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The Traditional and Contemporary Uses of Some Medicinal Plant Species

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İÇİNDEKİLER

BÖLÜM I

Some Plant Specıes Used In The Treatment Of Rheumatıc Dıseases Among The Publıc In Turkey

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Introduction

Rheumatism derives from the Greek word "rheuma." In contemporary usage, this term refers to bone, muscle, and joint pains whose causes cannot be precisely explained (Dal & et al., 2017). It is known that there are more than 100 rheumatic diseases. These diseases can often be recurrent, with some being less frequent. The severity of the disease varies depending on genetic and environmental factors. The prevalence of these diseases is higher in

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female patients compared to males. Rheumatic diseases hold significant importance for public health. According to a study, the prevalence of rheumatic diseases among chronic illnesses is reported to be 39%. It also ranks high in prescribed drug usage. Despite the use of medications in various dosages based on the type and frequency of observed symptoms, these drugs have not provided a definitive cure. This situation has led individuals to turn to traditional and complementary medicine practices (Güneş & Koşar, 2011).

Historical records demonstrate that plants have been an integral part of human life for thousands of years. According to these records, plants were initially used by humans as food and later for protection and treatment. Through trial and error, people discovered and incorporated locally accessible plants into their daily lives. Initially used merely as an alternative, plants have gained considerable attention today within the scope of a return to natural practices. Many individuals still consider plants as the sole treatment method, either to avoid the side effects of chemical drugs or due to economic and human limitations. Treating with plants is a method prone to error without the advice of experts in plants and their active ingredients.

Ethnobotanical studies on traditional folk remedies used in rheumatic diseases the main component of traditional folk remedies emerging from ethnobotanical studies is predominantly plants. Various parts of plant species have been preferred for the treatment of diseases using different methods. Our aim is to compile the studies conducted in Turkey regarding plant species used in rheumatic diseases, one of the most commonly observed diseases in society for which a definitive treatment method cannot be determined. The goal is to provide information about rheumatic diseases and plant species traditionally used in their treatment.

Definition and Classification of Rheumatism

Rheumatism encompasses a set of chronic diseases affecting the musculoskeletal system, including joints, bones, and muscles,

which can be chronically observed and whose exact causes are not fully understood. Although tissues such as muscles, bones, eyes, heart, and blood vessels can be affected by these diseases, connective tissue is the most commonly affected. The World Health Organization (WHO) defines rheumatism as a set of chronic and painful diseases affecting the locomotor system. Symptoms such as increased temperature, fatigue, joint deformities, pain, swelling, and redness in tissues are observed depending on the amount of inflammation. Excessive weight gain, smoking, aging, and inactivity affect the progression of the disease and the extent of discomfort in patients. The lifelong duration of the ailment both wears out the patient and the patient's family socially and economically.

Rheumatic diseases are classified based on the involvement of autoimmune, vasculitic, inflammatory, degenerative, and metabolic factors in the pathogenesis of their formation. Diseases within the category of rheumatic diseases include Sjögren's syndrome, systemic lupus erythematosus, acute rheumatic fever, scleroderma, gout, pseudogout, rheumatoid arthritis, ankylosing spondylitis, reactive arthritis, psoriatic arthritis, osteoarthritis, osteoporosis, familial Mediterranean fever, and fibromyalgia (http 1).

Some Plants Used in the Treatment of Rheumatic Diseases:

Rheumatic diseases significantly reduce the quality of life for patients. Challenges in accessing healthcare and medications, economic conditions, cultural beliefs, the inability of medications to provide a complete curative treatment, and the side effects of drugs have directed patients towards traditional treatments (Nacoulma et al., 2022). For this purpose, people have been benefiting from medicinal plants since ancient times. Elderly individuals known as healers, who have been using plants for many years, have gathered and verified their reliability and accuracy. Detailed information about their regional names, medical uses, botanical characteristics, and preparation methods has been obtained (Sutha et al., 2010). Providing a comprehensive explanation of the mechanisms of action

of traditional plants will assist in discovering new drug molecules for the treatment of diseases. Therefore, plants should be thoroughly researched and studied with sufficient depth (Setty & Sigal, 2005). For example, the pharmaceutical company Novartis in Switzerland derived artemisinin from the Artemisia annua plant, which was later used in malaria treatment under the name Coartem (Adams et al., 2009).

For these purposes, various parts of plants such as roots, stems, leaves, bark, branches, flowers, fruits, seeds, rhizomes, oil, latex, tubers, or the whole plant itself have been used directly. In the preparation of plants, generally infusion and decoction methods have been used, and occasionally the maceration method has been employed (Kamal et al., 2016).

However, the use of plants without conducting sufficient studies can lead to undesirable outcomes. After researching the toxicity of plants and their dosage and usage methods, paying attention to the conditions of interaction between the active substances in their contents and these substances with different active substances can be a significant source in the discovery of new drug molecules (Ataseven, 2021).

***Aesculus hippocastanum* L.**

Local Name: Known as horse chestnut because its seeds are reminiscent of a horse's eye and used in the treatment of fractures in horses.

Family: Hippocastanaceae

Growing Regions: Naturally found in Western Asia, cultivated as an ornamental plant in parks and gardens in the United States, Turkey, and many other countries (Akbel, 2010).

Botanical Features: It has strong roots and can grow up to 25 meters in height. The leaves are quite large, palmate-shaped, divided, and dark green in color. There are between 5-7 elongated, wedge-shaped leaflets that narrow towards the base and widen towards the tip,

suddenly tapering to a point. The leaflets are inversely oval-shaped. The flowers are generally white, in pyramid-shaped clusters measuring 15-30 cm in length. There are 4-5 dissimilar petals, and there are yellow spots under the petals, which darken and turn red as the flower ages. It has 7-8 filaments with upward-curved male organs. The sepal is bell-shaped with 5 teeth and easily falls off. The fruit is approximately 6 cm in diameter, round, spiky, and consists of a fleshy capsule with 1-3 seeds. The coffee-colored seed is about 1-4 cm in diameter. The tree usually flowers in April-May and bears fruit from August to October (Koçkar, 2014).

Figure 1. *Image of the leaf and flower of Aesculus hippocastanum species (http 2).*

Phytochemical Components: The bark contains compounds such as esculin, aesculetin, fraxin, scopoletin, fraxetin, scopoletin, allantoin, and quercetin. The flowers contain rutin, quercitrin, aescin, choline, purine, while the seeds contain starch, aescin, proteins, oils, sugars, and catechic tannins. The leaves contain compounds like quercitrin, isoquercitrin, and quercetin (Akbel, 2010).

Usage: The horse chestnut bark has antipyretic, hemorrhoid-reducing, and constipating effects. The seeds have preventive and vasoconstrictive effects on capillary rupture. The oil and extract are commercially available due to their strong antioxidant properties. They exhibit protective properties against ultraviolet rays and show strong anti-aging characteristics. They are used in shampoos, shower

foams, creams, lotions, toothpaste, hair formulations, and other cosmetic preparations (Eke, 2019). Decoction prepared from the seeds is used internally for rheumatism treatment, and an infusion made from dried and powdered seeds is used to alleviate rheumatic pains (Tuzlacı, 2006; Tuzlacı, 2016).

Crataegus monogyna JACQ. subsp. monogyna JACQ.

Local Name: Known by various names in different regions of Turkey, such as halıç, yaban gülü, yemişen, alıç, aluç, or ekşi muşmula (Balta, Karakaya & Ekici, 2015).

Family: Rosaceae

Growing Regions: It grows in Southern Europe, Northern Africa, Syria, Mediterranean countries, and various regions in Turkey, including Central Anatolia, Eastern Anatolia, Aegean, Mediterranean, and Northern Anatolia (Taylan, 2015).

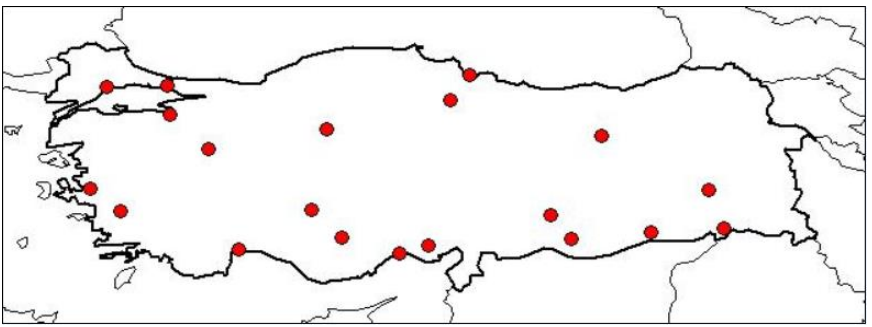

***Figure 2**. Distribution of Crataegus monogyna subsp. monogyna species in Turkey (http 3).*

Botanical Features: Although generally short, they can reach up to 10 meters, deciduous in winter, blooming in May, thorny trees or shrubs. Flowers are yellow, red, pink, or white; fruits are 1-3-seeded, 6-20 mm in diameter, slightly acidic, turning yellow, red, or orange; leaves are simple or lobed in winter. The flowers usually bloom

intensively in spring and are in cluster form. Thorny branches are red or reddish-brown (Balta, Karakaya & Ekici, 2015).

Phytochemical Composition: Fruit and flowers contain powerful antioxidant flavonoids (flavans), vitamins (especially vitamin C), saponin, organic acids, essential oil, and sugars (Taylan, 2015). It includes glucose, fructose, sucrose, sugar alcohols such as sorbitol, myo-inositol, glycosides, tannins, cratetegin, cardiotonic amines, acetylcholine, purine derivatives, amygdalin, and pectins from sugar groups. Additionally, its fruits contain high amounts of minerals such as Ca, P, K, Mg, and Fe (Balta, Karakaya & Ekici, 2015).

Usage: It has effects on arrhythmias, palpitations, heart failure, weakness of heart muscles after severe infectious diseases, high blood pressure, and cholesterol reduction following a heart attack. In addition to heart conditions, it can be used for hernia, indigestion, raising low blood sugar, anti-inflammatory, strengthening the immune system, protective against radiation, and protecting the liver. Its roots are boiled in water, and this water is used for baths for rheumatism treatment. Infusion from flowers and decoction from fruits are used internally to prevent joint pain and for rheumatic diseases. Besides medical use, it is also used as an ornamental and hedge plant in parks and landscaping (Aydemir, 2016).

***Ecballium elaterium* (L) A. RICH.**

Local Names: It is known by various names such as acı dülek, eşekhıyarı, cırtatan, cırtlatan, cırtlağan, ciritatan, şeytan keleği, yabani hıyar, acı kavun (Ekici & ark., 1998).

Family: Cucurbitaceae

Growing Regions: It grows in Albania, Belarus, Bulgaria, France, Greece, Italy, Malta, Portugal, Romania, Sicily, Sardinia, Spain, former Yugoslavia, and in Turkey in Istanbul, Amasya, Balıkesir, Bilecik, Denizli, Hatay, Mersin, Izmir, Kırklareli, Kahramanmaraş, Muğla, Sinop, Tekirdağ, Karaman (Güllü & Öcal, 2016).

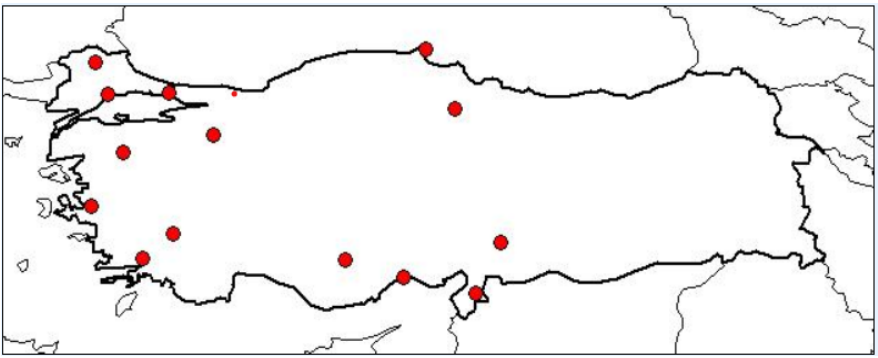

Figure 3. *Distribution of Ecballium elaterium species in Turkey (http 4)*

Botanical Features: It is a perennial herbaceous plant with tuberous roots and a prostrate stem. It has fleshy, cordate to triangular leaves. Both leaves and stem are covered with stiff hairs. The flowers with petaloid corollas are light yellow. The fruits are green, white-haired, oval-shaped, stalked, and hang down when mature. As they ripen, the fruits turn from green to yellow. With internal pressure, it forcefully ejects its seeds and juice. The seeds are brown, egg-shaped, and about 4-5 mm in size. Flowering occurs between April and November (Ekici & et al., 1998).

Phytochemical Composition: The major compound group cucurbitacins are found in various parts of the plant, especially in the fruit. Cucurbitacins are bitter, tetracyclic triterpenoid compounds with a 30-carbon cucurbitane skeleton. The plant also contains sterols, phenolic compounds, amino acids (serine, glycine, alanine, lysine, arginine, tyrosine, glutamic acid, and aspartic acid), fatty acids (lauric, myristic, palmitic, linoleic, and linolenic acid), flavonoids, alkaloids, resin, and starch. Sterols are synthesized in the root and stored in the leaf. The plant's sterol levels peak during flowering and decrease as the fruit matures (Memişoglu & Toker, 2001).

Usage: The juice obtained from the fruit has an anti-inflammatory effect, and this effect increases dose-dependently. Studies have revealed that the substance responsible for the anti-inflammatory effect is Cucurbitacin B. Due to its potent purgative effect, the plant has been used by individuals suffering from constipation and indigestion. In India, it has been used for the treatment of malaria and rabies, while in Anatolia, it has been applied fresh for abscess treatment and as a pain reliever. The roots, sold under the name Radix Mandragorae, have been marketed as a pain reliever. Ointments prepared from the roots have been used topically for chronic skin conditions such as eczema. In Egyptian pharmacies, preparations from the roots have been sold as potent purgatives, emetics, and wound healers. The decoction made from the roots (1 cup of water with 10-15 drops) is used internally to alleviate joint pain. For external rheumatism treatment, fresh fruits are pounded, and after soaking the seeds in alcohol with black pepper for 15 days, they are applied topically. (Memişoğlu & Toker, 2002; Tuzlacı, 2006).

Table 1. *Biological Activities of Cucurbitacins Found in Ecballium elaterium (Memişoğlu & Toker, 2001).*

Cucurbitacins	**Biological Activities**
Cucurbitacin B	Anti-inflammatory, cytotoxic, antitumor, hepatoprotective, antigibberellic, insect-repelling
Cucurbitacin E	Cytotoxic, antitumor, purgative, hepatoprotective, antihelminthic, insecticidal
Cucurbitacin D	Cytotoxic, antitumor, cardiovascular, hypnotic, antimicrobial
Cucurbitacin I	Cytotoxic, antitumor, antimicrobial, insect-repelling
Cucurbitacin L	Cytotoxic, antitumor, antihelminthic
Cucurbitacin R	Antifertility

***Hypericum perforatum* L.**

Local Name: Binbirdelik otu, sarı kantaron, kan otu, yara otu, koyun kıran, kılıç otu, püre, mayasıl otu, and known as St. John's wort in English (Hışıl, Şahin & Omay, 2005).

Family: Hypericaceae

Regions of Growth: It naturally grows in Europe, Asia, North Africa, the United States, and in various regions of Turkey, including Marmara, the Black Sea, Aegean, Eastern Anatolia, the Mediterranean, and Southeastern Anatolia (Aksu & Altınterim, 2015).

Botanical Features: It is a perennial plant with fibrous roots. The leaves are 10-35 mm long, elliptical, arranged singly, opposite, or spirally, and generally stalkless. The leaves have transparent pores that are visible in light, resembling perforations, giving rise to the Latin term "perforatum." The flowers are in branched clusters, the petals are golden yellow with small black dots on the edges, and there are numerous stamens, triadelphous. The ovary is superior and shows axial or parietal placentation. The seeds of the plant lack endosperm (Atalay, 2001; Öz, 2011).

Phytochemical Composition: *Hypericum perforatum* is a plant rich in active compounds, containing at least 10 different active components, including naphthodianthrone derivatives, flavonoids, floroglusinol derivatives, proanthocyanidins, tannins, volatile oils, amino acids, phenylpropanes, xanthones, and water-soluble compounds (organic acids, peptides, polysaccharides, etc.). The most important parts of these compounds include hyperforin, a floroglusinol derivative, hypericins from naphthodianthrones, quercetin glycosides, rutin, hyperoside, quercitrin, and biflavonoids from flavonoids. Biflavonoids are rare in nature. Hyperforin is a compound that can penetrate the brain and inhibits the reuptake of certain neurotransmitters such as norepinephrine, dopamine, serotonin, GABA, and L-glutamate. It is used in the treatment of skin

Compound Groups	Compounds
Volatile Oils	α-pinene, caryophyllene, limonene, myrcene, and cineol
Flavonoids	Hyperoside, quercitrin, isoquercitrin, quercetin, and rutin
Naphthodianthrone Derivatives	Hypericin, pseudohypericin, protohypericin, protohypericin
Biflavonoids	I3, II8-bi apigenin, amentoflavone
Floroglusinols	Hyperforin, adhyperforin
Phenolic Acids	Chlorogenic acid, caffeic acid, and ferulic acid
Sterols	β-sitosterol
Vitamins	Vitamins A and C
Other Compounds	Anthraquinones, proanthocyanidins, carotenoids, carbolic acids, xanthones, coumarin, certain amino acids, tannins, and resin

inflammations by inhibiting cyclooxygenase-1 and 5-lipoxygenase enzymes (Öz, 2011).

Table 2. *Active Compounds Found in Hypericum perforatum Plant (Baialieva, 2020).*

Hiperforin from the floroglusinol group exhibits an antidepressant effect by acting on the serotonin mechanism. It prevents the proliferation of peripheral blood mononuclear cells and tumor cells while inducing apoptosis (programmed cell death) (Öz, 2011). Hipericin and pseudohypericin from the naphthodianthrone group have a protective effect against photo damage (Aksu & Altınterim, 2015). In 2002, it was declared a medicinal plant by the World Health Organization (WHO). Popularly used, especially for its wound-healing effect, it has been employed in burn treatments. Due to its anti-tumor, antiviral, antidepressant, antibacterial, anti-inflammatory, analgesic, hepatoprotective, and antiseptic effects, the

plant has been used in Turkey for ulcers, diabetic conditions, colds, and stomach, liver, and gallbladder disorders (Baialieva, 2020). Decoction prepared from the flowering branches is used internally, and the above-ground parts, after soaking in olive oil for a period, are applied externally to treat rheumatic pains. Decoction made from the above-ground parts is used internally for arthritis treatment (Tuzlacı, 2006; Tuzlacı, 2016).

***Juglans regia* L.**

Local Names*:* In Turkey, it is known by various names such as Ceviz, Goz, Koz, Güz, Guz, Yandak, Ceviz ağacı, Cuz, Hingiç, Yondak, Guaz, Kuz, Giz, Cevz, Covs, Dara guzie, Adi ceviz, Cöoz, Gozıyr, Gozey, Cevız, Cozz, Ora, Boş, Giwez, Guwiz, Gerdikan, Hincik, Oreh, Anadolu cevizi, İran cevizi, and İngiliz cevizi (Demirkıran, 2008).

Family*:* Juglandaceae

Growing Regions: It is distributed in Kazakhstan, Uzbekistan, Kyrgyzstan, Northern India, Pakistan, Afghanistan, Tajikistan, Turkmenistan, Iran, Iraq, some parts of Azerbaijan, Armenia, Georgia, Bulgaria, Romania, Italy, France, Portugal, southern Germany, England, the United States, and throughout in Turkey. (Gidemen, 2021).

Botanical Features*:* It is a deciduous tree that can grow up to 18-30 m in height, presenting a splendid appearance. The leaves are imparipinnate, consisting of 5-9 leaflets with entire margins, and emit a strong fragrance. Male flowers are numerous, hanging in catkin-like clusters on the previous year's branches, with free stamens, typically 3-4, and short filaments. Female flowers are grouped in pairs or threes on the current year's young branches, with an ovary made up of two carpels, a short style, and a broad, two-branched stigma. The fruit is a drupe, approximately 4-5 cm in diameter (Özkan, 2007).

