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Assessing the combination of three plant species: Thyme (Thymus vulgaris), Damask Rose (Rosa damascena), and Stachys lavandulifolia vahl, to determine their synergistic effects on antimicrobial properties

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ABSTRACT

Plants, through their metabolic processes, produce phytochemicals commonly consumed in traditional medicine and nutrition for their potential health benefits. This study explores the biological and pharmacological evaluation of three distinct plant species: Stachys lavandulifolia vahl (mountain tea), Thyme (Thymus vulgaris), and Damask Rose (Rosa damascena). The primary focus is on assessing the synergistic effects of combining these plants and determining their impact on antimicrobial properties. The chemical structures of active compounds derived from these plants are presented, with a detailed classification based on their properties. The extract in our study showed strong antimicrobial activity against multiple microorganisms particularly *S. epidermidis* and *E. coli* with the inhibition zone 51 and 50 mm respectively. This analysis provides valuable insights into the potential therapeutic applications of these plants and their active compounds, thereby contributing to an enhanced understanding of their medicinal properties.

1. Introduction

The phytochemical profile and biological functionalities of the plants are very important field [1]. These species, Thyme (Thymus vulgaris), Damask Rose (Rosa damascena), and Stachys lavandulifolia vahl, are recognized for their potential antimicrobial activity (Fig. 1).

Fig. 1. Thyme (Thymus vulgaris), Damask Rose (Rosa damascena), and Stachys Lavandulifolia Vahl were bought in the local shop in Iran

Stachys lavandulifolia vahl, commonly known as mountain tea, is a medicinal plant native to certain regions. Various studies have been conducted to evaluate its biological and pharmacological properties. The active compounds found in Stachys lavandulifolia vahl have demonstrated significant medicinal properties [1]. The chemical structures of these active compounds, along with their classification based on their properties, are presented in this study. The specific properties and effects of these compounds are elaborated, providing insights into their potential therapeutic applications. Stachys lavandulifolia vahl spices (Chaye Koohi), has many species which is found in around world especially in Europe and Asia, Iran country has around 13 species of Stachys lavandulifolia vahl spices. The active components of Stachys lavandulifolia vahl spices were predominantly Hexadecanoic acid, α-pinene, germacrene-D, β-pinene, myrcene, and β-a-Phellandrene. However, their composition varied depending on the geographical area and extraction method employed, according to studies [2]. The activity of lavandulifolia vahl against both gram-negative and gram-positive bacteria, such as S. aureus, E. coli, Salmonella typhimurium, Candida tropicalis, S. agalactiae, B. cereus, K. pneumoniae, P. mirabilis, Salmonella enteritidis, Salmonella typhi, and P. aeruginosa, was highly evident. This effect is attributed to the monoterpenes present in

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lavandulifolia vahl, which possess excellent aqueous solubility and facilitate easy permeation of the microorganism's membrane [3].

Thyme, another plant examined in this study, is well-known for its culinary uses and traditional medicinal properties. It has been extensively studied for its bioactive compounds and their pharmacological activities [4]. The study highlights the chemical structures of the active compounds found in thyme and their classification based on their properties. The potential medicinal properties of these compounds are discussed, shedding light on their therapeutic potential in various health conditions. Thyme alone has been described in many studies for a wide range of pharmacological activities, which included anti-inflammatory, antitumoral, antifungal, antiparasitic, antioxidative, and antimicrobial. Thymus has a compound known as Thymol and Carvacrol which is commonly found as one of the predominant molecular compounds in Thymus vulgaris and Thymus Magnus Nakai species. Thymol and carvacrol inhibit microorganisms by the phenomenon involving a decrease in essential intracellular components and distraction of bacterial enzyme systems, alongside an elevation in the permeability of the cell membrane. Thyme oil extract in some studies has been shown activity against Pseudomonas aeruginosa and Candida albicans [5, 6].

Damask rose, a widely cultivated species of rose, is also included in this study. It is renowned for its fragrant flowers and has a long history of use in traditional medicine. The bioactive compounds present in Damask rose have been investigated for their biological activity [7]. The chemical structures of these active compounds are elucidated in this research, along with their classification based on their properties. This study provides an overview of the potential medicinal properties of Damask rose compounds, emphasizing their potential applications in health protection. Rosa damascena is a plant resembling a shrub with a delightful fragrance which is been used for many purposes [8]. The antimicrobial activity has been described and tested is some studies particularly, flowers (petals and sepals) which has phytochemical properties includes Alkanes, alcohols, phenols, terpenes and terpenoids furthermore, the extract from Rosa damascene showed activity against many organisms especially against Staphylococcus aureus, Pseudomonas aeruginosa and Candida albicana [9, 10].

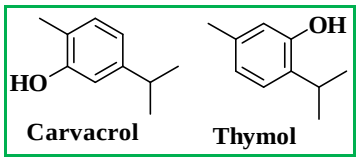
1-1. Thyme

Thyme (Thymus vulgaris) is indeed an aromatic and medicinal plant of significant economic importance in various regions, including North America, southern Europe, North Africa, and Asia. The word "thyme" originated from the practice of burning thyme as incense in ancient Greek temples, where the herb's pleasant aroma was believed to have purifying and cleansing properties. The plant is a perennial subshrub that typically grows to a height of 15-30 cm (6-12 inches) and spreads about 40 cm (16 inches) wide. It has a bushy growth habit, with woody stems at the base and small, gray-green leaves that possess a highly aromatic scent (Fig.2).

Fig. 2. Thyme Bushes (A), Thyme Flower (B), Thyme Leaves (C)

Thyme is widely used as a culinary herb due to its strong, distinctive flavor and aroma and in the cosmetic industry. Additionally, thyme has been valued for its medicinal properties for centuries and possesses significant antimicrobial effects against various human, animal, and plant pathogens. It contains various compounds, including essential oils, phenols, and flavonoids, that contribute to its potential health benefits. Thyme is known for its antimicrobial, antifungal, antioxidant, and anti-inflammatory properties, and it has been used to treat respiratory conditions, digestive issues, and skin ailments [11-15]. The use of plants as medicine dates back thousands of years, and evidence suggests that medicinal plant knowledge and practices existed as early as 4000-5000 B.C. The Chinese civilization is renowned for its long-standing tradition of using natural herbal preparations as medicines. In India, the use of plants as medicine can be traced back to ancient times as well. Today, the study of medicinal plants, known as ethnobotany, continues to play a crucial role in modern medicine. Many pharmaceutical drugs have been derived from plant compounds, and traditional herbal remedies are still used in many parts of the world for their healing properties [16-18]. Thymus vulgaris and its extracts have been extensively studied for their antimicrobial properties. Thyme extracts, including aqueous extracts, have demonstrated antibacterial efficacy against a range of bacteria and fungi in laboratory settings, for example, for treating respiratory disorders including whooping cough, bronchitis, and catarrh. This includes both drug-sensitive and drug-resistant strains. Thyme's antimicrobial effects are attributed to the presence of various bioactive compounds, particularly essential oils, such as Thymol and Carvacrol (Scheme 1), which exhibit strong antimicrobial activity. Indeed, in the 19th century, constituents of thyme oils (Thymol) were utilized by dentists for treating oral abscesses and inflammation, as well as for their antiseptic properties in endodontics [17-22]. Some of the attributed properties include analgesic (pain-relieving), anti-inflammatory, expectorant (promoting coughing up of mucus), digestive,

carminative (relieving flatulence), emmenagogue (promoting menstruation), anthelmintic (expelling intestinal worms), lithotriptic (aiding in the dissolution of kidney stones), diuretic (increasing urine production), and aphrodisiac (enhancing sexual desire). Also, thyme was utilized by the ancient Egyptians in various aspects of their culture, including the mummification process [23].



Scheme. 1. Structure of two more effective chemical compounds in Thyme

1-2. Damask Rose

Rosa damascena mill L, commonly known as Damask Rose, is indeed known as Gole Mohammadi in Iran. It is a well-known and highly valued flower in various cultures and is particularly associated with the production of rose oil and rose water. R. damascena is a perennial bushy shrub that typically grows to a height of 1 to 2 meters. The flowers of Damask Rose are renowned for their exquisite aroma and are used in the production of perfumes, cosmetics, and traditional medicines (Fig. 3) [24-27].

Fig. 3. Damask Rose Flower

The Damask Rose (Rosa Damascena) is believed to have originated in the Middle East, particularly in Iran, Syria, and Turkey, and Iran is associated with the production of rose water. Greece played a significant role in the production and trade of rose oil and extracts during the 7th century A.D., but the production of rose oil and extracts has expanded to various regions around the world over time [28-34]. The products derived from Damask Rose, such as rose absolute, rose water, dried petals, essential oil, dried flower buds, and rose concrete find extensive applications in several industries such as perfume, cosmetic, pharmaceutical, and food industries. A special place in these industries is due to its unique and captivating fragrance, therapeutic properties, versatility, and cultural significance attached to it [35-38].

1-3. Stachy Lavendulifolia Vahl.

Stachys lavandulifolia vahl, commonly known as chay-e-kouhi (Mountain Tea) is an herbaceous perennial plant belonging to the family Lamiaceae. It is native to several countries in the region, including Iran, Iraq, Armenia, Azerbaijan, Georgia, Turkey, and Turkmenistan. Stachys lavandulifolia vahl is a suffrutescent perennial plant and flowering stems are numerous and range from 10 cm to 30 cm in height. The inflorescence of Stachys lavandulifolia vahl consists of verticillasters, which are whorls of flowers along the stem. The pedicels, which are the stalks that connect the flowers to the stem, are short, measuring about 1.5-2 mm. (Fig. 4). The plant is known for its aromatic leaves and is often used in herbal tea preparations and typically grows in mountainous regions, hence the common name "Mountain Tea."

Fig. 4. Stachy Lavendulifolia Bush Vahl. (A), Bouquet (B), Flower (C)

In addition to its culinary uses, Stachys lavandulifolia vahl has been traditionally used in herbal medicine for various purposes, including its potential antispasmodic, anti-inflammatory, and diuretic properties. It is also sometimes cultivated as an ornamental plant due to its attractive foliage and delicate purple flowers. It is interesting to note that the species exhibits high phenotypic variability and can adapt to different habitats and altitudes, which further enhances its potential as a valuable genetic resource. The Lamiaceae family is one of the largest and most diverse families of flowering plants. With approximately 258 genera and around 7000 species worldwide, the family encompasses a wide range of aromatic herbs, ornamentals, and medicinal plants. The Lamiaceae family includes well-known plants such as mint, basil, rosemary, thyme, and sage. In the context of Iran, Stachys lavandulifolia vahl is just one of the many species within the Stachys genus that are cultivated and distributed throughout the country. With over 39 species from this genus grown in various regions of Iran. The utilization of Stachys lavandulifolia vahl and other members of the Lamiaceae family in traditional Iranian medicine underscores the importance of these plants in the cultural and medicinal practices of the region. Their natural products have been traditionally used for their potential therapeutic properties and are the subject of ongoing research for their bioactive compounds [39-42] (Fig. 5).

