Endemic Aromatic Medicinal Plants in the Holy Land Vicinity

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Abstract The Holy Land has a long history of settlement by many different nations, cultures and religions, as well as a long tradition of using plants for culinary, medicinal and liturgical purposes. This chapter describes a selected list of promising local Medicinal Aromatic Plants (MAP) from this region. The focus is on the most important native MAP and on their potential as new cultivated modern crops. The large climatic variations of this region, present in a relatively small area, create a wide range of natural habitats and high biodiversity of wild plants. Due to the geographical location of this area, which is in the meeting of four phyto-geographical regions, there is a rich diversity of herbaceous plants. Part of the common MAP in the Holy Land vicinity are endemic to this area, such as *Micromeria fruticosa, Origanum dayi, O. ramonense, O. syriacumvar syriacum, Chiliadenus iphionoides* and *Salvia domenica.* The rest are local ecotypes of a wider dispersion area, such *as Salvia fruticosa*, *Artemisia judaica*, *Achillea fragrantissima, Asteriscus graveolens*, *Coridothymus capitatus*, *Foeniculum vulgare* and *Mentha longifolia.* Cultivation of medicinal plants that were traditionally collected from the wild is necessary both for protection of plant species in their native habitats, and as a response to the increased demand for uniform high-quality sources of medicinal herbs.

Keywords Aromatic plants • The holy land • Domestication • Breeding • Folk medicine • Biological activity • Origanum • *Salvia fruticosa* • *Salvia dominica* • *Micromeria fruticosa* • *Chiliadenus iphionoide*

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Introduction

Medicinal plants, growing in the vicinity of the holy land, were traditionally used throughout history and many of them are mentioned in the scriptural sources (Duke 2007). The area traditionally considered to be the Holy Land of the Bible, is defined as the area from the mountains of Lebanon and Syria in the north, to the eastern banks of the Jordan River, to the northern reaches of the Sinai Peninsula in the south. Ethno-botanical surveys, conducted in recent years indicate that many of the traditional plants are still used in folk medicine today (Aburjai et al. 2007; Ali-Shtayeh et al. 2000; Dafni et al. 1984; Palevitch and Yaniv 2000; Lev and Amar 2000, 2002). Most of the plants are not common in the Western world today and are not cultivated in large scale, if at all. However, there is a great potential for future development of new crops and new products, mainly by domestication and breeding of selected unique local traditional Medicinal and Aromatic Plants (MAP). The great climatic variations in this region, in a relatively small area, create a wide range of natural habitats and high biodiversity of wild plants. Due to the geographical location of the Holy Land in the heart of the Levant, which is in the meeting area of four phyto-geographical regions, (Mediterranean, Irano-turanian, Saudi Arabian and Sudanian) there is a rich diversity of herbaceous plants. Mt. Hermon is in the north, where it snows in the winter. On this mountain, species such as *Nepeta italica L., Nepeta cilicia Boiss, Nepeta glomerata Bentham, and Trachonitica* can be found. Only 300–400 km away, in the desert region, we can find desert plants such as *Artemisia judaica*, *A. sieberi*, *Origanum dayi*, *O. ramonense*, *Achillea fragrantissima, Chiliadenus iphionoides* and *A. santolina* (Amzallag et al. 2005; Dudai et al. 2003; Putievsky et al. 1992, 1997; Tamir et al. 2011; Yaniv et al. 2011; Friedjung et al. 2013). In this chapter we describe a selected list of some interesting local medicinal species of this vicinity. We will focus on endemic aromatic plants and their potential as new cultivated crops.

Domestication and Breeding – Adapting the Traditional Former Glory to Modern Times

The increasing demand by industry for uniform and high-quality raw material, along with modern developments, results in the situation where fewer and fewer people still collect plants from the wild. In addition, some of the wild plant species are protected and as a result, not available. These facts have necessitated the cultivation of various species. This shortage of raw material has encouraged seed companies, researchers and farmers to select cultivars which could substitute for the raw material that once came from the wild. Therefore, the approach of the MAP research and development today is to develop modern agricultural methods for traditional crops. Most of them used to be collected by people in the wild, like oregano in Turkey and Greece or za'atar (*Origanum syriacum*) in Israel (Dudai 2012). The goal

is the domestication of plants and the development of optimal growth methods for modern industry in order to replace traditional methods.

The challenge of domestication of wild plants includes the need to acclimatize plants outside of their native region. For instance, although land distances in Israel are short, the variability and changeability of climate makes this type of plant domestication all the more difficult. Desert plants from the Negev, native to an arid climate, were acclimatized to a Mediterranean climate in the north of Israel. Moreover, when considering domestication of foreign wild plants such as *Origanum vulgare* (Putievsky et al. 1997) and *Salvia officinalis* (Putievsky et al. 1986b), the process should be accompanied by introduction, acclimation, and selection of suitable varieties to the local conditions.

The danger of extinction and the need for domestication has promoted the collection and conservation of plants in all their natural biodiversity. This important activity has been done in the last few years by Gene Banks in various countries (Heywood 2002). These collections can serve as a base for selection by screening of various traits, such as desirable natural products, bio-activity or adaptation of cultural practices (Dudai 2012).

Wild Aromatic Medicinal Plants as Potential New Crops

Part of the common aromatic plants in the Holy Land vicinity are endemic to this area, such as *Micromeria fruticosa, Origanum dayi, O. ramonense, O. syriacum ve syriacum, Chiliadenus iphionoides* and *Salvia domenica.* The rest are local ecotypes of a wider dispersion area. A selected list of the main common traditional plants and their references is given in Table 1.

The following species were chosen as the most promising endemic plants to be developed as new crops.

Origanum spp.

The genus *Origanum* (Lamiaceae) is divided into ten sections: *Amaracus* Bentham, *Anatolicon* Bentham, *Brevifilamentum* Ietswaart, *Longitubus* Ietswaart, *Chilocalyx* Ietswaart, *Majorana* Bentham, *Campanulaticalyx* Ietswaart, *Elongatispica* Ietswaart, *Origanum* Ietswaart, *Prolaticorolla* Ietswaart, and contains about 20 species (Ietswaart 1980). *Origanum* species are perennials herbs, the majority of them are distributed over the Mediterranean (Kokkini 1997). The culinary and medicinal herbs contain mainly carvacrol and/or thymol ("Oregano"), or terpinene-4-ol, linalool, and sabinene hydrate ("Marjoram") (Kokkini 1997). In the Holy Land vicinity there are 7 known endemic Origanum species, some of them belong of the unique section: *Campanulaticalyx.*

Table 1 Selected list of the most common local aromatic medicinal species in the wild