Phytochemical Composition: *Juglans regia* is a biologically rich and easily digestible plant. It has high protein and fat content, making it an essential component of a vegetarian diet. The plant's oil contains a higher proportion of polyunsaturated fatty acids (linoleic and alpha-linolenic acid) at 72%, monounsaturated fatty acids (oleic acid) at 18%, and saturated fatty acids at 10%. The components found in *Juglans regia* include water, macronutrients (fat, protein, carbohydrates, and dietary fibers), micronutrients-minerals (Calcium, Iron, Magnesium, Phosphorus, Potassium, Sodium, Zinc, Copper, Manganese, Selenium), micronutrients-vitamins (Vitamin C, Thiamine, Riboflavin, Niacin, Pantothenic Acid, Vitamin B6, Folate, Vitamin A, Vitamin E (alpha, delta, and gamma-tocopherol), Vitamin K), sterols (Stigmasterol, Campesterol, Beta-sitosterol), and other substances (Melatonin, Beta-carotene, Lutein, Zeaxanthin, Ellagic acid, Gallic acid) (Gidemen, 2021).

The leaves of *Juglans regia* contain bioactive compounds such as phenolic acids, flavonoids, organic acids, tocopherols, triterpenic acids, terpenes, terpenoids, tetralone derivatives, megastigman derivatives, and 5-hydroxy-1,4-naphthoquinone (juglone). Additionally, they contain volatile aroma compounds like caryophyllene oxide, β-caryophyllene, germacrene, α-pinene, and β-pinene. The most important phenolic compounds in Juglans regia include myricetin, rutin, ellagic acid, and juglone. Juglone is a characteristic phenolic compound found in leaves, fruit, shoots, and roots. Fresh leaves and fruit peels contain 1,4,5-trihydroxynaphthalene-4-D-glucoside, which transforms into juglone through drying and crushing (Salık & Çakmakçı, 2023).

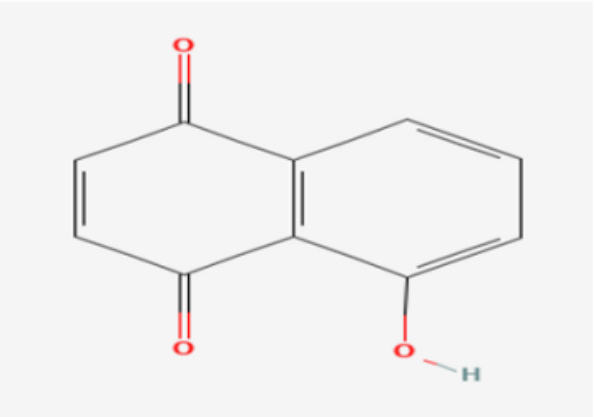

Figure 4. *Chemical structure of Juglone ($C_{10}H_6O_3$) (Salık & Çakmakçı, 2023)*

Usage: *Juglans regia* has a protective effect against cardiovascular diseases, cancer, and the negative effects associated with aging. It lowers LDL cholesterol levels, preventing artery blockages and increasing the elasticity of the blood vessels, thereby reducing the risk of cardiovascular diseases. Its melatonin content helps regulate the sleep cycle. The plant is rich in Omega-3 and Omega-6 unsaturated fatty acids. Insufficient intake of Omega-3 and Omega-6 fatty acids during pregnancy can lead to intellectual disability and sensory-motor function disorders in infants. Additionally, Omega-3 deficiency in children has been associated with sleep irregularities, excessive hyperactivity, learning difficulties, and behavioral disorders (Gidemen, 2021).

The oil of *Juglans regia* can be applied directly to corns for their treatment and can be used for facial massages to alleviate skin blemishes. Walnut leaves mixed into bathwater are employed for skin diseases, and the boiled leaves are used in the treatment of boils. A tea made from the leaves is consumed to stimulate appetite and strengthen the stomach (Demirkıran, 2008). The leaves, when wrapped fresh, are used to relieve rheumatic pains. The roots, soaked in olive oil from spring to autumn, are applied externally to reduce

rheumatic pains. A decoction made from young shoots, soaked into a cloth, is used to alleviate rheumatic pains (Tuzlacı, 2006).

***Laurus nobilis* L.**

Local Names: In Turkey, it is known by various local names such as defne, tehnel, teynel, tenel, tahnal, har, gar, ehnel, nehtel, tefrün, harve, taflan, defnün, tefrin (for non-fruit-bearing laurels), aşlı (for fruit-bearing laurels), açtı, tehni, talimi (Yılmaz & Çiftçi, 2021; Karık & et al., 2015).

Family: Lauraceae

Growing Regions: It is widespread in Algeria, Belgium, France, Greece, Mexico, Morocco, Portugal, Spain and the Canary Islands, Albania, Romania, the eastern coasts of Libya, the western part of Syria, Crimea, and extensively in Turkey, particularly in Balıkesir, Bursa, Yalova, Istanbul, Zonguldak, Kastamonu, Sinop, Trabzon, Rize, Izmir, Mugla, Antalya, Mersin, and Kahramanmaraş (Karık & et al., 2015).

Botanical Features: *Laurus nobilis* is an important element of vegetation in regions with a Mediterranean climate, characterized by hot and humid summers and mild and rainy winters. The plant, which does not shed its leaves in winter, can reach a height of 2-15 m. It is sensitive to frost in its early stages. As the altitude increases, the volatile oil content decreases, and the surface area of the leaves decreases (Yılmaz & Çiftçi, 2021). The leaves are elliptical-lanceolate, with undulate leathery edges and a strong, distinctive odor when crushed. The flowers are yellowish, located in the leaf axils and in clusters, with 4 petals; male flowers have 8-12 stamens, while females have 2-4 staminodes. The fruit is 1-1.5 cm in size, shiny black, with a well-developed seed similar to an olive (Tanker, Koyuncu & Coşkun, 2016). It is a plant with a high ability to produce shoots from the roots. The shoots are initially green and later turn red-black. The trunk has a dark gray, almost black bark. The branches are very dense, rising parallel to the trunk, giving a neat

and orderly appearance. Male and female flowers are found on separate plants (dioecious) (Karık & et al., 2015).

Phytochemical Composition: It is a valuable plant due to the presence of its essential oil in the leaves. The volatile oil contains 1,8-cineole, α-terpinyl acetate, α-terpineol, linalool, terpinen-4-ol, and sabinene (Yılmaz & Çiftçi, 2021). The leaves and fruits are also rich in mineral content (Özer, Sert & Öztürk, 2019).

***Table 3**. Mineral Content of Laurus nobilis Leaf and Fruit (Özer, Sert & Öztürk, 2019).*

Mineral Content (% Dry Weight)	**Leaf**	**Fruit**
Ca (Calcium)	1.3	0.18
K (Potassium)	0.22	0.56
Mg (Magnesium)	0.25	0.11
Na (Sodium)	0.19	0.14
P (Phosphorus)	0.1	0.19

Usage: The oil extracted from the fruits and leaves of the *Laurus nobilis* plant has various applications. The oil obtained from its fruits is mixed with olive oil to produce soap. This soap is effective against acne, softens hair, possesses good cleansing properties, and exhibits an anti-dandruff effect. Due to these characteristics, it is used in the preparation of mixtures for eczema, as well as for the treatment of hair dandruff and body rashes. Additionally, the fruits have appetizing, diuretic, parasiticidal (against parasites like lice, fleas, and ticks), and diaphoretic effects. The leaves, by increasing digestive secretions, prevent indigestion and are used in gargles for the treatment of tooth decay. They also have mucolytic, antifungal, antibacterial, muscle-relaxant, insecticidal, intestinal worm-expelling, and appetizing properties. Chewing the leaves can prevent bad breath. Tea made from the plant stimulates appetite, regulates

blood circulation, alleviates tonsillitis and colds, balances blood sugar, nourishes hair, provides softness, shine, and strength, relieves gas, and acts as a muscle relaxant (Özer, Sert & Öztürk, 2019). The fresh fruits, when pounded and mixed with honey, are used internally, and the oil obtained by boiling crushed fruits in water is used externally. Decoctions or infusions prepared from the leaves are used internally for rheumatism treatment. The oil obtained from fresh fruits is also used for lower back pain and disc displacement (Tuzlacı, 2016).

***Nerium oleander* L.**

Local Name: Known by names such as "zakkum," "ağı çiçeği," "zıkkım ağı," and "kan ağacı" in Turkey.

Family: Apocynaceae

Growing Regions: It grows in the western and southern regions of Anatolia in Turkey.

Botanical Features: *Nerium oleander* is a deciduous shrub that blooms from June to September, reaching a height of 2-5 meters. It is commonly used as an ornamental plant. The leaves are lanceolate, pointed, short-stalked, leathery, sometimes opposite, generally verticillate. There is a prominent main vein in the middle with parallel, less noticeable lateral veins around it. The calyx is dark red and small, while the corolla is pink or white. Pink-colored ones have white spots. Inside the corolla, there is a 5-part second corolla. There are 5 male organs with hairy tips of anthers, attached to the stigma and arrow-shaped; filaments are short and white. The ovary is 2-carpelled and multi-seeded. It has a cylindrical shape, yellow stigma, and a short style. The seeds are oval-shaped with tufts at the tip and are brown (Kizilay, 2015).

Phytochemical Composition: *Nerium oleander* contains ursolic acid, catechic compounds, sterols in small amounts, sapogenins, flavonoid glycosides, vitamin C, volatile oil, sapogenin, vitamin K, and carotene. Well-known toxic cardiac glycosides named oleandrin

and nerine are found in the plant. The bark contains volatile and fixed oil, resinous compounds, glycosides named rosaginin, nerin, and cortemerin; leaves contain tannins, glucose, resin, and vitamin C; and roots contain steroid compounds such as proceragenin and neridienone (Kizilay, 2015).

Usage: Unawareness of its toxicity by humans has led to poisoning through the chewing of leaves and flowers or exposure to the smoke produced by burning the plant. Poisoning symptoms include difficulty in breathing, strong or slowed pulse, gastrointestinal issues, numbness, rapid breathing, frequent urination, abdominal bloating, necrosis in renal tubules and collecting ducts, staining in heart muscle cells, and minor tissue damage. Some studies have shown that a single leaf has the potential to kill a human or a sheep, and a handful of leaves can be lethal to a horse (Sakarya, 2019). *Nerium oleander*, when soaked in alcohol for an extended period, has been used for the treatment of lower extremity pain and paralysis (inability to move facial muscles). When soaked in oil, it is used for the treatment of joint pain. The leaf-extracted juice has been used for abscesses and rheumatic conditions, while the fruit has been used for skin diseases and rheumatic conditions (Kizilay, 2015). The milky sap obtained after cutting young branches has been used externally for scorpion stings, and the decoction prepared from the leaves has been used internally for cancer treatment (Tuzlacı, 2016).

***Origanum onites* L.**

Local Names: Known in Turkey by various names such as "kekik" (thyme), "akkekik," "İzmir kekiği," "bilyalı kekik," "peynir kekiği," "eşek kekiği," "güveyotu," and "taş kekik."

Family: Lamiaceae (Labiatae)

Growing Regions: *Origanum onites* is found in Sicily, Greece, and in various regions of Turkey, including Antalya, Aydın, Balıkesir, Denizli, Silifke, Isparta, İzmir, Manisa, Muğla, Fethiye, and Uşak.

Botanical Features: It is a perennial plant with roots that can thicken up to 1 cm and dual branches that can extend up to 13 cm in its stem. The leaves are cordate, ovate, or elliptic in shape, growing upright, hairy, and with numerous stems. To prevent damage from drought, the plant has two types of leaves: small and large. Small leaves appear in summer, while large leaves emerge in winter. The edges of the leaves are slightly serrated, and they carry glandular hairs on their surfaces. The tips are pointed or elongated-pointed, with indistinct veins on the lower surface. The sepals are 2-3 mm long, unilaterally lipped, and the petals are 3-7 mm long. In the inflorescence, the flowers are arranged in oval or obovate shapes with slightly serrated edges, and each inflorescence has bracts in pairs, typically eight pairs per cluster. It generally thrives in calcareous soils and blooms between April and August (Poyraz, 2015; Oğuz & Kaplan, 2023).

Phytochemical Composition: One of the most notable features of *Origanum* species is their high content of volatile oil, obtained from dried leaves, flowers, stems, and buds. The main components of the essential oil are carvacrol and thymol. Additionally, some studies have identified linalool, p-cymene, γ-terpinene, borneol, α-pinene, β-pinene, sabinene, terpinen-4-ol, β-myrcene, α-thujene, caryophyllene, caryophyllene oxide, β-bisabolene, camphor, linalyl acetate, and 1,8-cineole in the oil (Poyraz, 2015). The leaves of Origanum onites also contain elements such as K, Ca, N, P, Fe, Zn, Mn, and Cu (Oğuz & Kaplan, 2023).

Usage: The volatile oil of *Origanum onites*, containing carvacrol and thymol, exhibits various biological activities. Carvacrol acts as antimicrobial, antioxidant, antibacterial, antifungal, and acetylcholinesterase enzyme inhibitor. Thymol, on the other hand, has antioxidant, antispasmodic, antimicrobial, and anti-inflammatory effects (Kete, 2022). Additionally, an infusion prepared from the leaves and flowering parts of *Origanum onites* has been used internally for colds, flu, nasal congestion, abdominal pain and cramps, relieving intestinal gas, lowering blood pressure,

reducing blood sugar, and externally for the treatment of hemorrhoids in decoction form, and against nausea (Tuzlacı, 2006).

The essential oil has been used internally for alleviating abdominal pain and cramps, reducing blood sugar; externally for the treatment of rheumatism and back pain. Fresh leaves, when boiled in water and applied as a poultice, have been used externally for the treatment of fractures and dislocations. After roasting, grinding into powder and mixing with flour and water, it has been used externally against sprains (Tuzlacı, 2016).

***Pancratium maritimum* L.**

Local Name: Sand lily

Family: Amaryllidaceae

Growing Regions: Sand lily is found in Greece, France, Spain, and along the sandy beaches of Kırklareli, Tekirdağ, Istanbul (Kilyos-Şile coastal areas), Bolu, Bartın, Sinop, Samsun, Giresun, Trabzon, Antalya, Mersin, and Adana in Turkey (Elibol, 2016).

Botanical Features: Sand lily, the only species naturally growing in our country, is a bulbous and perennial plant. It thrives in sand dunes a few meters away from the sea. Its coffee-colored, oval-shaped bulbs consist of fleshy scales, are encased, and can go as deep as 80 cm. It has a thick, flat stem called a scape, which is 12.5-35 cm tall and bears the flower cluster on its top. The plant blooms from June to October, with fragrant, funnel-shaped, white flowers measuring 10-15 cm. These flowers, 3-10 in number, cluster on the top of a stem. The flowers are surrounded by membranous, broad lanceolate bracts that envelop the flower cluster from the base. The flower stalks are short, measuring 5-13 mm from the ovary. The flower base is very thin. The flowers have a perianth, and the stamens are attached to the perianth. The leaves are long and lanceolate, fleshy, and linear, with a bluish-green color. They do not shed their leaves in winter, but leaves can dry out completely due to freezing events. Additionally, the leaves facilitate the growth and nutrient storage of

the bulb through photosynthesis. The capsule-shaped fruits contain small, black seeds. Due to the large size of the air-filled parenchyma, the seeds are light and easily transported to other locations by wind and water, germinating in the following spring (Kadim, 2020).

Phytochemical Composition: When the leaves, bulbs, and roots of *Pancratium maritimum* are examined, it is found to contain alkaloids such as licorine, tazettine, crinine, galanthamine, haemanthamine, and pancratistatin (Elibol, 2016).

Usage: The alkaloids obtained from the plant have been used against colon cancer and prostate cancer, as well as for antibiotic purposes. It has been observed that the alkaloids licorine, tazettine, crinine, and galanthamine exhibit activity against malaria. Some studies have indicated that due to its active ingredients, the plant has anti-tumor, antifungal, biopesticidal, hypotensive, laxative, and anti-inflammatory effects (Kadim, 2020). The bulbs, when pounded and wrapped in cloth, have been used externally for the treatment of joint, muscle, and rheumatic pains (Tuzlacı, 2016).

***Salix alba* L.**

Local Name: White willow, village willow

Family: Salicaceae

Regions of Growth: It is found in Turkey, Spain, Siberia, Cyprus, the northern part of Israel, the northeastern part of Iraq, the Caucasus, and the northwest of Iran.

Botanical Characteristics: The roots are dense, long, and thin, while the trunk is thick, cylindrical, brown, and exhibits longitudinal cracks as it ages. These trees can grow up to 25-30 meters in height. One of its most notable features is the white silky hairs covering the leaves, shoots, and buds. The silver-colored shoots are elastic and their tips hang downward. The leaves are elliptical-lanceolate, acuminate at the top, finely toothed, and thinly hairy, with more hairs on the lower surface. The number of stamens is 2. The small-sized

seeds are covered with tufts of hairs that assist in seed dispersal (İnceçayır, 2018; Tanker, Koyuncu & Coşkun, 2016).

Phytochemical Composition: *Salix alba* bark contains salicin, salicylic acid, salicyl alcohol, salicortin, salireposide esters, acetylated salicin, catechin, pheisin, triandrin, tannin, p-coumaric acid, flavonoids, and polysaccharides.

Usage: *Salix alba* is utilized for its potent antioxidant effects and its inhibition of the acetylcholinesterase enzyme, making it applicable in Alzheimer's treatment. Internally, it is used for calming, strengthening, reducing fever, and treating constipation, as well as for the treatment of rheumatic fever and subacute bacterial endocarditis due to the salicin derivatives present in its bark structure (İnceçayır, 2018). A decoction prepared from the trunk, leaves, and branch bark is used externally. Fresh leaves, when boiled in water and turned into a poultice by wrapping them in cloth, are employed for the treatment of rheumatism. Charcoal obtained from the trunk is powdered and used to alleviate bloating in animals. A decoction made from the leaves is applied externally to eliminate dandruff, and drinking a cup on an empty stomach in the mornings is recommended for lowering blood sugar levels (Tuzlacı, 2016).

***Tribulus terrestris* L.**

Local Name: In Turkey, it is known by the names "demir dikeni, çoban çökerten, demirleyen, deve çökerten, çarık dikeni, and demir bıtırağı."

Family: Zygophyllaceae

Growing Regions: It is found in India, China, Southern United States, Mexico, Spain, Bulgaria, and in Turkey in Istanbul, Çanakkale, Kocaeli, Sakarya, Zonguldak, Amasya, Samsun, Artvin, Ankara, Kayseri, Elâzığ, Kars, Antalya, Adana, Gaziantep, İzmir, and Denizli (Chhatre et al., 2014).

Botanical Features: These are annual herbaceous plants with a height ranging from 10 to 60 cm. The roots are thin, cylindrical, fibrous when fresh, densely branched, and brown. The leaves are paripinnate, elliptical or rectangular, covered with fine silver-colored hairs. The flowers are small and sparse, with sepals measuring 5 mm, covered with silky hairs, and petals of 4-5 mm in light yellow color, easily shedding. The fruits are pale green-yellow, mostly smooth, spherical, with two pairs of sharp hard spines, slightly aromatic, and have a slightly bitter taste. The carpel is star-shaped, and the seeds are oily (Chhatre et al., 2014).

Phytochemical Composition: Studies conducted on the *Tribulus terrestris* plant have identified saponins, flavonoids, glycosides, alkaloids, and tannins. The saponin composition includes furostanol, tigogenin, neotigogenin, gitogenin spirostanol saponins, neogitogenin, hecogenin, neohecogenin, diosgenin, chlorogenin, ruscogenin, and sarsasapogenin. The compound protodioscin is observed as the most important saponin type in the plant. Kaempferol, kaempferol-3-glucoside, kaempferol-3-rutinoside, and tribuloside flavonoids have been identified in the leaves and fruits of *Tribulus terrestris*. Additionally, the plant contains terrestribisamide, tribulusterine, aurantiamide acetate, xanthosin, fatty acid esters, ferulic acid, vanillin, p-hydroxybenzoic acid, β-sitosterol, stigmasterols, harmine and norharmane alkaloids, β-carboline, tribulusterin, and α-amyrin compounds (Chhatre et al., 2014).

Usage: The fruits have been used for eye disorders, increasing edema, treating sexual dysfunction, abdominal distension, and leukorrhea in women. Popularly, it has been used as an aphrodisiac, lithotriptic, urinary disinfectant, for skin diseases, sexual weakness, diuretic, and antihypertensive purposes. It has also been used for headaches, vitiligo, mastitis, swelling, acute conjunctivitis treatment, as a tonic, and mild laxative. Due to its saponin content, it is used for infertility and libido irregularities in both men and women, as well as in heart conditions (Chhatre et al., 2014). In

Turkey, a decoction prepared from the above-ground parts in the Denizli region has been used externally for rheumatism treatment (Tuzlacı, 2016).