Fig. 5. Map Distribution of Iranian Stachys lavandulifoliavahl

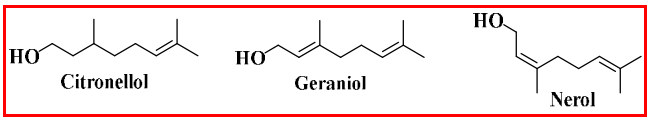
2. Applications

2-1. Applications of Thyme

Thyme contains compounds such as Thymol and Carvacrol, which have been shown to have antimicrobial properties. These compounds can help inhibit the growth of bacteria, fungi, and viruses, making thyme a potential natural remedy for certain infectious diseases. Thyme is also believed to act as a stress reliever. Its aromatic compounds, when inhaled, may have a calming effect on the nervous system and help reduce stress and anxiety. In addition to the previously mentioned nutrients, thyme also contains vitamin K, vitamin E, and folic acid. Indeed, thyme essential oil has been found to possess strong antimicrobial properties against certain strains of bacteria. The studies suggest that thyme essential oil was particularly effective against Staphylococcus aureus and Klebsiella pneumonia, two common pathogens that can cause infections in humans [43, 44]. The antimicrobial activity of thyme essential oil can be attributed to its bioactive compounds, such as thymol and carvacrol, which have been shown to exhibit potent antimicrobial effects. Thymol, in particular, has been extensively studied for its antibacterial and antifungal properties, particularly its effect on Candida species. The findings studies imply that thyme essential oil has the potential to be used as a natural antiseptic, both in the pharmaceutical and food industries as a preservative. However, it is important to note that the efficacy of thyme essential oil against different strains of bacteria can vary and may be dose-dependent [45, 46]. The researchs has demonstrated that thyme essential oil can inhibit the growth of fluconazole-resistant C. albicans isolates. The oil was found to be fungistatic (inhibiting fungal growth) and fungicidal (killing the fungi) at low doses. This suggests that thyme essential oil may have potential as a natural antifungal agent [47].

2-2. Applications of Damask Rose

Rose water is indeed a popular product derived from Rosa Damascena and has been used for centuries for various purposes due to its pleasing fragrance and potential therapeutic properties. Rose water is a common ingredient in skincare products such as facial toners, and makeup removers, or as an ingredient in face masks and moisturizers due to its soothing and hydrating properties. It is believed to help balance the skin's pH, reduce redness and inflammation, and provide a refreshing sensation. Aromatherapy, culinary applications, flavoring, and fragrance are other usages of rose extraction. Regarding the composition of rose oil, depending on factors such as the extraction method, rose variety, and geographical region, it contains various components, including volatile compounds responsible for its fragrance. While rose oil primarily consists of odorless Stearoptene, which is a solid fraction, it also contains other compounds such as aliphatic hydrocarbons (C14-C23 normal paraffin). These components contribute to the characteristic scent and properties of rose oil (Scheme 2). The oil content of rose water can vary, it typically contains about 10-50% rose oil [48- 53].



Scheme 2. The structures of the main chemicals in Rose oil

Anti-HIV activity due to certain compounds such as tannins and flavonoids, have shown inhibitory effects against HIV replication in laboratory experiments [54]. The plant's antimicrobial effects have been attributed to the presence of compounds like phenethyl alcohol, phenolic compounds, terpenes, and flavonoids. The essential oil of Rosa damascena has been studied for its antimicrobial effects, including antibacterial activity against various gram-positive and gram-negative strains such as Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus, Chromobacterium violaceum, Erwinia carotovora. Antidiabetic effects of extracts from the plant have shown promising results in reducing blood glucose levels may be attributed to the presence of bioactive compounds like phenolics, flavonoids, and tannins.

The R. damascena extracts have been reported to exhibit bronchodilatory properties, which could potentially be beneficial in respiratory conditions characterized by bronchoconstriction, such as asthma. The relaxation of tracheal chains has been attributed to the presence of certain compounds like flavonoids and terpenes in the plant [55-63]. Rosa damascena has been studied for its potential anti-inflammatory effects because of its vitamin C content. Hydroalcoholic extract of R. damascena on paw edema induced by carrageenan, which is an inflammatory agent. The anti-inflammatory effect of R. damascena extract in reducing paw edema may be attributed to its ability to inhibit the mediators of acute inflammation via various inflammatory mediators, such as prostaglandins and cytokines. Vitamin C is known for its antioxidant and anti-inflammatory effects. Vitamin C acts as a scavenger of free radicals and it can help alleviate inflammation (Fig. 6) [64-67].

2-3. Applications of stachy lavendulifolia

Stachys lavandulifolia vahl has been traditionally used for various purposes, including its potential benefits for dandruff treatment, scalp hair re-growth, and its antimicrobial, antiviral, and antifungal properties [68]. Various polyphenols found in Stachys lavandulifolia vahl, such as flavonoids, have been shown to possess antioxidant properties. Polyphenols, including those present in Stachys lavandulifolia vahl, have been attributed to various biological effects. These effects are often associated with their antioxidant activities, which

include scavenging free radicals, inhibiting peroxidation (the process of free radical-induced damage to lipids), and chelating transition metals.

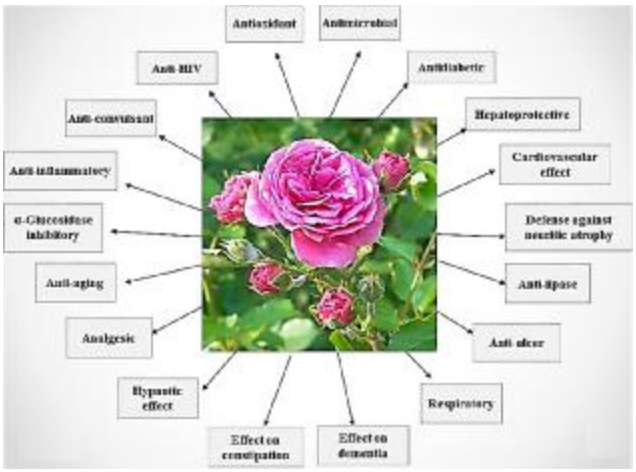


Fig. 6. All Biological activity of Damask Rose in a frame

It is important to note the possibility of abortion depends on the dosage in animals. Stachys lavandulifolia vahl may be useful in managing symptoms associated with postmenopausal syndrome (such as mood swings, bloating, and breast tenderness) and primary dysmenorrhea (menstrual pain) due to its reported properties, including antispasmodic effects and potential analgesic (pain-relieving) properties. Some studies have suggested that Stachys lavandulifolia vahl may have anxiolytic effects in animals, indicating potential benefits in reducing anxiety symptoms. Stachys lavandulifolia vahl has been reported to strengthen the stomach and potentially prevent gastric ulcers induced by alcohol consumption. Stachys lavandulifolia vahl has been investigated for its potential use in treating Leishmania Major, a parasitic disease transmitted through sandflies. This plant has been reported to possess sedative and hypnotic effects, which may have implications for promoting relaxation and aiding sleep, and also may exhibit analgesic (pain-relieving) and anti-inflammatory effects, which could potentially be beneficial in managing pain and reducing inflammation. It has been suggested as a potentially effective treatment for fatigue, nausea, and vomiting associated with primary dysmenorrhea. Its reported antispasmodic effects may contribute to these benefits [68-80].

Stachys lavandulifolia vahl may possess antipyretic (fever-reducing) and spasmolytic (muscle-relaxing) effects. These properties could potentially contribute to its therapeutic applications in managing fever and alleviating spasms or cramps. Stachys lavandulifolia vahl, particularly in Iranian folk medicine, has been used as an anxiolytic (anxiety-reducing) and sedative agent, and reported anxiolytic effects may offer potential benefits. Its sedative properties have also been associated with aiding insomnia, anti-depressive effect, and its potential to stimulate appetite. Stachys species, including Stachys lavandulifolia vahl, have been traditionally used in herbal medicine for digestive disorders. Infusions or decoctions of Stachys species are consumed as tonics and have been used to treat stomach disorders. In Anatolia and Iran as a traditional remedy is used, particularly for ailments such as headache, stomachache, gastritis, and nerve disorders. Additionally, some compounds found in Stachys lavandulifolia vahl extracts have shown antibacterial properties, suggesting potential use as a traditional treatment for infectious diseases. It also known as mountain tea has been reported for its potential benefits in preventing Helicobacter pylori infection [81-93].

3. Chemical composition

3-1. Chemical Composition of Thyme

Thyme contains various chemical compounds (Table 1) that contribute to its distinctive flavor and potential health benefits [94-99]. The chemical composition of thyme includes:

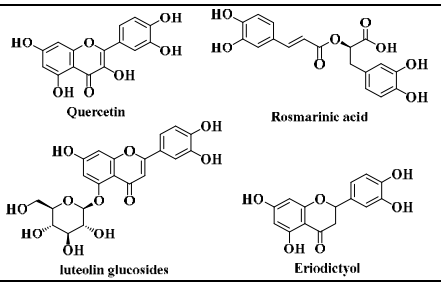
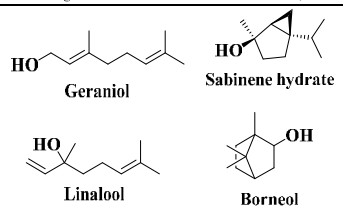
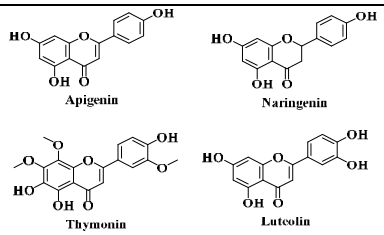
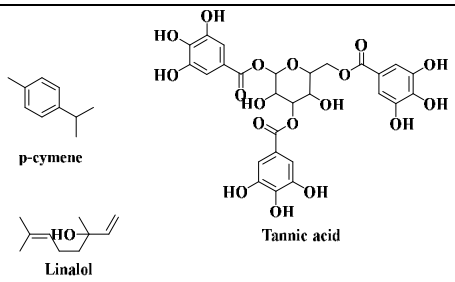
Phenolic acids: Thyme contains phenolic acids like rosmarinic acid, caffeic acid, and ferulic acid. These compounds possess antioxidant and anti-inflammatory properties [100-112].

Essential oils: Thyme essential oil is rich in compounds such as thymol, carvacrol, p-cymene, myrcene, and terpinene. These compounds give thyme its strong aroma and are known for their antimicrobial and antioxidant properties [113-122].

Flavonoids: Thyme contains flavonoids like apigenin, luteolin, naringenin, and thymonin. Flavonoids have antioxidant effects and may contribute to the herb's potential health benefits [123-131].

