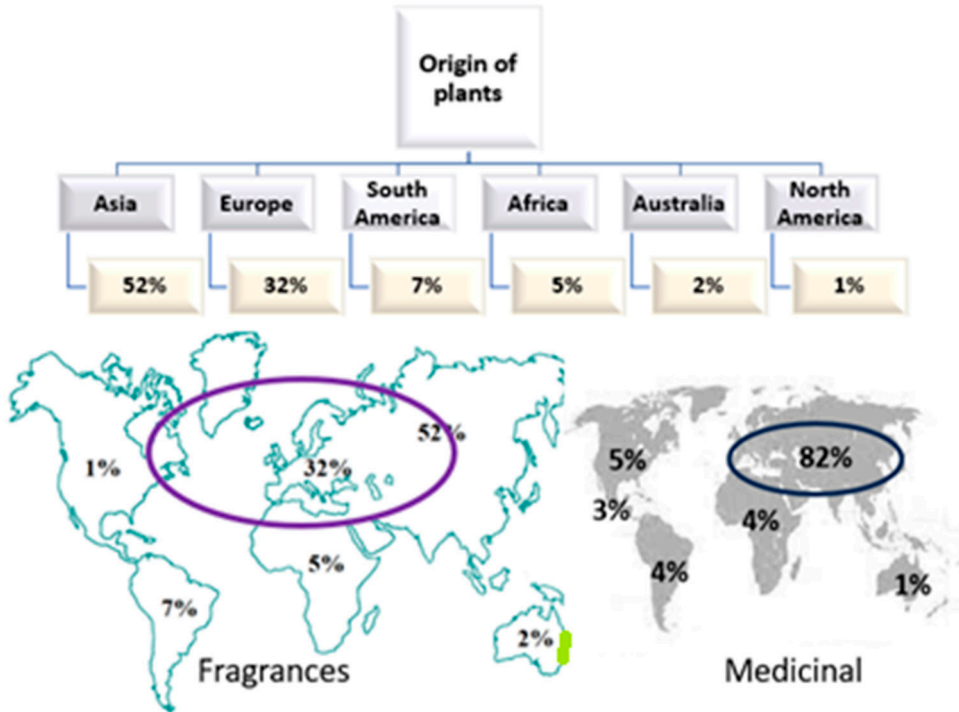


Figure 6. Regional origin of the plants used in perfumes and fragrances according to this work and origin of the medicinal plants that appear in the Spanish Pharmacopoeia V edition [28]. Own elaboration.

This figure almost coincides with the origin of the plants or their medicinal derivatives that appear in the Royal Spanish Pharmacopoeia (the same as the European one) (82%) [68]. It could be

deduced then] that the human being, while searching for medicinal plants, has also found plants producing essences to perfume himself, not in vain many of the molecules responsible for the aromas also have therapeutic action (1,8-cineole, hesperidin, zingiberenes, etc.).

Figure 7 shows the percentages of the most used organs. It can be observed that all parts (depending on the plant) can be sources of essences, although the use of the flower (34%) and the leaf (30%) predominates. On the opposite side are resins (e.g., Tolu balsam) (10%), stems (e.g., *Santalum album*), rhizomes (e.g., *Zingiber officinale*) and roots (e.g., *Chrysopogon zizanioides*) (8%).

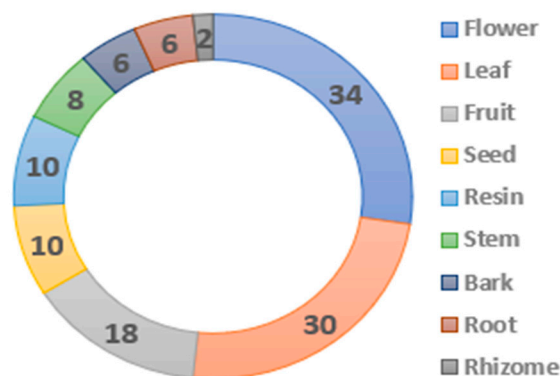


Figure 7. Part of the plant used to obtain extracts. Own elaboration.