Phytochemical Composition: Studies conducted on the *Tribulus terrestris* plant have identified the presence of saponins, flavonoids, glycosides, alkaloids, and tannins. The saponin composition includes furostanol, tigogenin, neotigogenin, gitogenin spirostanol saponins, neogitogenin, hecogenin, neohecogenin, diosgenin, chlorogenin, ruscogenin, and sarsasapogenin. The most significant saponin type in the plant is the compound protodioscin. Flavonoids such as kaempferol, kaempferol-3-glucoside, kaempferol-3-rutinoside, and tribuloside have been identified in the leaves and fruits of *Tribulus terrestris*. Additionally, compounds like terrestribisamide, tribulusterine, aurantiamide acetate, xanthosine, fatty acid esters, ferulic acid, vanillin, p-hydroxybenzoic acid, β-sitosterol, stigmasterols, harmine, and norharmane alkaloids, β-carboline, tribulusterin, and α-amyrin have been detected in the plant (Chhatre et al., 2014).

Usage: The fruits have been used for eye disorders, to increase edema, in the treatment of sexual dysfunction, abdominal distension, and leukorrhea in women. Among the public, it has been utilized as an aphrodisiac, lithotriptic, urinary disinfectant, for skin disorders, sexual weakness, as a diuretic and antihypertensive, for headaches, vitiligo, mastitis, swelling, acute conjunctivitis treatment, as a tonic, and mild laxative. Due to its saponin content, it is used for infertility and libido irregularities in both women and men, as well as for heart conditions (Chhatre et al., 2014). A decoction prepared from the above-ground parts in the Denizli region of our country has been used topically for the treatment of rheumatism (Tuzlacı, 2016).

***Urtica dioica* L.**

Local Name: Known as dızlağan, çızlağan, cızgan, dalagan, cınçar, ağdalak, ısırgı, and ısırgan otu in Turkey.

Family: Urticaceae

Regions Where It Grows: Thrives in temperate and tropical terrains (Çolak, Çömlekcioğlu & Aygan, 2020).

Botanical Features: *Urtica dioica* is a perennial, dioecious, and herbaceous plant. It ranges from 30 to 150 cm in height, with creeping roots and stinging hairs present throughout the plant. The leaves are arranged in a decussate pattern, cordate, oblong, or ovate at the base, with toothed margins, dark green upper surfaces, and lighter-colored lower surfaces. The flowers are green, arranged in axillary clusters, false spikes, racemes, or rarely globose head clusters. Fruiting perianth parts are hairy on the entire surface (Davis, 1982).

Phytochemical Composition: The main compounds found in *Urtica dioica* include flavonoids, tannins, volatile oils, fatty acids, polysaccharides, lectins, sterols, terpenes, proteins, vitamins, and minerals. Compounds causing the burning sensation in the leaves are acetylcholine, histamine, 5-hydroxytryptamine (serotonin), leukotrienes, and formic acid, located inside the trichomes. The leaves are rich in B, C, K vitamins, calcium, iron, magnesium, phosphorus, potassium, and sodium minerals. Volatile oils contain carvacrol, carvone, naphthalene, e-anethole, hexahydrofarnesyl, acetone, e-geranyl acetone, (E)-β-ionone, and phytol. Flavonoids include isorhamnetin, quercetin, isoquercetin, astragalin, rutin, 3-rutinosides, and 3-glycosides. The plant also contains shikimic acid, phenylpropanes, caffeic acid, chlorogenic acid, caffeoyl, malic acid, carotenoids, β-carotene, hydroxy-β-carotene, luteoxanthin, lutein, epoxide, violaxanthin, essential amino acids, glucokinins, and chlorophyll (Joshi, Mukhija & Kalia, 2014).

Usage: Traditionally, in the Balkan countries, nettle is used in the form of an infusion to treat diarrhea, vaginal discharge, and stomach pain, and to stop internal and external bleeding. It has been observed that ancient Egyptians also used nettle infusion to alleviate arthritis and lumbago (sudden pain in the lower back caused by exposure to cold). In Europe, the flowers, leaves, and seeds are utilized as a diuretic, vasoconstrictor, and tonic. Nettle tea and tincture have been

employed for gout, feverish gout, fever, and malaria treatment. Boiling leaves and stems are applied for skin disorders, dried leaves are used for inhalation to relieve asthma and similar bronchial issues, and nettle is used for sciatic pain, weight loss, facilitating breathing, cough, paralysis, suppression of menstrual flow in women, rheumatism, and muscle energy deficiency. The roots are used as an anti-inflammatory in the treatment of rheumatoid arthritis to prevent prostate enlargement. Ethnobotanical studies conducted in Turkey have identified the preparation of a decoction from fresh nettle leaves, left on the painful area, used for bathing, boiled leaves wrapped in a cloth for the treatment of rheumatism and relief of joint pain. Additionally, a mixture of nettle leaves with semolina and flour is applied externally for the treatment of fractures, dislocations, and joint rheumatism (Çolak, Çömlekcioğlu & Aygan, 2020).

***Allium sativum* L.**

Local Name: Garlic

Family: Liliaceae (Asphodelaceae)

Growing Regions: It grows and is cultivated in Asia, Europe, North Africa, China, India, Egypt, the USA, Mexico, and Turkey (Dikel, 2015; Ayaz & Alpsoy, 2007).

Botanical Features: Garlic is an herbaceous annual plant, 25-100 cm in height, with 4-10 leaves, 4-25 mm in width, flat-veined, rarely flowering, and pink flowers arranged in an umbel (a spathe at the base of the umbel). Flowering occurs between the 6th and 8th months. The flower cover parts (1-3 mm) are lanceolate and acuminate. The filament is shorter than the flower cover parts. The bulb is flat, egg-shaped, white, or pinkish in color, consisting of 5-15 almost equal bulbs, all enclosed by a single skin (Baytop, 1999; Kaya, 2007).

Phytochemical Composition: *Allium sativum* contains over 200 components, including vitamins, sulfur compounds, amino acids, proteins, lipids, trace elements, flavonoids, and antioxidants. It

contains minerals such as Selenium, Germanium, and Tellurium, as well as myricetin, ellagic acid, gallic acid, quercetin, phenolic compounds, alliin, allicin, ajoene, allylpropyl disulfide, diallyl trisulfide, S-allyl cysteine, S-allyl mercapto cysteine sulfur compounds, allinase, peroxidase, myrosinase enzymes, caffeic acid, quercetin. Additionally, it contains vitamins A, B1, B2, Niacin, and C, sucrose, glucose, and sulfur-containing volatile oil that imparts the characteristic odor and taste to the plant (Kır & Yünlü, 2016).

Usage: *Allium sativum* has been used for millennia to combat various diseases. During the Middle Ages, physicians used masks soaked in garlic water to protect themselves from infectious diseases. In World War II, crushed garlic was applied to the wounds of Russian soldiers to prevent infections. Studies have shown that garlic lowers high levels of cholesterol, triglycerides, and LDL cholesterol while increasing HDL cholesterol. Individuals consuming daily *Allium sativum* experienced a reduction in systolic blood pressure by 12-30 mm Hg and diastolic blood pressure by 7-20 mmHg. The sulfur compound allicin in garlic prevents the formation of fibrin and plaque in the blood, reducing the risk of a heart attack. It increases the number of macrophages, leading to the death of pathogens. The compound allicin is also used as an antibacterial agent against Gram-negative and Gram-positive bacteria such as *Helicobacter pylori*, *E.coli*, and *Lactobacillus casei*. Fresh garlic is used topically as a poultice for wound healing, mobilizing the immune system to enhance the body's defense against infectious organisms. Garlic is known to lower blood sugar, benefit stomach cancer, and reduce symptoms of chronic lead poisoning (Ayaz & Alpsoy, 2007).

In Turkey, among the public, crushed garlic cloves are externally used for the treatment of lumbago, and a paste made with salt is applied externally to alleviate rheumatic pains in the legs and joints. Crushed and heated garlic cloves are wrapped in a warm cloth and used externally for compress treatments (Tuzlacı, 2016).

***Amygdalus communis* L.**

Local Name: Almond

Family: Rosaceae

Regions Grown: Almonds are cultivated in Greece, Spain, Italy, Iran, Syria, Palestine, North America, and various regions in Turkey such as the Aegean, Mediterranean, Southeastern Anatolia, Inner Anatolia, and Marmara.

Botanical Features: *Amygdalus communis* is a tree that can grow up to 8 meters tall, flowering with pink or white flowers before leaves emerge in spring. The flowers are solitary or in clusters of 2-3; the stem is very short, and the receptacle is concave. Both calyx and corolla have 5 members each, numerous stamens, one ovary, and they are free at the base of the receptacle. In young fruits (green almonds), there is a soft pericarp, which gradually becomes woody, transforming into a porous, hard endocarp (Tanker, Koyuncu & Coşkun, 2016).

Phytochemical Composition*:* Almond bark contains triterpenoids, betulinic, ursolic, and oleanolic acids, flavonol glycosides, and phenolic acids. Seeds contain linoleic and oleic acids, proteins, fats, sugars, vitamin E, vitamin B, calcium, magnesium, phosphorus, sodium, potassium, chlorine, sulfur, iron, zinc, manganese, copper, cobalt, and fluorine elements. Amygdalin and prunasin are found in fruits and leaves (Sfahlan & et al., 2009).

Usage: Almond oil derived from *Amygdalus communis* strengthens and adds shine to hair, heals wounded and burned skin, regulates intestines, and is used to treat constipation in children. Bitter almond seeds are used in pharmacy for their good taste and odor-removing properties in the composition of some medicines. Bitter almonds are also used internally as cough suppressants, demulcents, diuretics, vermifuges, and for treating sore throats. Externally, bitter almonds are used to treat skin cracks. Bitter almond oil has hypoglycemic effects. Studies on almond seeds have reported that the unsaturated fatty acids in them lower LDL cholesterol, raise HDL cholesterol, and prevent heart attacks (Başkurt, 2005). In Turkey, locally, oil

obtained from *Amygdalus communis* seeds is used externally to alleviate rheumatic pains (Tuzlacı, 2016).

***Viscum album* L. subsp. *album* L.**

Local Names: In Turkey, it is known by various names such as "ökseotu, burç, purç, çekem, gevele, gökçe otu, gökçe, gövelek, güvelek, çampir, gelimkara, pura, biriç, and fitri."

Family: Loranthaceae (Viscaceae)

Regions Grown: It is found in Europe, Africa, Central Asia, East Australia, America, and all regions of Turkey.

Botanical Features: *Viscum album* is a semi-parasitic shrub that grows on the slender branches of trees, developing slowly. It has a root system that absorbs water, sugar, and amino acids from the host tree. The stem is yellow-green, leaves are stalkless, with smooth edges, green throughout the year, lanceolate or spatulate, and have veins on the underside. Leaf size varies depending on the host tree. Flowers are dioecious, about 2-3 mm in diameter, yellow-green, and located at the tips of young branches. Fruits are about 8 mm in diameter, covered with a gel-like substance, 1-2-seeded, spherical, and white. *Viscum album* is a plant that can live up to 70 years, producing new branches every year (Yüksel, Akbulut & Keten, 2005; Nazaruk & Orlikowski, 2016).

Figure 4. *Fruit and Morphological Image of Viscum album (http 5)*

Phytochemical Composition: The chemical composition of *Viscum album* varies depending on the host plant. Some components can be

obtained from the host plant since the plant itself cannot produce them. The important compounds found in the plant include lectins, alkaloids, viscotoxins, polyphenolic compounds (protocatechuic, p-hydroxybenzoic, caffeic, salicylic, ferulic, and sinapic acids, syringin, coniferin, rosmarinic acid, etc.), terpenoid compounds, lignans, flavonoids (chalcones and flavanones), flavonols, polysaccharides, amines, and carbohydrates. Lectins (ML I, ML II, ML III) are the main components of the plant and are classified as proteins that inactivate the type II ribosome. Triterpenes (β-amyrin acetate, oleanolic acid, betulinic acid), phytosterols (stigmasterol, β-sitosterol), and their glycosides are included in the terpenoid compounds. In addition to these compounds, long-chain fatty acids, hydrocarbons, and trace amounts of volatile components (trans-a-bergamotene, trans-b-farnesene, loliolide, and vomifoliol) are also present (Kleszken et al., 2022).

Usage: The fruit and leafy branches of *Viscum album* are utilized in the treatment of epilepsy, as a blood pressure regulator, blood purifier, heart strengthener, diuretic, urinary antispasmodic, and spasm reliever. The crushed fruits are applied to areas affected by boils, promoting the opening of the boil and draining the pus. Additionally, crushed fruits, when combined with mastic gum (black gum), are used to alleviate rheumatic pains. However, when taken orally, the fruits are toxic. *Viscum album* tea is believed to be beneficial for chronic cramps, hysteria seizures, imbalances leading to diabetes, and arteriosclerosis. One of the significant applications of *Viscum album* is in cancer treatment. It has been reported to have beneficial effects on breast cancer, pancreatic cancer, laryngeal cancer, bladder cancer, and leukemia. Furthermore, it is noted for its positive impact on neurological disorders, as well as its antiviral, antibacterial, anti-inflammatory, antiepileptic, and immune-stimulating effects (Yüksel, Akbulut & Keten, 2005).

DISCUSSION AND CONCLUSION

Rheumatic diseases, particularly by causing damage to the musculoskeletal system, induce inflammation in patients.

Inflammation leads to symptoms such as pain, swelling in tissues, increased temperature, joint deformities, carditis, speech and balance disorders, muscle weakness, joint sensitivity, fatigue, diarrhea, constipation, dysphagia, and more. The emergence of these diseases can be attributed to factors such as medications, hormones, diseases, bacteria, viruses, communal living spaces, enzymes (DNAase, hyaluronidase, streptokinase, etc.), age, gender, occupational factors, obesity, inadequate nutrition, pregnancy, lactation, exercise, pubertal development, physical activity, race, ethnic origins, and exposure to ultraviolet and sunlight. Rheumatic diseases are more prevalent in women than in men. Some studies suggest a higher incidence of rheumatic diseases in women of childbearing age compared to men, implying that hormones may play a role in the development of the disease, although a definitive conclusion has not been reached (Köksal, Soylu, & Özdemir, 2016).

As the etiology of the disease is not fully understood, it cannot be completely cured. Therefore, the goal is to minimize the symptoms of patients, reduce mortality and morbidity. To achieve this goal, corticosteroids, non-steroidal anti-inflammatory drugs, disease-modifying drugs, and anti-TNF agents are used in pharmacological treatment. In addition to pharmacological treatment, physical methods such as patient education, exercise, massage, hydrotherapy, hot application, cold application, movement restriction-rest, acupuncture, tens, massage, and therapeutic touch are also employed (Demiray & Alpözgen, 2022).

Gastrointestinal side effects such as nausea, vomiting, diarrhea, and abdominal pain, as well as side effects like myopathy, megaloblastic anemia, azoospermia in males, elevated liver enzymes, leukopenia, and thrombocytopenia may occur in patients depending on the dosage of medications (Kasapçopur & Arısoy, 2006; Ugan & Ermiş, 2011). Due to observed side effects and difficulties in accessing medications, along with economic conditions, cultural beliefs, and the inability of drugs to provide complete curative treatment, patients have turned to traditional

remedies (Nacoulma & et al., 2022). For this purpose, various parts of plants such as roots, stems, leaves, bark, branches, flowers, fruits, seeds, rhizomes, oils, latex, bulbs, or the entire plant itself have been used (Kamal & et al., 2016). Infusions and decoctions prepared from the roots, stems, branches, leaves, seeds, fruits, and flowers of plants, fresh leaves boiled in water and applied as a poultice, onions crushed and wrapped in a cloth, and externally applied oils obtained from fruits and seeds have been used in the treatment of rheumatic diseases (Tuzlacı, 2006; Tuzlacı, 2016).

In our study, information about plants traditionally used in the treatment of rheumatic diseases has been compiled. It is essential to emphasize the development of new drug molecules and active substances for the treatment of rheumatic and other diseases, as well as to increase research on plants used in traditional medicine in this regard. The fact that many active ingredients of past medications were derived from plants used in traditional treatment should not be forgotten. Additionally, the adjuvant effect of plants used in traditional treatment should not be overlooked, with particular attention paid to plant-drug interactions.

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BÖLÜM II

Some Plant Species With Antitussive Effects Used As Folk Remedies In Turkey

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Introduction

Cough, essentially serving as a defense mechanism in the body, is a vital protective reflex in the lungs and bronchi that prevents the settling of inhaled foreign objects or particles in the lower respiratory tract, and plays a role in expelling irritant substances that occur following mucosal inflammation. It also

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prevents secretion in the lungs. It serves to protect the lungs and respiratory system against thermal, mechanical, and chemical factors (Özdilekcan, 2018).

Cough holds a significant place as a reason for hospital admissions across all age groups worldwide. According to the results of epidemiological studies, the symptom of cough ranks among the most common complaints that influence physicians' decisions to conduct a general medical examination. The persistence of a patient's cough for an extended period or its severity, whether it has been present for a long time or started recently, negatively affects the patient's daily life. It disrupts sleep patterns, causes physiological harm, and, as the duration of occurrence increases, not only induces stress but also has negative psychological effects on the patient. Patients often feel the need to frequently visit the hospital for a persistent cough, increasing not only the number of medications taken by the patient but also the workload of the physician (Çildağ, 2005).

Our study aims to compile research related to the use of certain plants in folk medicine for the treatment of cough. The use of plants for medicinal purposes dates back to the dawn of human history. People have employed various methods, such as observing animals or trial-and-error approaches, to treat diseases using many plants readily available in their environment. Ethnobotanical studies have contributed to the discovery of numerous new drug molecules by revealing substances obtained or synthesized by mimicking traditional knowledge. Therefore, the information obtained from ethnobotanical studies is highly valuable, facilitating the translation of many insights into a laboratory setting and subsequently into a clinical context for medical interpretation.

The Physiology of Cough

Coughing is a result of irritation in the respiratory tract and some other areas. If the cough reflex center in the medulla oblongata is under control, it results in involuntary coughing, while if it is under the control of the cerebral cortex, it leads to voluntary coughing.

However, fundamentally, it occurs in response to the stimulation of sensory receptors connected to the vagus nerve located in the larynx or the tracheobronchial tree. These stimulations in the airways can be of a chemical, mechanical, inflammatory, or thermal nature. Chemical receptors are mainly located in the bronchi and larynx and are sensitive to harmful gases such as smoke. Mechanical receptors, on the other hand, are found in the trachea, carina, and larynx and are sensitive to factors such as displacement and contact (Çağlar, 2012).

The mentioned sensory receptors are not only present in the trachea, bronchi, and larynx but also in other organs such as the external ear canal, stomach, pleura, esophagus, paranasal sinuses, pericardium, and diaphragm. The receptors in the tracheobronchial tree and larynx respond to both mechanical and chemical stimuli, whereas the receptors in the other mentioned areas only respond to mechanical stimuli (Kartaloğlu, Okutan & İlvan, 2001).

Cough Reflex Receptors

For the occurrence of a cough, the stimulation of cough receptors is necessary. The sensory receptors involved in this reflex are of three types:

1. Slowly adapting receptors (SAR)
2. Rapidly adapting receptors (RAR)
3. Unmyelinated vagal afferent fibers (J receptors or C fibers)

One of the most sensitive regions that initiate the cough reflex is the branching areas of the tracheobronchial tree and the carina, and another is the larynx. The receptors in these areas are stimulated by the impact of a foreign body, and after a series of events, coughing begins. Unmyelinated vagal afferent fibers (J receptors or C fibers) are receptors found in the tracheobronchial tree, bronchial, and alveolar walls. While irritant receptors are also present in large bronchi, agents that stimulate these receptors do not activate the

receptors in unmyelinated vagal afferent fibers and do not cause coughing. Studies have shown that C fibers do not have a role in initiating cough but facilitate the physiology of cough by increasing sensitivity during reflex formation. Rapidly adapting receptors (RAR) are myelinated A delta fibers and are located in the laryngeal region. They are stimulated by chemical and mechanical factors. The crucial step in the initiation of the cough reflex is the stimulation of A delta fibers. Slowly adapting receptors (SAR), like C fibers, play a role in facilitating the formation of the cough reflex. This is because these receptors do not respond to classical stimuli (İğde & Öksüz, 2015).

