## THE ESSENTIAL OIL OF LEMON BALM (Melissa officinalis L.), ITS COMPONENTS AND USING FIELDS

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**ABSTRACT:** Lemon balm (*Melissa officinalis* L.), member of *Lamiaceae* (formerly *Labiatae*) family, is one of the important medicinal plant species. Today, it is used in different branches of industry (such as medicine, perfume, cosmetic, and food etc.) in many countries of the world. The main components of lemon balm essential oil, ranged from 0.01 to 0.25%, are 39% citronellal, 33% citral (citronellol, linalool) and geraniol. It is traditionally used as a mild sedative, spasmolytic and antibacterial agent. In addition, results of a lot of clinical researches have showed that essential oil of lemon balm can be used in treatment of Alzheimer's disease, as antioxidant against negative effects of free radicals and an antitumoral agent and it has positive effect on immune system and stress. By means of its antimicrobial activity it was found to be effective in inhibiting the spoilage yeast growth in food industry. As to, another popular usage field of this plant is in perfume and cosmetic industry, due to hydrosol in its essential oil.

Key Words: Lemon balm, essential oil rate, essential oil components, antioxidant, medicinal usage.

### OĞULOTU (Melissa officinalis L.)' NUN UÇUCU YAĞI, BİLEŞENLERİ VE KULLANIM ALANLARI

ÖZET: Lamiacea failyasından olan oğulotu (Melissa officinalis L.) önemli tibbi bitki türlerinden birisidir. Günümüzde dünyanın birçok ülkesinde çeşitli sanayi dallarında (tıp, parfümeri, kozmetik ve gıda vb) kullanılmaktadır. Oğulotunda % 0.01 ile 0.25 arasında uçucu yağ bulunur. Bu uçucu yağın ana bileşenleri %39 citronellal, 33% citral (citronellol, linalool) ve geraniol'dür. Geleneksel olarak yaygın bir şekilde sakinleştirici, spazm giderici ve antibakteriyel olarak kullanılmaktadır. Bir çok klinik araştırma sonuçları, oğulotu uçucu yağının Alzheimer hastalığının tedavisinde, serbest radikallerinin olumsuz etkilerine karşı antioksidan ve tümör oluşumunu engelleyen ajan olarak kullanılabileceğini, ayrıca bağışıklık sistemi ve stres üzerine de olumlu etkilerinin olduğunu göstermiştir. Antimikrobiyel etkisi sayesinde, gıda sanayinde gıdaların bozulmasına neden olan mayaların gelişimini önleyici etkisi bulunmuştur. Diğer güncel kullanım alanı ise uçucu yağındaki hidrosol nedeniyle parfümeri ve kozmetik sanayidir.

Anahtar Kelimeler: Oğulotu, uçucu yağ oranı, uçucu yağ bileşenleri, antioksidan, tıpta kullanımı.

## 1. INTRODUCTION

Herbal remedies have been used for thousands of years. Early in human history, people practiced herbal medicine as a magical or religious healing art (Baker, 1965). Today, a lot of people use herbal medicine or rely on them. There are many various drug plants. One of them is lemon balm (*Melissa officinalis* L.), in other words bee herb or sweet balm.

Lemon balm, member of the family *Lamiaceae* (formerly *Labiatae*) in scientific classification is a perennial herb that is, one that lives at least three years. It is bushy and upright, reaching a height of about 1 m. The soft, hairy leaves are 2 to 8 cm long and either heart-shaped. The leaf surface is coarse and deeply veined, and the leaf edge is scalloped or toothed. White or pale pink flowers which consist of small clusters of 4 to 12 blossom in the summer. It is commonly referred to as Lemon Balm because of its lemon-like flavor and fragrance (Ilisulu, 1992; Anonymous, 2003).