Tannins: Thyme contains tannins, which contribute to its astringent properties [132-140].

Table 1: Isolated Organic Compounds from the whole herb of Thyme

Entry	Chemical material	Chemical structure	Phytochemical Status	Pharmacology
1	Phenolic acids		Polyphenolic compounds	Anti-Alzheimer, Anti-cancer, Anti diabetic, Antimicrobial, Cardioprotective, Nephroprotective, Anti-aging, Hepatoprotective, Anti-inflammatory, Anti-allergic, Anti-Depressant [90-102]
2	Essential oil		Terpene alcohol	Antibacterial, Antifungal, Antispasmodic, Antitussive, Anxiolytic, Neuroprotective, Antihypertensive, Antioxidant, Antihyperlipidemic, Anti-inflammatory, Immunomodulatory, Anti-cancerous, Analgesic [103-112]
3	Flavonoids		Flavone	Antioxidant, Anti-inflammatory, Antimicrobial, Antidiabetic, Anticancer, Neuroprotective, Cardiovascular, Hepatoprotective [113-121]
4	Tannins		Phenolic compound	Sedative, Antiviral, Anti-inflammatory, Antioxidant, Anti-nociceptive, Analgesic, Anesthetic, Antimicrobial, Anxiolytic, anti-Hyperlipidemic, Antinoceptive, Antidepressive, Neuroprotective [122-130]

3-2. Chemical Composition of Damask Rose (Rosa Damascena)

Damask rose is a species of rose known for its fragrant flowers, which are commonly used in perfumes, cosmetics, and culinary applications. The chemical composition (Table 2) of Damask rose includes:

Essential oil: The essential oil of Damask rose is highly valued for its fragrance and therapeutic properties. It contains compounds such as citronellol, geraniol, nerol, eugenol, and linalool. These compounds contribute to the distinctive aroma and potential health benefits of Damask rose [141-143].

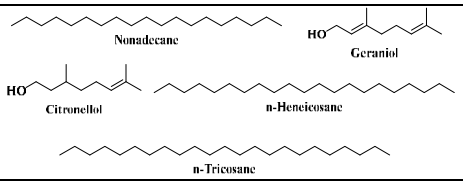
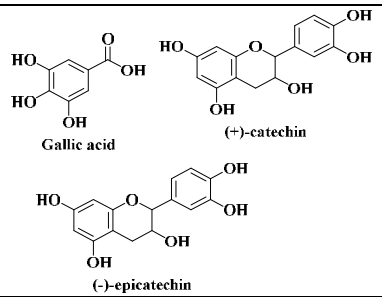
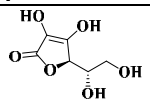
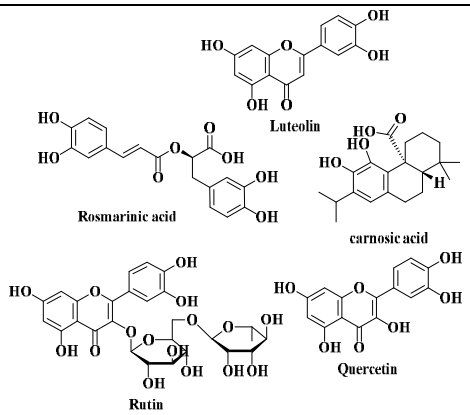
Phenolic compounds: Damask rose contains various phenolic compounds, including flavonoids (such as quercetin and kaempferol) and phenolic acids (such as gallic acid and ellagic acid). These compounds have antioxidant and anti-inflammatory properties [144-146].

Vitamin C: Damask rose is a good source of vitamin C, which is known for its antioxidant properties and its role in collagen synthesis [147-149].

Flavonoids: Damascene rose contains various flavonoids, including quercetin, kaempferol, and myricetin derivatives. These compounds contribute to the plant's antioxidant properties and are believed to have potential health benefits when consumed. Quercetin, for instance, is known for its antioxidant and anti-inflammatory properties, while kaempferol is associated with potential cardioprotective effects and has been studied for its anti-cancer properties. Flavonoids in Damascene rose can vary based on factors like growing

conditions, environmental factors, and extraction methods used in obtaining these compounds. The presence and quantity of flavonoids may differ in different parts of the plant (petals, leaves, etc.) and in extracts derived from it [150-153].

Table 2: Isolated Organic Compounds from the whole herb of Damask Rose

Entry	Chemical material	Chemical structure	Phytochemical Status	Pharmacology
1	Essential oils		Terpenoid	Antibacterial Anti-inflammatory Obesity Antioxidant Brain system [131-133]
2	Phenolic Compounds		Coumarin	Antimutagenic Antioxidant Anti-inflammatory Anticancer Free-radical scavenger Antidepressant [134-136]
3	Vitamin C		Ascorbic acid	Antioxidant Anti-inflammatory [137-139]
4	Flavanoids		Quercetins, Hydroxyflavone	Anti-HIV Antibacterial Antioxidant Antitussive Hypnotic Antidiabetic Relaxant effect [140-143]

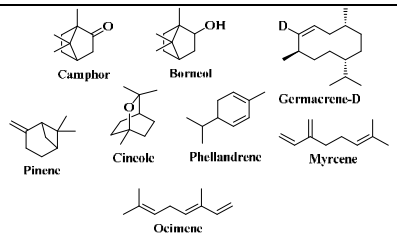
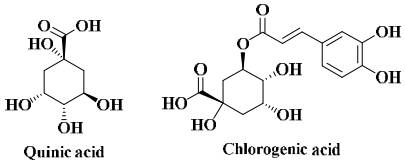
3-3. Chemical Composition of Stachys Lavandulifolia

Stachys lavandulifolia vahl, commonly known as lavender cotton or Spanish lavender, is an aromatic herb native to the Mediterranean region. While there is limited information available on its specific chemical composition (Table 3), it is known to contain some common constituents found in other members of the Stachys genus, which may include:

Essential oils: Stachys lavandulifolia vahl may contain essential oils with compounds like camphor, borneol, cineole, and various terpenes. These compounds contribute to its characteristic fragrance and potential therapeutic properties [154-157].

Phenolic compounds: Similar to other Stachys species, Stachys lavandulifolia vahl may contain phenolic compounds, such as flavonoids and phenolic acids, which possess antioxidant and anti-inflammatory properties [158-161].

Table 3: Isolated Organic Compounds from the whole herb of Stachys lavandulifolia

Entry	Chemical material	Chemical structure	Phytochemical Status	Pharmacology
1	Essential oils & Terpenoids		Terpenes	Antimicrobial Anti-inflammatory Anticandidal, Antibacterial Antioxidant [144-147]
2	Phenolic compounds		Polyphenol acids	Antioxidant Anti-inflammatory, Anti-cancer [148-151]

4- Antibacterial Activity

4-1. Materials and Methods:

4-1-1. Extraction and Microbial strains

The maceration extraction method served as a fitting approach for extracting effective plant substances [162]. The aerial parts of Thymus vulgaris, Rosa damascena, and Stachys lavandulifolia vahl were prepared and dried to remove excess moisture, ensuring optimal extraction efficiency (This collection was purchased from a store that harvests all its herbal products from the fields and mountains of Sanandaj, located in Kurdistan, Iran). The dried plant material was then finely crushed to increase the surface area for solvent interaction and facilitate the release of bioactive compounds. Subsequently, the plant material from each species was mixed in equal proportions to create a homogeneous blend. Given the nature of our target compounds and their susceptibility to heat, we opted for a solvent that ensures effective extraction without compromising the integrity of the bioactive constituents. In this study, we utilized a solvent mixture of water and alcohol to achieve the desired extraction efficiency (50:50). The prepared plant mixture was then subjected to maceration, wherein it was immersed in the solvent mixture for four days. During this period, the solvent selectively dissolves the desired bioactive compounds from the plant material, resulting in an enriched extract. Following the extraction period, the solvent-extract mixture underwent straining and filtration processes to separate the liquid extract from the residual plant material. Finally, the obtained extract was concentrated under reduced pressure to remove excess solvent and obtain a concentrated extract rich in bioactive compounds. The extract was then stored under appropriate conditions to maintain its stability and bioactivity for subsequent analyses or applications.

To evaluate the Mixture of three Extracts' antibacterial properties, six common microbial strains were used. These strains were two Gram-positive bacteria (Staphylococcus epidermidis ATCC 12228, S. aureus ATCC 29737), Three Gram-negative bacteria (Escherichia coli ATCC 10536, Pseudomonas aeruginosa ATCC 27853, Salmonella abony ATCC 6017) and the fungal strain of Candida albicans ATCC 10231, that obtained from the Microbiology Laboratory of Medical Analysis Department at Tishk International University, Erbil- Iraq. Re-grown all microbial strains from 15% glycerol-storage medium, subcultured on Brain Heart Infusion BHI medium at 37 C for 24 hours for bacterial strains, and SDA used for Candida spp. subculturing for 48 hours [163].

4-1-2. Microbial Suspension Preparation

Bacterial Suspension Preparation: A single Pure colony of Bacterial growth was suspended in 2 ml of sterile saline then the turbidity of each Bacterial suspension (500 µL) was adjusted to the 0.5 McFarland standard and contained approximately $1x10^8$ CFU/mL [164].

4-2. Yeast Suspension Preparation: The inoculum was prepared by choosing distinct colonies of diameter 1 mm from 18 to 24 hrs. cultures and suspended in 5 mL of sterile distilled water then shaking it on a vortex mixer for 15 seconds. The cell density has been adjusted to the density of a 0.5McFarland standard by adding sterile distilled water and measuring absorbance in a spectrophotometer at a wavelength of 530 nm. This gave a yeast suspension of 1±5 x 10^\6 cfu/mL [165].

4-3. Antimicrobial Bioassay

The Antimicrobial activity of the extract was determined by the agar-well diffusion technique, the protocol of the Clinical and Laboratory Standards Institute (CLSI, 2012) was employed in this method. Mueller-Hinton agar and PDA were prepared for bacterial and fungal strains, respectively. 0.1 mL of standardized inoculum of each bacterium and yeast was spread on the surface of the Solidified Medium. Then, 6 mm diameter wells were punched, and sequentially, 80 µL of the extract was

poured into the wells with distilled water as the Negative control and the positive control (AK; Amikacin G-ve, AP; Ampicillin G+ve and Fluconazole; Yeast) to the bacterial and Fungi, respectively. the plates were incubated at 37 °C for 24 and 48 hours, respectively. After incubation, the diameters of the growth inhibition zones around each well were measured in mm by Normal Ruler. Minimum inhibitory concentration (MIC) and Minimum Bactericidal Concentration (MBC): Nzeako et al.'s (2006) description of the agar well diffusion method used for MIC and MBC determination [166]. Aqueous extracts with concentrations of 50, 25, 12.5, 6.25, 3.12, 1.56, and 0.78 g/ml were divided by two and diluted with distilled water. Every time a new batch of dilutions was to be utilized; they were made. On MHA and PDA, 6 mm diameter wells were constructed, and they were swabbed as previously reported with the appropriate organism suspension. 80 L of each dilution in triplicates were separately poured into each well. For 24 and 48 hours, respectively, the plates were incubated aerobically at 37° C with bacteria and yeast. The average zone size for each dilution was determined by measuring the zones of inhibition. The lowest dilution of an extract at which the growth of the organisms was inhibited was considered the endpoint of activity for each extract (Fig. 7).