Cough Phases

Coughing begins with taking a deep breath, forming the inspiratory phase. The inspiratory phase is followed by the compression phase, where the glottis temporarily narrows and closes. The compression phase, where the glottis is closed, transitions to the expulsive phase with the sudden opening of the glottis, leading to a rapid, explosive air flow (expulsive phase). The compressive and expulsive phases together constitute the expiratory phase in the physiology of the cough reflex (Kartaloğlu, Okutan & İlvan, 2001).

Taking a deep breath to initiate the inspiratory phase prepares the airways for clearing during the expiratory phase. In this phase, the glottis is in an open position. During the compression phase, also called the compression phase, the glottis temporarily closes. Throughout this phase, intraabdominal pressure and intrathoracic pressure increase. This is communicated to the central system and can lead to complications in skeletal, muscle, gastrointestinal, cardiovascular, neurological, and other systems. The expiratory phase, which is the final phase of coughing, begins with the opening of the glottis. Coughing occurs in a burst-like fashion with a sudden, rapid, and transient airflow. The opened airways are also cleared. Glottis closure and the expulsive phase can repeat without the inspiratory phase.

Physiologically, there are two types of cough (Erdoğan, 2021):

1. Laryngeal (true expiratory reflex)
2. Tracheobronchial (voluntary, distal to the larynx)

Cough Classification

Cough is categorized into three groups based on the duration:

1. Acute cough: Lasts less than 3 weeks.
2. Subacute cough: Lasts between 3 and 8 weeks.
3. Chronic cough: Lasts longer than 8 weeks.

Cough Treatment

There are various types of cough based on different symptoms, durations, and causes. However, cough treatment can be broadly categorized into two types:

Expectorant Treatment

This treatment aims to enhance the effectiveness of cough by using medications and herbs with expectorant properties. Pharmacologically or mechanically, the intensity of cough is increased, clearing the lower respiratory tract. This treatment can be applied in diseases such as pneumonia, bronchiectasis, and cystic fibrosis, showing beneficial effects.

Antitussive Treatment

Contrary to exacerbating cough, antitussive treatment prevents, controls, or suppresses cough. It suppresses the cough reflex by exerting peripheral or central effects. Antitussive treatment is divided into specific antitussive treatment and non-specific antitussive treatment.

Specific Antitussive Treatment

Specific antitussive treatment targets the cause of the cough. Physiopathological mechanisms causing cough are regulated or

eliminated. Due to its specific nature, it achieves a high success rate, ranging from 84% to 98%.

Non-specific Antitussive Treatment

In non-specific antitussive treatment, cough is not prevented but rather controlled. The treatment does not target the physiopathological mechanism; instead, it focuses on the symptom. Non-specific treatment is preferred when specific treatment cannot be applied or when there is no response to treatment.

Some Herbal Species with Antitussive Effects Used Among the Public in Turkey

In the treatment of cough, herbal remedies have gained significant importance alongside pharmaceutical drugs such as antitussive medications and antihistamines. Challenges and deficiencies in patient-doctor communication, the increasing cost of medication, fear of side effects associated with pharmaceutical treatment, a preference for natural solutions, the desire for a trustworthy treatment option, and the inclination of patients to be informed and have a say in their treatments make herbal remedies appealing. The utilization of plant extracts, consumption as herbal tea, herbal baths, raw consumption, volatile oils, and extracts indicate the extensive use of herbal remedies among the public. Active ingredients and antitussive medications are also derived from herbal products and plants. In productive cough, essential oil drugs are used, while in dry cough, mucilage drugs are employed to cover the mucosa, forming a protective layer (Pars, Suluhan & Ercan, 2020).

***Pimpinella anisum* L.**

Pimpinella anisum L., commonly known as anise, is a species belonging to the Apiaceae (Umbelliferae) family and Pimpinella L. genus. It is also known by various regional names such as Mesir otu (Karamanlı-Burdur), Ezeltere (Sivas), Ezertene (Sivas), Ezerteri (Pınarbaşı-Kayseri), Ezanteri (Gümüşhane), and Enisen (http 1).

Botanical Characteristics of *Pimpinella anisum* L.:

Pimpinella, belonging to the Apiaceae (Umbelliferae) family, is a herbaceous plant that can be either annual or perennial, occasionally appearing in a shrubby form. Species within this genus can be either simple or highly branched. The plant features small yellow/green seeds and white flowers. Its leaves may be arranged alternately or opposite each other. The plant typically has five petals, and their lengths are equal. Occasionally, outer petals may be longer than inner ones. The petals are positioned in a backward-curving manner at the top. They come in colors such as light blue, white, pink, or yellow. The fruit can be compressed from the sides or dorsally, or it may have a cylindrical shape. The fruit is schizocarp, meaning it is a split fruit. The mericarp can be smooth/hairy, prickly/rough, or scaly. There are five primary ridges (prominences) and four secondary ridges on the mericarp. These may have undulating/winged forms. Between the ridges, vittae (furrows) are present. Secretory canals are found either where the vittae are located or on the opposite faces of the mericarps. The mericarps separate when the fruit ripens.

Chemical Composition of *Pimpinella anisum* L. Species:

Parts Used as Medicinal Material: The parts used as a drug are its fruits.

Chemical Composition*:* The fruits contain about 2-6% volatile oil. The composition of the volatile oil is as follows: Trans-anethole: 80-95%, Pseudoisoeugenol, Estragole, Anisic acid, Anisaldehyde, Anisic ketone, Limonene, Linalool, Coumarin as farnesyl-oxy-coumarin, Flavonoids such as nobiletin and tangeretin (Gülçın &ark., 2003).

Uses of *Pimpinella anisum* L. Species:

Pimpinella anisum L. plant has therapeutic effects in various physiopathological conditions such as respiratory disorders, gynecological and neurological disorders, and digestive disorders. Additionally, it possesses mucolytic, carminative, anticonvulsant,

anesthetic, and hypothermic properties due to its content of estragole and eugenol. Its muscle-relaxant effect comes from anethole. It's important to note that anethole may cause allergic reactions in some individuals. The use of its essential oil is not recommended for inflamed, dermatitis-prone, or sensitive skin as it may cause sensitivity. The safety of its use during pregnancy and breastfeeding is not definitively known. However, some studies suggest that, under doctor supervision, it can be used in infusion form at recommended doses. In Turkish folk medicine, it is used for its diuretic, appetite stimulant, and sedative effects, particularly in the use of its seeds (Büyükkök, Güngör & Genç, 2022).

Geographical Distribution of Pimpinella anisum L. Species in Turkey

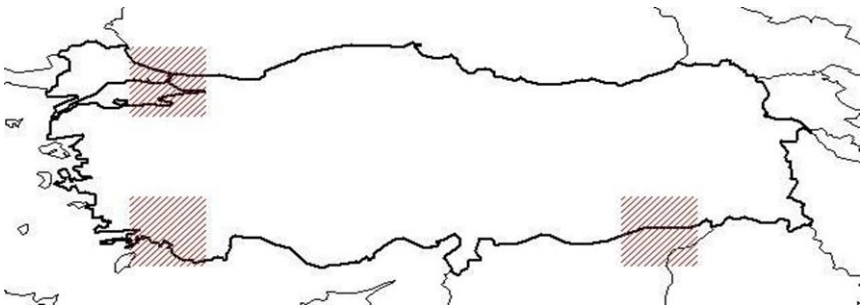

Figure 1. Distribution of *Pimpinella anisum* L. Species in Turkey According to the Grid Mapping System (A2, C2, C8) (http 1)

Pimpinella anisum L. plant is distributed in Western, Northwestern, and Eastern Anatolia regions of Turkey, with a particularly common occurrence in the provinces of Mardin, Denizli, and Kocaeli. Globally, its general distribution includes Western Russia, Eastern Russia, Egypt, Central Europe, Southern Europe, Iran, India, Cyprus, Syria, and various hot regions around the world (Gülçin &ark., 2003).

Eucalyptus globulus Labill.

The plant known by the name Eucalyptus, scientifically classified as *Eucalyptus globulus* Labill., is a large genus belonging to the Myrtaceae family. The *Eucalyptus* genus is native to the continent of Australia and consists of evergreen trees. The tree is utilized in the battle against marshes due to its ability to absorb a significant amount of water from the soil and evaporate it through its leaves. Additionally, it is cultivated to combat malaria by controlling mosquitoes.

The Botanical Characteristics of *Eucalyptus globulus* Labill.

Eucalyptus globulus Labill. is a tree that reaches a height of 20 m. It exhibits heterophyllous leaves with a leathery texture. The leaves on young branches are opposite and lanceolate; on mature branches, they are arranged alternately and falcate. Falcate leaves contribute to the Eucalypti folium drug (Tanker, Koyuncu & Coşkun, 1998).

The Chemical Composition of *Eucalyptus globulus* Labill.

Extracts obtained from *Eucalyptus* species contain volatile oils, tannins, triterpenes such as ellagic acid and ursolic acid, monoterpenes, phenols, saponins, cyanogenic heterosides, cardiotonic heterosides, and steroids. The parts of the *Eucalyptus globulus* Labill. plant utilized as a drug are its leaves (**Eucalypti folium**) and the volatile oil obtained from the plant (**Eucalypti aetheroleum**). *Eucalyptus globulus* Labill. contains approximately 1.5-3.5% volatile oil. Within this volatile oil, α-pinene, p-cymene, and a high percentage of 1,8 cineole (eucalyptol), ranging from 54-95%, are found. All Eucalyptus species contain one or more types of inositol, with myo-inositol being the most common type (Süzgeç-Selçuk & Eyisan, 2012).

Uses of *Eucalyptus globulus* Labill. Species

The aerial parts of the *Eucalyptus globulus* plant are used as the drug. The volatile oil of *Eucalyptus globulus* has a wide range of applications in medicine and pharmacy. The inhalation (steam) of eucalyptus essential oil is commonly used for respiratory complaints, throat pain, and cold-related conditions. This method of inhalation with the volatile oil is also employed for treating nasal congestion and runny nose. **Eucalypti aetheroleum** is also a stimulating oil used in throat lozenges, tinctures, and cough syrups to soothe the throat.

The leaves of *Eucalyptus globulus* Labill. act as an expectorant and respiratory tract antiseptic. The essential oil and leaves are used by the general public for various conditions such as bronchitis, asthma, cystitis, flu, fever, colds, and laryngitis. Due to the presence of tannins, the leaves of the plant are effective against constipation and possess tonic properties. For the purpose of suppressing coughs, the powder (5-10 grams/day) or infusion (2%) is used.

In traditional medicine, *Eucalyptus globulus* leaves are utilized in China for burns, enterocolitis, and arthritis treatment; in Mexico, they are chewed to strengthen gums; in Venezuela, leaves soaked in water are used for the treatment of colds and flu-like illnesses; in Asia, it serves as an anesthetic and dewormer; in Cuba, its volatile oil is used for stomach, lung, and liver disorders, as well as in the treatment of malaria.

Due to the potential risk of laryngospasm associated with its cineole content, its use is not recommended for infants under 30 months. Its use is not recommended in children under 12 years of age, pregnant women, and nursing mothers due to insufficient studies and data. Internal use should be diluted. It should not be used by diabetes patients as it may interact with antidiabetic drugs. It is not used with drugs metabolized by liver detoxification enzymes such as CYP1A2, CYP3A4, CYP2C19, and CYP2C9, as it induces these enzymes.

The Distribution Areas of *Eucalyptus globulus* Labill. Species

While this species is native to Southeastern Australia, it is also found in Mexico, Africa, Venezuela, Cuba, and many Asian countries (Başer & et al., 1998).

Thymus vulgaris L.

Belonging to the Lamiaceae family and commonly known as 'thyme,' *Thymus vulgaris* is a plant species within the Thymus genus. It is also known as 'za'atar' in Arabic. In addition to the 40 species found in Turkey, there are numerous subspecies, species, and varieties within this genus. It grows during the seasons of spring, summer, and autumn, with flowering occurring in the summer months (Golshan, Diker & Çankaya, 2022).

Botanical Features of *Thymus vulgaris* L.

The leaves of *Thymus vulgaris* L. can grow up to 20-30 cm, with a width of about 3 mm, and are stemless or very short-stemmed, ranging from 4-12 mm in length. The lamina can vary in shape from stiff lanceolate to ovate. The calyx is green, tubular, and often dotted with lilac-colored spots. After flowering, the calyx tube is long, rigid, and covered with stiff hairs. The length of the corolla is approximately twice that of the calyx, usually brownish in dry conditions, and slightly bilabiate. *Thymus vulgaris* is a perennial flowering plant consisting of evergreen, small shrubs (WHO monographs, 1999).

Chemical Composition of *Thymus vulgaris* L.

It carries volatile oil in the range of 1.0-2.5% (with the total ratio of thymol and carvacrol reaching up to 64%), flavonoids such as sirsilineol and thymonin, methylated flavones, phenolic glycosides, monoterpenoid phenyl compounds, monoterpenoid glycosides, phenolic acids including caffeic acid and rosmarinic acid, saponins, aliphatic aldehydes, aliphatic alcohols, and acetophenones (ESCOP Monographs, 2003).

Uses of *Thymus vulgaris* L. Species

The aerial parts (**Thymi herba**) and the volatile oil (**Thymi aetheroleum**) of *Thymus vulgaris* L. are used as the drug (Süzgeç-Selçuk & Eyisan, 2012).

Thymus vulgaris L. is widely used in both traditional medicine and culinary practices. Thyme is known for its mucolytic effects and is considered as an antitussive, expectorant, antiseptic, antimicrobial, astringent, anthelmintic, and carminative. Thyme infusion and extract are commonly used for diseases such as sore throat, severe cough, acute bronchitis, bronchial diseases, inflammation, laryngitis, pharyngitis, and whooping cough, as well as in chronic gastritis, diarrhea, and loss of appetite. These effects are attributed to the flavonoids it contains and the volatile oil used.

Additionally, thymol, an active component of thyme, is effective against bacteria and enterobacteria, exhibiting antifungal and antibacterial properties. Its use is common in infections caused by gram-negative and gram-positive bacteria, as well as fungi such as *Candida albicans*, intestinal infections caused by hookworms, and oral and throat inflammation to prevent bad breath. A 5% infusion is used to prevent oral bacteria, and it is applied topically for bacterial and fungal skin diseases. Externally, its volatile oil can be used by rubbing for rheumatic and joint pains, and in the treatment of Tinea pedis (athlete's foot). It is also used for dermatitis, eczema, acne-prone and oily skin, as well as insect bites and stings. The carvacrol contained in thyme water and thyme volatile oil has a strong analgesic effect. Thyme tea, prepared through maceration, is commonly used in the treatment of cough and bronchitis (PrasanthReddy & et al., 2014)."

Thyme's aerial parts should not be used internally or externally in children under the age of 12, and its volatile oil should not be used in individuals under the age of 18. Its use in pregnant and breastfeeding women is not considered safe, as there is insufficient research conducted. Stomach complaints may be observed during use. If cough or fever occurs after use, it should be discontinued, and

a healthcare professional or pharmacist should be consulted. The use of thyme essential oil in bathwater should not exceed 10-20 minutes. The use of thyme tea in hypertensive patients is harmful (http 3).

Geographical Distribution of *Thymus vulgaris* L.

Thymus vulgaris L., although native to Southern Europe, is found in various countries and regions worldwide, including Poland, Spain, South Africa, Russia, the United States, Eastern and Southern Asia, the Mediterranean, thriving in diverse and varied climatic conditions (Stahl-Biskup & Venskutonis, 2012).

Tussilago farfara L.

Tussilago farfara L. belongs to the *Tussilago* L. genus within the Asteraceae (Compositae) family. Commonly known as 'Coltsfoot,' it is also referred to by various names such as 'Öksürük otu' (Cough herb), 'kavalak,' 'kabalak,' 'gabalah,' 'şabla,' 'gabalak,' 'kınaçiçeği,' 'kınaotu,' 'lapaza,' 'devetabanı,' 'deveşaplağı,' 'kusut' (Sürmene-Trabzon), and 'sulandık otu' (Tekirdağ) (http 2).

Tussilago farfara L. Species Botanical Features

Tussilago farfara L. is a perennial herbaceous plant that grows in loose and moist soils on slopes. In spring, the flower heads are observed before the leaves, appearing yellow and emerging individually from the stem. The leaves, on the other hand, emerge after the plant's flowers have withered, and they are approximately 5-10 cm, angular to orbicular, tomentose on the lower surface with a dirty white color, and fleshy. Farfarae folia, the Coltsfoot leaf as a herbal remedy, can be used alone or in combination with other herbs (Tanker, Koyuncu & Coşkun, 1998).

Chemical Composition of *Tussilago farfara* L. Species

Tussilago farfara L. contains approximately 7% mucilage, various sugars such as inulin and galactose as carbohydrates, alkaloids like tussilagin and pyrrolizidine, flavonoids including flavonols and glycosides, acids such as tannic acid, ferulic acid, caffeic acid, gallic acid, tartaric acid, p-hydroxybenzoic acid, malic

acid, phytosterols, triterpenes, choline, tussilagon, and volatile oils (Tetik, 2019).

Tussilago farfara L. Species Uses

The flowers of *Tussilago farfara* L. are used as a herbal remedy (**Farfarae flos**). As the name suggests, the herbal remedy exhibits expectorant and antitussive effects. It is effective in asthma, bronchitis, laryngitis, pharyngitis, whooping cough, influenza, and the common cold, particularly in cases of productive coughs and acute or chronic coughs. It moisturizes the lungs and prevents lung congestion. Studies have shown that tussilagon, a component in Coltsfoot, has anti-inflammatory properties. The leaves are made into poultices for use on burns, wounds, eye inflammations, and injuries, benefiting from the herbal remedy's anti-inflammatory and antibacterial effects. The soothing effect of mucilage is utilized to alleviate throat soreness. The flowers, when made into poultices, are used for skin diseases such as eczema, ulcers, and insect bites. The plant is available in syrup, extract, and tincture forms, and the dried leaves and flowers can be brewed in boiling water to make tea. It is also added to salads and dishes in folk cuisine (Lım, 2012).

The Distribution Areas of *Tussilago farfara* L. Species

Tussilago farfara L. is commonly found in Europe, China, Siberia, North America, Korea, and Turkey. In Turkey, it grows in various provinces including Tekirdağ, Ankara, Osmaniye, Sivas, Bolu, Samsun, Istanbul, Niğde, Kastamonu, Konya, Antalya, İzmir, Çanakkale, Isparta, Elazığ, Gümüşhane, and Erzurum (http 2).

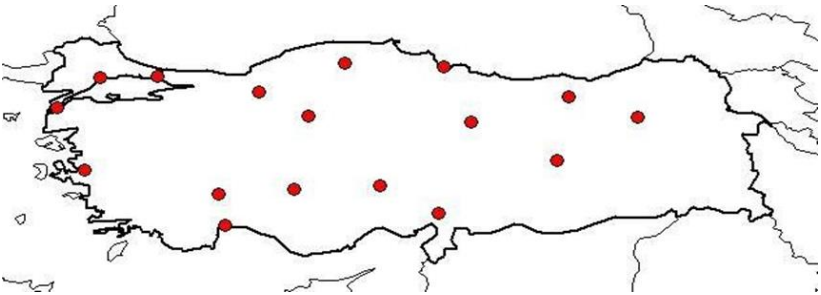

Figure 2. *The provincial distribution of Tussilago farfara L. species in Turkey (http 2)*

Tilia cordata MILLER

Tilia cordata MILLER belongs to the *Tilia* genus in the Tiliaceae family. It is known by the names "Linden" and "Winter Linden," as well as "Small-leaved linden." The flowers and leaves of the linden tree, which grows naturally in the wild, are harvested in July and August. Linden trees show slow growth in their early years but accelerate in development in later years. They have the ability to produce shoots (Sarıkaya & Doğdu, 2021).

Botanical Features of *Tilia cordata* MILLER

Tilia cordata MILLER is generally in the form of a tree but can also be found in the form of a tall shrub. It is a deciduous woody species, and it holds significance among deciduous woody plants. Its leaves are alternate, undivided, generally cordate or truncate at the base, serrate, petiolate, and its flowers are yellowish-white, pleasantly fragrant, arranged in an elongated cyme attached to an elongated membranous bract. The sepals are 5, free, petals 5, free, stamens numerous, free; sometimes staminodes are present. The ovary is superior, with 5 locules, each with 2 ovules, and a weakly 5-lobed style with a stigma. The fruit is obovate, indehiscent, usually 3-5 longitudinally veined, and sparsely pubescent. The entire fruit structure is attached to persistent bracts, and seeds are 1-2 in number (Yaltırık, 1966).