Species	Family	References
Achillea fragrantissima (Forssk) Sch. Bip	Compositae	Fleisher and Fleisher (1993) and Ravid et al. (1995)
Artemisia arborecescence L.		Dudai and Amar (2005) and Yaniv et al. (2011)
Artemisia judaica L.	Compositae	Putievsky et al. (1992) and Yaniv et al. (2011)
Artemisia sieberi Besser	Compositae	Feuerstein et al. (1986), Fleisher et al. (2002), and Yaniv et al. (2011)
Asteriscus graveolens (Forssk.) Less	Compositae	
Chiliadenus iphionoides (Boiss. & Blanche) Brullo	Compositae	Tamir et al. (2011)
Coridothymus capitatus L.	Lamiaceae	Fleisher and Fleisher (2002)
Foeniculum vulgare Mill. var. *vulgare*	Umbelliferae	Barazani et al. (2002)
Mentha longifolia L.	Lamiaceae	Segev et al. (2012)
Micromeria fruticosa (L.) Druce	Lamiaceae	Dudai et al. (2001)
Origanum dayi Post.	Lamiaceae	Dudai et al. (2003) and Amzallag et al. (2005)
Origanum remonense Danin	Lamiaceae	Danin et al. (1997)
Origanum syriacum var *syriacum*	Lamiaceae	Dudai (2012)
Origanum isthmicum Danin	Lamiaceae	Danin and Künne (1996)
Origanum jordanicum Danin & Künne	Lamiaceae	Danin and Künne (1996)
Origanum petraum Danin	Lamiaceae	Danin (1990)
Origanum punonense Danin	Lamiaceae	Danin (1990)
Salvia domenica L.	Lamiaceae	Werker et al. (1985b) and Ravid and Putievsky (1985a)
Salvia fruticosa Mill	Lamiaceae	Putievsky and Ravid (1984) and Putievsky et al. (1986b)
Salvia sclarea L.	Lamiaceae	Elnir et al. (1991a, b)
Satureja thymbra L.	Lamiaceae	Ravid and Putievsky (1985b)
Thymbra spicata L.	Lamiaceae	Ravid and Putievsky (1985b)

Syrian marjoram

Origanum syriacum is one of the main important native plants in the Holy Land vicinity. Syrian marjoram is an aromatic perennial herb in the mint family, Lamiaceae. The local common name of this plant is "**Za'atar**" or "**Ezov matzuy**". This herb is a very important one for the local population, with a long history of traditional uses. This herb was identified as the biblical hyssop which is mentioned in the bible as a medicinal and antiseptic plant (Fleisher and Fleisher 1988), and fits today as a part of the trend of "natural products" and "functional food" (Dudai 2008).

Description

The Syrian marjoram undergoes dramatic morphological variation during the year, probably as a mechanism of adaptation for the extreme seasonal climatic changes in its dispersion area: During the winter and spring upright thick stems bear large (1–3 cm long) and soft leaves. In the summer these foliage abscise, while new small leathery leaves are expressed on thin prostrate stems. The flowering starts in the beginning of May. Full bloom is observed in the beginning of June. About 50 days later (end of July) most of the inflorescences dry up and abscise. New flowers are produced sporadically during the summer and early autumn. The last flowers appear in September (Dudai et al. 1989, 1992).

Classification

In the past Syrian marjoram was defined as *Majorana syriaca* (Labiatae). In the revision of Ietswaart (1980) it is classified as a species of the genus *Origanum*, and belongs to the section *Majorana*, named *Origanum syriacum.* In the Middle East there are three varieties of this species: *O. syriacum* var *syriacum O. syriacum* var *bevanii* (mainly in Turkey and Syria) (Lukas et al. 2009) and *O. syriacum* var *sinaicum* (in Egypt) (Başer et al. 2003).

Origin and Distribution

Majorana syriacum is endemic to the Middle East in Mediterranean maquis and forest, Batha, Phrygana, hard rock outcrops, mainly in Lebanon, Syria, Israel, Jordan and the Sinai Desert (Feinbrun-Dothan 1978; Ietswaart 1980).

Folk Medicine

The word *ezov* refers in the Bible to a plant tied into branches and used as a brush to sprinkle blood on the doorposts and lintels when the house was cleansed against leprosy (Leviticus 14:4), as well as for purposes of worship: “And a clean person shall take hyssop and dip it in the water and sprinkle it upon the tent, and upon all the vessels, and upon the persons that were there, and upon who touched a bone, or one slain, or one dead, or a grave” (Numbers 19:6) (Zohary 1982). Due to its association with cleaning, the hyssop plant was thought to possess powers of spiritual purification: “purge me with hyssop and I shall be pure: wash me, and I shall be whiter than snow” (Psalms 51, 7). At the same time it was supposed to exemplify the stunted discredited plants that grow out of walls: “From the cedar tree that is in Lebanon even unto the hyssop that springeth out of the wall” (I Kings 4:33), although it is actually a handsome plant, tall, and does not sprout on walls (Zohary 1982).

The identity of the Biblical *ezov* with *O. syriacum* is confirmed by a Samaritan custom whereby Origanum is traditionally used by Samaritans to sprinkle the blood

of the Passover sacrifice. The hair on the stems is said to prevent coagulation of the blood (Zohary 1982).

The Syrian marjoram is known as a remedy for intestinal worms since Jesus' time (Palevitch and Yaniv 2000). Today, among Israeli Arabs, a tea is prepared from the leaves to relieve colds and stomach aches. Syrup prepared by scalding Syrian marjoram leaves is known as a remedy for several diseases, in the folk medicine of the Middle-East.

The Yemenite Jews use an infusion of hyssop to relieve labor pains, and use it in combination with sage and various aromatic leaves to reduce the pain of heart diseases, headaches and earache.

The plant is believed to promote verbal dexterity and can act as a charm against witchcraft.

An ethnobotanocal survey conducted in Israel revealed the following ethnic uses of Syrian marjoram (Dafni et al. 1984).

1. To relieve toothaches: Green leaves are crushed and placed on the aching tooth.
2. To treat gum infections: Dried leaves are crushed with salt and rubbed on the inflamed area.
3. To strengthen heart function: Tea is prepared with honey.
4. To treat infections of the digestive tract and urinary system: decoction is prepared and 2–4 spoons are taken daily.
5. To treat colds: tea is prepared.
6. To clear worms: An extract is made from leaves in olive oil, left for 2 weeks in the sun, the oil is absorbed in sugar lumps and 1–3 spoon are taken twice daily.

Biological Activities

The high quantities of carvacrol and thymol in oregano spp. oil, are responsible for its potent biological properties such as antioxidant (Yanishlieva et al. 1999), antibacterial (Ultee et al. 2002; Si et al. 2006; Esen et al. 2007), fungicide (Muller-Riebau et al. 1995), insecticide (Cetin et al. 2007), herbicide (Dudai et al. 1999b) and nematicide activities (Oka et al. 2000).

Many diverse activities of carvacrol, such as antimicrobial, antitumor, antimutagenic, antigenotoxic, analgesic, antispasmodic, anti-inflammatory, angiogenic, antiparasitic, antiplatelet, ache inhibitory, antielastase, insecticidal, antihepatotoxic and hepatoprotective activities have been described (Baser 2008). In addition, uses such as a feed additive, in honeybee breeding and in gastrointestinal ailments have been shown.

Major Chemical Constituents and Bioactive Compounds

O. syriacum essential oil is primarily comprised of the phenolic monoterpenes carvacrol and thymol (Lukas et al. 2009). Usually there are two identified chemotypes: one contains mainly carvacrol (60–80 %) and a small amount of thymol;

whereas the other contains mainly thymol and little carvacrol (Dudai et al. 1989). There is a huge seasonal variation in the essential oil content and composition: The essential oil content of plants harvested in February is only one-fifth of that in plants harvested in August. Their composition also varies significantly within the season; whereas during most of the Summer the main component of a thymol chemotype is thymol, in the Winter the thymol content falls to only 36 %, and p-cymene becomes the main component of the essential oil. The carvacrol chemotype shows a similar trend (Dudai et al. 1992). In addition, it contains other important phenolic compounds such as thumoquinon (0.04–23.7 % DW) (Lukas et al. 2009), oleanolic acid (0.15–1.2 % DW), ursolic acid (0.5–2.5 % DW) and rosmarinic acid (0.2–2.0 % DW) (Dudai 2012).