5. Result and Discussion

5-1. Result

The antimicrobial activities of Stachys lavandulifolia-Damask rose-Thyme- mix Aqueous extract against five bacterial strains and a yeast. examined in the current study and their potential was evaluated by the diameter of inhibition zones and endpoint extract activity of this mixture extract of mixture of these three herbals. The antibacterial activities of Extract done by Agar well diffusion method is shown in Tables 4.

Table 4: Zone of Inhibition of Aqueous Extraction against Gram positive, Gram negative and Yeast species.
*¹(Fluconazole 25 µl), * AK: Amikacin, *AMP: Ampicillin, *D.W: Distilled Water.

Microbial	Positive Control/Ak *AMP	Negative Control/ D. W	Aqueous Extract (80 µl)
Staphylococcus aureus	29 mm (AMP)	0	34 mm
Staphylococcus epidermidis	14 mm (AMP)	0	51 mm
E. coli	16 mm (Ak)	0	50 mm
Pseudomonas aeruginosa	15 mm (Ak)	0	30 mm
Salmonella abony	17 mm (Ak)	0	25 mm
Candida albicans	19 mm*¹	0	22 mm

The results revealed that in plant mixture extract, the highest antibacterial activity were against *S.epidermidis* and *E. coli* with the inhibition zone diameters 51 and 50 mm respectively. And showed a large inhibition zone against *S.aureus, P.aeruginosa, and salmonella abony* 34, 30, and 25 mm than the standard antibiotics that have been used as the positive control. Moreover, less activity was observed against Yeast species (*Candida albicans*) to compared with their antibacterial activity.

Table 5. The endpoint of antimicrobial activity of water (Aqueous extracts) at % v/v dilution

Microbes	End- point Extract activity v/v %
Staphylococcus aureus	0.5% (500 µl /ml)
Staphylococcus epidermidis	0.125% (125 µl /ml)
E. coli	0.5% (500 µl /ml)
Pseudomonas aeruginosa	0.125% (125 µl /ml)
Salmonella abony	0.25% (250 µl /ml)
Candida albicans	0.25% (250 µl /ml)

Table 5 and (Fig.8) represent the concentration endpoints of the antimicrobial activities of Mixture extract for all tested strains and zone of inhibition of each diluted concentration. All three herbal has different antimicrobial activity against all bacteria and yeast tested. The endpoint evaluation has been tested for the extract mixture, the lowest endpoint concentration of the liquid extraction was 0.12% (125 µl) against *S.epdermidis and P.aeruginosa,* The mixture had a middle concentration endpoint at 0.25% (250 µl) *with C. albicans and Salmonella Abony*, while the concentration end-points *for S.aureus and E.coli* were 0.5% (500 µl).

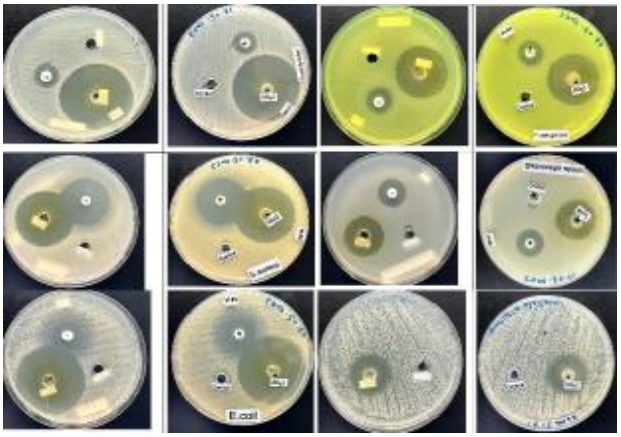


Fig. 7. Zone of inhibition of 5 bacterial strains and Candida albicans.

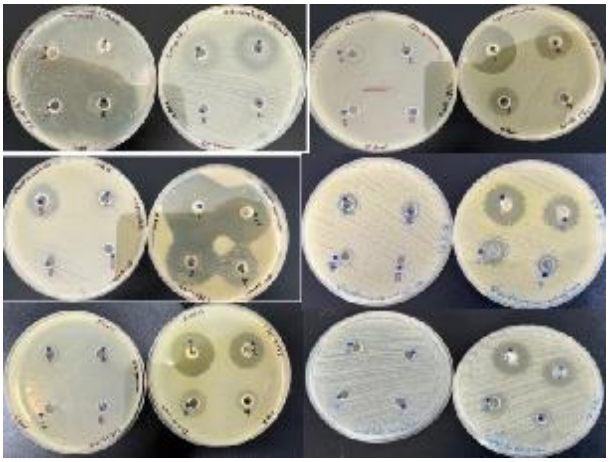


Fig. 8. Endpoint antimicrobial activity of Two-fold diluted Watery Extract by Well Diffusion Method

5-2. Discussion

Our study revealed that the antimicrobial activity against staphylococcus aureus, pseudomonas aeruginosa, and E. coli was significantly more effective with inhibiting

zones measuring 34 mm, 30 mm, and 50 mm respectively, when compared to the activity of stachys Lavandula alone, which only measured 12.5 mm, 25 mm, and 12.5 mm, respectively [167].

Another study conducted by Nasser and his colleagues for antimicrobial activity rosa damascean extract inhabiting zone among staphylococcus aureus and E. coli was 32 mm and 22 mm while our extract was further efficacious with inhabiting zone 34 mm and 50 which was more effective than Rosa damascene extract alone [168]. Similar study conducted in regards of Thymus vulgaris extract alone for antimicrobial activity different concentration have used for showing antibacterial activity in 20 ml Staphylococcus aureus, Pseudomonas aeruginosa and E. coli which was 31.4 ± 0.47, 14.13 ± 0.19 and 34.99 ± 0.19 respectively, meanwhile activity in our extract was 34 mm, 30 mm, and 50 mm eventually our product most robust compared to thymus vulgaris extract solely [169].

Our study has uncovered that a combination of three specific plant species exhibits significantly higher efficacy against certain bacterial strains. Notably, we observed extensive activity against Staphylococcus epidermidis, E. coli, and Staphylococcus aureus. Consequently, further investigation is recommended to explore the potential activity of this plant extract against other bacterial strains.

6. Conclusion

Today, even in spite of scientific advances and the increase in the use of advanced and man-made technologies, using nature as a rich source of food, dyes, effective drugs for treatment, textures, fibers, and fuel still remains. Stachys lavandulifolia vahl (mountain tea), Thyme, and Damask rose are all plants known for their medicinal uses. These plants produce various phytochemicals, which are natural compounds that contribute to their therapeutic effects. In this study, the biological and pharmacological evaluation of these plants was conducted, focusing on the active compounds responsible for their medicinal properties. Additionally, the chemical structures of these active compounds were examined, and they were classified based on their properties. Stachys lavandulifolia vahl, commonly known as mountain tea, is a perennial herbaceous plant found in mountainous regions. It has been traditionally used in herbal medicine for its numerous health benefits. The active compounds in Stachys lavandulifolia vahl include flavonoids, phenolic acids, and terpenoids. Flavonoids such as apigenin, luteolin, and hesperidin are present in this plant and have demonstrated antioxidant, anti-inflammatory, and anticancer activities. Phenolic acids, such as rosmarinic acid, possess antioxidant and antimicrobial properties. Terpenoids, including ursolic acid and oleanolic acid, exhibit anti-inflammatory and hepatoprotective effects. Thyme (Thymus vulgaris) is an aromatic herb widely used in cooking and traditional medicine. It contains several active compounds, including thymol, carvacrol, and flavonoids. Thymol and carvacrol are phenolic compounds known for their antimicrobial, antifungal, and antioxidant properties. They have been investigated for their potential in treating respiratory infections and as natural preservatives. Flavonoids present in thyme, such as apigenin and luteolin, contribute to its antioxidant and anti-inflammatory activities. The damask rose (Rosa damascena) is a fragrant flower extensively used in perfumery and cosmetics. It also possesses medicinal properties attributed to its bioactive compounds. The major active compounds found in Damask rose are phenolic compounds, including gallic acid, quercetin, and kaempferol derivatives. Gallic acid exhibits antioxidant and anti-inflammatory effects. Quercetin and kaempferol derivatives have been associated with antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. The chemical structures of the active compounds in Stachys lavandulifolia vahl, Thyme, and Damask rose vary depending on the specific compound. However, they generally belong to the classes of flavonoids, phenolic acids, and terpenoids. Flavonoids are characterized by their flavone or flavonol structure, which includes a flavan nucleus with hydroxyl and methoxy substitutions. Phenolic acids, such as rosmarinic acid and gallic acid, possess a carboxylic acid group attached to a phenolic ring. Terpenoids, including ursolic acid and oleanolic acid, consist of repeating isoprene units and are commonly found in essential oils. In summary, Stachys lavandulifolia vahl (mountain tea), Thyme, and Damask rose contain various active compounds with medicinal properties. These compounds, such as flavonoids, phenolic acids, and terpenoids, contribute to the plants' antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. The chemical structures of these active compounds exhibit structural diversity within their respective compound classes. Understanding the biological and pharmacological evaluation of these plants and their active compounds can provide insights into their potential therapeutic applications in traditional medicine and nutrition.