Tilia cordata MILLER Species Chemical Composition

Flavonoids (quercitrin, isoquercitrin, astragalin, hyperoside, rutin, tiliroside), essential oils (linalool, geraniol, geranyl acetate, farnesol), mucilage (rhamnogalactans, oronic acids), phenolic acids (caffeic acid, chlorogenic acid, p-coumaric acid), condensed tannins (proanthocyanidin B2), and amino acids are present in the above-ground parts of the plant (Toker et al., 2001).

Uses of *Tilia cordata* MILLER Species

The flower heads of *Tilia cordata* MILLER, known as "Tiliae flos," are used as the drug. Linden is one of the frequently employed plants in the treatment of colds during the winter season. From ancient times to the present, it has been utilized for its ability to induce sweating and its antipyretic effects. The drug is effective in conditions such as dry cough, febrile influenza/cold, bronchitis, and upper respiratory tract infections. It exhibits antitussive, antispasmodic, anti-inflammatory, analgesic, and expectorant effects. Additionally, it is used for migraines, gastric inflammations, throat pain, and as a diuretic. Linden tea is used for colds, and the steam from linden tea is used to relieve nasal congestion. Linden tea reduces stress and promotes sleep due to its sedative effect. Its use during breastfeeding and pregnancy is not recommended due to insufficient data (Sarıkaya & Doğdu, 2021).

Tilia cordata MILLER Species Distribution

Tilia cordata MILLER is naturally distributed in Istanbul, Turkey, and globally, it is found in the southern and northern extremes of Europe, as well as in the Caucasus region (http 4).

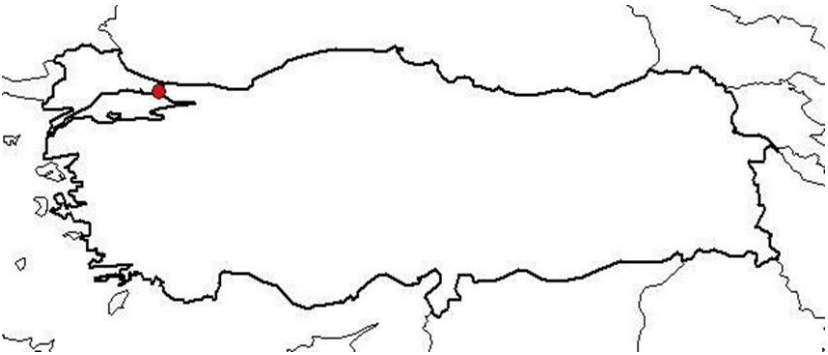

***Figure 3**. Provincial distribution of Tilia cordata MILLER species in Turkey (http 4).*

***Crocus sativus* L.**

Crocus sativus L. is a perennial herbaceous plant belonging to the *Crocus* L. genus in the Iridaceae (Iris) family. It is commonly known as "Saffron," "Saffron crocus," and "Saffron flower." The **Croci stigma (=Crocus)** drug is obtained from its flowers. The drug consists of the dried 3-branched stigmas collected from the flowering plant.

Botanical Features of Crocus sativus L. Species

Crocus sativus L. is a cormous, perennial herbaceous plant with a height of 20-30 cm, featuring purple flowers. Each flower of the plant contains three red stigmas. The flowers are singular or found in clusters at the end of a short scape, without a spathe. The perianth is actinomorphic, with 6 tepals fused at the base. The leaves are basal, developing together with or after the flowers, narrow, linear, and the upper surface is flat or channelled. The fruit type is a capsule. The corm is covered with brown, membranous scales (Özoğul & Kılıç, 2023; Tanker, Koyuncu & Coşkun, 1998).

***Crocus sativus* L. Species Chemical Composition**

Crocus sativus L. is a plant rich in volatile oils and aromas. These include various carotenoids such as lycopene, zeaxanthin, and carotenes. It carries volatile oil in the range of 0.4-1.5%, with crocin

and picrocrocin as its main components. The compound crocin is responsible for the bright yellow-red color of saffron (Gül, 2014).

Uses of *Crocus sativus* L. Species

While the primary use of Crocus sativus L. is in the kitchen due to its aromatic and pungent taste, it has also found its place in traditional medicine for the treatment of various ailments. Recent studies have indicated its antitussive, anti-inflammatory, sedative, antidepressant, anticonvulsant, cytotoxic, and anti-hyperlipidemic effects. In traditional medicine, it is used as an expectorant, for dysentery, measles, jaundice, stomach disorders, and insomnia. Ibn Sina mentioned in his work "Al-Qanun fi al-Tibb" that saffron was used for respiratory ailments. He stated that the fragrance of saffron eliminates inflammation of the lung membranes and that saffron oil facilitates breathing. Additionally, it has been noted to be effective in mucous membrane and skin inflammations, acute ear infections (swelling), and impotence. Ayurveda also mentions its effectiveness in diseases such as colds, asthma, cough, and arthritis. In Iran, it has been used for its hypnotic and sedative effects, while in ancient Rome, it was used for lung inflammations, cough suppression, liver disorders, and eye inflammations. In Azerbaijan, it has been employed in the treatment of boils. A mixture of egg yolk and saffron is applied to the boil for treatment. The combination of saffron, ginger, and cloves brewed into tea is believed to have a sedative effect. Saffron extracts and tinctures are used as pain relievers in stomach and intestinal disorders (Paşayeva & Tekiner, 2014).

Crocus sativus L. Species Distribution

Crocus sativus L. is a species naturally found in the Balkans, Eastern Mediterranean countries, and India. In Turkey, it is still cultivated in Safranbolu (Özkan, 2007)."

Inula britannica L.

Inula britannica L. is a perennial herbaceous plant belonging to the Inula L. genus in the Asteraceae (Daisy) family. It is commonly known as "Meadow Fleabane."

Botanical Features of *Inula britannica* L. Species

I. britannica is a biennial or perennial plant species, often found in disturbed meadow areas. It ranges from 15 to 75 cm in height, and its stem can be covered with spreading hairs or be glabrous. The flowers of the plant are bright yellow and occur singly or in clusters of 2-3. The plant prefers sandy, clayey, and loamy soil (Khan et al., 2010).

Chemical Composition of *Inula britannica* L. Species

The **Inulae flos** drug contains various flavonoids such as luteolin, isorhamnetin, isoquercetin, quercetin, 6-methoxyluteolin, spinacetin; terpenoids, steroids; lactones such as inulisin, britannin, and britannilactone; caffeic acid, chlorogenic acid, taraxasterol, mucilage, and the most important component, inulin (Özer, Çoban & Bouljak, 2020).

Uses of *Inula britannica* L. Species

The **Inulae flos** drug typically exhibits antitussive, diuretic, and antiemetic effects. Due to its antitussive effect, it is effective in productive cough and bronchitis. The flavonoids it contains reduce histamine levels to normal limits, decrease bronchial hyperactivity, and affect connective tissue. It acts as an expectorant by accelerating metabolism in the bronchi and has applications against asthma. The drug is also used for hiccups and indigestion. In severe symptoms, the flowers of the species are used, while the leaves are used for milder symptoms. Additionally, there are studies indicating its lipid-lowering, antidiabetic, antioxidant, anti-inflammatory, and anticancer effects. It is contraindicated in cases of diarrhea and chronic dry cough (Özer, Çoban & Bouljak, 2020).

***Inula britannica L.* Species Distribution in Turkey**

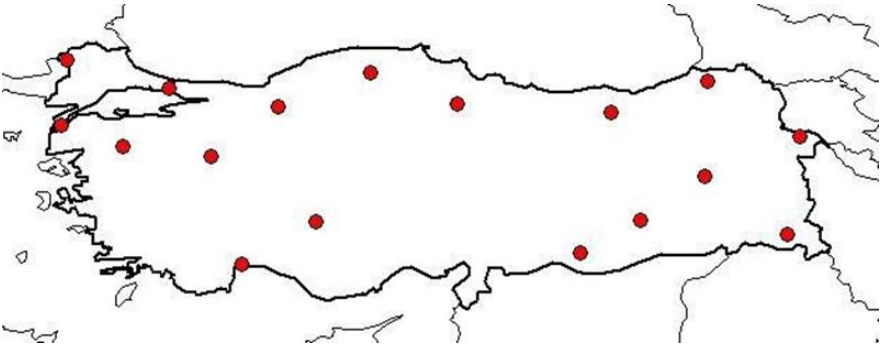

Figure 4. *Regional Distribution of Inula britannica L. in Turkey by Province (http 5).*

The species *Inula britannica* L. is distributed in Western, Eastern, and Central Europe, as well as in Iran, China, and the Caucasus. In Turkey, it is widespread in various regions, including Bolu, Şanlıurfa, Istanbul, Muş, Iğdır, Kütahya, Hakkari, Konya, Kastamonu, Gümüşhane, Ağrı, Edirne, Amasya, Diyarbakır, Antalya, Çanakkale, Artvin, and Balıkesir (http 7).

***Hedera helix* L.**

Hedera helix L. is a perennial, climbing plant belonging to the *Hedera* L. genus of the Araliaceae family. It is characterized by its evergreen nature, utilizing adventitious roots to climb walls or trees, and remains green throughout all seasons (Tanker, Koyuncu & Coşkun, 1998). Commonly known as 'Ivy,' 'English Ivy,' or 'Common Ivy,' it is also referred to colloquially as 'Wall Ivy,' 'Forest Ivy,' and 'Black Leaf (Akseki-Antalya)' (http 8).

Botanical Features of *Hedera helix* L. *Hedera helix* L. is an evergreen, woody perennial plant. Its leaves, with a maximum length of 8 centimeters, are shiny, green, and possess a leathery texture. Due to its persistent greenery, it has a long lifespan. The leaves are harvested in spring and early summer. The leaves emerging on the flowering stem are larger and lance-shaped compared to others. The plant's stem is climbing, long, and creeping, with a potential length

of up to 30 meters. The stem can have a diameter of more than 10 centimeters, and as it widens, it may give rise to shorter branches. The plant produces green-yellow flowers with a diameter of 5-7 mm, arranged in terminal clusters. The fruits are initially green and turn purple-black after maturing in winter. Each fruit contains 2 to 5 seeds (Lutsenko et al., 2010).

Chemical Composition of *Hedera helix* L.

Hedera helix L. contains approximately 3% hederacozide C (hederasaponin C), which is considered the active compound of the species. Triterpenoid saponins, ranging from 2.5% to 6%, are present, with trace amounts of monodesmosidic saponins. Small quantities of monodesmosidic compounds, such as hederagenin-3-O-β-D-glucoside and α-hederin, can be found in fresh leaves. The plant also contains various flavonoids, including quercetin, rutin, and caffeolquinic acid, as well as phytosterols and falkarinol (Büyükkök, Güngör & Genç, 2022).

Uses of *Hedera helix* L.

The leaves of *Hedera helix* L. are dried and used as a drug. The extract of dried leaves exhibits therapeutic effects as an expectorant, mucolytic, and antispasmodic in respiratory tract diseases such as bronchitis and coughs associated with the common cold. The secretolytic effects are attributed to glycoside saponins. Studies have also demonstrated the antimicrobial and anti-inflammatory properties of *Hedera helix* leaf extract. In addition to its use for weight loss, it is employed in creams, shampoos, and lotions as an anti-itch and moisturizing agent (Lutsenko et al., 2010).

It is not recommended to use *Hedera helix* in conjunction with antitussive medications containing dextromethorphan and codeine. Its use is not recommended for children under the age of 2, but for children aged 2-4 with persistent cough, it may be recommended by a physician (Büyükkök, Güngör & Genç, 2022).

Distribution Areas of *Hedera helix* L. Species in Turkey

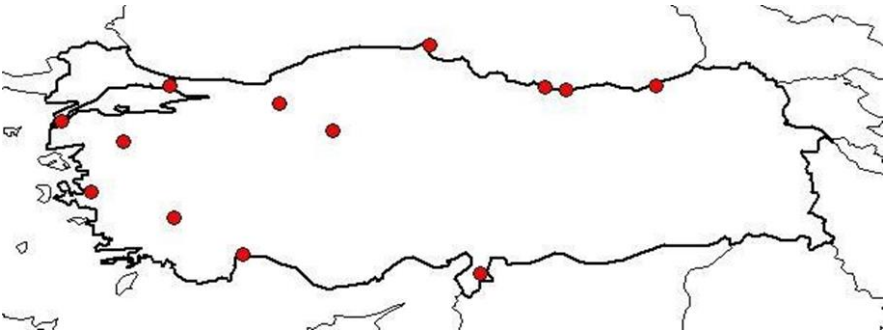

Figure 5. *Regional Distribution of Hedera helix L. Species in Turkey by Province (http 5)*

The species *Hedera helix* L. is distributed in temperate regions of Northern-Central Asia and Europe; in Turkey, it is found in Balıkesir, Bolu, Antalya, Ankara, Çanakkale, Istanbul, Ordu, Rize, Giresun, Sinop, Denizli, Izmir, and Hatay (http 5)

***Plantago major* L. subsp. *major* L.**

Plantago major L. is a perennial herbaceous plant species belonging to the *Plantago* L. genus in the *Plantaginaceae* family. Commonly known as "Sinir otu" (Nerve plant), "Damar otu" (Vein plant), and "Büyük sinirli ot" (Greater nerve plant) in Turkish folklore (Samuelsen, 2000).

Botanical Features of *Plantago major* L. Species

The height of *Plantago major L.* can reach up to 15 cm, but it may vary depending on the habitat in which it grows. The plant's leaves are toothed, have irregular margins, and are devoid of hairs. They exhibit parallel venation and form a rosette. The flowers of the plant are brownish-green, small, and located at the tips of non-branched spikes. The seeds are oval-shaped, with a maximum diameter of 1.5 mm, and have a bitter taste. Each capsule surrounds the seeds, and there are 8-16 seeds inside each capsule (Samuelsen, 2000).

Chemical Composition of *Plantago major* L. Species

Studies on *Plantago major L.* have revealed that the plant contains alkaloids, phenolic compounds such as caffeic acid derivatives, lipids, terpenoids, iridoid glycosides, and vitamin C (Akbaş, 2019).

Uses of *Plantago major* L. Species

The plant is used as an expectorant for coughs caused by colds, particularly effective in loosening phlegm. It plays a significant role in respiratory diseases such as shortness of breath, asthma, and bronchitis. Additionally, it is employed in circulatory system disorders, such as heart conditions. The plant is also utilized in the treatment of ulcers. It finds application in the treatment of skin diseases, inflammations, and wounds.

The tea obtained by brewing the leaves of *Plantago major* L. is used in the treatment of coughs and for gargling. The water obtained from the plant is used for dressing eye inflammations. The seeds or leaves of the plant are crushed into a poultice and applied to painful wounds (Korkmaz & Karakurt, 2015)."

Distribution Areas of *Plantago major* L. Species in Turkey

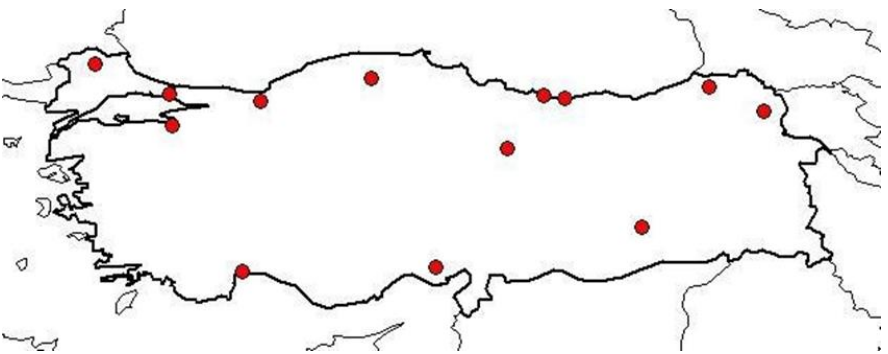

Figure 6. *Distribution of Plantago major L. species in provinces of Turkey (http 6)*

The *Plantago major* L. species grows in temperate regions worldwide, including Central Asia, North America, Southern Australia, North Africa, and Europe. In Turkey, it is distributed in Sivas, Adana, Ordu, Düzce, Kırklareli, Istanbul, Giresun, Kars, Diyarbakır, Bursa, Kastamonu, Artvin, Antalya, and Ağrı (http 6).

***Althaea officinalis* L.**

Althaea officinalis L. is a perennial herbaceous plant species belonging to the Malvaceae family within the *Althaea* L. genus. Commonly known as "Marshmallow" or "Hollyhock," it is utilized for its roots, leaves, and flowers (Sağlam, 2007).

Botanical Features of *Althaea officinalis* L. Species

Althaea officinalis L. typically thrives in damp areas like riverbanks. It usually reaches a height of 1-1.5 meters, occasionally reaching up to 2 meters. The plant has an upright growth habit, and its flowers are white to pink and hermaphroditic. The leaves are either entire or three-lobed, rounded/oval in shape, and have short stems. Both sides of the leaves are covered with numerous velvety hairs. The roots are fibrous, easily breakable, and can appear as yellowish-white or grayish cylindrical pieces (Baytop, 1999; Kaya et al., 2010).

Chemical Composition of *Althaea officinalis* L. Species

In the roots of *Althaea officinalis* L., constituents such as scopoletin, quercetin, kaempferol, chlorogenic acid, caffeic acid, p-coumaric acid, α-D-glucan, flavonoid glycosides, phenolic acids, coumarin, tannin compounds, and 18-21% mucilage are present. Additionally, amino acids are found. In the leaves and flowers, phenolic acids, coumarin compounds, flavonoid aglycones, aspartic acid, and glutamic acid are identified (Sağlam, 2007).

Usage Areas of *Althaea officinalis* L. Species

The leaves, flowers, and roots of the species have various uses related to coughs caused by the common cold. It has an antitussive effect on coughs caused by colds, emollient effects in soothing chest

irritation due to coughs, and a protective and soothing effect in the inflammation of gastric mucosa and pharyngeal mucosa, as seen in conditions like ulcerative colitis, peptic ulcer, and gastroenteritis.

The infusion, maceration, or decoction of the root of Althaea officinalis L., containing mucilage, is effective in the treatment of dry cough, throat soreness, and bronchitis. It is used as a mouthwash or gargle for irritation in the pharynx. Topically, it is utilized for the treatment of dermatitis, eczema, furunculosis, providing a protective and wound-healing effect on skin wounds. Studies on the species have revealed not only the mentioned effects but also antimicrobial, cytotoxic, antiprotozoal, antioxidant, and hypoglycemic effects (Kaya et al., 2010).

Distribution Areas of *Althaea officinalis* L. Species in Turkey

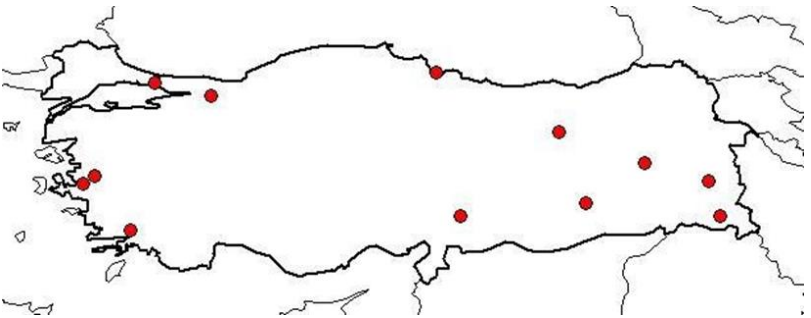

Figure 7. *Regional Distribution of Althaea officinalis L. Species in Turkey (http 7)*

The *Althaea officinalis* L. species is distributed globally in countries such as America, Russia, China, and Europe. In Turkey, it is found in various regions including Van, Istanbul, Samsun, Hakkari, Sakarya, Diyarbakır, Muş, Erzincan, Muğla, İzmir, Kahramanmaraş, and Manisa (Lim, 2012).

Primula veris L.

Primula veris L. is a perennial herbaceous plant species belonging to the Primulae L. genus of the Primulaceae family. It is commonly known as "Cowslip," "Oxlip," or "Keyflower."

Drug Name: Primulae radix, Primulae flos

Botanical Features of *Primula veris* L. Species

Primula veris L. is a perennial plant with underground rhizomes, ranging from 8 to 45 cm in length, and associated thick roots. The plant is known for its common names, including "Cowslip," "Oxlip," or "Keyflower. The leaves are 2.5-34 x 1-7 cm in size, with an ovate, oblong, or elliptic lamina. They are cordate, truncate, or cuneate at the base, with winged or unwinged petioles of varying lengths. The leaf margins are irregularly crenate. The flower arrangement consists of 2-6 flowers. Bracts are linear-triangular, shorter or longer than the pedicel. Pedicels are 1-20 mm in length. The calyx is 10-20 mm, obconical, with lobes measuring 3-6 mm, triangular-acute, nearly flat, and glandular-hairy. The corolla tube is 13-25 mm, equal to or longer than the calyx, with lobes measuring 5-10 mm, spreading, and golden-yellow in color. The fruit, in the form of a capsule, is shorter than the calyx (Davis, 1978).