Development as a New Cultivated Crop

Lately, due to the danger of extinction as a result of the excess collection in the wild, *O. syriacum* has become a "protected species" by law, so its domestication for agricultural production becomes necessary. A project of domestication and breeding in Israel has been conducted over the last 30 years (Dudai 2012). First, vegetative propagation materials of *O. syriacum* were systematically collected to represent their natural diversity, and are grown in experimental fields under intensive conditions. The genetic variability of the essential oil content and compositions, as well as other ingredients such as ursolic acid and rosmarinic acid in various clones of the representative populations, grown in uniform conditions, was very high. The selection process yielded new high quality and uniform commercial varieties (Fig. 1). Two clones were registered as cultivars: "Carmel" (a carvacrol type) and "Tavor" (a thymol type) (Dudai 2012). Study of the factors affecting the yield components (Dudai et al. 1992) and a series of field agro-technical experiments were necessary to optimize the cultivation of the new crop in the various areas. Agronomic aspects studied included search of selective herbicides, the effect of fertilization, irrigation, and harvest regime and plant height on yield components during at least 2 years of growth. Most of the experiments were carried out with different clones in order to find the best treatments for each of the expected ones to be used for commercial purposes (Putievsky et al. 1997).

Other Endemic *Origanum* Species as Potential New Crops

In addition to *O. syriacum*, six species, *Campanulaticalyx* (Ietswaart 1980) are distributed in the limited desert area in Southern Israel, Jordan and Sinai (Egypt) *O. dayi* (Dudai et al. 2003; Amzallag et al. 2005; Friedjung et al. 2013), *O. remonense* (Danin et al. 1997), *O. jordanicum* (Danin and Künne 1996), *O. petraeum*, *O. punonense* (Danin 1990) and *O. isthmicum* (Danin and Künne 1996). Table 2 represents the main components of the essential oils extracted from dry material of the various species. *O. petraeum O. punonense, O. dayi* (Fig. 2) and *O. ramonenese* (Fig. 2),

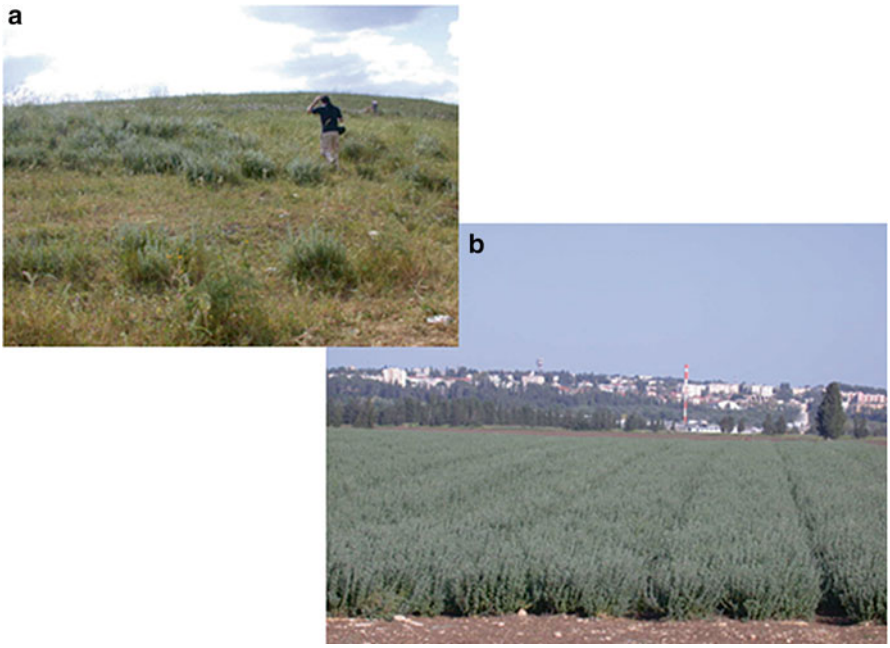

Fig. 1 *Origanum syriacum* population in the wild (**a**) and a domesticated variety in an commercial open field in Israel (**b**) (Dudai, unpublished data)

containing substantial amounts of α-terpineol and terpinen-4-ol, belong to the "marjoram" culinary type, while *O. isthmicum and O. jordanicum*, belonging to "oregano" type, contain mainly carvacrol derivatives.

The common "oregano" (*Origaum vulgare* or other species used for this spice) is not native to the Holy Land vicinity, but was introduced to Israel due to its popularity in the world, together with some other Mediterranean herbs. The selection process yielded a few clonal cultivars which have been used for the production of dry or fresh herbs for export (Basker and Putievsky 1978; Putievsky et al. 1988, 1997). Recently, interspecific cross breeding yielded some interesting hybrids of *O. vulgare* × *O. syriacum* (Fig. 2), which are used for further breeding (Dudai, unpublished data).

Salvia spp.

The genus *Salvia* (Lamiaceae) includes more than 1,000 species (Alizar 1993; Rivera et al. 1994; Tucker et al. 1995). *Salvia* species are either herbaceous or shrubby perennials and many of them are used as herbs or ornamentals and garden plants (Clebsch and Barner 2003).

Table 2 Volatile composition of *Origanum* spp. of *Campanulaticalyx* section collected in Israel and Jordan[a]

Components	*O. ramonense*	*O. dayi*	*O. petraeum*	*O. punonense*	*O. isthmicum*	*O. jordanicum*
α-Pinene	1	tr	1	3	3	–
Camphene	–	1	1	1	4	2
β-Pinene				2		
3-Octanone					1	8
para-Cymene	4	10	8	8	13	7
Limonene	–	3				
1,8-Cineole	27	tr	10	22		
γ-Terpinene	2	1	2	9	tr	1
Linalool	–	tr	tr	1	tr	4
Borneol	2	9	3	3	9	4
Terpinen-4-ol	6	14	11	17	1	
α- Terpineol	41	43	38	18	1	
2α-Hydroxy 1,8-cineole	2	2	1			
Carvacrol methyl ether					tr	16
Thymoquinone					11	1
Linalyl acetate			7			
Bornyl acetate	tr	2	1	1		tr
Thymol				tr	2	
Carvacrol				–	44	17
iso-Ascaridol				2		
Carvacryl acetate						29
cis-p-Menth-2-en 1,8-diol	2					
trans-Caryophyllene	tr		1	1	3	2
Caryophyllene oxide					2	1
Cadinol			1			
Caryophylla-4(14),8(15)-dien-5-beta-ol					1	
Intermediol	–	1	2	2		

tr traces (<1 %), *n.d.* not detected (<0.05 %)
[a]Collected by Prof. Avinoam Danin and analyzed by GCMS on Rtx-5MS column
Larkov (2009)

Greek Sage (Salvia fruticosa, *syn.* S. triloba)

Salvia fruticosa is a common native herb and very popular which is growing in wide areas in the Holy land vicinity and the Mediterranean regions. Salvia is an aromatic perennial herb in the mint family, Lamiaceae (Rivera et al. 1994). It is known as

Fig. 2 Three endemic Origanum species to the Holy Land vicinity and a hybrid (*O. vulgare* × *O. Syriacum*) obtained by cross breeding in Israel. The pictures were taken in the Aromatic Plants Living Germplasm collection at the Newe Ya'ar Research Center, Israel (Dudai, unpublished data)

having a few local common name, depending on the region and the language, such as: Mariamia, Marmaria, Joa'sas, Shijeri (Arabic) and Marva – Meshuleshet (Hebrew).