Lemon balm, one of the important medicinal plant species mainly grown in natural flora -especially in Mediterranian region- of Turkey, is native to southern Europe and northern Africa, and east as far as the Caucasus and northern Iran. Its wild types are in all Mediterranean countries and South part of the Alps. There are exist on other three subspecies which are naturally expended in our wild flora; subsp. officinalis,

subsp. *altissima* and subsp. *inodora* (Davis, 1982; Ilisulu, 1992; Anonymous, 2003). It is recorded that the plant is mainly grown in Germany, France, Italy, Romania, Bulgaria, and North America (Ceylan, 1987, Tansı ve Özgüven 1995). Özhatay et al. (1997) reported that the subspecies of *M. officinalis*' are evaluated in domestic markets and they are also on the list of the exported medicinal and aromatic plants.

It is used in traditional medicine from ancient times. French monks and nuns, and Paracelsus (1493-1541), Swiss physician and chemist, prepared tonics, called as "life elixir", contain lemon balm, and used. English writer John Evelyn (1620-1706), described this plant as "ruler of brain, strengthening to mental, and removing from melancholia". Its essential oil was named "bal-smin" or "leader of the oils" in Hebrew. Avicenna recommends that lemon balm strengthened heart (Asımgil, 2001; Anonymous, 2003).

Today, lemon balm is used in various branches of industry (such as medicine, perfume and cosmetic, and food etc.) in a lot of countries of the world.

# 2. THE ESSENTIAL OIL OF LEMON BALM AND ITS COMPONENTS

Lemon balm essential oil, obtained from fresh or dried flower, leaf, and branches of this plant by water steam distillation or chemical extraction, is characteristic with fresh lemon odor, and light yellow colored. Its viscosity is lighter than that of water (Anonymous, 2003). It was desired that this value should not be lower than 0.05 % (Baytop, 1984).

The main components of the essential oil are 39% citronellal, 33% citral (citronellol, linalool) and 2% geranial. In addition, this oil contains such as threeterpinene, phenol carbon-acid (rosmarinic acid), and flavonglychoside acids in low ratio. There are also caffeic acid (a kind of tannin), several flavonoids (luteolin-7-O-glucoside, isoquercitrin, apigenin-7-Oglucoside, and rhamnocitrin), rosmarinic acid, ferulic acid, methyl carnosoate, hydroxycinnamic acid, and 2-(3', 4'-dihydroxyphenyl)-1,3-benzodioxole-5-aldehyde and some other aldehydes: beta-caryophyllene, neral, and geranyl acetate. (Kucera and Herrmann, 1967; 1984; Zevbek, 1985; Mulkens and Baytop, Kapetanidis, 1987; Peake et al., 1991; Dimitrova et al., 1993; Vaverkova et al., 1995; Chevallier, 1996; Ceylan, 1997; Tagashira and Ohtake, 1998; Hohmann et al., 1999).

Variability in both the content and quality of essential oil has been observed in herb and leaf drugs depending on the harvest cut height of plant (Mrlianova et al., 2001 b), time and number of cut (Ceylan, 1987).

Results from selected studies currently undertaken on lemon balm essential oil and its compenent are as follow.

That the essential oil content in the leaves at the stage just prior to blooming, or at the onset of blooming, ranged from 0.06 to 0.16 % (V/m), and the maximal essential oil content (0.09 to 0.45%) was in the plants from the second harvest in lemonbalm from 17 European regions; the essential oil content in cultivar Citra from Bratislav was 0.13% and 0.23-0.27%, in 1<sup>st</sup> harvest and 2<sup>nd</sup> harvest, respectively were determined by Mrlianova et al. (2001 a).

Mrlianova et al. (2001 b) were recorded that three different cuts were carried out on cv. Citra and the oil content in the herb was highest in the top third (0.13% V/m), satisfactory in the herb including both and middle thirds (0.08% V/m) and lowest in the whole herb (0.06% V/m). The essential oil content in the leaves of respective herbs was in the range 0.39%-0.14% V/m (top third part-whole aerial part). Citrals (A and B) were 55.79, 48.46, and 59.74 and 56.87% in the top third part of the herb, the whole herb, and the leaves from those parts, respectively. Likewise, beta-caryophyllene was 5.01, 3.87, and 6.97 and 5.13%; beta-caryophyllene oxide was 17.19, 24.07, and 15.64 and 17.82%; citronellal was 2.73, 5.51, and 2.82 and 6.44%.