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References

[1] (a) A. K. O. Aldulaimi, A. H. Idan, A. H. Radhi, S. A. Aowda, S. S. S. A. Azziz, W. M. N. H. W. Salleh, A. K. O. Aldulaimi, N. A. M. Ali, Gcms analysis and biological activities of iraq zahdi date palm phoenix dactylifera l

volatile compositions. *Res. J. Pharm. Tec.,13*(11) (2020) 5207-5209. doi:10.5958/0974-360X.2020.00910.5; (b) S. S. S. A., Azziz, A. K. O. Aldulaimi, S. A. Aowda, Y. M. Bakri, A. A. Majhool, R. M. Ibraheem, F. Abdullah, Secondary metabolites from leaves of polyalthia lateriflora and their antimicrobial activity. *Int. J.Res. Pharm. Sci. 11*(3), (2020) 4353-4358. doi:10.26452/ijrps.v11i3.2652; (c) S.Mahzooni-Kachapi, M.Mahdavi, L.Roozbeh-Nasira'ei, M .Akbarzadeh, F. Rezazadeh, Antimicrobial activity and chemical composition of essential oils of Stachys lavandulifolia Vahl. from Mazandaran. Iran. *J. Med. Plant Res.*, 6(2012) 4149- 4158; (d) L. Lahrizi; F. Errachidi; H. Nekhla; L. E. Ghadraoui, Ajuga iva L.: An overview of phytochemical profile and biological functionalities, Chem. Rev. Lett. 7 (2024) 31-44. 10.22034/crl.2024.413946.1241; (e) P. Abbasi; K. Shayesteh; V. Vahidfard; H. Jangara, Removal of Cadmium in the Cold Purification Step by Semi-batch Process, Chem. Rev. Lett. 6 (2023) 449-460. 10.22034/crl.2023.408052.1234; (f) M. Sheydaei; S. Shahbazi-Ganjgah; E. Alinia-Ahandani; M. Sheidaie; M. Edraki, An overview of the use of plants, polymers and nanoparticles as antibacterial materials, Chem. Rev. Lett. 5 (2022) 207-216. 10.22034/crl.2022.343015.1168; (g) Soma Majedi; Tola Abdulsattar Faraj; Heshu Jalal Ahmed; Faiq H.S. Hussain, A review of biochemical structures of Urtica dioica metabolites and their pharmaceutical effects, Chem. Rev. Lett. 4 (2021) 206-212. 10.22034/crl.2021.316199.1131; (h) E. C. Emenike; C. Onyema, Phytochemical, Heavy Metals and Antimicrobial Study of the Leaves of Calopogonium mucunoides, J. Chem. Lett. 3 (2022). 10.22034/jchemlett.2022.327443.1049; (i) N. Salehi, Chemical composition of the Essential oil from stems, leaves and flowers of Salvia verticillate L., J. Chem. Lett. 2 (2021) 50-55. 10.22034/jchemlett.2021.276845.1026; (j) N. Salehi, Chemical composition of the Essential oil from Aerial parts of Achillea filipendulina Lam. From Iran, J. Chem. Lett. 1 (2020) 160-163. 10.22034/jchemlett.2021.271773.1019; (k) P. Ghiasvandnia; M. Edraki; F. Shahimi; M. Sheydaei, Evaluation of concentration of heavy metals and microbial contamination in parsley (Petroselinum crispum) vegetable, Chem. Res. Technol. 1 (2024) 2-7;10.2234/chemrestec.2023.181245; (l) M. Sheydaei; M. Edraki, Antimicrobial evaluation of Garcinia cambogia-impregnated sodium montmorillonite, Chem. Res. Technol. 1 (2024) 16-21. 10.2234/chemrestec.2024.187183.

[2] M. Mahdavi, M., Jouri, M. H., M.Kachapi, S., H. Jelodar, S,Study of chemical composition and antibacterial effects of essential oils of Stachys lavandulifolia Vahl., Salvia verticillata L., and Tanacetump olycephalum Schultz-Bip. on some microbial lineages. *Intl. J. Farm. & Alli. Sci*, 4 (2015) 197-206.

[3] A. Rezakhanlo, SM.Talebi, Trichomes morphology of stachys lavandulifolia vahl. (Labiatae) of Iran. *Procedia Soc. Behav. Sci.*, 2 (2010) 3755-3763.

[4] E. Pandur, G. Micalizzi, L. Mondello, A .Horváth, K. Sipos, G. Horváth, G.Antioxidant and Anti-Inflammatory Effects of Thyme (Thymus vulgaris L.) Essential Oils Prepared at Different Plant Phenophases on Pseudomonas aeruginosa LPS-Activated THP-1 Macrophages. *Antioxidants,* 11(2022) 1330.

[5] A. Kowalczyk, M. Przychodna, S .Sopata, A. Bodalska, I Fecka, Thymol and Thyme Essential Oil—New Insights into Selected Therapeutic Applications. *Molecule,*25 (2020) 4125.

[6] E. Vassiliou, O .Awoleye, A. Davis, S. Mishra, Anti-Inflammatory and Antimicrobial Properties of Thyme Oil and Its Main Constituents. *Int. J. Mol. Sc,*24 (2023) 6936.

[7]R Kumar, S .Sharma, S.Sood, VK. Agnihotri,Evaluation of several Rosa damascena varieties and Rosa bourboniana accession for essential oil content and composition in western Himalayas. *J. Essent. Oil Res,* 26(2014) 147–152.

[8]A.Kumar, RD.Gautam, S.Singh, R.Chauhan, M. Kumar, D .Kumar, A. Kumar, S. Singh, Phenotyping floral traits and essential oil profiling revealed considerable variations in clonal selections of damask rose (Rosa damascena Mill.). *Sci Rep,* 13 (2023) 8101.

[9]H. Baydar, S .ERBAŞ, S. Kazaz,Variations in floral characteristics and scent composition and the breeding potential in seed-derived oil-bearing roses (Rosa damascena Mill.). Turkish *J. Agric. For,*40 (2016) 560–569.

[10] M. Yaghoobi, MM. Farimani, Z. Sadeghi, S. Asghari, H. Rezadoost, Chemical analysis of Iranian Rosa damascena essential oil, concrete, and absolute oil under different bio-climatic conditions. *Ind. Crops Prod,* 187(2022) 115266.

[11] K Singletary, Thyme: history, applications, and overview of potential health benefits. *Nutrition Today,* 51(2016) 40-49.

[12] M .Gavahian, A. Farahnaky, K .Javidnia, Comparison of ohmic-assisted hydrodistillation with traditional hydrodistillation for the extraction of essential oils from Thymus vulgaris L. *Innovative Food Science & Emerging Technologies*, 14(2012)85-91.

[13] V. Kuete, *Medicinal* spices and vegetables from Africa: therapeutic potential against metabolic, inflammatory, infectious, and systemic diseases. Edition: 1, *Elsevier*, (2017) ISBN: 9780128092866.

[14] N. Jain, P. Choudhary, Phytochemistry, Traditional Uses and Pharmacological Aspect of Thymus vulgaris: A Review. *Indian Journal of Pharmaceutical Sciences*, 84(2022)1369-1379.

[15] S. Hosseinzadeh, A. Jafarikukhdan, A. Hosseini, R. Armand, The application of medicinal plants in traditional and modern medicine: a review of Thymus vulgaris. *International Journal of Clinical Medicine*, 6(2015)635-642.

[16] S. Jarić, M. Mitrović, P. Pavlović, Review of ethnobotanical, phytochemical, and pharmacological study of Thymus serpyllum L. *Evidence-based complementary and alternative medicine*, (2015)1019781-10.

[17] Akbar.S., Akbar.S, Thymus vulgaris L. (Lamiaceae) (Syns.: T. chinensis K. Koch; T. ilerdensis González ex Costa; T. sublaxus Rouy). Handbook of 200 Medicinal Plants*: A Comprehensive Review of Their Traditional Medical Uses and Scientific Justifications*, (2020)1795-1810.

[18] E. Basch, C. Ulbricht, P. Hammerness, A. Bevins, D. Sollars, Thyme (Thymus vulgaris L.), thymol. *Journal of herbal pharmacotherapy*, 4(2004) 49-67.

[19] Stahl-Biskup, E. and Sáez, F. eds. (2002). Thyme: the genus Thymus. *CrC press.*

[20] P. Satyal, BL. Murray, RL. McFeeters, WN. Setzer , Essential oil characterization of Thymus vulgaris from various geographical locations. *Foods, 5(2016)70.*

[21] Q. Benameur, T. Gervasi, V. Pellizzeri, M. Pľuchtová, H. Tali-Maama, F.Assaous, B.Guetto, Antibacterial activity of Thymus vulgaris essential oil alone and in combination with cefotaxime against bla ESBL-producing multidrug resistant Enterobacteriaceae isolates. *Natural product research,* 33(2019)2647-2654.

[22] MS.Taher, YF.Salloom, R.Al-Asadi, ZJ.Al-Mousswi, HA Alamrani, The medicinal importance of Thyme plant (Thymus vulgaris). *Biomedicine,* 41(2021)531-534.

[23] VK.Kaul, VS.Singh,BS.Singh, Damask rose and marigold: prospective industrial crops. *J. Medicin. Aromat. Plant Sci,*22(2000)313-318.

[24] V. Farnia, M.Shirzadifar, J.Shakeri, M.Rezaei, H. Bajoghli,E.Holsboer-Trachsler, S.Brand,Rosa damascena oil improves SSRI-induced sexual dysfunction in male patients suffering from major depressive disorders: results from a double-blind, randomized, and placebo-controlled clinical trial. *Neuropsychiatr Dis Treat,*11(2015)625-635.

[25] S.Gudin**,**Rose: genetics and breeding. *Plant Breed.* Rev, 17 (2010)159-189.

[26] M. H. Boskabady, M. N. Shafei, Z. Saberi, S.Amini,Pharmacological effects of Rosa damascena. *Iran. J. Basic Med. Sci.* 14(2011)295-307.

[27] N.Kovacheva, K.Rusanov, I.Atanassov, Industrial cultivation of oil bearing rose and rose oil production in bulgaria during 21 ST century directions and challenges. *Biotechnol.* Biotechnol. *Equip.* 24(2010)1793–1798.

[28] M.Mahboubi, Rosa damascena as holy ancient herb with novel applications. *Journal of traditional and* complementary *medicine,* 6(2016), pp.10-16.

[29] M. Omidi, A. Khandan-Mirkohi, M. Kafi, O. Rasouli, A. Shaghaghi, M .Kiani, Z. Zamani, Comparative study of phytochemical profiles and morphological properties of some Damask roses from Iran. *Chemical and Biological Technologies in Agriculture,* 9(2022).51.

[30] B. Mahdood, B. Imani, S. Khazaei, Effects of Inhalation Aromatherapy with Rosa damascena (Damask Rose) on the State Anxiety and Sleep Quality of Operating Room Personnel During the COVID-19 Pandemic: A Randomized Controlled Trial. *J. Perianesth Nurs.* 37(2022)493-500.

[31] A. Nikbakht, M. Kafi, A study on the relationships between Iranian people and Damask rose (Rosa damascena) and its therapeutic and healing properties. In VIII International People-Plant Symposium on Exploring Therapeutic Powers of Flowers, *Greenery and Nature* 790(2008) 251-254.

[32] Alizadeh, Z., Fattahi, M. (2021). Essential oil, total phenolic, flavonoids, anthocyanins, carotenoids, and antioxidant activity of cultivated Damask Rose (Rosa damascena) from Iran: With chemotyping approach concerning morphology and composition. Scientia *Horticulturae,* 288 (2021).110341.

[33] Guenther, E. and Althausen, D, The essential oils. *New York: Van Nostrand.* 1(1984)81

[34] G. Busetta, M. Ponte, M. Barbera, A. Alfonzo, A. Ioppolo, G .Maniaci, R. Guarcello, N. Francesca, Influence of Citrus Essential Oils on the Microbiological, Physicochemical and Antioxidant Properties of Primosale Cheese. *Antioxidants (Basel),* 11(2022) 2004.