There are many legends revolving this plant in the folklore of the region. There is a story about Mary, mother of Jesus, who, while fleeing to Egypt to escape Herod, with her son in her arms, wiped her face with sage leaves to refresh herself and her son in the oppressive heat. From this legend the Arabic name, "mariamiah" – "the blessed one" is derived. The Latin name: "Salvia" is a contraction of the Latin word Salvameaning "to rescue".

The three-lobed sage is now a protected plant, due to excessive gathering from the wild by healers and users. (Palevitch and Yaniv 2000).

Description

Salvia fruticosa is an evergreen shrub growing up to 1 m height. The unique leaf with three main parts (Fig. 3) is probably the reason of the former name *tri* (three) *loba* (lobes or leaves). The stems are upright and hairy, the flower color is lilac. Flowering starts in February–March. Anthesis and seed maturation continue until the end of June (Putievsky and Ravid 1984; Putievsky et al. 1986a).

Fig. 3 Sage "Newe Ya'ar": an Inter-specific hybrid (Dudai et al. 1999a) of local Israeli *S. fruticosa* with introduced Dalmatian sage

Folk Medicine

In ancient Greece a tea prepared from leaves of the plant was believed to purify the blood and impart a feeling of well-being.

The Yemenite Jews use the plant to relieve earache. Tunisian Jews use it to ease stomach ache, and the Jews of Morocco use it as a diuretic medication.

In the traditions of the Arabs in this region sage is used mainly to treat colds and disorders of the digestive system, including stomach ache, diarrhea, indigestion and flatulence (Dafni et al. 1984).

In Lebanon a water infusion of the leaves is used as a cure for liver diseases. Herbal healers in the Middle East recommend using sage to regulate menstruation, to enhance fertility, to strengthen the muscles of the womb before and after childbirth, and to treat problems associated with menopause. Sage helps opening the respiratory canals, and eases catarrh and sore throats. A gargle prepared from an infusion of sage leaves is used to treat coughs and painful gums.

Sage is attributed with the virtue of prolonging life, in both Arabic and European folklore.

In an ethnobotanical survey, conducted among the Arabs in Israel, the following uses were found to be the most popular (Dafni et al. 1984)

1. To treat mouth sores: fresh leaves are chewed.
2. To cure external sores: fresh leaves are placed on the sore.
3. To accelerate wound healing: dried crushed leaves are spread on the wound.
4. To treat colds: a vapor bath is prepared with sage leaves. The vapor is inhaled.
5. To relive aching joints and rectal pains: Sit over a vapor bath containing sage leaves.

Biological Activities and Modern Medicine

Thujones are some of the essential-oil components of *S. fruticosa*. They are known to depress the central nervous system, counter the activity of various poisons, and induce hallucinations. The use of large dosages of thujones is liable to induce side effects such as convulsions and loss of consciousness. However, using the plant according to tradition is usually safe.

The essential oil also contains phenols, which are active against microbes (Palevitch and Yaniv 2000 and human fungi (Adam et al. 1998).

The effect of extracts obtained from selected Salvia species was tested against oxidative and alkylation damage to DNA in human HCT15 and CO115 cells. Data showed that sage tea protected colon cells against oxidative and alkylating DNA damage and may also interfere with efficacy of alkylating agents used in cancer therapy (Ramos et al. 2012).

Antiproliferative activity of crude ethanol extracts from nine Salvia species grown in Jordan was studied against a panel of breast cancer cell lines.

Cytotoxic activity was evaluated in human tumor models of breast cancer; MCF-7, T47D, ZR-75-1, and BT 474 by the sulforhodamine B assay. In addition, the extracts were evaluated using a non-transformed cell line (Vero) and normal fibroblast cells in order to demonstrate their selectivity and safety (Abu-Dahab et al. 2012).

The results show that three of the plant extracts under investigation exhibited antiproliferative activity against breast cancer cells and were shown to be safe and selective. They are*: S. fruticosa, S. hormium* and *S. syriaca*. These could be considered as a potential source for novel anticancer therapy (Abu-Dahab et al. 2012).

Major Chemical Constituents and Bioactive Compounds

While the main components of the essential oil of *S. fruticosa* in Europe are 1, 8 cineol, thujone and camphor (Máthé et al. 2010), thujones were not reported as a significant component in plants sampled from wild populations in Israel (Putievsky and Ravid 1984). Antioxidant activity and phenolic antioxidants such as rosmarinic acid, caffeic acid, ursolic acid, oleanolic acid and carnosic acid in *S. fruticosa* were also reported (Máthé et al. 2010; Pizzale et al. 2002; Skoula et al. 2000).

Development as a New Cultivated Crop

Domestication and selection of *S. fruticosa* were studied in Israel in the 1980s (Putievsky and Ravid 1984), but any wide scale cultivation of this crop today does not exist. However, the main benefit of this work was obtained by interspecific hybridization with the European common Sage species (Putievsky et al. 1990). Crossing of *S. officinalis*, introduced to Israel from Dalmatia, (Putievsky et al. 1986b; Zutic et al. 2003) with local *S. fruticosa* (Putievsky et al. 1986a) yielded a new commercial cultivar of sage (Fig. 3) (Dudai et al. 1999a). This cultivar has aroma and appearance similar to those of *S. officinalis* (Dudai 2012) but grows in the Israeli Winter and Spring as well as the local *S. fruticosa*, and today it is the main cultivar grown for the fresh herbs market (Dudai et al. 1999a; Dudai 2012).

Salvia dominica

S. dominica is an endemic species to the Holy Land vicinity. Its local common names are Chuecha in Arabic and Marva Reichanit in Hebrew (Dafni et al. 1984). The aroma of its leaves, stems and inflorescences is strong and very similar to that of *S. sclarea* (Werker et al. 1985b).

Description

Salvia dominica is an evergreen shrub growing up to 0.8 m height. The stems are upright and hairy, the flower color is white. The flowering starts in February–March. Anthesis and seed maturation continue until the end of May. The trichoms are very similar to those of *S. sclarea* (Werker et al. 1985b).

Major Chemical Constituents and Bioactive Compounds

The essential oil content in leaves and flowers of *S dominica* is 0.2–0.3 %. The main components of the essential oil are (−) linalyl acetate, lonalool, trpineol, neryl acetate, geranyl acetate geraniol and nerol (Ravid and Putievsky 1985a; Ravid et al. 1994).

Folk Medicine

S. dominica is used to relieve pains, by means of poultices made of crushed leaves, placed on the painful limb. Sweet gall nuts of a peach-like taste develop on the stems of this plant. The local inhabitants are very fond of them. They are called: “little peach” (Palevitch and Yaniv 2000).

Biological Activity

Khalil et al. (2005) reported on anti-microbial activity of crude extract of *S. dominica* against *stapylococus aureu*, but not against other tested pathogenic bacteria. *S. dominica* extracts also showed cytotoxic and antiproliferative activity on choriocarcinoma, endometrium adenocarcinoma, B lymphoblast (Fiore et al. 2006) and breast adenocarcinoma (Abu-Dahab and Afifi 2007) tumor cell lines. Dal Piaz et al. (2009) identified 24 sesterterpene lactones isolated from *S. dominica*, 18 of them interact with tubulin – tyrosine ligase, an enzyme involved in the tyrosination cycle of the C-terminal of tubulin, and inhibit its activity in cancer cells.

A weak nematocidal activity was found in the essential oil components against root-kinot nematodes (Oka et al. 2000).

Clary Sage

A new and unique chemotype of clary sage, *Salvia sclarea* L., was identified recently in wild populations of this species in the northern part of Israel (Elnir et al. 1991a).