Sarı and Ceylan (2002) reported that the essential oil ranged from 0.03 to 0.067% besides, the main component in essential oil was geraniol (33.13 to 53.68%), and the others were neral, citronellal, and  $\beta$ -pinen in the study, carried out with 11 Melissa populations in Menemen and Bozdağ.

Tinmaz et al (2001) was reported that the highest essential oil's ratio (0.14%) was obtained from the plants, cut in the beginning of blooming, grown in Çanakkale ecological conditions.

Essential oil obtained from a few different populations of *Melissa officinalis* L. cultivated in Poland had been investigated by Patora et al. (2003). In their study, the content of essential oil in the leaves and herb were recorded as 0.08-0.25 ml/100g and 0.06-0.167 ml/100g, respectively. In addition, essential oil was in the plant material from experimental patch then that from commercial cultivations, and essential oil of the fresh material was slightly higher than one of the dried one. Also, it was observed that the contents of citral, citronellal, linalool, nerol, geraniol beta-caryophyllene and beta-caryophyllene oxide among the populations were different greatly.

Patora and Klimek (2002) have isolated six flavonoids from the leaves of lemon balm. These flavonoids have been luteolin, luteolin 7-O-beta-D-7-O-beta-Dglucuronopyranoside, apigenin 7-*O*-*beta*-*D*glucopyranoside, luteolin 3'-*O*-*beta*-*D*glucuronopyranoside, luteolin 7-*O*-*beta*-*D*glucuronopyranoside and *luteolin* glucopyranoside-3-Obeta-D-glucuronopyranoside. The last three glycosides have been found in lemon balm for the first time and luteolin 7-O-beta-Dglucopyranoside-3'-Obeta-D-glucuronopyranoside is a new compound in plants.

## 3. USING FIELD OF LEMON BALM ESSENTIAL OIL a- In Medicine:

The World Health Organization reported that there are approximately four millions people on the world (which are constituing 80% of the total population) trying to cure their health problems with herbal drogs. In addition, in the developed countries, 25% of the medicines -sold with rescription- were obtained from herbal origined (vimblastin, reserpine, quinine, aspirin etc.) plants (Farnsworth, 1990; Principe, 1991). There are made numerous clinical and epidemiological studies on herbs all over the world, with using several enzymatic systems for exposing the bioactive material in them and maintaining the research studies for producing the high productive material. Almost huge International Medicine Companies have, well or medium equipped, an "herbal products research unit" in their constitution (Baser, 2004).

There are numerous herbs which have traditionally been used in folk medicine. Including lemonbalm (*Melissa officinalis* L.), marijuana (*Cannabis sativa*), ginger (*Zingiber officinale*), ginkgo (*Ginkgo biloba*) and Peppermint oil topically was found to be as effective as oral paracetamol for headache control and now being investigated as possible migraine prophylactics (Baldwin, 1987; Gobel, 1996).

Lemon balm has traditionally been used due to its memory enhancing properties, but using of which is currently more widely used as sedative or calm, spasmolytic and antibacterial agent and sleep aid has been more popular recently (Coleta et al., 2001; Kennedy et al., 2002; Kennedy et al., 2003; Sadraei et al., 2003; Kennedy et al., 2004; de Sousa et al., 2004). In addition these properties that are very important to human healthy, today researches about essential oil of lemon balm have been continued intensively.

Khayyal et al. (2001) have prepared the extracts from the plants Iberis amara, Melissa officinalis, Matricaria recutita, Carum carvi, Mentha piperita, Glycyrrhiza glabra, Angelica archangelica, Silybum marianum and Chelidonium majus, singly and combined in the form of a commercial preparation, STW 5 (Iberogast) and a modified formulation, STW 5-II, lacking the last 3 constituents. These extracts were tested for their potential anti-ulcerogenic activity against indometacin induced gastric ulcers of the rat as well as for their antisecretory and cytoprotective activities. All extracts produced a dose dependent antiulcerogenic activity associated with a reduced acid output and an increased mucin secretion. According to this study results, the anti-ulcerogenic activity of the extracts was also confirmed histologically. On the other hand, the cytoprotective effect of the extracts could be partly due to their flavonoid content and to their free radical scavenging properties. Free radicals occur in body chemistry, in processes such as the destruction of invading organism by white blood cells. Free radicals might play a role in various maladies, such as arthritis, heart disease, and Alzheimer's disease. When natural enzyme controls fail, free radicals in the body attack lipids, proteins, and nucleic acids. Especially, the beta glucan in essential oil, protects the body from free radicals destroying effects taking the role of antioxidant.