[35] K .Rusanov, N .Kovacheva, B .Vosman, L .Zhang, S. Rajapakse, A .Atanassov, I. Atanassov, I,.Microsatellite analysis of Rosa damascena Mill. accessions reveal genetic similarity between genotypes used for Rose oil production and old Damask rose varieties. *Theoretical and Applied Genetics,* 111(2005) 804-809.

[36] SR.Tabaei-Aghdaei, A.Babaei, M.Khosh-Khui, K. Jaimand, MB .Rezaee, MH .Assareh, Morphological and oil content variations amongst Damask rose (Rosa damascena Mill.) landraces from different regions of Iran. *Scientia Horticulturae,* 113(2007)44-48.

[37] MB. Hassanpouraghdam, Y .Salimi, MR .Morshedloo, M. Asadi, F. Rasouli, S. Ercisli, H. Fidan, Stachys lavandulifolia Populations: Volatile Oil Profile and Morphological Diversity. *Agronomy,* 12(2022)1430.

[38] K Morteza-Semnani, M. Akbarzadeh, S. Changizi, Essential oils composition of Stachys byzantina, S. inflata, S. lavandulifolia and S. laxa from Iran. *Flavour and fragrance journal,*21(2006).300-303.

[39] POWO, Plants of the World Online. Facilitated by the Royal Botanic Gardens, Kew. Published on the Internet (2021)

[40] K. Semnani, M.Akbarzadeh, S.Changizi,Essential oils composition of Stachys byzantina, S.inflata, S. lavandulifolia and S. laxa from Iran. *Flavour and Fragr* ,21(2006)300–3.

[41] H. Akhani, P. Trimborn, H Ziegler,Photosynthetic pathways in Chenopodiaceae from Africa, Asia, and Europe with their ecological, phytogeographical and taxonomical importance. *Plant Systematics and Evolution,* 206 (1997)187-221.

[42] T. Özdöl, Ö .Güner, A. Sefalı, E. Akcicek, T .Dirmenci, H. Yıldırım, Three new records for the flora of Turkey: Campanula lyrata subsp. icarica (Campanulaceae), Erysimum aureum (Brassicaceae) and Stachys benthamiana (Lamiaceae). *Phytotaxa,* 531(2022)147-150.

[43] EMA. Dauqan, A. Abdullah, A,Medicinal and functional values of thyme (Thymus vulgaris L.) herb. *Journal of applied biology and biotechnology*, 5(2017)017-022.

[44] B. Salehi, MS. Abu-Darwish, AH. Tarawneh, C. Cabral, AV. Gadetskaya, L. Salgueiro, Thymus spp. plants-Food applications and phytopharmacy properties. *Trends in Food Science & Technology,* 85(2019)287-306.

[45] A. Drioiche, FZ. Radi, A. Ailli, A. Bouzoubaa, A. Boutakiout, S. Mekdad, OAL. Kamaly, A. Salehr, Correlation between the chemical composition and the antimicrobial properties of seven samples of essential oils of endemic Thymes in Morocco against multi-resistant bacteria and pathogenic fungi, Saudi Pharmaceutical Journal, 30 (2022) 1200-1214.

[46] NA. Alshaikh, K. Perveen, Susceptibility of Fluconazole-Resistant Candida albicans to Thyme Essential Oil. *Microorganisms,* 9(2021)2454.

[47] G. Nieto,A review on applications and uses of thymus in the food industry. *Plants (Basel),* 9(2020)1-29

[48] A. Dobreva, D. Nedeltcheva-Antonova, Comparative Chemical Profiling and Citronellol Enantiomers Distribution of Industrial-Type Rose Oils Produced in China. *Molecules,* 28(2023)1281.

[49] M. Moein, Y. Ghasemia, F. Karami, H. TavallaliComposition of the essential oil of Rosa damascenea Mill. from South of Iran. *Iranian Journal of Pharmaceutical Sciences,* 6(2010)59-62.

[50] H. Baydar, NG. Baydar, The effects of harvest date, fermentation duration and Tween 20 treatment on essential oil content and composition of industrial oil rose (Rosa damascena Mill.). *Industrial crops and products,* 21(2005)251-255.

[51] N Yasa, F. Masoumi, RSE. ROUHANI, AA. HAJICorrespondence chemical composition and antioxidant activity of the extract and essential oil of Rosa damascena from Iran, *Guilan. Daru. J,* 17(2009)175–180.

[52] A. Zargari, Medicinal plants. *Tehran University of* Medical *Sciences*, (1997).

[53] A. Nikbakht, M. Kafi, M. Mirmasoudi, M. Babalar, Micropropagation of Damask rose (Rosa damascena Mill.) cvs Azaran and Ghamsar. Inter. J. Agri. Bio, 7(2004) 535–538.

[54] M. Kurkcuoglu, KHC. Baser, Studies on Turkish rose concrete, absolute, and hydrosol. *Chemistry of natural compounds,* 39 (2003)457-464.

[55] L. Bakhtyari, L. Shirbeigi, M. Tabarrai, R. Rahimi, A Ayatollahi, Efficacy of a Polyherbal Syrup Containing Lemon Balm, Damask Rose, and Fennel to Treat Melasma: A Randomized, Triple - Blind, Controlled Clinical Trial. *Jundishapur J Nat Pharm Pro,*18(2023)1-9.

[56] S. Ulusoy, G. Boşgelmez-Tınaz, H. Seçilmiş-Canbay carotene, phenolic contents, and antibacterial properties of rose essential oil, hydrosol and absolute. *Current microbiology,* 59 (2009)554-558.

[57] S. Gateva, G. Jovtchev, T. Angelova, T. Gerasimova, A. Dobreva, M. Mileva Cytogenetic Studies on Genoprotective Effect of Rosa damascena Mill. Hydrosol in Plant and Lymphocyte Test Systems. *Life (Basel).* 13(2023) 1753.

[58] A. Dadkhah, F. Fatemi, MRM. Malayeri, MHK. Ashtiyani, SK. Noureini, A. Rasooli, Considering the Effect of Rosa damascena Mill. Essential Oil on Oxidative Stress and COX-2 Gene Expression in the Liver of Septic Rats. *Turk J Pharm Sci.* 16(2019) 416-424.

[59] BC. Andoğan, H Baydar, S. Kaya, M. Demirci, D. Özbaşar, E. Mumcu,Antimicrobial activity and chemical composition of some essential oils. *Archives of pharmacal research,* 25 (2002860-864.

[60] V. Gochev, K. Wlcek, G. Buchbauer, A. Stoyanova, A. Dobreva, E. Schmidt, L. Jirovetz, L,Comparative evaluation of antimicrobial activity and composition of rose oils from various geographic origins, in particular Bulgarian rose oil. *Natural Product Communications,* 3(2008)1063-1068.

[61] M. Etschmann, W. Bluemke, D. Sell, J. Schrader, Biotechnological production of 2-phenylethanol. *Appl. Microbiol. Biotechnol.* 59(2002)1-8.

[62] A. Gholamhoseinian, H. Fallah, F. Sharifi-Far, M. Mirtajaddini,The Inhibitory Effect of Some Iranian Plants Extracts on the Alpha Glucosidase', *Iranian Journal of Basic Medical Sciences,* 11(2008) 1-9.

[63] A. Gholamhoseinian, H. Fallah, H.,Inhibitory effect of methanol extract of Rosa damascena Mill. flowers on α-glucosidase activity and postprandial hyperglycemia in normal and diabetic rats. *Phytomedicine,* 16(2009)935-941.

[64] N. Mahmood, S. Piacente, C. Pizza, A. Burke, AI. Khan, AJ. Hay, The anti-HIV activity and mechanisms of action of pure compounds isolated fromrosa damascena. *Biochemical and biophysical research communications,* 229(1996)73-79.

[65] A. Maleev, G. Neshtev, S. Stoianov, N. Sheikov, The ulcer protective and anti-inflammatory effect of Bulgarian rose oil. *Eksperimentalna meditsina i morfologiia,* 11(1972)55-60.

[66] SR. Tannenbaum, JS. Wishnok, CD. Leaf, Inhibition of nitrosamine formation by ascorbic acid. *The American journal of* clinical *nutrition,* 53(1991)247S-250S.

[67] V. Hajhashemi, A. Ghannadi, M. Hajiloo,Analgesic and anti-inflammatory effects of Rosa damascena hydroalcoholic extract and its essential oil in animal models. *Iranian journal of pharmaceutical research: IJPR,* 9(2010)163.

[68] K. Javidnia, F. Mojab, SA. Mojahedi, Chemical constituents of the essential oil of Stachys lavandulifolia Vahl from Iran. Labiatae family in folk medicine in Iran: from ethnobotany to pharmacology. *Iranian Journal of Pharmaceutical Research,* 3(2004)61-63.

[69] J. Kukić, S. Petrović, M. Niketić, Antioxidant activity of four endemic Stachys taxa. *Biological and Pharmaceutical* Bulletin, 29(2006)725-729.

[70] N. sadat Tabatabaei, M. Mazandaranee, Autocology and ethnopharmacology of Mespilus germanica L. in the North of Iran. In *AIP Conference Proceedings* ,971 (2008)248-251.

[71] Erdemoglu, N., Turan, N.N., Cakõcõ, I., Sener, B. and Aydõn, A, Antioxidant activities of some Lamiaceae plant extracts. Phytotherapy Research: *An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives,* 20(2006)9-13

[72] L. Jafarzadeh, A. Asgari, IF. GOLSHAN, S. KHEYRI, N. Parvin, M. RAFIEIAN, F. Taji,Abortificient effects of Stachys lavandulifolia Vahl in mice. *Journal of Shahrekord University of Medical Sciences,* 11(2010)26-31

[73] F. Olfati, S. Azarbaijani, M. Hadizadeh, T. Sadeghi, E. Hajseiedjavadi,E.,Effect of powder of Stachys lvandulifolia flowers on primary dysmenorrhea. *Journal of Medicinal Plants,* 9(2010).

[74] M. Rabbani, SE. Sajjadi, HR. Zarei, Anxiolytic effects of Stachys lavandulifolia Vahl on the elevated plus-maze model of anxiety in mice. *Journal of ethnopharmacology,* 89(2003)271-276.

[75] F. Nabavizadeh, AM. Alizadeh, S. Adeli, M. Golestan, H. Moloudian, M. Kamalinejad., Gastroprotective effects of Stachys Lavandulifolia extract on experimental gastric ulcer. *Afr J Pharm Pharmacol,* 5(2011),155-9.