Chemical Composition of *Primula veris* L. Species

In the roots of *Primula veris* L., phenolic glycosides such as primulaverin, 5-methoxy-methyl salicylate, and primeverin are present. Additionally, triterpenic saponins like primulasaponin and priverosaponin B22 acetate can be found. The flowers contain flavonoids such as rutin, kaempferol-3-O-rutinoside, isorhamnetin robinoside, quercetin robinoside, triterpenic saponins, and volatile oil (PDR for Herbal Medicines, 2004).

Uses of *Primula veris* L. Species

The flowers and roots of *Primula veris* L. are used as a drug. Thanks to the triterpenic saponins they contain, the flowers and roots exhibit expectorant, secretolytic, and diuretic effects. The high

proportion of saponins in the plant increases secretion in the bronchi, respiratory tract, and throat through the parasympathetic reflex pathway, reducing the viscosity of phlegm and demonstrating a mucolytic effect. Due to this effect, it is indicated in the treatment of chronic bronchitis. The plant also has anti-inflammatory effects. Its use is not recommended for children under 12 years old, individuals with gastric ulcer disorders, or those using aspirin. When used in high doses, vomiting and diarrhea may occur (Büyükkök, Güngör & Genç, 2022).

Distribution Areas of *Primula veris* L. Species in Turkey

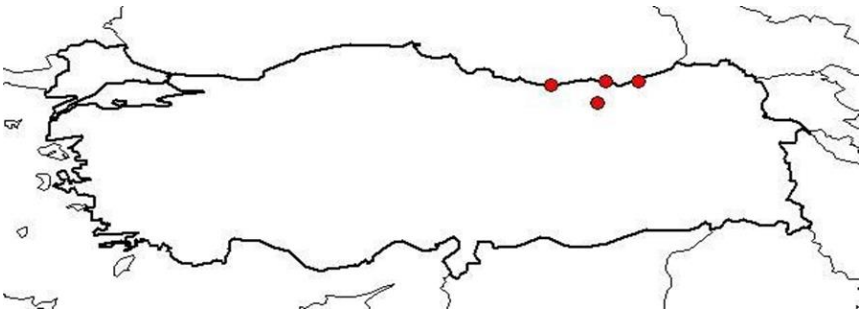

Figure 8. *Regional Distribution of Primula veris L. Species in Turkey (http 8)*

The *Primula veris* L. species is distributed globally in Western Asia, Central Asia, and Europe. In Turkey, it is found in regions such as Trabzon, Giresun, Rize, and Gümüşhane (http 8).

***Marrubium vulgare* L.**

Marrubium vulgare L. is a perennial herbaceous plant species belonging to the Marrubium L. genus of the Lamiaceae family. It is commonly known as "White Horehound," "Common Horehound," "Hound's Bane," "Marrubium," or "Horehound."

Common Names: Mayasıl otu, Yalancı ısırgan, Kara derme, Kukas otu, Boz ot, Köpek otu, İt sineği (Koç, 2019).

Drug Name: Marrubii herba

Botanical Features of *Marrubium vulgare* L. Species

Marrubium vulgare L. is a branched, herbaceous plant. The leaves of the species are serrated and stalked, covered in dense hairs. The stem can reach a height of 20-60 cm. The flowers are sessile, small, and arranged in clusters. The fruits are brownish-gray, approximately 2 mm in length, and can be round or flat at the tip (Koç, 2019).

Chemical Composition of *Marrubium vulgare* L. Species

The main component of the dried drug of *Marrubium vulgare* L. plant is the compound marrubiin, found at a rate of 0.7%. The precursor substance of marrubiin is premarrubiin, another diterpene variety. *Marrubium vulgare* L. contains marrubenon, peregrinin, ursolic acid, izoquercetin, caffeic acid, gallic acid, apigenin, vitexin, marruboside, vulgarin, vulgarol, monoterpenes, phenylpropanoic esters, steroids, tannins, alkaloids, and sugars (Koç, 2019; Büyükkök, Güngör & Genç, 2022).

Uses of *Marrubium vulgare* L. Species

In traditional usage, *Marrubium vulgare* L. is known for its expectorant, antipyretic, analgesic, diuretic, and carminative effects against coughs caused by the common cold. The flowering branches are used as a chest softener in pulmonary inflammation and asthma. It is present as an active ingredient in lozenges, herbal teas, and essential oils. Studies have shown that the drug of the species has antihypertensive, antimicrobial, antispasmodic, antioxidant, anti-inflammatory, hepatoprotective, antibacterial, hypolipidemic, and gastroprotective effects. The plant is also studied for its potential as a uterine stimulant and ulcer preventive. If cough symptoms persist after a week of use, usage should be discontinued, and medical advice sought. Individuals sensitive to the plant's content and children under 12 should avoid using it (Bağcı et al., 2019).

The Distribution Areas of *Marrubium vulgare* L. Species in Turkey

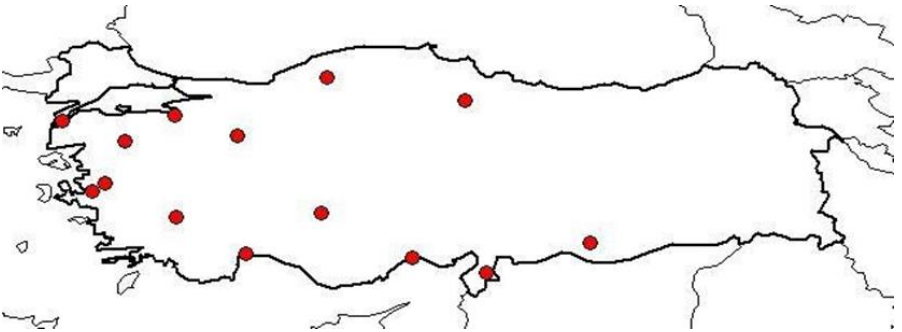

Figure 9. *Provincial Distribution of Marrubium vulgare L. Plant (http 9)*

The *Marrubium vulgare* L. species is distributed globally, being found in countries such as Cyprus, Italy, Kazakhstan, Iraq, Sweden, Uzbekistan, the United Kingdom, Belgium, the Netherlands, Denmark, Russia, Portugal, Egypt, and France. In Turkey, it is observed in various provinces including Karabük, Şanlıurfa, Amasya, Manisa, Antalya, Konya, Balıkesir, İzmir, Bursa, Mersin, Çanakkale, Hatay, Denizli, and Eskişehir (Koç, 2019).

***Angelica sylvestris* L. var. *sylvestris* L.**

Angelica sylvestris L. is a perennial herbaceous plant species belonging to the *Angelica* L. genus of the Apiaceae family. It is commonly known as "Wild Angelica" and "Kekire" in local parlance (http 10).

Botanical Features of *Angelica sylvestris* L. Species

Angelica sylvestris L. is a perennial herbaceous plant that can reach a length of 2 meters. It thrives in wet meadows, along riverbanks, and in moist areas of temperate regions. The flowers of the species are pinkish-greenish, arranged in umbels, and multi-layered. Each umbel contains 35 flowers, and the flowers are divided into two parts. The male organ of the plant matures before the female

organ. The leaves are arranged in a whorled pattern, and the stem is purple and erect (Elif & Ömeroğlu, 2019).

Chemical Composition of *Angelica sylvestris* L. Species

The content of *Angelica sylvestris* L. includes coumarins, polyphenols, tannins, resin, pectin, acetylenic compounds, sterols, phenolic acids, polysaccharides such as sugar and starch, sesquiterpenes, chalcones, and volatile oil. The volatile oil content is around 0.5-1%, and one of the significant components is Angelica acid (Sarker & Nahar, 2004; Gül, 2014).

Uses of *Angelica sylvestris* L. Species

Angelica sylvestris L. is used for expectorant purposes in coughs associated with the flu and the common cold, respiratory tract diseases such as chronic bronchitis and asthma, digestive system disorders including loss of appetite, gastrointestinal issues, and indigestion, as well as for urinary and joint-related problems like joint pain, rheumatism, and sciatica. The plant also exhibits anticancer, antimicrobial, antitumor, and hepatoprotective effects. Due to its estrogenic properties, it is used to alleviate menopausal symptoms in women. In Asian countries, it is used as a dietary supplement. The dried roots are powdered and used through infusion, and the volatile oil is applied to the body (Koç & Ömeroğlu, 2019).

Distribution Areas of *Angelica sylvestris* L. Species in Turkey

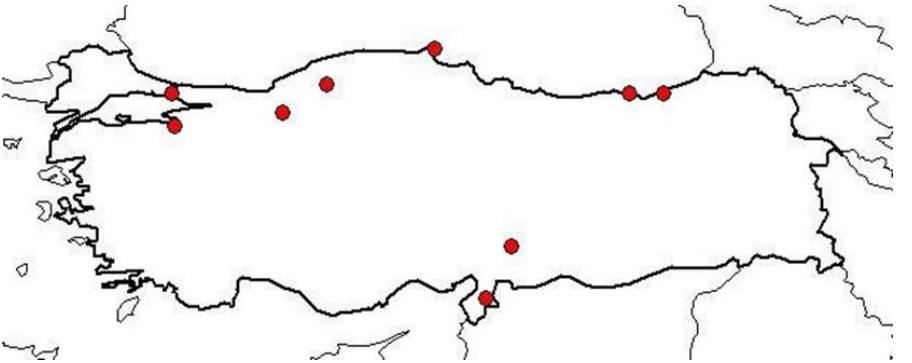

Figure 10. *Provincial Distribution of Angelica sylvestris L. Species in Turkey (http 13)*

The *Angelica sylvestris* L. species is found globally in Georgia, Europe, the Caucasus, Southern Russia, and Siberia. In Turkey, it is distributed in Bolu, Trabzon, Istanbul, Sinop, Karabük, Rize, Bursa, Kahramanmaraş, and Hatay (http 10).

***Mentha* x *piperita* L. Species**

Mentha x *piperita* L. is a perennial herbaceous plant species belonging to the Lamiaceae family and the *Mentha* L. genus. It is a hybrid of *Mentha aquatica* and *Mentha spicata*. In Turkey, it is known as "Bahçe nanesi" (Garden mint), "İngiliz nanesi" (English mint), and "Tıbbi nane" (Medicinal mint). The leaves of the plant are used as the drug (**Menthae piperitae folium**). The volatile oil obtained by steam distillation of the aerial parts (**Menthae piperitae aetheroleum**) is also widely used as a drug (Demirez, Nilufer & Ergun, 2014).

Botanical Features of *Mentha* x *piperita* L. Species

Mentha x *piperita* L. plant reaches a height of 45-80 cm. The flowers of the species are purple, pointed, and small. The roots branch towards the top, have a channelled and hairy structure, and are purple in color. The leaves are dark green, pointed and oval-

shaped, with opposing stems. Glandular trichomes are present on both sides of the leaves, with a higher count on the lower surface compared to the upper surface (Taştan-Onay, 2021).

Chemical Composition of *Mentha* x *piperita* L. Species

The most significant chemical component of *Mentha* x *piperita* L. plant is menthol, which is found in its essential oil. The majority of studies on the chemical composition of the species focus on the volatile oil present in the leaves. While the volatile oil component is around 0.5-1%, it contains approximately 40-60% menthol, 8-10% menthone, and monoterpenes such as mentofuran. Additionally, flavonoid varieties such as hesperidin, apigenin, rutin, eriocitrin, and luteolin, and terpenes including izomenton, mentofuran, eucalyptol, cineol, pulegone, carvone, limonene, β-pinene, α-pinene, germacrene, and viridiflorol are present in the chemical composition of the species. Phenolic acids such as rosmarinic acid are also part of the chemical constituents of Mentha x piperita L. The ratio of menthol, mentofuran, menthone, and pulegone determines the quality of the essential oil obtained from the Mentha x piperita L. plant. In a high-quality Mentha x piperita L. plant, the percentage of menthol and menthone is high, while the percentage of pulegone and mentofuran is low (Demirez, Nilufer & Ergun, 2014).

Uses of *Mentha* x *piperita* L. Species

The *Mentha* genus, including *Mentha* x *piperita* L., is the third most commonly used genus for respiratory system disorders in Turkey. The menthol derived from the leaves' essential oil has expectorant and soothing effects on the bronchi, making it effective as an antiseptic and expectorant in upper respiratory tract diseases like colds and flu. The plant exhibits antiemetic, carminative, and spasmolytic effects. Internally, menthol is used for nausea, stomach spasms, and gas elimination, while topically, it is applied for toothaches, sciatica, myalgia, arthritis, and migraines due to its cooling and local anesthetic properties. The extract of *Mentha* x *piperita* L. has antimicrobial effects against bacteria, viruses, and

fungi. Inhaling the vapor of the volatile oil is beneficial for nasal congestion, and a tea made from the leaves helps with throat inflammations, coughs, bronchitis, asthma, and alleviates muscle and abdominal pain. Studies have also observed the beneficial effects of a mixture of peppermint oil, beeswax, coconut oil, and eucalyptus oil applied to the chest for relieving coughs (Sıcak & et al., 2013).

Distribution Areas of *Mentha* x *piperita* L. Species in Turkey

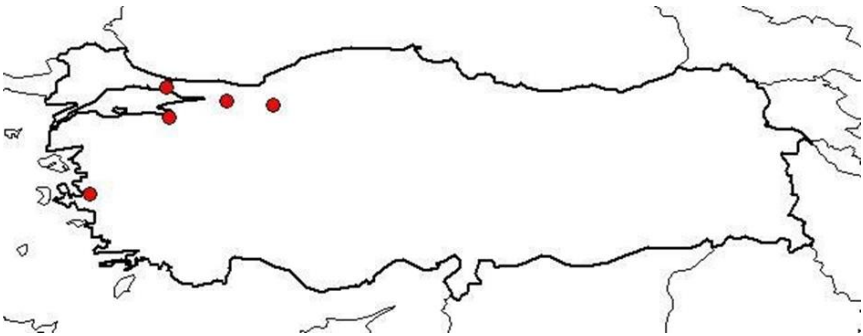

Figure 11. *Provincial Distribution of Mentha x piperita L. Species in Turkey (http 11)*

Mentha x *piperita* L. species is distributed in Bolu, Sakarya, Istanbul, Izmir, and Bursa in Turkey (http 11)."

***Malva neglecta* WALLR.**

Malva neglecta is an annual herbaceous plant species belonging to the *Malva* genus of the Malvaceae family. Commonly known as "common mallow" or "cheeseweed" among the public, it typically grows along roadsides and in gardens. The parts of the plant used as a drug include the roots, seeds, and leaves (Özer, Çoban & Bouljak, 2020).

Botanical Features of *Malva neglecta* WALLR.

Malva neglecta is a gray, hairy plant that reaches a height of 8-45 cm and possesses a thick taproot system. Its stem is commonly ascending or prostrate, rarely erect, often woody at the base except

for the tips, round, usually turning dark purple towards the lower part, occasionally entirely green, densely covered with star-shaped hairs from the base. The leaves of the species have long stalks. Although the plant's stem is generally in a prostrate position, an upright form is also occasionally observed. The stem base is woody, branching as it progresses towards the tips. The flowers are mostly axillary, 3 or 4 in number, rarely solitary. The corolla is egg-shaped, hairy along the base like a claw, and pink-colored. The petals are kidney-shaped, with fine wrinkles, having whitish-colored hilum and dark brown seeds. The fruit is cylindrical and hangs down. Its length is greater than the length of the leaves but shorter than the length of the flowers (Batsatsashvili & et al., 2017).

Chemical Composition of *Malva neglecta* WALLR. Species

The essential chemical components of *Malva neglecta* include mucilage, glycosides, flavonoids, and pectins. The leaves used as a drug (Malvae folium) contain approximately 8% mucilage. The flowers (Malvae flos) consist of around 7% anthocyanins such as malvidin, malvin, definidin, along with 10% mucilage and small amounts of tannins and coumarin (Özer & et al., 2020).

Malva neglecta WALLR. Species Uses

Malva neglecta, with its main component, mucilage, exhibits a protective effect on mucous membranes. Thanks to this effect, it is used in the treatment of nonproductive coughs, respiratory disorders such as bronchitis and pharyngitis, and inflammations of the mouth and throat. Additionally, Malva neglecta is employed in the form of infusion for stomach disorders like gastritis and ulcers. It is used as a decoction for soothing the chest and, when combined with nettle, meadowsweet, and willow leaves, it is used as a decoction for rheumatism (Yeşilyurt & et al., 2017).

Distribution Areas of *Malva neglecta* WALLR. Species in Turkey

Şekil 12. *Malva neglectaWALLR. .türünün Türkiye'de il bazında dağılımı (http 12).*

Figure 12. *Distribution of Malva neglecta WALLR. species on a provincial basis in Turkey (http 12).*

Malva neglecta species is distributed globally in Asia, Europe, and Africa. In Turkey, it is found in Adana, Karaman, Gaziantep, Şanlıurfa, Kars, Tekirdağ, Mardin, Sivas, Karabük, Samsun, Amasya, Konya, Artvin, and Kayseri (http 12).

Examples of Herbal Origin Active Ingredients Used in Cough Treatment

Medications used in the treatment of cough are beneficial in the symptomatic treatment of respiratory conditions such as asthma, bronchitis, and upper respiratory tract infections, including diseases like the flu and the common cold. In addition to antitussive, mucolytic, and expectorant-effective drugs, decongestants, antihistamines, and their combinations are also among the medications used in cough treatment (İmamoğlu, 2019).

Codeine

Codeine, found in the capsules of the *Papaver somniferum* L. (poppy) plant at a concentration of 0.5-3%, can also be synthetically produced through the methylation of morphine. Codeine acts by

inhibiting the cough reflex and is a potent antitussive medication. Due to its respiratory system-depressant effects, its use is not recommended for children under the age of 12. Codeine usage may lead to side effects such as dependency and sedation (Arslan & et al., 2008).

Noscapine

Noscapine, present in opium at a concentration of 2-10%, is known for its antitussive effects, which are equivalent to codeine (Arslan & et al., 2008).

CONCLUSION

Cough, fundamentally serving as both a reflex and a defense mechanism in the body, facilitates the expulsion of irritants resulting from inflammation in the mucosa, prevents the formation of secretions in the lungs, and hinders the entry of inhaled foreign substances into the respiratory system (Özdilekcan, 2018). Cough occurs in response to various stimuli in the airways, which can be thermal, inflammatory, chemical, or mechanical in nature (Çağlar, 2012). Cough consists of three consecutive phases, with the inspiratory phase forming the first phase. The inspiratory phase begins with a deep breath, the glottis is open, laying the groundwork for the clearance of the airways. The second phase is the compression phase, where the glottis temporarily closes, and pressure increases in the abdominal muscles. The expiratory phase is the final phase. The glottis suddenly opens, and coughing occurs with an explosive and rapid airflow (Ergen, 2018).

There are three types of cough based on the duration of persistence. Cough lasting less than three weeks is classified as acute cough, lasting three to eight weeks is subacute cough, and cough persisting for more than eight weeks is defined as chronic cough. Initially, every cough is acute, and depending on the cause or duration, it may transform into other types of coughs. The main cause of acute cough is upper respiratory tract infection, viral infection is the main cause of subacute cough, and gastroesophageal

reflux, upper/lower respiratory tract diseases are observed as the main causes of chronic cough. In addition, diseases such as asthma, chronic obstructive pulmonary disease, bronchiectasis, heart failure, colds, etc.; harmful gases such as some medications, cigarette smoke, allergens, humidity, and air pollution are significant factors in the formation and persistence of cough. If none of these specific factors are found in an examination, psychogenic cough should be considered. Psychogenic cough is generally observed in adolescents and children. The cause of psychogenic cough may be a desire for attention, an effort to attract attention, having an introverted character, or a presence in a controlling/uninterested family environment. No symptoms are observed in physical examinations. Cough is not observed during sleep or during an activity. Patients diagnosed with psychogenic cough should seek the help of a psychiatrist (Yanık, 2021).