Akhondzadeh et al. (2003) carried out the investigation to asses the efficacy and safety of lemon balm extract using a fixed dose (60 drops/day) in patients with mild to moderate Alzheimer's disease. Patients with mild to moderate Alzheimer's disease aged between 65 and 80 years were treated for four months, and divided two groups randomly to placebo or fixed dose of lemon balm extracts. At four months, Melissa extract produced a significantly better outcome on cognitive function than placebo. Besides, there were no significant differences in the two groups in terms of observed side effects except agitation, which was more common in the placebo group. With respect to conclusions, Melissa officinalis extract is value in the management of mild to moderate Alzheimer's disease and has a positive effect on agitation in such patients.

Drozd and Anuszewska (2003) reported that the effect of water extracts from leaves of Melissa influenced on the immune system, in both humoral and cellular response.

Kennedy et al. (2004) have suggested that the potential for lemon balm to mitigate the effects of stress.

De Sousa et al. (2004) performed the study on antitumoral and antioxidant activities of lemon balm essential oil. The chemical composition and the biological activities of lemon balm essential oil obtained under controlled harvesting and drying conditions. Obtained findings showed that this oil was very effective against a series of human cancer cell lines (A549, MCF-7, Caco-2, HL-60, and K562) and mouse cell line (B16F10). Also, this oil possessed antioxidant activity, as evidence by reduction of *1*, *1-diphenyl-2-picryl-hydrazyl* (DPPH). These results pointed out to the potential use of lemon balm essential oil as an antitumoral agent.

Savino et al., (2005) invastigated that the colic in breastfed infant. The result of their studies shows that the colic in breastfed infant improves within 1 week of treatment with an extract based on *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis*.

Bolkent et al., (2005) reported that the administration of *Melissa officinalis* L. extract reduced total cholesterol, total lipid, ALT, AST and ALP levels in serum, and LPO levels in liver tissue, moreover increased glutathione levels in the tissue. As a result, it was suggested that *Melissa officinalis* L. extract exerted an hypolipidemic effect and showed a protective effect on the liver of hyperlipidemic rats.

#### b- In Food:

The lemon-scented leaves add flavor to jellies, liqueurs, fruit salads, and cold drinks (İlisulu, 1992; Anonymous, 2003). In addition, results of a lot of researches have showed that essential oil of lemon balm and extracts (*Melissa officinalis* subsp. *officinalis* and of *Melissa officinalis* subsp. *inodora*) can be used as antioxidant (Marangui et al., 2004). As known, antioxidant, type a molecule that neutralizes harmful compounds is called as free radicals (Anonymous, 2003).

The essential oils from aerial parts of Melissa officinalis, Lavandula angustifolia, Salvia officinalis, and Mentha piperita were analyzed using gas chromatography and gas chromatography-mass spectrometry by Araujo et al. (2003). Their antimicrobial activities were evaluated against five food spoilage yeasts, Torulaspora delbrueckii, Zygosaccharomyces bailii, Pichia membrainifaciens, Dekkera anomala, and Yarrowia lipolytica. Saccharomyces cerevisiae was also used as a reference. According to results of this research, the essential oil of M. officinalis at 500 microg/ml completely inhibited the growth of all yeast species. The main component of the oil of lemon balm was citral (neral plus geranial) (58.3%), which showed a marked fungi toxic effect, contributing to its high activity.

Mimica et al. (2003) have described antimicrobial and free radical scavenging capacity (RSC) together with the effects on lipid preoxidation (LP) of lemon balm essential oil in their study. The antimicrobial activity was tested against 13 bacterial strains and six

fungi. The examined essential oil exhibited very strong RSC; the most powerful scavenging compounds were monoterpene aldehydes and ketons (neral/geranial, citronellal, isomenthone, and menthone) and mono- and sesquiterpene hydrocarbons (E-caryophyllene). The most effective antibacterial activity was expressed on a multiresistant strain of *Shigella sonei*. A significant rate of antifungal activity was exhibited on *Trichophyton* species.