[76] M. Asadi, S. Bahrami, SR. ANSARI,The effect of Stachys Lavandulifolia Vahl. and Mespilus Germanica L. leaves hydroalcoholic extracts on Leishmania Major (MRHO/IR/75/ER) in vitro. *Jundishapur. J. Nat. Pharm.* 5(2010)39-43.

[77] S. Andalib, A. Vaseghi, G. Vaseghi, AM. Naeini., Sedative and hypnotic effects of Iranian traditional medicinal herbs used for treatment of insomnia. *EXCLI journal,* 10(2011).192.

[78] V. Hajhashemi, A. Ghannadi, S. Sedighifar., Analgesic and anti-inflammatory properties of the hydroalcoholic, polyphenolic and boiled extracts of Stachys lavandulifolia. *Research in Pharmaceutical Sciences,* 1(2007)92-98.

[79] E. Jenabi, M. Asltoghiri, M. Hajiloomohajeran, M. Torkamani Effect of Stachys lavandulifolia on fatigue, nausea and vomiting associated with primary dysmenorrheal. *Procedia Soc Behav Sci*,31(2012) 124.

[80] P. Mirabi, F. Mojab, M203 Effects of Stachys Lavandulifolia on the Severity and Systemic Manifestations of Dysmenorrhea. *International Journal of Gynecology & Obstetrics,* 119 (2012) S598-S598

[81]F. Naghibi, M. Mosaddegh, SM. Motamed, A. Ghorbani, Labiatae family in folk medicine in Iran: *from ethnobotany to pharmacology. Iranian Journal of Pharmaceutical Research,* 4(2022)63-79.

[82]R. Tundis, L. Peruzzi, F. Menichini., Phytochemical and biological studies of Stachys species in relation to chemotaxonomy: a review. *Phytochemistry,* 102 (2014)7-39.

[83] GH.Amin., Popular medicinal plants of Iran. *Ministry of health,* (1991).40-47.

[84] M. Ramezani, MK. Hassanzadeh, DM. Safdarabadi., Volatile constituents of Stachys lavandulifolia Vahl growing in Iran, (2002): 20-23.

[85] M. Khanavi, M. Hajimahmoodi, M. Cheraghi-Niroomand, Z. Kargar, Y. Ajani, A. Hadjiakhoondi, Comparison of the antioxidant activity and total phenolic contents in some Stachys species. *African Journal of Biotechnology*, 8(2009).

[86] M. Öztürk, ME. Duru, F. Aydoğrmuş-Öztürk, M. Harmandar, M. Mahlıçlı, U. Kolak, A. Ulubelen.,GC-MS analysis and antimicrobial activity of essential oil of Stachys cretica subsp. *smyrnaea. Natural product communications,* 4(2009)1934578X0900400124.

[87] M. Taheri, A. Majd, T. Nejadsattari, H. Hekmatshoar, S. Mehrabian,Ethanolic extract of aerial organs of Stachys lavandulifolia Vahl in generative phase has more efficient antimicrobial effects. *Advances in* Environmental *Biology,* (2013)4016-4022.

[88] B. Minae, M. Sardari, H. Sharifi, MSR. Abadi, O. Sadeghpour. Stachys lavandulifolia Vahl. and its relation with marmazad activities in traditional manuscripts. *Iranian Red Crescent Medical Journal,* 17(2015).

[89] M. Khanavi, M. Sharifzadeh, A. Hadjiakhoondi., Phytochemical investigation and anti-inflammatory activity of aerial parts of Stachys byzanthina C. Koch. *Journal of ethnopharmacology,* 97(2005)463-468.

[90] H. Skaltsa, P. Bermejo, D. Lazari, AM. SILVAN, AL. SKALTSOUNIS, A. SANZ, MJ. ABAD,Inhibition of prostaglandin E2 and leukotriene C4 in mouse peritoneal macrophages and thromboxane B2 production in human platelets by flavonoids from Stachys chrysantha and Stachys candida. *Biological and Pharmaceutical Bulletin,* 23(2000)47-53.

[91] S. Grujic-Jovanovic, HD. Skaltsa, Marin, M. Sokovic, Composition and antibacterial activity of the essential oil of six Stachys species from Serbia. *Flavour and Fragrance Journal,* 19(2004)139-144.

[92] Z. Amirghofran, M. Bahmani, A. Azadmehr, K. Javidnia,Anticancer effects of various Iranian native medicinal plants on human tumor cell lines. *Neoplasma,* 53(2006)428-433.

[93] G Stamatis, P Kyriazopoulos, S Golegou, A Basayiannis, S Skaltsas, H Skaltsa, In vitro anti-Helicobacter pylori activity of Greek herbal medicines. *Journal of ethnopharmacology, 88(2003).175-179.*

[94] AK. Al-Asmari, MT. Athar, AA. Al-Faraidy, MS. Almuhaiza, Chemical composition of essential oil of Thymus vulgaris collected from Saudi Arabian market. *Asian Pacific Journal of Tropical Biomedicine,* 7(2017)147-150.

[95] W. Abdelli, F. Bahri, A. Romane, M. Höferl, J. Wanner, E. Schmidt, L. Jirovetz,Chemical composition and anti-inflammatory activity of Algerian Thymus vulgaris essential oil. *Natural product communications,* 12(2017)1934578X1701200435.

[96] I. Stefanis, D. Hadjipavlou-Litina, AR. Bilia, A. Karioti ,LC-MS-and NMR-guided isolation of monoterpene dimers from cultivated Thymus vulgaris varico 3 hybrid and their antityrosinase activity. *Planta Medica,* 85(2019)941-946.

[97] NK. Fayad, OHS. AL-Obaidi, TH. Al-Noor, MO. Ezzat, Water and alcohol extraction of Thyme plant (Thymus vulgaris) and activity study against bacteria, tumors and used as antioxidant in margarine manufacture. *Innovative Systems Design and Engineering,* 4(2013)41-51.

[98] D. Asha, L. Mathew, Chemical profiling of Thymus vulgaris L. using HPTLC. *Journal of Pharmacognosy and Phytochemistry,* 6(2017)1017-1023.

[99] SM. Patil, R. Ramu, PS. Shirahatti, C. Shivamallu, RG. Amachawadi, A systematic review on ethnopharmacology, phytochemistry and pharmacological aspects of Thymus vulgaris Linn. *Heliyon,* 7(2021)07054.

[100] U. Ejaz, M. Afzal, M. Mazhar, M. Riaz, N. Ahmed, WY. Rizg, AA. Alahmadi, MY. Badr, RY. Mushtaq, Characterization, Synthesis, and Biological Activities of Silver Nanoparticles Produced via Green Synthesis Method Using Thymus Vulgaris Aqueous Extract, *International Journal of Nanomedicine*, 19 (2021) 453-469.

[101] YSB. Baraya, KK. Wong, NS. Yaacob, The immunomodulatory potential of selected bioactive plant-based compounds in breast cancer: a review. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents), 17(2017)770-783.

[102] L. Zhang, J. Zhang, B. Zhao, X. Zhao-Wilson, Quinic acid could be a potential rejuvenating natural compound by improving survival of Caenorhabditis elegans under deleterious conditions. *Rejuvenation Research,* 15(2012).573-583.

[103] M. Nadeem, M. Imran, T. Aslam Gondal, A. Imran, M. Shahbaz, R. Muhammad Amir, Therapeutic potential of rosmarinic acid: A comprehensive review. *Applied Sciences,* 9(2019)3139.

[104] T Hase, S Shishido, S Yamamoto, R Yamashita, H Nukima, S Taira, T Toyoda, K Abe. , Rosmarinic acid suppresses Alzheimer's disease development by reducing amyloid β aggregation by increasing monoamine secretion. Scientific *Reports,* 9(2019)8711.

[105] KMM. Espíndola, RG. Ferreira, LEM. Narvaez, ACR. Silva Rosario, AHM. Da Silva, AGB. Silva, Chemical and

pharmacological aspects of caffeic acid and its activity in hepatocarcinoma. Frontiers in oncology, 9(2019)541.

[106] A. Duangjai, N. Nuengchamnong, N. Suphrom, K. Trisat, N. Limpeanchob, S. Saokaew,Potential of coffee fruit extract and quinic acid on adipogenesis and lipolysis in 3T3-L1 adipocytes. *Kobe Journal of Medical Sciences,* 64(2018)84.

[107] S. Habtemariam, Protective effects of caffeic acid and the alzheimer's brain: an update. *Mini Reviews in Medicinal Chemistry,* 17(2017)667-674.

[108] SJ. Pragasam, V. Venkatesan, MK. Rasool, Immunomodulatory and anti-inflammatory effect of p-coumaric acid, *a common dietary polyphenol on experimental inflammation in* rats. *Inflammation,* 36(2013) 169-176.

[109] Saibabu, V., Fatima, Z., Khan, L.A. and Hameed, S. (2015). Therapeutic potential of dietary phenolic acids. *Advances in pharmacological sciences.*

[110] Y. Shen, X. Song, L. Li, J Sun, Y. Jaiswal, J. Huang, C. Liu, W. Yang, L. Williams, H. Zhang, Protective effects of p-coumaric acid against oxidant and hyperlipidemia-an in vitro and in vivo evaluation. *Biomedicine & Pharmacotherapy,* 111(2019)579-587.

[111] C. Cueva, MV. Moreno-Arribas, PJ. Martín-Álvarez, Antimicrobial activity of phenolic acids against commensal, probiotic, and pathogenic bacteria. *Research in* microbiology, 161(2010)372-382.

[112] OA. Flausino, L. Dufau, LO. Regasini, MS. Petronio, D HS. Silva, T. Rose, VS. Bolzani, Alkyl hydroxybenzoic acid derivatives that inhibit HIV-1 protease dimerization. *Current medicinal chemistry,* 19(2012)4534-4540.

[113] C. Seidel, M. Schnekenburger, A. Mazumder, MH. Teiten, G. Kirsch, M. Dicato, M. Diederich,4-Hydroxybenzoic acid derivatives as HDAC6-specific inhibitors modulating microtubular structure and HSP90α chaperone activity against prostate cancer. *Biochemical pharmacology,* 99(2016).31-52.

[114] M Abotaleb, A. Liskova, P. Kubatka, D. Büsselberg,Therapeutic potential of plant phenolic acids in the treatment of cancer. *Biomolecules,* 10(2020)221.

[115] F. Abedi, BM. Razavi, H. Hosseinzadeh, A review on gentisic acid as a plant derived phenolic acid and metabolite of aspirin: Comprehensive pharmacology, toxicology, and some pharmaceutical aspects. *Phytotherapy research,* 34(2020)729-741.

[116] C. Srinivasulu, M. Ramgopal, G. Ramanjaneyulu., Syringic acid (SA)–a review of its occurrence, biosynthesis, pharmacological and industrial importance. *Biomedicine & Pharmacotherapy,* 108(2018)547-557.