This chemotype contains relatively high citral, geranyl- acetate and geraniol, while the major essential-oil components of the common clary sage in the world are linalool and linalyl-acetete. Comparison of the new chemotype with a Russian type showed a great difference in composition and organoleptic character between the two oils. The relative quantity of most components of hybrid oils was intermediate between those of the parent plants (Elnir et al. 1991b).

White Micromeria

(*Micromeria fruticosa* (L.). Druce. Lamiaceae is a perennial herb found in Northern and central Israel, Lebanon, Syria, Jordan and Turkey. Thanks to its nice minty aroma, this is a popular herb, used for tea consumption, giving a feeling of coolness during the typical hot summer in the area. Its local common names are Zuta Levana in Hebrew and Zofa or Ishbat Al Shay in Arabic.

Description

White Micromeria is a dwarf- shrub growing up to 0.2–0.8 m height. The plant spreads vegetatively mainly at the end of winter and spring. The flowering starts in July and continues until November. The flower color is white (Dudai et al. 2001).

Major Chemical Constituents and Bioactive Compounds

The major component of the white micromeria is enantiomerically pure (+)-pulegone (Ravid et al. 1994). In addition to (+)-pulegone, major components of the essential oil are other monoterpenes such as isomenthol, isomenthone, limonene, menthol, α-pinene, β-pinene, piperitone, piperitenone oxide and the sesquiterpenes b-caryophyllene and germacrene. (Werker et al. 1985a; Fleisher and Fleisher 1991; Dudai et al. 2001; Kirimer et al. 1993). Dudai et al. (2001) found a significant seasonal variation in the essential oil composition: During the summer months, when growth rates are maximal, (+)-pulegone constituted up to 80 % of the essential oil, while in early winter, a period of growth-rest in Mediterranean climates, (+)-pulegone levels dropped dramatically to a few percent, while isomenthol constituted up to 80 % of the essential oil. Additionally, in this study there were marked differences in the extracts obtained from individual leaf along the stems: In young upper leaves, the main component was (+)-pulegone, constituting up to 70 % of the total essential oil extracted. During maturation, levels of this component dropped steadily, while reciprocally, levels of isomenthol increased steadily with leaf position, from 0 % in young leaves to more than 60 % in older leaves (Dudai et al. 2001).

Folk Medicine

Tea made of leaves is used to ease breathing of people suffering from colds and also to relieve stomach aches. In Nazareth they prepare an infusion of the leaves to relieve heart pains (Palevitch and Yaniv 2000). The aerial parts of *M. fruticosa* are widely used in the eastern Mediterranean region as medicinal teas, to treat many ailments including abdominal pains, diarrhea, eye infections, heart disorders, high blood pressure, weariness, exhaustion, colds and open wounds (Yaniv et al. 1982; Dafni et al. 1984).

Biological Activity

Evaluation of the allelochemical properties of white micromeria essential oils and its main component (+)-pulegone has demonstrated strong inhibition of seed germination and plant development (Dudai et al. 1999b, 2000, 2009). Pulegone and pulegone-derived lactones have anti-feedant, antibacterial, antifungal and insecticide activity (Szczepanik et al. 2005; Zielińska and Matkowski 2014).

Pulegone is also known as toxic, mainly hepato- and neurotoxicity (Moorthy et al. 1989). **Nevertheless,** De Sousa et al. (2011) reported that (+)–pulegone is a psychoactive compound and has the profile of an analgesic drug, it exhibited antinociceptive activity against chemically induced pain in mice, as well as CNS-depressing and anticonvulsant effects (de Sousa et al. 2011).

Sharp Varthemia

Chiliadenus (syn. *Varthemia*) *iphionoides* (Boiss. et Blanche) Brullo is a member of the Composites. *C. iphionoides* is an aromatic plant whose aerial parts were used in the traditional medicine of the eastern Mediterranean region, and is endemic to the Holy Land vicinity. Its local common names are Salimania in Arabic and Ktela Harifa in Hebrew.

Description

C. iphionoides is an evergreen dwarf shrub with small leaves covered with hairs and glands containing essential oil which gives the plant its unique aroma (Feinbrun-Dothan 1978). All the flowers are tubular. The flowering season is from September to December.

Classification

Chiliadenus iphionoides (Boiss. et Blanche) Brullo (syn. *Varthemia iphionoides* Boiss. et Blanche and Jasonia iphionoides (Boiss. & Blanche) Botsch), a member of the Asteraceae family, tribe Inuleae.

Origin and Distribution

It is found throughout most of Israel, from Mount Hermon to the southern Negev, as well as in Syria, Lebanon, Jordan, and Sinai (Greuter 2008), (Danin 1983).

Folk Medicine

Sharp varthemia is traditionally used for anti-diabetic treatment (Al-Mustafa and Al-Thunibat 2008). In an ethno-botanical survey, conducted among the Arabs in Israel, the following uses were found to be the most popular (Dafni et al. 1984)

1. To relieve headaches and stomach aches, and to clear flatulence: an infusion is prepared. Also fresh leaves are chewed.
2. To treat eye complaints: soaked leaves are placed on the eye.
3. To treat sick babies: The baby is washed in boiled leaves, and then covered to sweat.

4. To treat urine retention: Drink a water infusion of crushed leaves.
5. To relieve internal and external bodily pains: A steam bath is prepared from leaves.
6. To dress wounds: Fresh or dried leaves are placed on the wound.

The Yemenite Jews use sharp vartemia leaves mixed with honey to strengthen their heart and brain, as well as their mental power. They use the leaves cooked in water to relieve melancholia and nervousness, and to treat coughs and mild colds (Palevitch and Yaniv 2000). In traditional eastern Mediterranean medicine, *C. iphionoides* is used to treat influenza, fever, stomach ache, depression and nervousness (Palevitch and Yaniv 1991).

Biological Activity

Various studies demonstrated cytotoxic, anti-oxidant, anti-bacterial activities (Al-Dabbas et al. 2006; Al-Mustafa and Al-Thunibat 2008), anti-diabetic (Gorelick et al. 2011) and hypoglycemic activity (Afifi et al. 1997). Al-Dabbas et al. (2005) isolated eudesmane sesquiterpene with antibacterial activity.

T-cadinol, found in one chemotype, has muscle relaxing activity, possibly due to its calcium antagonistic properties (Zygmunt et al. 1993), and may be useful in immunotherapy (Takei et al. 2006).

Intermedeol has therapeutic potential for treatment human leukemia (Jeong et al. 2002), as well as repelling activity against mosquitoes (Cantrell et al. 2005), ticks (Soares et al. 2010), and ants (Chen et al. 2008).

Major Chemical Constituents and Bioactive Compounds

Avato et al. (2004) described the composition of *C. iphionoides*'s essential oil in a plant sampletaken from the Jordan Valley in Jordan, with borneol as the main compound of this essential oil. Other major compounds were 1, 8-Cineole, α-Terpinol, Camphor, Bornyl formate, Terpinen-4-ol and Bornyl acetate (Tamir et al. 2011). Even though several similar compounds were found, mostly monoterpens, these populations were rich in Intermedeol (not found in the Jordanian oil), Chrysanthemic acid and τ- Cadinol. In contrast to the Jordanian population, seven primary compounds were found in the essential oil of Israeli populations: Borneol, Camphor, 1,8-Cineole, τ-Cadinol, Chrysanthemic acid, fokienol and Intermedeol (Tamir et al. 2011). In 10 representative populations, chosen according to geographical location, climate and topography, 161 volatile compounds were found in the extracts, of which 75 were minor components and not identified. Considerable variation in essential oil composition was found among populations, enabling the identification of three main chemotypes: (A) camphor - α-pinene-fokienol chemotype,

(B) τ-cadinol-1,8 cineole-transchrysanthemol chemotype, and (C) intermedeol chemotype. The main compound of the southern populations was Camphor; therefore they belong to the "Camphorial" chemotype. Only the populations of Judea, Samaria and the northern Negev contain Intermedeol, therefore they belong to the "Intermedeolial" chemotype (Tamir et al. 2011).