Uzun et al., (2004) studied the traditional medicine in North-West of Turkey (Sakarya province) by interviewing local informants from several villages. Plant species used to treat infections were tested for antimicrobial activity. Information was collected for 46 plant species from 30 families and for 5 animal species. Twenty four of the plant species were cultivated. Most used families were Asteraceae, Cucurbitaceae, Lamiaceae and Rosaceae and the most used plants were Artemisia absinthium, Equisetum telmateia, Lavandula stoechas, Melissa officinalis, Tussilago farfara and Urtica dioica. A total of 139 medicinal uses were obtained. Plants are used mainly for infectious diseases (18%), for neurological and psychological disorders (13.7%), cardiovascular disorders (13%), skin disorders (12.2%) and respiratory disorders (10.1%). Extracts were tested in vitro for antimicrobial activity against Staphylococcus aureus ATCC 65538, Staphylococcus epidermidis ATCC 12228, Escherichia coli ATCC 8739, Klebsiella pneumonia ATCC 4352, Pseudomonas aeruginosa ATCC 1539, Salmonella typhi, Shigella flexneri, Proteus mirabilis and Candida albicans ATCC 10231, using microbroth dilution technique according to National Committee for Clinical Laboratory Standards (NCCLS). This research showed that Arum maculatum, Datura stramonium, Geranium asphodeloides and Equisetum telmateia petroleum either extracts had MIC values of 39.1 microg/ml, 78.1 microg/ml, 78.1 microg/ml and 39.1 microg/ml, respectively against Staphylococcus epidermidis. Datura stramonium petroleum either extract had a MIC value of 39.1 microg/ml against Escherichia coli and Trachystemon orientalis ethanol extract had a MIC value of 39.1 microg/ml against *Escherichia coli*. The antimicrobial activity of Arum maculatum, Equisetum telmateia, Geranium asphodeloides, Plantago intermedia, Senecio vulgaris Trachystemon orientalis has been reported here for the first time

Yadav et al. (2005) assessed various leaf structural and chemical features as possible predictors of the size of the phyllosphere bacterial population in the Mediterranean environment. They examined eight perennial species, naturally occurring and coexisting in the same area, in Halkidiki (northern Greece). They are Arbutus unedo, Quercus coccifera, Pistacia lentiscus, and Myrtus communis (evergreen sclerophyllous species), Lavandula stoechas and Cistus incanus (drought semideciduous species), and Calamintha nepeta and Melissa officinalis (nonwoody

perennial species). *M. communis, L. stoechas, C. nepeta* and *M. officinalis* produce essential oil in substantial quantities. It is fond that, the aromatic plants are on average more highly colonized than the other species, whereas the nonwoody perennials are more highly colonized than the woody species. Leaves with water content >73% are the bacteria most highly colonized.

### c- In Perfume and Cosmetic Industry:

Due to hydrosol its essential oil and the strongly scented leaves are also used in perfumes and natural cosmetics. Hydrosol is the watery solution of the distillation that contains both the water-soluble plant components and micro-drops of essential oil. Because of they acidify the water or the product which is beneficial to the skin or in the body. Thus the hydrosol acts as a healing anti-inflammatory and mild but therapeutic antiseptic. Bacteria do not live well an in acidic environment which is why acids such as vinegar make good preservatives for such food items as pickles Chilé peppers and Olives. Acidic environments are astringent and so the hydrosols are useful in skin care products as astringents that constrict and contract the tissues.

The hydrosols can be used externally in skin care products as a douche or internally diluted and taken as a tonic drink (Rose, 2000).