These facts may have multiple biological meanings, plants are immobile organisms and are subject to aggression by herbivores and phytophagous or climatic variations throughout their vegetative development, hence they produce secondary metabolites as a form of protection, but in the case of pollination, the odor of flowers (pleasant or unpleasant, day or night) is related to the attraction of the type of pollinating agent-usually insects [69].

A high percentage of the plants considered here come from warm climates, with high seasonal temperatures. The Lamiaceae (*Rosmarinus*, *Lavandula*, *Thymus*, *Mentha*, etc.) are mainly Mediterranean plants, very aromatic and rich in essences. These essences evaporate with high temperatures and help to cool the plant [57]. The same consideration can be made for the Apiaceae, which have resiniferous canals throughout the plant, especially in the fruit [70]. But this explanation is different in the case of pollination, the odor of flowers (pleasant or unpleasant, day or night) The case of the Rutaceae family may be somewhat different. While the flowers of the genus *Citrus* are very fragrant, essential oils are very abundant in the mesocarp of the fruit, especially rich lysigenous cavities). The citrus family is native to China and has spread to temperate areas of southern Africa, Australia, the Mediterranean region and other warm regions of the world, forming what is called the "Citrus Belt" [70]. It is possible that its preponderance in the composition of fragrances is the easy obtaining of its components (Limonene, Mircene, Geraniol, Linalool, Citronellol) by the simple method of expression of the fruit.

Figure 8 shows, as an example, some macroscopic and microscopic images of three plant genera or species that form an essential part in the form of natural extracts for the preparation of these products: *Rosmarinus officinalis* (Lamiaceae), *Pimpinella anisum* (Apiaceae) and *Citrus* (Rutaceae).