Plants from the Apiaceae family such as *Pimpinella anisum* L. (anise), *Angelica sylvestris* L. (angelica); from the Myrtaceae family *Eucalyptus globulus* L. (eucalyptus); from the Lamiaceae family *Thymus vulgaris* L. (thyme), *Marrubium vulgare* L. (white horehound), *Mentha* x *piperita* L. (peppermint); from the Asteraceae family *Tussilago farfara* L. (coltsfoot), *Inula britannica* L. (British yellowhead); from the Tiliaceae family *Tilia cordata* MILLER. (lime); from the Iridaceae family *Crocus sativus* L. (saffron); from the Araliaceae family *Hedera helix* L. (ivy); from the Plantaginaceae family *Plantago major* L. (common plantain); from the Malvaceae family *Althaea officinalis* L. (marshmallow), *Malva neglecta* WALLR. (common mallow); from the Primulaceae family *Primula veris* L. (cowslip) are frequently used in the community for cough treatment. These mentioned plants exhibit antitussive, expectorant, and mucolytic effects and are used in various forms.

The physician should take a detailed medical history and consider all symptoms during the physical examination of a patient who presents to the hospital with a complaint of cough. The questions asked during the medical history should be clear and understandable, and the most suitable treatment should be applied to

the patient. Severe or prolonged cough negatively affects the patient's daily life and can lead to psychological distress. Therefore, seeking medical attention due to cough is quite common. Despite the frequent visits to hospitals, patients often turn to traditional practices instead of pharmacological treatments in the first step. Miscommunication between the doctor and patient, the patient's reluctance to ask questions, unwillingness to use medication, avoidance of side effects of drugs, and the desire for a natural approach have increased the tendency towards alternative medicine. Plants play a significant role in traditional practices, and results obtained through trial and error over the years have popularized the use of plants among the public. In this context, many plants have been used in folk medicine for cough treatment.

Plants have always held a significant place in human life throughout history. Initially used solely for nutritional purposes, plants were later employed for shelter and protection. Subsequently, as their healing properties were discovered, they became utilized in the treatment of diseases. In the present day, the widespread but often uninformed use of plants in traditional treatment methods can lead to undesirable outcomes in some patients.

The benefit-to-risk ratio of well-analyzed plants or various herbal remedies can be advantageous when used at appropriate doses determined by experienced and trained healthcare professionals, with close monitoring of potential side effects. This is beneficial not only for the treatment of symptoms but also for preventive purposes. The scarcity of clinical studies in the field is noteworthy.

Pharmacists, being the healthcare professionals closest to and trusted by individuals seeking advice in the health domain, play a crucial role. The presence of experienced pharmacists with knowledge in this field is essential. Pharmacists receive various courses related to plants throughout their undergraduate education and graduate with fundamental knowledge about herbal drugs. Therefore, they constitute an important professional group that should have a say in this field. They are among the primary groups

of healthcare professionals that can be consulted by the community regarding herbal drugs.

Plants have a widespread use in traditional folk remedies. Therefore, systematically compiling and sharing ethnobotanical studies conducted in the field, along with laboratory research on the mechanisms of action of plants used in traditional treatments, would contribute to the discovery of new drug molecules and active ingredients in the field.

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BÖLÜM III

Medicinal plants and cosmeceuticals used in hyperpigmentation and hypopigmentation

Leyla GÜVEN[1]

Introduction

Plants constitute a very rich resource for the development of potential dermocosmetic candidates due to their traditional use in therapy. Likewise, traditional uses of plants are used in the development of cosmetic products for skin care. (Wang & ark., 2006) The use of herbal extracts or phenolic compounds obtained from plants in cosmetic products has gained importance in recent years.(Mukherjee & ark., 2011)

Cosmetic; Prepared to be applied to various external parts of the human body such as epidermis, nails, hair, lips and external genital organs, teeth and oral mucosa, its sole or main purpose is to clean these parts, give fragrance, change the appearance, and /or correct body odors, and/or protect or all preparations and substances

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whose purpose is to keep them in good condition.(Sağlık Bakanlığı, 2005)

Cosmeceuticals; They are also known as “active cosmetics” and are among drugs and cosmetics. Cosmeceuticals; They are products that have a cosmetic effect by changing the structure and functions of the skin and skin patches positively through biophysiological effects.(Çomoğlu, 2012) Although people initially used cosmetic products to improve their psychology, to give fragrance, and to color, recently they have been used for many reasons such as repairing damaged skin, preventing or delaying aging, preventing damage from ultraviolet rays, and increasing the protective effect of the skin There are also many reasons to choose cosmetic products. These can be given as age, gender, socioeconomic level, and underlying diseases. Cosmetic products are especially preferred for acne, skin moisturizing, blemish problems, reducing the effects of aging and protecting against adverse conditions.(Kaymak &Tırnaksız, 2007) The structure of cosmetic products is very complex. When the structure of these products is examined, many of them contain herbal extracts and natural active ingredients.(Mukherjee & ark., 2011)

Many naturally sourced formulations have been used for the treatment of hypopigmentation, hyperpigmentation and melasma, which are cosmetic problems. Plant-derived products used in these formulations are used more than animal-derived products. Natural skin care products should be hypoallergenic and easily absorbed by the upper layers of the skin. The high number of side effects of animal products have made herbal extracts more preferred.(Şenol, 2016)

Long-term topical skin care solutions (both cosmetic and cosmeceutical) are required to solve the hyperpigmentation problem on the skin. Although conventional treatment agents such as hydroquinone, corticosteroids, and kojic acid are highly effective, local or systemic side effects (e.g., ochronosis, atrophy, carcinogenesis) occur with long-term exposure. Therefore, in order

to eliminate pigmentation problems, it is necessary to develop new products with less side effects and to investigate natural and herbal sources. Active isolated compounds from plants such as arbutin, aloesin, gentisic acid, flavonoids, hesperidin, licorice, niacinamide, yeast derivatives and polyphenols inhibit melanogenesis without melanocytotoxicity by different mechanisms.(Zhu &Gao, 2008) Hypopigmentation and hyperpigmentation products are available as commercial preparations for dermocosmetic purposes to achieve a lighter skin appearance. They are also used in the clinical treatment of pigment disorders such as melasma, post-inflammatory hyperpigmentation and hypopigmentation. Raw materials and active ingredients obtained from natural sources, especially herbal sources, are increasingly used. Modern phytocosmetics require standardized defined extracts from the plant matrix. In recent years, both cosmetic oils of plant origin and plant natural cosmetics have been reintroduced to the market following consumer demand. The term phytocosmetics has begun to be used frequently with the use of plants, plant extracts, volatile or fixed oils in cosmetic products, especially skin and hair care products.(Koluman &Süzgeç-Selçuk, 2016) In this review study, plants used as topical treatment in hyperpigmentation and hypopigmentation disorders and literature containing natural active ingredients were examined. In addition, cosmeceutical products used commercially in Turkey were researched using the Rx Media Pharma program, and plant or natural active ingredients in their formulations that may be responsible for the effect were presented in our study.

2. General information

2.1. Structure of the Skin

Skin, which is of indispensable importance for human life, is the largest organ of our body. Skin originating embryogenically from ectoderm and mesoderm; It consists of epidermis, dermis and subcutis. The epidermis is listed from bottom to top as Stratum basale, Stratum spinosome, Stratum granulosum, Stratum lucidum and Stratum corneum. Stratum lucidum is located in the thick

epidermis and provides transition from Stratum granulosum to Stratum corneum. Stratum basale is the lowest layer and consists of kerenocytes and melanocytes. Cells called melanocytes are dentric cells that synthesize melanin from organelles called melanosomes and deliver it to keratonocytes. New keranocytes formed by the division of basal cells form the spinous. It is also the largest layer of the epidermis. Stratum corneum is the outermost layer consisting of dead cells called corneocytes that are not capable of division.(Miloglu & ark., 2023)

2.2. Deride Pigmentasyon Mekanizması

Pigmentation in our skin occurs as a result of physiological events, and these are: The development and density of melanocytes, structural and enzymatic events in melanosomes, melanin production, transfer of melanosomes to dendrites, transfer of melanosomes to keranocytes, distribution of melanin in the subbasal layer. The first three are genetic steps and the others are the steps targeted by cosmetic products. Apart from genetic factors, another important factor is exposure to UV rays. Events that cause skin pigmentation due to UV (sun rays) are as follows: Pigmentation polymerization of melanin, change in the distribution of melanosomes in the skin, activation of responsible enzymes in melanin-producing cells, increased release of the hormone that stimulates melanocyte production, and transfer of melanin to the upper epidermis to prevent damage to the skin from UV (sun rays). Melanin is synthesized in melanosome organelles in melanocytes. Melanogenesis is the production of melanin. Melanin production; Its activity is determined by three enzymes: tyrosinase, tyrosinase-related protein 1 and tyrosinase-related protein 2. The main determinant in melanogenesis is the tyrosinase enzyme. The first step in obtaining melanin is tyrosinase enzyme transformations and the formation of pheomelanin with the presence of eumelanin, cysteine and glutathione. Other stages proceed spontaneously if the physiological pH is appropriate. While genetic factors are also effective in melanogenesis, the hormone, which is a peptide derived

from proopimelanocortin, stimulates pigmentation as a result of sun exposure.(Alğın Yapar, 2017)

2.3 Tyrosinase Enzyme inhibitors

It is also necessary to mention the tyrosinase enzyme and its functions, as it is an enzyme frequently mentioned in in vitro experiments in spot treatment. Tyrosinase is a copper-containing enzyme that is widely found in plants, microorganisms and animals and is involved in the synthesis of melanin in skin and hair. It is an enzyme required for melanin pigments, which are abundant in plants and animals, and catalyzes melanin biosynthesis in three steps: hydroxylation of tyrosine to 3,4-dihydroxyyphenylalanine (DOPA), oxidation of DOPA to dopaquinone, and oxidation of 5,6-dihydroxyindole (DHI) to indolquinone. Abnormal production of melanin pigment has been a serious aesthetic problem since the beginning of humankind (Thody, 1993). Tyrosinase inhibitors are widely used in the cosmetic industry and food industry due to their skin whitening effect (Shimizu & ark., 2000). Some of the medicinal plants with high tyrosinase inhibitor effect are widely used in cosmetics. Tyrosinase inhibitors have attracted strong interest from both the cosmetics industry and the food industry. Some of the naturally occurring medicinal plants with high tyrosinase inhibitory effects are widely used in cosmetics. Tyrosinase inhibitors also have strong antioxidant activity. Because plants that receive high amounts of sunlight induce harmful active oxygen radicals in order to protect themselves from the harmful rays of the sun. Therefore, plants must have an effective antioxidation system for their strong antioxidative components to protect themselves from damage. As a result of tyrosinase inhibitor activity studies: Skin beauty and health can be supported by protecting the skin from external and internal harmful agents with cosmetic products. (Masuda & ark., 2005)

2.4 Vitiligo

Clinically, milky-white depigmented macules, which begin with melanocyte destruction and manifest themselves with the loss of melanocytes in number and function, are known as an

asymptomatic, chronically progressive pigmentation disorder of unknown cause. Areas where pigment loss occurs expand towards the environment and merge. (Parsad & ark., 2003) Hypopigmentation is a cosmetic problem that can be seen at any age, the cause of which is unknown, but it is not fatal, but it also creates a visual discomfort that negatively affects the human mood. (Önder & ark., 2018) Hypopigmentation, which has an idiopathic etiology, is thought to develop through genetic, autoimmune biochemical and neural mechanisms. (Ortonne, 2012) Additionally, psychological problems frequently occur after a physical trauma. It can occur as a result of losing a family member, job loss, traffic accident, heat, UV, pressure, contact with chemicals, sunburn, and the use of various medications. (Spritz, 2012). The epidemiology of vitiligo does not differ greatly between races and genders in terms of the incidence of the disease. While vitiligo is more difficult to detect in white-skinned patients unless they are exposed to the sun, the disease is more obvious in dark-skinned patients because the color difference occurs. (Karıncaoğlu &Doğan, 2001)

2.4.1 Treatment Methods in Vitiligo

Interest in natural products and the tendency to treat diseases with natural products is increasing day by day. The products that nature offers us protect our health and provide us with many benefits both in treatment and in our daily lives. The main natural products we benefit from are plants and the compounds obtained from them. Plants; It offers us various treatment opportunities to eliminate various skin diseases and many other ailments, from flu infections to cancer. Plants and their active compounds are used in various ways in the treatment of vitiligo. Plants, especially those containing furocoumarin, are known to be the most mentioned plants in the treatment of vitiligo. Besides; Different plants are also mentioned that are used in the treatment of vitiligo, but do not contain this group of compounds. Not only plants, but also secondary compounds obtained from plants are involved in the treatment of vitiligo. Furocoumarin (psoralens) and furochromone compounds are

frequently encountered among natural products used in the treatment of vitiligo.(Yıldız & ark. 2013)

2.4.1.1 Furocoumarins

It is also included as a group of coumarins, a subgroup of secondary compounds known in the plant kingdom with a furan ring attached to a coumarin unit. In addition, there are also synthetically produced furocoumarins. Furocoumarins are widely used in photochemical treatments against different skin conditions such as psoriasis and vitiligo. (Santana & ark., 2004) The use of psoralens group of compounds, known with their most basic structure, among the furocoumarins, in vitiligo dates back to ancient times. Mechanistically, thymine acts by binding to the DNA nucleotide, thereby inhibiting the spread of pathogenic cells or the production of highly reactive singlet oxygen in damaged tissues. (Ashwood-Smith & ark., 1986)Psoralens are linear furocoumarins that are quite common in plants. In general, plants containing psoralens are used internally and externally to support skin pigmentation and tanning. Psoralen absorbs nearby ultraviolet light thanks to its large chromophore, allowing this radiation to stimulate the formation of melanin pigments. Body areas that respond best: It is determined as face and body, and the most common side effects are vomiting and erythema. (McNeely &Goa, 1998)

2.4.1.2 Furokromon

Kellin is a furochromone compound and is known as a compound found in the ripe fruits of Ammi visnaga, a Mediterranean plant. This plant also carries the compound visnagi (Table 1)(Önder & ark., 2018)**.**

Table 1: *Plants Used in the Treatment of Vitiligo (Önder & ark., 2018)*

Plant	Family	The part of plant
Acronychisa baerverlenii	Rutaceae	Whole plant
Ammi majus	Apiaceae	Fruit
Angelica sinensis	Apiaceae	Root
Brosimum gaudichaudi	Moraceae	Root bark
Camella sinensis	Theaceae	Leaf
Capparis spinosa	Capparaceae	Root bark and seed
Citrus bergamia risso	Rutaceae	Oil
Cnidum monnieri	Apiaceae	Fruit
Dorstenia brasliensis	Moraceae	Rhizome
Ficus carica	Moraceae	Leaf
Ginkgo biloba	Ginkgoaceae	Leaf
Gundelia tournefortii var. tournefortii	Asteraceae	Seed, latex
Nigella sativa L.	Ranunculaceae	Seed
Pastinaca sativa	Apiaceae	Root
Polypodium leucotomas	Polypodiacea	Herba
Psoralea corylifolia	Leguminosa	Seed, Fruit
Pyrostegia venusta	Bignoniaceae	Leaf and flower
Vernonia anthelmintica	Asteraceae	Seed
Ruta montana L.	Rutaceae	Herba
Treculia obovoidea	Moraceae	Herba

2.5. Hyperpigmentation

Hyperpigmentation, which is a darkening of the skin color, may occur due to exposure to sun/UV rays, various chemicals (drugs, cosmetics, etc.) or the presence of certain diseases. Additionally, it may occur in response to mechanical trauma, chemical peeling, laser applications, acne or some skin diseases. Hyperpigmentation, especially when it occurs in the facial area, can

negatively affect individuals socially. Causes of acquired hyperpigmentation include i. skin diseases (melasma, post-inflammatory hyperpigmentation) or other causes. Sun rays, chemicals and hormones are the most common causes of acquired hyperpigmentation, and as a general approach, avoiding sun rays and UV sources, choosing alternatives to hormone preparations (oral contraceptives), avoiding chemicals/cosmetic products that increase/cause skin sensitivity (sensitization) and sun protection. It is recommended to use the products.(Perez-Bernal & ark., 2000)

Hyperpigmentation can pose a significant cosmetic problem and psychosocial stress for patients. Treatment of diseases caused by hyperpigmentation involves a very long process, and treatment is more difficult, especially in people with dark skin. The aim of treatment is to reduce the number of melanosomes and prevent the proliferation of melanocytes. In the treatment of hyperpigmentation, identifying the underlying cause is important in choosing the most appropriate treatment for the patient. Understanding the etiopathogenesis of diseases that cause hyperpigmentation and histologically determining the pigment level in the skin are guiding in the selection of treatment. The amount of color change depends on the location of melanin deposition. While epidermal involvement manifests itself as brown discoloration, dermal deposition appears as blue-gray. Pigmentation at the epidermal level is more common than dermal pigmentation and responds better to treatment.(Korkmaz &Erturan, 2010)

2.5.1 Melasma

Melasma, also known as Chloasma and Pregnancy Mask, is a hyperpigmentation condition with distinct borders that is commonly seen as irregular spots and spots on the face, neck and forearms. It is generally seen in women, especially those of Spanish and Asian origin. While dark-skinned races from India, Pakistan and the Middle East experience this problem in the early stages, it develops in adolescence and later years in other populations. This condition can last for years, with pigmentation increasing in the summer

months due to excessive exposure to the sun. The exact cause of melasma is unknown. But there are multiple factors among the reasons. The most important of these factors are genetic tendency and UV exposure. At the same time, birth control pill use, pregnancy and cosmetics are among these factors. Estrogen and perhaps progesterone can also cause melasma. Frequent development of the disease during pregnancy, use of birth control pills, diethyl stilbestrol administration and post-menopausal hormone therapy has led to this belief. This disease, known as the "mask of pregnancy", decreases or disappears after birth, especially in lightly pigmented individuals, but it can continue as long as birth control pills are taken. Other hormones such as melanotropic peptide and β-lipotropin secreted from the pituitary gland may also play a role in the origin of the disease. Some cosmetic products can cause stains. However, although the majority of women with melasma use cosmetic products, a specific chemical substance has not been identified so far. Melasma lesions occur only on skin exposed to the sun. Brown, gray and even blue spots turn into irregular spots. Lesions may occur linearly or in a starburst distribution. Although there is no definitive cure for melasma, some approaches have been developed. While it may disappear after birth, it may remain for years or for life. It is important to determine which histological type of melasma is present before starting treatment. Wood's light examination is usually sufficient, but biopsy may be required in very darkly pigmented patients. If melasma is dermally located, what can be done to lighten the pigment color is limited. Regardless of location, however, sun exposure should be minimized and broad-spectrum sunscreens should be used daily to protect the skin from UV rays. In patients with epidermal type melasma, lightening agents may be beneficial when used for a long time. It is a very important preventive measure for women prone to melasma to avoid frequent pregnancies.(Çelebi &Kahraman, 2005)

2.5.2 Treatment Methods Used in Hyperpigmentation

It is known that the demand for skin whitening applications is increasing in the world and that systemic or locally effective skin

whitening products are used both to lighten the natural skin color and to remove spots that occur due to various reasons. It is known that hyperpigmentation, which is a darkening of the skin color, can occur due to exposure to sun/UV rays and various chemicals (medicines, cosmetics, etc.) or in response to some diseases, acne or some skin diseases. In order to eliminate skin spots due to hyperpigmentation, after examining the cause, depigmentation products, chemical peeling, cryoscopy, laser application or surgical procedures can be applied. Active compounds for depigmentation can be grouped according to their mechanism of action as those effective before melanin synthesis, during melanin synthesis, after melanin synthesis, and others. When skin whitening active ingredients and formulations are examined structurally, it is seen that biotechnological, botanical or chemical origin compounds are applied as pharmaceutical preparations applied to the skin (cream, emulsion, gel, solution, etc.) or orally taken preparations (capsule, tablet, etc.). These compounds have been prepared in recent years by using nanotechnology and modern pharmaceutical carrier systems (nanoemulsion, nanosphere, nanocapsule, nanosome, solid lipid nanoparticle, nanostructured lipid carriers, niosome, ethosome, liposome, etc.) and are marketed in the pharmaceutical, cosmetic or food category in line with international legal differences. appears to be presented.(Alğın Yapar, 2017)

Skin whitening active compounds, which can be used alone or in combination, generally show their effects in three ways. These; i. eliminating skin tone discrepancy, ii. removing pigmentation disorders (freckles, age or sun spots, melasma, acne scars, etc.), iii. It lightens skin tone by reducing natural skin pigmentation (common examples of applications for naturally dark skin in Asia and Africa). The mechanisms of action of active compounds applied externally within the scope of skin whitening generally target various stages of melanin synthesis (pre-melanin synthesis, synthesis phase, post-melanin synthesis), and in order to obtain a synergistic effect, physical/chemical effective skin peelers or device applications