Conclusion

Many special and unique local medicinal plants grow in the Holy Land, all with a long history of use, including scriptural documentation of many of them. However, most of them, although still used by the local population, are almost unknown in the western world. During the last decades a few ethno-botanical surveys have been conducted, in order to preserve the knowledge accumulated throughout the past. There is a great need to conserve the natural biodiversity of these plants, which has been damaged by recent intensive urban development. We think that these plants could be preserved by becoming agricultural commodities, since they have great potential as new crops and could become a source for novel bioactive compounds and drugs. In addition, some new culinary herbs could be developed by classical or by interspecific crossbreeding, as was demonstrated with oregano and sage. New products based on ancient plants and practices could bring the herbal traditions of the Holy Land to the rest of the world.

References

Abu-Dahab R, Afifi F (2007) Antiproliferative activity of selected medicinal plants of Jordan against a breast adenocarcinoma cell line (MCF7). Sci Pharm 75:121–136

Abu-Dahab R, Afifi F, Kasabri V, Majdalawi L, Naffga R (2012) Comparison of the antiproliferative activity of crude ethanol extracts of nine salvia species grown in Jordan against breast cancer cell line models. Pharmacogn Mag 32:319–324

Aburjai T, Hudaib M, Tayyem R, Yousef M, Qushawi M (2007) Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Heights region. J Ethnopharmacol 110:294–304

Adam K, Sivropoulou A, Kokkini S, Lanaras T, Arsenakis M (1998) Antifungal Activities of *Origanum vulgare* subsp. *hirtum, Mentha spicata, Lavandula angustifolia*, and *Salvia fruticosa* essential oils against human pathogenic fungi. J Agric Food Chem 46:1739–1745

Afifi F, Saket M, Jaghabir M, Al-Eisawi D (1997) Effect of *Varthemia iphionoides* on blood glucose level of normal rats and rats with streptozonic-induced diabetes mellitus. Curr Ther Res 58:888–892

Al-Dabbas MM, Hashinaga F, Abdelgaleil SA, Suganuma T, Akiyama K, Hayashi H (2005) Antibacterial activity of an eudesmane sesquiterpene isolated from common Varthemia, *Varthemia iphionoides*. J Ethnopharmacol 97:237–240

Al-Dabbas MM, Suganuma T, Kitahara K, Hou DX, Fujii M (2006) Cytotoxic, antioxidant and antibacterial activities of *Varthemia iphionoides* Boiss. extracts. J Ethnopharmacol 108(2):287–293

Ali-Shtayeh MS, Yaniv Z, Mahajna J (2000) Ethnobotanical survey in the Palestinian area: a classification of the healing potential of medicinal plants. J Ethnopharmacol 73:221–232

Alizar G (1993) Catalogue Synonymique des Salvia du Monde. (Lamiaceae) VI. Biocosme Mésogéen. Nice 10(3–4):33–117

Al-Mustafa AH, Al-Thunibat OY (2008) Antioxidant activity of some Jordanian medicinal plants used traditionally for treatment of diabetes. Pak J Biol Sci 11:351–358

Amzallag N, Larkov O, Ben Hur M, Dudai N (2005) Soil microvariation in the wild as a source of variability: the case of secondary metabolism in *Origanum dayi* Post. J Chem Ecol 31(6):1135–1254

Avato P, Raffo F, Aldour NA, Vartanian ST (2004) Essential oil of *Varthemia iphionoides* from Jordan. Flavour Fragr J 19:559–561

Barazani O, Cohen Y, Fait A, Diminstein S, Dudai N, Ravid U, Putievsky E, Friedman J (2002) Chemotypic differentiation in indigenous populations of *Foeniculum vulgare* var. *vulgare* in Israel. Biochem Syst Ecol 30:721–731

Baser KHC (2008) Biological and pharmacological activities of carvacrol and carvacrol bearing essential oils. Curr Pharm Des 14:3106–3119

Başer KHC, Kürkçüoğlu M, Demirci B, Özek T (2003) The essential oil of *Origanum syriacum* L. var. *sinaicum* (Boiss.) letswaart. Flavour Fragr J 18(2):98–99

Basker D, Putievsky E (1978) Seasonal variation in the yield of herb and essential oil in some Labiatae species. J Hortic Sci 53:179–183

Cantrell CL, Klun JA, Bryson CT, Kobaisy M, Duke SO (2005) Isolation and identification of mosquito bite deterrent terpenoids from leaves of American (*Callicarpa americana*) and Japanese (*Callicarpa japonica*) beautyberry. J Agric Food Chem 53:5948–5953

Cetin H, Erler F, Yanikoglu A (2007) A comparative evaluation of *Origanum onites* essential oil and its four major components as larvicides against the pine processionary moth, *Thaumetopoea wilkinsoni* Tams. Pest Manag Sci 63:830–833

Chen J, Cantrell CL, Duke SO, Allen ML (2008) Repellency of callicarpenal and intermedeol against workers of imported fire ants (Hymenoptera: Formicidae). J Econ Entomol 101:265–271

Clebsch B, Barner CD (2003) The new book of Salvias. Timber Press, Portland, pp 125–127. ISBN 978-0-88192-560-9

Dafni A, Yaniv Z, Palevitch D (1984) Ethnobotanical survey of medicinal plants in northern Israel. J Ethnopharmacol 10(3):295–310

Dal Piaz F, Vassallo A, Lepore L, Tosco A, Bader A, De Tommasi N (2009) Sesterterpenes as tubulin tyrosine ligase inhibitors. First insight of structure-activity relationships and discovery of new lead. J Med Chem 52:3814–3828

Danin A (1983) Chilliadenus iphionoides. In: Flowering plants, the fauna and flora of Israel. Ministry of Defense – Publications, Tel Aviv, p 138 (Hebrew)

Danin A (1990) Two new species of *Origanum* (Labiatae) from Jordan. Willdenowia 25:601–602

Danin A, Künne I (1996) *Origanum jordanicum* (*Labiatae*), a new species from Jordan, and notes on other species of *O.* sect *Campanulaticalyx*. Willdenowia 25:601–611

Danin A, Ravid U, Umano K, Shibamoto T (1997) Essential oil composition of *Origanum ramonense* Danin leaves from Israel. J Essent Oil Res 9:411–417

De Sousa DP, Nobrega FF, de Lima MR, de Almeida RN (2011) Pharmacological activity of (R)-(+)- pulegone, a chemical constituent of essential oils. Z Naturforsch 66(7–8):353–359

Dudai N (2008) Optimization and improvement of phenolic monoterpenes production by oregano (*Origanum* sp.). Acta Hortic 778:15–28

Dudai N (2012) Domestication and breeding of wild medicinal and aromatic plants – 30 years of experience in Israel. Acta Hortic (ISHS) 955:175–183

Dudai N, Amar Z (2005) Tree wormwood (*Artemisia arborescens*) – a medicinal plant that arrived in the region of Israel from Western Europe during the Crusaders. Haya'ar 7:35–40 (Hebrew)

Dudai N, Putievsky E, Palevitch D, Halevy AH (1989) Environmental factors affecting flower initiation and development of *Majorana syriaca* L. (syn. *Origanum syriacum* var. *syriacum*). Isr J Bot 38:229–239