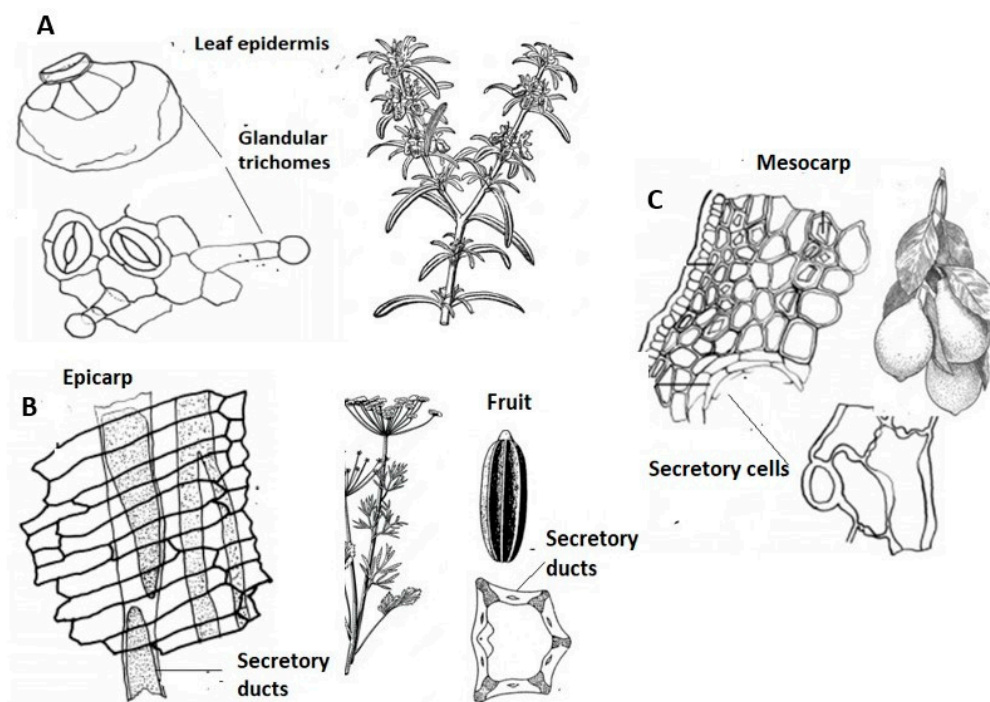


Figure 8. Microscopic images of secretory cells. A: Glandular trichomes of the leaf of *Rosmarinus officinalis* (Lamiaceae). B: Secretory ducts in the pericarp (epicarp) of *Pimpinella anisum* (Apiaceae). C. Secretory cells of the pericarp (mesocarp) of the genus *Citrus* (Rutaceae). Own elaboration based on Real Farmacopea Española (European) [28].

3.3. Chemical considerations on extracts in perfumes and fragrances

Currently more than 3000 chemicals, either natural fragrances or synthetic chemicals responsible for the odorous properties of scented products, while a perfume can be composed of a mixture of 20 to more than 200 of them [30].

In this work, 110 molecules were found to be part of perfume essences and fragrances. Table 1 shows the most frequent ones: linalool (13.8%), (α and β pinene-12.74%), limonene (12.74%), 1,8-cineole (10.92%), eugenol and derivatives (9.1%), geraniol (7.28%), vanilla and derivatives (7.28%), β -cariophyllene (4.55%), p-cymene (4.55%) and farnesene and derivatives (3.64%). In general, terpenoids predominate, with an overall presence of more than 80% in the molecules shown in Table 1. The concept of terpenoid refers to a very numerous set of molecules of plant origin whose precursor is isopentenyl diphosphate and are assembled and modified in many different ways, always based on the isopentane skeleton. Most terpenoids have multicyclic structures, which differ from each other not only in functional group but also in their basic carbon skeleton [71]. These functional groups of volatile terpenoids (alcohols, ketones, aldehydes, esters) are responsible for the different odors of extracts to elaborate fragrances. In these extracts in Table 1, we can also find other non-terpenoid compounds such as eugenol, hesperidin, vanillin, etc. (Figure 9).

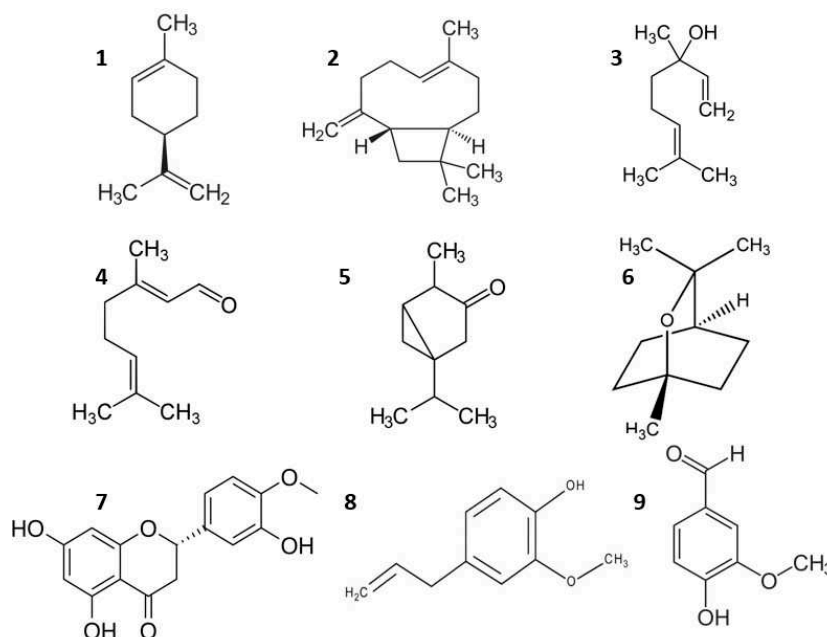


Figure 9. Some molecular structures found in essential oils. 1: Limonene. 2: β -cariophyllene. 3: Linalool. 4: Citral (Geranial). 5: Thujone. 6: 1,8-cineole. 7: Hesperidin. 8: Eugenol. 9: Vanillin.