(ultrasound, ultrasound, etc.) It is known that laser etc.) are used.(John & ark., 2005)

With the developing world order, individuals' increasing desire to live comfortably and to be healthy, beautiful and well-groomed enables the rapid development of the cosmetics and dermocosmetics industry and increases the demand for the use of these products. In recent years, people's increasing interest in natural products, especially herbal ones, instead of synthetic chemicals in every field has led to the increase of phytocosmetics in the cosmetics industry. Plants, herbal oils and extracts, which have been used with simple methods for centuries to stay young and beautified, have now begun to be included in phytocosmetic products. As they are preferred, their number and variety are increasing day by day. Although there are not many scientific studies on phytocosmetic products and the most preferred plants in this field, the increasing demand day by day attracts the attention of scientists and directs them to research in this field. (Koluman &Süzgeç-Selçuk, 2016) (Table 2)

Table 2. Plants Used in Hyperpigmentation (Ghafari & ark., 2017) (Kim & ark., 2015) (Han & ark., 2014) (Dej-adisai & ark., 2014)(Tengamnuay & ark., 2006) (Jin & ark., 2006)

Plant	**Family**	**Part of Plant**
Achillea ptarmica	Asteraceae	Root
Alcea digitata	Malvaceae	Flower
Althaea officinalis	Malvaceae	Flower
Alkanna tinctoria	Boraginaceae	Leaf and Root
Allium cepa	Alliaceae	Seed
Allium sp.	Alliaceae	Seed and Root
Althaea officinalis	Malvaceae	Flower
Alyssum sp.	Brassicaceae	-
Amygdalus communis	Rosaceae	Seed, Root, Oil
Androsace umbellata	Primulaceae	-
Apium graveolens	Apiaceae	Leaf, branch
Aristolochia sp.	Aristolochiaceae	Root

Artocarpus lacoocha	Moraceae	Wood
Artocarpus sp.	Moraceae	Root
Arum italicum Mill.	Araceae	Root
Astragalus sp.	Fabaceae	Mastix
Beta vulgaris	Chenopodiaceae	Leaf
Brassica nigra	Brassicaceae	-
Brassica oleracea	Brassicaceae	Seed, Leaf
Bryonia sp.	Cucurbitaceae	Root
Caesalpinia bonduc	Caesalpiniaceae	-
Capparis sp.	Capparaceae	Fruit
Carthamus tinctorius	Asteraceae	Fruit
Chrysanthemum morifolium	Compositae	Leaf
Cicer arietinum	Leguminosae	-
Citrus medica	Rutaceae	Fruit
Convolvulus scammonia	Convolvulaceae	Branche
Costus sp.	Costaceae	Root
Cucumis colocynthis	Cucurbitaceae	Cortex
Cucurbita mexicana	Cucurbitaceae	Cortex
Cucumis melo	Cucurbitaceae	Seed, Cortex
Cucumis sativus	Cucurbitaceae	Fruit
Curcuma zedoaria	Zingiberaceae	Root
Daphne mezereum	Thymelaeaceae	Leaf
Dorema sp.	Cucurbitaceae	Fruit
Eruca sativa	Brassicaceae	Seed
Fagopyrum tataricum	Polygonaceae	-
Ficus carica	Moraceae	-
Flemingia grahamiana	Acanthaceae	Fruit
Gentiana lutea	Gentianaceae	Root
Gypsophila struthium	Caryophyllaceae	Root
Hemerocallis sp.	Hemerocallidacee	Root
Hypericum sp.	Clusiaceae	Flower
Hyssopus officinalis	Lamiaceae	Aerial part
Indigofera tinctoria	Fabaceae	-
Iris sp.	Iridaceae	Seed, Root
Jasminum sp.	Oleaceae	Leaf, Fruit
Laurus nobilis	Lauraceae	-
Lepidium draba	Brassicaceae	Aerial part
Lepidium sativum	Brassicaceae	Seed
Linum sp.	Linaceae	Seed
Lolium temulentum	Poaceae	Seed

Lupinus termis	Fabaceae	Seed
Lycium afrum	Brassicaceae	Leaf, Seed
Mandragora officinarum	Solanaceae	Branche
Moringa arborea *M. oleifera*	Moringaceae	Seed
Muscari comosum	Hyacinthaceae	Bulb
Myrtus communis	Myrtaceae	Leaf
Narcissus sp.	Amaryllidaceae	Flower, Seed
Nerium sp.	Apocynaceae	Leaf
Nymphaea sp.	Nymphaeaceae	Root
Persicaria hydropiper	Polygonaceae	Arial parts
Pistacia sp.	Anacardiaceae	Fruit
Plumbago europaea	Plumbaginaceae	
Polygonum hydropiper	Polygonaceae	Fruit
Portulaca oleracea	Portulacaceae	Leaf
Raphanus sp.	Brassicaceae	Seed, Leaf
Rheum sp.	Polygonaceae	Root
Rhodiola sachalinensi	Crassulaceae	Leaf
Ricinus communis	Euphorbiaceae	Seed
Rosa canina *R. moschata*	Rosaceae	Flower
Rubia tinctorum *R. cordifolia*	Rubiaceae	Root
Ruta graveolens	Rutaceae	Leaf
Senna sp.	Caesalpiniaceae	Leaf
Terminalia chebula	Combretaceae	Leaf
Terminalia chebula	Combretaceae	Leaf
Trachyspermum copticum	Apiaceae	Seed
Trigonella foenum-graecum	Fabaceae	Seed
Triticum vulgare	Poaceae	Seed
Urginea maritima	Hyacinthaceae	Root
Vicia ervilia	Fabaceae	Seed
Vicia faba	Fabaceae	Bark, Fruit

2.6 Active Ingredients Used in Hyperpigmentation

Considering the color changes seen in skin and hair, we see that the compositions of melanins are arranged differently. However, altered cutaneous melanin production can cause significant aesthetic

problems. These can be listed as melasma, post-inflammatory hyperpigmentation, freckles and age spots. In Western culture, achieving a tan is still desired. In recent years, the tanning industry has expanded despite warnings about overexposure to the sun and UV rays. In Eastern culture, light skin, a tradition that has lasted for a century, is considered to equal youth and beauty. One of the challenges for the cosmetic industry is the development of preparations to bleach hyperpigmented lesions or achieve safe whitening. In recent years, interest in skin whitening has increased greatly. Targeting the enzyme tyrosinase, as the key enzyme of melanogenesis, is one of the most prominent targets for depigmentation. Tyrosinase inhibitors can be classified as competitive, non-competitive or mixed type. Knowledge of the type of inhibition is important to achieve better skin whitening. Synergistic effects may occur as a result of combined treatments. Arbutin is an example of a competitive tyrosinase inhibitor and aloesin is an example of a non-competitive tyrosinase inhibitor. The antioxidant capacities of extracts obtained from plants can be tested.(Smit & ark., 2009)

Arbutin: Arbutin, a naturally occurring β-D-glucopyranoside derivative of hydroquinone, is found in the dried leaves of some plants. Kojic Acid has an effect similar to azelaic acid. It reduces skin discoloration in a short time (8-12 weeks) by blocking excess melanin in the skin. It is one of the active ingredients effective in the treatment of blemishes or hyperpigmentation. It prevents excess tyrosine oxidation by combining with enzymes immediately after application to the skin. It has been clinically proven that it is also effective in pigmentation caused by UV.(Gökce & ark., 2016; Zhu &Gao, 2008)

Aloesin: Aloesin, a compound isolated from the aloe plant, has been proven to competitively inhibit tyrosinase from human, fungal sources. Aloesin, together with arbutin, appears to synergistically inhibit melanin production by mechanisms combining competitive and non-competitive inhibitions of tyrosinase activity.(Choi & ark., 2002)

Hesperidin: Hesperidin is a bioflavonoid commonly found in the peel and membranes of citrus fruits. Hesperidin has demonstrated the ability to inhibit melanin synthesis without cytotoxicity. Therefore, hesperidin offers potential skin-lightening benefits, including improving overall skin tone and anti-aging effects.(Zhang & ark., 2008) (Proteggente & ark., 2003)

Niasinamid : Niacinamide is a biologically active form of niacin (vitamin B3) commonly found in many root vegetables and yeasts. Using cultures of human melanocytes and keratinocytes, we showed that niacinamide inhibited the transfer of melanosomes from melanocytes to keratinocytes. Topically applied niacinamide has shown a reversible reduction in hyperpigmented lesions and increased skin size. Topical niacinamide has also been shown to reduce collagen oxidation products and improve yellowing or wilting caused by aging.(Bissett & ark., 2004; Hakozaki & ark., 2002)

Licorice root extracts: Licorice root extracts have several active compounds that can stimulate or suppress melanogenesis. Other active compounds isolated from licorice root extracts, such as glabrene, isolikiritigenin licuracid, isolikiritinin and lycochalcone A, have also been shown to inhibit tyrosinase activity. Liquirit has no effect on tyrosinase; however, it causes depigmentation by other mechanisms.(Fu & ark., 2005; Lee & ark., 2002)

Mulberry: Dried mulberry (*Morus alba*) leaves (85% ethanol extract) have been shown to inhibit tyrosinase activity. Morus alba acts as an ingredient in brightening cosmetics. (Katsube & ark., 2006; Lee & ark., 2002)

Polyphenols: Polyphenols are a class of compounds that have antioxidant capacity and are commonly found in plants. Inhibition of melanogenesis has been observed with many polyphenol plant extracts. Proanthocyanidins or procyanidins, classified as polyphenols, are found in red wine and cranberry juice; Grape seeds are a rich source. The antioxidant activities of proanthocyanidins

were found to be stronger than the activity of vitamin C or E in aqueous systems.(Yoshimura & ark., 2005)

Gingko: Extracts from the leaves of the gingko tree have shown potent free radical scavenging activity when applied to the skin. Ginkgo flavone glycosides, mostly quercetin and kaempferol derivatives, can inhibit tyrosinase activity by chelating copper in the enzyme.(Hibatallah & ark., 1999)

Ascorbic acid: Considered a skin whitening agent.(Smit & ark., 2009)

2.7. Herbal Cosmetic Products Used in Blemish Treatment Sold in Pharmacies

When we examine the contents of cosmetic products sold in pharmacies, we see that many cosmetic products for blemish treatment use herbal active ingredients alone or in combination, or herbs and extras that are effective in blemish treatment. While some of the products contain only the Turkish and Latin names of the plants, some contain the extract, oil, essence, water, aroma, leaf, petals, flower, bark, root, seed, gum, enzyme, protein, ferment, milk of the plants used. and we see that its polysaccharides are included. A product may contain a single herb or more than one herb. We can list the contents of the products examined as products that lighten the skin and remove blemishes on the skin, products that protect against sun rays and provide tanning, products that provide hypopigmentation and products that remove melasma pregnancy mask spots. Frequently used herbal active ingredients; We often see that kojic acid, arbutin, ascorbic acid, aloesin, furocoumarins and furochromones are frequently used, and some of the plants that are effective in spot treatment are used in cosmetic products that are effective in spot treatment. Some of these plants; *Tymus vulgaris, Citrus aurantifolia,* Arctostapylo uva ursi, *Cucumis sativus, Artocarpus integer, Artocarpus lacoocha roxb, Fagopyrum tataricum, Punica granatum Ammi majus, Morus alba, Glycyrrhiza glabra, Gentiana lutea, Ficus carica.* These are some of the

examples of plants used in cosmetic preparations.(Koluman &Süzgeç-Selçuk, 2016) (Table 3)

Table 3. *Dermocosmetics Used in Blemish Treatment Available in Pharmacies*.("RX Media Pharma İnteraktif İlaç Bilgi Kaynağı ", 2019)

Commercial Company Name / Product Name ®	**Formulation**
AGI DERMATİS; Clarifying concentra	Ascorbic acid *Simmondsia chinensis* oil
ASOSS İLAÇ ;Vitix Jel	*Cucumis melo* Fruit extract
ASSOS İLAÇ; Tritone krem	Arbutin Kojic acid Ascorbic acid, Licorice leaf extract
ASSOS İLAÇ; Tritone SPF 30 Krem	Alpha-arbutin Kojic acid *Glycyrrhiza Glabra* (licorice) root extract
ASSOS İLAÇ; Fadeaway skın doctors	*Glycyrrhiza glabra* root extract *Arctostaphylos uva ursi* leaf extract
ASSOS İLAÇ; Tritone Forte Krem	Alpha-arbutin *Glycyrrhiza Glabra* (licorice) root extract *Lavandula angustifolia* Peppermint oil Linalool Limonen
BENEV ;İntensive holistic lightener	Azelaic acid *Aloe barbadensis* leaf juice *Glycyrrhiza Glabra* (licorice) root extract *Morus alba* leaf extract *Arctostaphylos uva ursi* leaf extract *Camellia oleifera* leaf extract
BİODERMA; White objective active cream	*Andrographis paniculata* leaf extract *Glycyrrhiza glabra* root extract Ascorbyl glucoside

BİODERMA; White objective hand cream	*Andrographis paniculata* leaf extract *Glycyrrhiza glabra (licorice)* root extract
BİOTA LABORATUVARLARI; Ton Düzenleyici Peeling Jel	Arbutin Niasinamid Glycerine Glycolic acid Apricot kernel extract
CORTEX PHARMA; D-clar gotas/drops rılastıl cumlase lab	*Acer saccharum* extract *Citrus medica limonum* fruit extract *Citrus aurantiyum* dulsis fruit extract *Glycine soja*-seed extract *Leuconostoc*/radish root ferment filtrate *Saccharum officinarum* extract *Vaccinium myrtillus* fruit extract *Paeonia officinalis* flower extract
DARPHİN; Anti dark spot perfevting treatment perfect	*Trametes versicolor* extract *Curcuma longa* (turmeric) root extract *Gentiana lutea* root extract *Scutellaria lateriflora* extract Vitamin C *Betula alba* leaf extract
CORTEX PHARMA; D-clar gotas/drops rılastıl cumlase lab	*Acer saccharum* extract *Citrus medica limonum* fruit extract *Citrus aurantiyum* dulsis fruit *Glycine soja* seed extract *Leuconostoc*/radish root ferment filtrat *Saccharum officinarum* extract *Vaccinium myrtillus* fruit extract *Paeonia officinalis* flower extract
DARPHİN; Anti dark spot perfevting treatment perfect	*Trametes versicolor* extract *Curcuma longa* (turmeric) root extract *Gentiana lutea* root extract *Scutellaria lateriflora* extract Vitamin C *Betula alba* leaf extract
CORTEX PHARMA; D-clar gotas/drops	*Acer saccharum* extract *Citrus medica limonum* fruit extract

rılastıl cumlase lab	*Citrus aurantiyum* dulsis fruit *Glycine soja* seed extract *Leuconostoc*/radish root ferment filtrate *Saccharum officinarum* extract *Vaccinium myrtillus* fruit extract *Paeonia officinalis* flower extract
DARPHİN; Anti dark spot perfevting treatment perfect	*Trametes versicolor* extract *Curcuma longa* (turmeric) root extract *Gentiana lutea* root extract *Scutellaria lateriflora* extract Vitamin C *Betula alba* leaf extract
DDF Protect and correct spf 15	*Glycyrrhiza glabra* (licorice) root extract *Zea mays* seed oil *Macadamia ternifolia* seed oil *Helianthus annuus* (sunflower) seed oil *Camellia sinensis* leaf extract Ascorbic acid
DDF; Brightening cleanser	Azelaic acid Kojic acid
DDF; Discolation reversel pod p	*Macadamia ternifolia* seed oil *Helianthus annuus* (sunflower) seed oil *Zea mays* oil *Spirulina platensis* extract *Glycyrrhiza glabra* (licorice) root extract *Camellia sinensis* leaf extract
DENGE İLAÇ; Nopigden-B Krem	*Butyrospermum parkii* Kojic acid Panthenol
DENGE İLAÇ; Nopigden-F Krem	Kojic acid *Eijitsu ekisu*, Pomegranate seed oil Shea butter, Panthenol

DERMAHAEL; Dermahael sl skin lightening gel	Arbutin, Vitamin C *Camellia sinensis* leaf extract *Glycyrrhiza uralensis* (Licorice) root extract *Ginkgo biloba* leaf extract
DERMAHEAL; Dermaheal DC Dark Eye Circle Gel	*Camellia sinensis* leaf extract *Glycyrrhiza uralensis* root extract Arbutin
DERMAHEAL; Dermaheal SB Skin Brightening	*Glycyrrhiza uralensis* (Licorice) root extract Vitamin C Arbutin
DERMAHEAL; Dermaheal SL Skin Lightening Gel	*Camellia sinensis* leaf extract *Glycyrrhiza uralensis* root extract *Ginkgo biloba* leaf extract Arbutin
DERMOTOLOGICA; Dark bright spf 15	*Melissa officinalis* leaf extract *Actinidia chinensis* fruit juice *Sophora angustifolia* root extract
DERMOTOLOGİA ;Extreme c chromawhıte trx	*Camellia sinensis* leaf extract Alg extract Yeast extract
DROGSAN ;Vitilex krem	*Capparis spinosa* fruit extract Apricot seed oil
DUCRAY; Melascreen depigmentant	Azelaik asit
ISIS PHARMA; Vitiskin jel Vıtıskın	Vitamin B12
KMY GLOBAL; Cuıq intense dark spot correcting cream spf 20	*Triticum aestivum* seed oil *Artocarpus heterophyllus* seed extract
KUGER FARMA ;Coverderm luminous SPF15	Alfa-arbutin *Pisum sativum* extract *Saxifraga sarmentosa* extract *Vitis vinifera* (grape) seed extract *Scutellaria baicalensis* extract *Saxifraga sarmentosa* extract Vitis vinifera (grape) seed extract *Scutellaria baicalensis* extract

KUGER FARMA; Luminous Exfolia	Jojoba oil Vitamin C Arbutin
KUGER FARMA; Luminous Tri-Activ Duo Pack	Vitamin C Arbutin Bioflavonoids Alpha-arbutin
LA ROCHE-POSAY; Mela-D anti Brown spot spf 15	kojic acid
LOTİS PHARMA; Exuviance Skin Brightening gel	2% Kojic acid 3% Glycolic Acid 5% Gluconolactone, 1% Citric Acid, 1% Lactic Acid, 3% Color Lightening Complex (bearberry extract, mulberry extract and licorice root extract), 0.5% Vitamin C
LOTİS PHARMA; Neostrata Hiperpigmentasyon Kremi SPF 15	Arbutin
LOTİS PHARMA; Neostrata Hiperpigmentasyon Pedi	30% Citric Acid 3% Kojic Acid, 2% Arbutin
LOTİS PHARMA; NeoStrata Pigment Jel	2% Kojic Acid 3% Color Lightening Herbal Complex 0.5% Vitamin C
SABRİL; leke önleyici bakım kremi	*Chamomilla recutita* (matricaria) flower extract
SKINCEUTICALS; Pyhto+botanıcal gel for hyperpigmentation	*Thymus vulgaris* flower/ leaf extract Arbutin Kojic acid, *Cucumis sativus* fruit extract *Citrus aurantifolia (lime)* flower extract *Arctostaphylos uva ursi* leaf extract
NÜVEM PHARMACİST ‘S LABORATORY; Vitisun	*Citrus aurantium bergamia* fruit extract *Avena sativa* (oat)- extract

	*Cucumis mel*o fruit extract *Pimenta racemosa* meyve leaf extract *Piper nigrum* fruit extract Vitamin C Sweet almond seed oil *Prunus amygdalus ama*ra seed oil *Sesamum indicum* seed oil *Nigella sativa* seed oil *Corylus avellana* seed oil *Juglans regia* seed oil *Triticum vulgare* seed oil *Punica granatum* seed oil *Persea gratissima* seed oil *Linum usitatissimum* seed oil *Vitis vinifera*
SKİN DOCTORS; Dermabrite	Bearberry extract *Glycyrrhiza glabra* (licorice) root extract
SYNCHROLINE; Enerpeel hands	20% Trichloroacetic Acid 10% Lactic Acid 5% Kojic Acid
URIAGE; Depiderm soin Dépigmentant intensif	Vitamin C *Glycyrrhiza glabra* root extract *Camellia sinensis* leaf extract
VİCHY; Bi White advanced	*Rosa gallica* flower extract *Glycyrrhiza glabra* (licorice) leaf extract Ascorbic acid

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