Dudai N, Putievsky E, Ravid U, Palevitch D, Halevy AH (1992) Light, temperature and flowering affecting monoterpenes content in *Origanum syriacum* L. Physiol Plant 84:453–459

Dudai N, Lewinsohn E, Larkov O, Katzir I, Ravid U, Putievsky E (1999a) Dynamics of yield components and essential oil production in a commercial hybrid sage (*Salvia officinalis* × *fruticosa* var. "Newe Ya'ar No 4"). J Agric Food Chem 47:4341 ± 4345

Dudai N, Poljakoff-Mayber A, Mayer AM, Putievsky E, Lerner HR (1999b) Essential oils as allelochemicals and theirs potential use as bioherbicides. J Chem Ecol 25:1079–1089

Dudai N, Larkov O, Putievsky E, Lerner HR, Ravid U, Lewinsohn E, Mayer AM (2000) Biotransformation of constituents of essential oils by germinating wheat seed. Phytochemistry 55:375±382

Dudai N, Larkov O, Ravid U, Putievsky E, Lewinsohn E (2001) Developmental control of monoterpenes content and composition in *Micromeria fruticosa* (L.) Druce. Ann Bot 88(3):349–354

Dudai N, Larkov O, Chaimovitsh D, Lewinsohn E, Freiman L, Ravid U (2003) Volatile compounds of *Origanum dayi* Post. Flavour Fragr J 18(4):334–337

Dudai N, Chaimovitsh D, Larkov O, Ficsher R, Blaicher Y, Mayer AM (2009) Allelochemicals released by leaf residues of *Micromeria fruticosa* in soils, their uptake and metabolism by inhibited wheat seed. Plant Soil 314:311–317

Duke JA (2007) Medicinal plants of the bible. CRC Press, Atlanta, 488 pp

Elnir O, Ravid U, Putievsky E, Dudai N, Ladzinsky G (1991a) Genetic affinity between two chemotypes of clary sage (*Salvia sclarea* L.). Euphytica 54:205–208

Elnir O, Ravid U, Putievsky E, Dudai N, Ladezinsky G (1991b) The chemical composition of two clary Sage chemotypes and their hybrids. Flavour Fragr J 6:153–155

Esen G, Azaz AD, Kurkcuoglu M, Baser KHC, Tinmaz A (2007) Essential oil and antimicrobial activity of wild and cultivated *Origanum vulgare* L. subsp. Hirtum letswaart from the Marmara region, Turkey. Flavour Fragr J 22:371–376

Feinbrun-Dothan N (1978) Flora Palestina. Part III, The Israel Academy of Science and Humanity, Jerusalem

Feuerstein I, Mueller D, Hobert K, Danin A, Segal R (1986) Constitution of essential oils from *Artemisia herba-alba* populations of Israel and Sinai. Phytochemistry 25:2343–2347

Fiore G, Nencini C, Cavallo F, Capasso A, Bader A, Giorgi G, Micheli L (2006) *In vitro* antiproliferative effect of six *salvia* species on human tumor cell lines. Phytother Res 20:701–703

Fleisher A, Fleisher Z (1988) Identification of biblical hyssop and origin of the traditional use of oregano-group herbs in the Mediterranean region. Econ Bot 42(2):232–241

Fleisher Z, Fleisher A (1991) The essential oil of *Micromeria fruticosa* (L.) Druce subsp. Barbata (Boiss et Kotschy.), P.H. Davis: aromatic plants at the Holy Land and the Sinai, Part VII. J Essent Oil Res 3:477–479

Fleisher Z, Fleisher A (1993) Volatiles of *Achillea fragrantissima* (Forssk.) Sch. Bip. Aromatic plants of the Holy Land and the Sinai. XL. J Essent Oil Res 5:211–214

Fleisher Z, Fleisher A (2002) Volatiles of *Coridothymus capitatus* chemotypes growing in Israel: aromatic plants of the Holy Land and Sinai part XV. J Essent Oil Res 14:105–106

Fleisher Z, Fleisher A, Nachbar RB (2002) Chemovariation of *Artemisia herba-alba* Asso. Aromatic plants of the Holy land and the Sinai. Part XVI. J Essent Oil Res 14:156–160

Friedjung A, Choudhary S, Dudai N, Rachmilevitch S (2013) Physiological conjunction of allelochemicals and desert plants. PLoS ONE 8(12):e81580. doi:10.1371/journal.pone.0081580

Gorelick J, Kitron A, Pen S, Rosenzweig T, Madar Z (2011) Anti-diabetic activity of *Chiliadenus iphionoides*. J Ethnopharmacol 137(3):1245–1249

Greuter W (2008) Med-checklist. A critical inventory of vascular plants of the circum-Mediterranean countries, 2nd edn, Dicotyledones (Compositae). Palermo, Genève/Berlin

Heywood VH (2002) The conservation of genetic and chemical diversity in medicinal and aromatic plants biodiversity. In: Şener B (ed) Biodiversity. Springer, New York, pp 13–22

Ietswaart JH (1980) A taxonomic revision of the genus Origanum (Labiatae). Leiden University Press, The Hague

Jeong SH, Koo SJ, Choi JH, Park JH, Ha J, Park HJ, Lee KT (2002) Intermedeol isolated from the leaves of *Ligularia fischeri* var. *spiciformis* induces the differentiation of human acute promyeocytic leukemia HL-60 cells. Planta Med 68:881–885

Khalil A, Hassawi DS, Kharma A (2005) Genetic relationship among salvia species and antimicrobial activity of their crud extracts against pathogenic bacteria. Asian J Plant Sci 4:544–549

Kirimer N, Tumen G, Ozek T, Baser KHC (1993) The essential oil of *Micromeria fruticosa* (L.) Druce subsp. Barbata (Boiss et Kotschy.) P.H. Davis of Turkish origin. J Essent Oil Res 5:79–80

Kokkini S (1997) Taxonomy, diversity and distribution of *Origanum* species. In: Proceedings of the IPGRI international workshop on Oregano, 8–12 May 1996, CIHEAM, Valenzano, Bari, Italy, p 2–12

Larkov O (2009) Aromatic plants as a source of natural chiral semiochemicals. Ph.D. thesis, Hebrew University of Jerusalem (submitted)

Lev E, Amar Z (2000) Ethnopharmacological survey of traditional drugs sold in Israel at the end of the 20th century. J Ethnopharmacol 72:191–205

Lev E, Amar Z (2002) Ethnopharmacological survey of traditional drugs sold in the Kingdom of Jordan. J Ethnopharmacol 82:131–145

Lukas B, Schmiderer C, Franz C, Novak J (2009) Composition of essential oil compounds from different Syrian populations of *Origanum syriacum* L. (Lamiaceae). J Agric Food Chem 57(4):1362–1365

Máthé I, Máthé Á, Hohmann J, Janicsák G (2010) Volatile and some non-volatile chemical constituents of Mediterranean Salvia species beyond their native area. Isr J Plant Sci 58(3–4):273–277

Moorthy B, Madyastha P, Madyastha KM (1989) Hepatotoxicity of pulegone in rats: its effects on microsomal enzymes *in vivo*. Toxicology 55:327–337

Muller-Riebau F, Berger B, Yeged O (1995) Chemical composition and fungitoxic properties to phytopathogenic fungi of essential oils of selected aromatic plants growing wild in Turkey. J Agric Food Chem 43:2262–2266

Oka Y, Nacar S, Putievsky E, Ravid U, Yaniv Z, Spiegel Y (2000) Nematicidal activity of essential oils and their components against the root-knot nematode. Phytopathology 90:710–715