#### 4. CONCLUSION

Lemon balm is a potential medicinal and aromatic plant grown commonly most of our wild areas. Its essential oil is currently used in medicine and pharmacology (anti-tumor, anti-bacterial, microbial, antihistaminic, antispasmodic antioxidant, by means of its antiviral effect curing of the herpes (Allahverdiyev et al., 2004), antiulcerogenic, moderate Alzheimer's modulation of mood and cognitive performance, stimulating the immune system (against anti HIV-1) (Yamasaki et al., 1998) and the heart, insect bites, painful menstruation, colds, headaches, mumps, insomnia, mild sedative and anti-depressant), (Foster and Duke, 1990), in food industry (using it's essential oil for food spoilage yeasts to extending the storage periods, in soft drinks industry because its fresh lemon tastes and herbal tea industry) and in cosmetic industry (containing hydrosol for curing dermatogical problems).

Valuable essential oil which the plant contains a very less amount has already been imported although it's large extension in our flora unfortunately, this condition causes a loss of foreign currency approximately one million \$ every year, according to data of Under Secretariat of The Prime Ministry for Foreign Trade. There are some studies about lemon balm just recently in our country. In order to meet industry's demand and export, new lines and cultivars containing acceptable volatile oil should be improved. With connect this, The Central Research Instituted for

Field Crops and Field Crops Department of Ankara University started the project in order to provide high quality raw material for industry without depending on flora.

#### 5. REFERENCES

- Allahverdiyev A, Duran N, Ozguven M, Koltas S., 2004 Antiviral activity of the volatile oils of Melissa officinalis L. against Herpes simplex virus type-2. Phytomedicine. 2004 Nov;11(7-8):657-61.
- Akhondzadeh, S., Nooroonzian, M., Mohammadi, M., Ohadinia, S., Jamshidi, A.H. and Khani, M., 2003. Melissa officinalis extract in the treatment of patient with mild to moderate Alzheimer's disease: a double blind, randomised, placebo controlled trial. Food Prot. Apr. 6 (4):625-632.
- Anonymous, 2003. Microsoft Encarta Encyclopedia, 1993-2003 Microsoft Corporation
- Araujo, C., Sousa, M.J., Ferreira, M.F. and Leao, C., 2003. Activity of essential oils from Mediterranean *Lamiaceae* species against food spoilage yeasts. Plant Physiol. Apr.; 131(4):1816-1825.
- Asımgil, A., 2001. Şifalı Bitkiler. Timaş Yayınları, İstanbul. 352 s.
- Backer, H.G. 1965. Plant and Civilization. Wadsworth Publishing Company, Inc. Belmont, California. 145-157 p.
- Baldwin, C A., 1987. What pharmacists should know about feverfew. Pharm J; 239:237–238.
- Başer, K.H.C., 2004. TEB Mised Sayı: 3-4 (12.01.2004)
- Baytop, T., 1984. Türkiye'de Bitkiler ile Tedavi. İst. Üni. Yav. No:3255.
- Bolkent S, Yanardag R, Karabulut-Bulan O, Yesilyaprak B., 2005. Protective role of Melissa officinalis L. extract on liver of hyperlipidemic rats: a morphological and biochemical study. Ethnopharmacol. 2005 Jul 14:99(3):391-8.
- Ceylan, A., 1987. Tıbbi Bitkiler II. Ege Üni. Ziraat Fak. Yay. No: 481. İzmir. 306 S.
- Chevallier, A., 1996. The Encyclopedia of Medicinal Plant. Kindersley Dorling Limited London, 111p.
- Coleta, M., Campos, M.G., Cotrim, M.D. and Proenca da Cunha, A. 2001. Comparative evaluation of *Melissa* officinalis L., *Tilia europaea* L., *Passiflora edulis* Sims. and *Hypericum perforatum* L. in the elevated plus maze anxiety test. Pharmacopsychiatry. 2001 Jul;34 Suppl 1:S20-1.
- Davis, P.H. 1982. Flora of Turkey and the East Aegean Islans, Vol.7, Edinburgh.
- Dimitrova, Z., Dimov, B. and Manolova, N., 1993. Antiherpes effect of Melissa officinalis L. extracts. Acta Microbiol Bulg 1993;29:65–72
- Drozd, J. and Anuszewska, E., 2003. The effect of the *Melissa officinalis* extract on immune responce in mice. Acta Pol Pharm. Sep-Oct., 60(5):395-400.
- Farnsworth, N.R. 1990. The role of entnopharmacology in drug development. In: Bioactive compounds from plants, CIBA Fondation Symposium, 154 pp. 2-21, John Wiley & Sons, Chichester, NewYork Brisbane, Toronto, Singapore.
- Foster, S. and Duke, J. A., 1990. Peterson Field Guides. A field guide to medicinal plants; Eastern and Central North America. Boston, Houghton Mifflin company, 1990.366p
- Gobel H, Fresenius J and Heinz A. 1996. Peppermint oil in headache. Nervenartz; 67:672–678.