Table 1 does not indicate the concentrations of these molecules, since the percentages of essence vary within the same species, there are varieties that require optimal conditions of climate, soil, adequate cultivation and collection at the time of the year in which the essential oils are of the highest quality. This is what a professor of botany and partner of a cosmetics company tells in a web page, referring to the case of vanilla, a molecule in great demand nowadays, for which it can be obtained by chemical synthesis (Kraf process), although the public prefers that of natural origin [72]. In the case of citrus fruits, it is worth mentioning the results of Bourgou's research [39], in which the proportion of essential oil molecules in the pericarp of four *Citrus* species (*Citrus aurantium*, *C. limon*, *C. sinensis* and *C. reticulata*), ranges from 0.46 to 2.70% depending on the ripening stage of the fruit.

In recent years, both official institutions and the industry have become aware of the problem of fragrance allergy and there have been important changes in legislation. Until a few years ago manufacturers were not obliged to specify the chemical compounds considered as fragrances contained in the product, now they are committed to declare them in some cases under a confidentiality contract since their composition is subject to analysis by chromatography, spectroscopy, mass spectrometry and electronic nose methods [73,74]. Previously, people allergic to fragrances had to avoid any hygiene and household products containing fragrances in their composition, which was a significant limitation considering the wide distribution of these substances. The current European regulation requires the mandatory declaration of 26 fragrances recognized as contact allergens on cosmetic product labels since 2005 (Geraniol, *Evernia prunasti*, Eugenol, Cumarine, Farnesol, Linalool, Limonene, etc.). These fragrances should be indicated on the label if present in a concentration ≥ 10 ppm. [74]. Perfume or similar is regulated by European legislation within the cosmetics section and is controlled by the Spanish Agency of Medicines and Health Products, in which incidence is made on labeling, the toxic or allergenic nature of some of the components [75]. Like the rest of cosmetics, perfumes and their components require rigorous quality controls to ensure their safety, since their natural origin is not synonymous with safety. An example is bergamot essential oil, which in the presence of sunlight can cause Berloque dermatitis, characterized by the presence of erythema and brown pigmentation in the exposed area. In addition to phototoxicity, as in the previous case, essential oils can produce photosensitization, irritation, or short- and long-term toxicity by accumulation, either by systemic or inhaled routes [74,76]. Finally, we would like to emphasize that in the elaboration of quality fragrances it would not be correct to mix certain molecules (which can be obtained by chemical synthesis to obtain a fragrant product).

The most advisable is to use combinations of extracts, in which the majority molecules are accompanied by others in lower concentration, but which can give the fragrance a special characteristic, which is why the experience of the perfumer is very important, who must apply the Latin phrase *Fiat Secundum artem* or let it be done according to art (empirical and personal knowledge, often secret).

4. Conclusions

Today's society increasingly uses cosmetics and fragrances to contribute to a better opinion of itself. This has been a constant in history and in different civilizations. People have more information about what is going on around them, in this case about personal hygiene issues. The quality, origin and production of fragrances are no exception, since the individual in particular likes to know as much as possible about the process that the product he/she buys undergoes, especially because it can be expensive.

The composition of perfumes is very complex, using multiple plant extracts combined with each other, sometimes joined with molecules produced by chemical synthesis. This study tries to highlight the traditional and current importance of plants (bio-renewable raw material) together with the most innovative chemical and modern technological transformation, without forgetting that some plant derivatives can be toxic.

These general considerations (traditional and current) must be taken into account by the pharmacist, as a specialist who must meet the needs of the public. All this is closely related to Pharmaceutical Botany as a "Green Science" and source of many resources in the future".

In short, this work offers general, synthetic and at the same time representative information, and interdisciplinary researchers are encouraged to continue to delve into all aspects of this subject.

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