Palevitch D, Yaniv Z (1991) Medicinal plants of Israel. Tamuz-Modan Publishing, Tel-Aviv

Palevitch D, Yaniv Z (2000) Medicinal plants of the Holy Land. Modan, Tel-Aviv, 358 pp

Pizzale L, Bortolomeazzi R, Vichi S, Uberegger E, Conte LS (2002) Antioxidant activity of sage (*Salvia officinalis* and *S. fruticosa*) and oregano (*Origanum onites* and *O. indercedens*) extracts related to their phenolic compound content. J Sci Food Agric 82:1645–1651

Putievsky E, Ravid U (1984) Selection and cultivation of *Salvia fruticosa* from wild population in Israel. In: Genetic resources of aromatic and medicinal plants, Organized by EUCARPIA, F.A.O., Oeiras, Portugal, p 87–94

Putievsky E, Ravid U, Dudai N (1986a) The essential oil and yield components from various plant parts of *Salvia fruticosa* Mill. (syn. S. *triloba*). J Nat Prod 49:1015–1017

Putievsky E, Ravid U, Dudai N (1986b) The influence of season and harvest frequency on essential oil and herbal yield from a pure clone of sage (*Salvia officinalis*) grown under cultivated conditions. J Nat Prod 49:326–329

Putievsky E, Ravid U, Dudai N (1988) Phenological and seasonal influences on essential oil of a cultivated clone of *Origanum vulgare* L. J Sci Food Agric 43:225–248

Putievsky E, Ravid U, Diwan-Rinzler N, Zohary D (1990) Genetic affinities and essential oil composition of *Salvia officinalis* L., *S. fruticosa* Mill., *S. tomentosa* Mill. and their hybrids. Flavour Fragr J 5(2):121–123

Putievsky E, Ravid U, Dudai N, Katzir I, Carmeli D, Eshel A (1992) Variation in essential oil of *Artemisia judaica* chemotypes related to phenological and environmental factors. Flavour Fragr J 7:253–257

Putievsky E, Dudai N, Ravid U (1997) Cultivation, selection and conservation of oregano species in Israel. In: Padulsi S (ed) Proceedings of the IPGRI international workshop on Oregano, (CIHEAM, Valenzano (Bari), Italy, p 103–110

Ramos AA, Pedro D, Collins AR, Pereira-Wilson C (2012) Protection by Salvia extracts against oxidative and alkylation damage to DNA in human HCT15 and CO115 cells. J Toxicol Environ Health A 75(13–15):765–775

Ravid U, Putievsky E (1985a) Essential oils of Israeli wild species of Labiatae. In: Baerheim Svendsen A, Scheffes JC (eds) Essential oils and aromatic plants. Martinus Nijhoff, Dordrecht, pp 155–161

Ravid U, Putievsky E (1985b) Composition of essential oils of *Thymbra spicata* and *Satureja thymbra* chemotypes. Planta Med 51:337–339
Ravid U, Putievsky E, Katzir I (1994) Chiral GC analysis of (R)(+) pulegone with high enantiomeric purity in essential oils of some lamiaceae aromatic plants. Flavour Fragr J 9:205–207
Ravid U, Putievsky E, Katzir I (1995) Determination of the enantiomeric composition of α-terpineol in essential oils. Flavour Fragr J 10(4):281–284
Rivera D, Obon C, Cano F (1994) The botany, history and traditional uses of three-lobed sage (Salvia fruticosa Miller) (Labiatae). Econ Bot 48:190–195
Segev D, Nitzan N, Chaimovitsh D, Eshel A, Dudai N (2012) Chemical and morphological diversity in wild populations of *Mentha longifolia* in Israel. Chem Biodivers 9(3):577–588
Si W, Gong J, Chanas C, Cui S, Yu H, Caballero C, Friendship RM (2006) In vitro assessment of antimicrobial activity of carvacrol, thymol and cinnamaldehyde towards *Salmonella* serotype Typhimurium DT104: effects of pig diets and emulsification in hydrocolloids. J Appl Microbiol 101:1282–1291
Skoula M, Abbes JE, Johnson CB (2000) Genetic variation of volatiles and rosmarinic acid in populations of *Salvia fruticosa* mill growing in Crete. Biochem Syst Ecol 28(6):551ERLI
Soares S, Borges L, Braga R, Ferreira L, Louly C, Tresvenzol L, de Paula J, Ferri P (2010) Repellent activity of plant-derived compounds against *Amblyomma cajennense* (Acari: Ixodidae) nymphs. Vet Parasitol 167:67–73
Szczepanik M, Dams I, Wawrzenczyk C (2005) Feeding deterrent activity of Terpenoid Lactones with the *p*-Menthane system against the Colorado Potato Beetle (Coleoptera: Chrysomelidae). Environ Entomol 34(6):1433–1440
Takei M, Umeyama A, Arihara S (2006) T-cadinol and calamenene induce dendritic cells from human monocytes and drive Th1 polarization. Eur J Pharmacol 537:190–199
Tamir H, Satovicb Z, Gorelick J, Danin A, Fischer R, Chaimovitsh D, Dudai N (2011) Intraspecific variation of *Chiliadenus iphionoides* essential oil in Israel. Chem Biodivers 8:1065–1082
Tucker AO, Maciarello MJ, Clebsch BB (1995) Volatile leaf oils of cultivars of *Salvia clevelandii* (Gray) Greene X S. *leucophylla Greene*. J Essent Oil Res 7:101–104
Ultee A, Bennik MHJ, Moezelaar R (2002) The phenolic hydroxyl group of carvacrol is essential for action against the food-borne pathogen *Bacillus cereus*. Appl Environ Microbiol 68:1561–1568
Werker E, Putievsky E, Ravid U (1985a) Structure of glandular hairs and identification of the main components of their secreted material in some species of Labiatae. Isr J Bot 34:35±45
Werker E, Ravid U, Putievsky E (1985b) Glandular hairs and their secretions in the vegetative and reproductive organs of *Salvia sclarea* and *S. dominica*. Isr J Bot 34:239–252
Yanishlieva NV, Marinova EM, Gordon MH, Raneva VG (1999) Antioxidant activity and mechanism of action of thymol and carvacrol in two lipid systems. Food Chem 64:59–66
Yaniv Z, Dafni A, Palevitch D (1982) Labiateae as medicinal plants in Israel. In: Margaris N, Koedam A, Vokou D (eds) Aromatic plants: basic and applied aspects. Martinus Nijhoff Publishers, The Hague, pp 265–269
Yaniv Z, Dudai N, Bacharach U (2011) *Artemisia* spp. In: Singh RJ (ed) Genetic resources, chromosome engineering and crop improvement: medicinal crops, vol 6. CRC Press, Boca-Raton, pp 338–359
Zielińska S, Matkowski A (2014) Phytochemistry and bioactivity of aromatic and medicinal plants from the genus *Agastache* (Lamiaceae). Phytochem Rev 13(2):391–416. doi:10.1007/s11101-014-9349-1
Zohary M (1982) Plants of the bible. Cambridge University Press, New York
Zutic I, Putievsky E, Ravid U, Dudai N (2003) Influence of harvest dynamics and cut height upon yield components of sage (*Salvia officinalis* L.). J Herb Spices Med Plant 10(4):49–61
Zygmunt PM, Larsson B, Sterner O, Vinge E, Hogestatt ED (1993) Calcium antagonistic properties of the sesquiterpene T-cadinol and related substances: structure-activity studies. Pharmacol Toxicol 73:3–9