- Hohmann, J., Zupko, I. and Redei, D., 1999. Protective effects of the aerial parts of Salvia officinalis, Melissa officinalis and Lavandula angustifolia and their constituents against enzyme-dependent and enzymeindependent lipid peroxidation. Planta Med 1999; 65:576–578.
- İlisulu, K. 1992. İlaç ve Baharat Bitkileri. Ank. Üniv. Ziraat Fak. Yayın No: 1256/360, Ankara, 198-208 p. 302 p.
- Kennedy, D.O., Scholey, A.B., Tildesley, N.T., Perry, E.K. and Wesnes, K.A. 2002. Modulation of mood and cognitive performance following acute administration of *Melissa officinalis* (lemon balm). Planta Med. Feb., 68(2):178-180.
- Kennedy, D.O., Wake, G., Savelev, S., Tildesley, N.T., Perry, E.K., Wesnes, K.A. and Scholey, A.B. 2003. Modulation of mood and cognitive performance following acute administration of single doses of *Melissa officinalis* (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties. Fitoterapia, Jul., 74(5):445-452.
- Kennedy, D.O., Little, W. and Scoley, A.B., 2004. Attenuation of laboratory-induced stres in humans after acute administration of *Melissa officinalis* (lemon balm). J Pharm Pharmacol. May; 56 (5):677-681.
- Khayyal, M.T., el-Ghazaly, M.A., Kenawy, S.A., Seif-el-Nasr, M., Mahran, L.G., Kafafi, Y.A. and Okpanyi, S.N. 2001. Antiulcerogenic effect of some gastrointestinally acting plant extracts and their combination. Arzneimittelforshung.2001; 51(7):545-53.
- Kucera LS and Herrmann EC, 1967. Jr. Antiviral substances in plants of the mint family (Labiatae). I. Tannin of *Melissa officinalis*. Proc Soc Exp Biol Med 1967;124:865–869.
- Marongiu B, Porcedda S, Piras A, Rosa A, Deiana M, Dessi MA.,2004. Antioxidant activity of supercritical extract of *Melissa officinalis* subsp. *officinalis* and *Melissa officinalis* subsp. *inodora*. Phytother Res. 2004 Oct;18(10):789-92.
- Mimica-Dukic, N., Bozin, B., Sokovic, M. and Simin, N. 2003. Antimicrobial and antioxidant activities of Melissa officinalis L. (Lamiaceae) essential oil. Acta Pol. Pharm. Nov.-Dec., 60(6):467-470.
- Mrlianova, M., Tekel'ova, D., Felklova, M., Reinohl, V. and Toth, J. 2001 a. The influence of the harvest cut height on the quality of the herbal drugs *Melissa* folium and melissae herba. Ceska Slov Farm. Nov., 50 (6): 299-302
- Mrlianova, M., Tekel'ova D., Felklova M., Toth, J., Musil, P. and Grancai, D. 2001 b. Comparision of the quality of *Melissa officinalis* L. cultivar Citra with Mellissas of European origin. Pharmacospsychiatry. Jul., 34 Suppl 1: S20-1.
- Mulkens, A. and Kapetanidis, I., 1987. Flavonoides des feuilles de *Melissa officinalis* L. (Lamiaceae). Pharm Acta Helv 1987; 62(1):19–22.
- Özhatay, N., Koyuncu, M., 1997. Türkiye'nin doğal tıbbi bitkileri hakkında bir çalışma. Doğal Hayatı Koruma derneği Yayınları, İstanbul.
- Patora, J.and Klimek, B., 2002. Flavonoids from lemon balm (*Melissa officinalis* L., *Lamiaceae*). Clin Psychiatry. July., 63(7):553-558.
- Patora, J., Majda, T., Gora, J. and Klimek B. 2003. Variability in the content and composition of essential oil from lemon balm (*Melissa officinalis* L.) cultivated in Poland. J. Endocrinol Invest. Oct., 26(10):950-955.

- Peake, PW., Pussell, BA. and Martyn, P., 1991. The inhibitory effect of rosmarinic acid on complement involves the C5 convertase. In J Immunopharmac 1991;13(7): 853-857.
- Principe, P.P. 1991. Valling the biodiversity of medicinal plants. In: Akerele, O.,Heywood, V., Synge,H.(eds), Conservation of medicinal plants, pp. 79-124, Cambridge Univ.Press, Cambridge.
- Rose, J., 2000. An Herb for Skin Care. Aromatic Plant Project Pres Release, March 2000.
- Sadraei, H., Ghannadi, A. and Malekshahi, K. 2003. Relaxant effect of essential oil of *Melissa officinalis* and citral on rat ileum contractions. Phytother Res. Jun., 17(6):599-604.
- Sarı, A. O. and Ceylan, A., 2002. Yield characteristics and Essential oil composition of lemon balm (*Melissa officinalis* L.) grown in the Aegean Region of Turkey. Turkish Journal of Agriculture and Forestry, 22 (4): 217-224
- Savino F, Cresi F, Castagno E, Silvestro L, Oggero R., 2005. A randomized double-blind placebo-controlled trial of a standardized extract of Matricariae recutita, *Foeniculum vulgare* and *Melissa officinalis* (ColiMil) in the treatment of breastfed colicky infants. Phytother Res. 2005 Apr; 19(4): 335-40.
- De Sousa, A.C., Alviano, D.S., Blank, A.F., Alves, P.B.;
  Alviano, C.S. and Gattas, C.R., 2004. *Melissa officinalis*L. Essential oil: antitumoral and antioxidant activities. J
  Agric Food Chem. May, 52 (9):2485-2489.
- Tagashira M and Ohtake Y., 1998. A new antioxidative 1,3-benzodioxole from *Melissa officinalis*. Planta Med 1998; 64:555–558.

- Tansı, S., Özgüven, M. 1995. Farklı ekolojilerde limonotu (*Melissa officinalis* L.)' nun uygun çoğaltma tekniklerinin belirlenmesi. Ç.Ü. Ziraat Fak. Dergisi 10(2): 33-42, Adana.
- Tinmaz, A.B., Gökkuş, A., Çetin, K. And Erdoğan, S.S., 2001. Determining of the voletile oil content and drug herbage yield of lemon balm (*Melissa officinalis* L.) applied different harvesting time and planting distances grown in Çanakkale ecological conditions. Proceeding of the workshop on Agriculturel and Quality Aspects of medicinal and Aromatic plants, Adana, 197-202p.
- Uzun E, Sariyar G, Adsersen A, Karakoc B, Otuk G, Oktayoglu E, Pirildar S., 2004. Traditional medicine in Sakarya province (Turkey) and antimicrobial activities of selected species. J Ethnopharmacol. 2004 Dec;95(2-3):287-96.
- Vaverkova, S., Tekel, J. and Holla, M., 1995. The effect of herbicides on the qualitative properties of medicinal plants. Part 3: Content and composition of the essential oil from *Melissa officinalis* L. after application of basagran. Pharmazie 1995; 50:835–836.
- Yadav RK, Karamanoli K, Vokou D., 2005. Bacterial Colonization of the Phyllosphere of Mediterranean Perennial Species as Influenced by Leaf Structural and Chemical Features. Microb Ecol. 2005 Oct 13.
- Yamasaki, K., Nakano, M., Kawahata, T., Mori, H., Otake, T., Ueba, N., Oishi, I., Inami, R., Yamane, M., Nakamura, M., Murata, H., Nakanishi, T., 1998. Anti-HIV-1 activity of herbs in Labiatae. Aug; 21(8): 829-33
- Zeybek, N., 1985. Farmasötik Botanik. Ege Üni. Eczacılık Fak. Yay No: 1, İzmir.