[117] T. Tanaka, N. Kawaguchi, N. Zaima, T. Moriyama, Y. Fukuta, N. Shirasaka, Antiosteoporotic activity of a syringic acid diet in ovariectomized mice. *Journal of natural* medicines, 71(2017)632-641.

[118] A. Chaudhary, VS. Jaswal, S. Choudhary, A. Sharma, V. Beniwal, HS. Tuli, S. Sharma, Ferulic acid: a promising therapeutic phytochemical and recent patents advances. *Recent Patents on Inflammation & Allergy Drug Discovery,* 13(2019)115-123.

[119] C. Mancuso, R. Santangelo, Ferulic acid: pharmacological and toxicological aspects. *Food and Chemical Toxicology,* 65 (2014)185-195.

[120] B. Salehi, AP. Mishra, I. Shukla, M. Sharifi-Rad, MM. Contreras, A. Segura-Carretero, H. Fathi, Thymol, thyme, and other plant sources: *Health and potential uses. Phytotherapy research,* 32(2018)1688-1706.

[121] KH. Can Baser, K.H, Biological and pharmacological activities of carvacrol and carvacrol bearing essential oils. *Current* pharmaceutical *design,* 14(2008)3106-3119.

[122] Z. Heidari, A. Salehzadeh, SA. Sadat Shandiz, S. Tajdoost, Anti-cancer and antioxidant properties of ethanolic leaf extract of Thymus vulgaris and its bio-functionalized silver nanoparticles. *3 Biotech,* 8(2018).1-14.

[123] Y. Lei, P. Fu, X. Jun, P. Cheng,Pharmacological properties of geraniol–a review. *Planta medica,* 85(2019)48-55.

[124] I. Pereira, P. Severino, AC. Santos, AM. Silva, EB. Souto, Linalool bioactive properties and potential applicability in drug delivery systems. Colloids and *Surfaces B: Biointerfaces,* 171(2018)566-578.

[125] G. Kiskó, S. Roller,Carvacrol and p-cymene inactivate Escherichia coli O157: H7 in apple juice. *BMC* microbiology, 5(2005)1-9.

[126] LR. Bonjardim, ES. Cunha, AG. Guimarães, MF. Santana, MGB. Oliveira, MR. Serafin, Evaluation of the anti-inflammatory and antinociceptive properties of p-cymene in mice. *Zeitschrift für Naturforschung* C, 67(2012)15-21.

[127] A. Marchese, CR. Arciola, R. Barbieri, AS. Silva, SF. Nabavi, AJ. Tsetegho Sokeng, M. Izadi,Update on monoterpenes as antimicrobial agents: *A particular focus on p-cymene. Materials,* 10(2017)947.

[128] MK. Swamy, MS. Akhtar, UR. Sinniah , Antimicrobial properties of plant essential oils against human pathogens and their mode of action: an updated review. *Evidence-based complementary and alternative medicine (2016)*

[129] FFB. Passos, EM. Lopes, JM. de Araújo, DP. de Sousa, LMC. Veras, JRSA. Leite, FRC, AlmeidaInvolvement of Cholinergic and Opioid System in γ-Terpinene-Mediated Antinociception. *Evid Based* Complement *Alternat Med*. (2015)829414.

[130] MC. Foti, KU. Ingold, Mechanism of inhibition of lipid peroxidation by γ-terpinene, an unusual and potentially useful hydrocarbon antioxidant. *Journal of agricultural and food chemistry,* 51(2003)2758-2765.

[131] YM. Mukhtar, M. Adu-Frimpong, X. Xu, J. Yu,Biochemical significance of limonene and its metabolites: future prospects for designing and developing highly potent anticancer drugs. *Bioscience Reports,* 38(2018). BSR20181253

[132] C. Sharma, JM. Al Kaabi, SM. Nurulain, Polypharmacological properties and therapeutic potential of β-caryophyllene: a dietary phytocannabinoid of pharmaceutical promise. *Current pharmaceutical design,* 22(2016)3237-3264.

[133] B. Salehi, S. Upadhyay, I. Erdogan Orhan, A. Kumar Jugran, S. LD Jayaweera, DA. Dias, Therapeutic potential of α-and β-pinene: A miracle gift of nature. Biomolecules, 9(2019)738.

[134] C. Khaleel, N. Tabanca, G. Buchbauer,. *α-Terpineol, a natural monoterpene: A review of its biological properties. Open Chemistry,* 16(2018)349-361.

[135] B. Salehi, A. Venditti, M. Sharifi-Rad, D. Kręgiel, J. Sharifi-Rad, A. Durazzo, M. Lucarini, A. Santini, The therapeutic potential of apigeninInt. *J. Mol. Sci.,* 20(2019)1305.

[136] F. Ali, S. Jyoti, F. Naz, M. Ashafaq, M. Shahid, YH. Siddique,Therapeutic potential of luteolin in transgenic Drosophila model of Alzheimer's disease. *Neuroscience letters,* 692(2019).90-99.

[137] Y. Lin, R. Shi, X. Wang, HM. Shenuteolin, a flavonoid with potential for cancer prevention and therapy. *Current cancer drug targets,* 8(2008)634-646.

[138] A. Mahmood, HZ. Alkhathlan, Isolation, synthesis, and pharmacological applications of cirsimaritin—A short review. *J. Med. Plants Res,* 7(2019)252-260.

[139] S. Guo, X. Wu, J. Zheng, N. Charoensinphon, P. Dong,Anti-inflammatory effect of xanthomicrol, a major colonic metabolite of 5-demethyltangeretin. *Food & function,* 9(2018)3104-3113.

[140] M. Fattahi, RM. Cusido, A. Khojasteh, M. Bonfill, J. Palazon, Xanthomicrol: A comprehensive review of its chemistry, distribution, biosynthesis, and pharmacological activity. *Mini Reviews in Medicinal Chemistry,* 14(2014)725-733.

[141] N. Oka, A. Ikegami, M. Ohki, K. Sakata, A. Yagi, Citronellyl disaccharide glycoside as an aroma precursor from rose flowers. *Phytochemistry,* 47(1998)1527-1529.

[142] N. Kumar, B. Singh, VK. Kaul, Flavonoids from Rosa damascena mill. *Natural Product Communications,*1(2006)1934578X0600100805.

[143] J. Buckle, Aromatherapy in the context of nursing, the nature of aromatherapy. Clinical Aromatherapy in Nursing London: *Arnold* Publisher(1887)2-48.

[144] S. GHASEMI, R. HOSSEINZADEH, M. JAFARI,Antitussive effect of Rosa damascena in guinea pigs(2003) 231-234

[145] N. Mahmood, S. Piacente, C. Pizza, A. Burke, AI. Khan, AJ. Hay ,The anti-HIV activity and mechanisms of action of pure compounds isolated fromrosa damascena. Biochemical *and biophysical research communications,* 229(1996)73-79.

[146] H. Loghmani-Khouzani, Essential oil composition of Rosa damascena Mill cultivated in central Iran. *Scientia Iranica*. 14(2007)316-319.

[147] M. Chishti A., Akram, M., Laila, U., Zainab, R., Ifthikar, M., Ozdemir, F. A.Kebede, I. A., Rosa Damescana: A review of its conventional uses Phytochemistry and Pharmacology, Glob Acad. *J Agri Biosci;* 5(2023) 61-67.

[148] N. Yasa, F. Masoumi, RSE. ROUHANI, AA. HAJI, Chemical composition and antioxidant activity of the extract and essential oil of Rosa damascena from Iran, population of Guilan (2009): 175-180.

[149] FC. Huang, G. Horváth, P. Molnár, E. Turcsi, J. Deli, *a carotenoid* cleavage *oxygenase from Rosa damascena. Phytochemistry,* 70(2009) 457-464.

[150] AY. Aldhebiani, WA. Yaslam, Flavonoid Detection and Antioxidant Estimation in Rosa Damascena Mill. Growing in Taif and Al-Madinah Cities, Saudi Arabia. Pakistan Journal of Botany, 55(2023) 995–999.

[151] TB. Ng, F. Liu, ZT. Wang,Antioxidative activity of natural products from plants. *Life sciences,* 66(2000)709-723.

[152] V. Butterweck, G. Jürgenliemk, A. Nahrstedt, H.WinterhoffF,lavonoids from Hypericum perforatum show antidepressant activity in the forced swimming test. *Planta medica,* 66(2000)3-6.

[153] RS. Verma, RC. Padalia, A. Chauhan, A. Singh, AK. Yadav,Volatile constituents of essential oil and rose water of damask rose (Rosa damascena Mill.) cultivars from North Indian hills. *Natural product research,* 25(2011)1577-1584.

[154] G. İşcan, B. Demirci, F. Demirci, F. Göger, N. Kırımer, YB. Köse, KHC. Başer, Antimicrobial and antioxidant activities of Stachys lavandulifolia subsp. lavandulifolia essential oil and its infusion. *Natural product communications,* 7(2012)1241-1244.

[155] AG. Pirbalouti, M. Mohammadi, Phytochemical composition of the essential oil of different populations of Stachys lavandulifolia Vahl. *Asian Pacific Journal of Tropical Biomedicine,* 3(2013)123-128.

[156] H. Sadeghi, V. Zarezade, H. Sadeghi, MA. Toori, MJ. Barmak, A. Azizi, M. Ghavamizadeh,,Anti-inflammatory Activity of Stachys Pilifera Benth. Iranian Red Crescent medical journal, 16(2014)19259.

[157] R. Tundis, M. Bonesi, A. Pugliese, F. Nadjafi, F. Menichini, MR. Loizzo, Tyrosinase, acetyl-and butyryl-cholinesterase inhibitory activity of Stachys lavandulifolia Vahl (Lamiaceae) and its major constituents. *Records of Natural Products,* 9(2015)81-93.

[158] MB. Bahadori, G. Zengin, L. Dinparast,The health benefits of three Hedgenettle herbal teas (Stachys byzantina, Stachys inflata, and Stachys lavandulifolia)-profiling phenolic and antioxidant activities. *European Journal of Integrative Medicine,* 36(2020)101134.

[159] M. Rabbani, SE. Sajjadi, A. Jalali,Hydroalcohol extract and fractions of Stachys lavandulifolia vahl: effects on spontaneous motor activity and elevated plus-maze behaviour. Phytotherapy Research*: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 19(2005)854-858.*

[160] MR. Delnavazi, P. Saiyarsarai, S. Jafari-Nodooshan, M. Khanavi, S. Tavakoli, H. Hadavinia,Cytotoxic flavonoids from the aerial parts of Stachys lavandulifolia Vahl. *Pharmaceutical Sciences,* 24(2018)332-339.

[161] SE. Sajjadi, SM. Ghanadian, M. Rabbani, F. Tahmasbi, Isolation and Identification of Secondary Metabolites from the Aerial Parts of Stachys lavandulifolia Vahl. *Iranian journal of pharmaceutical research: IJPR,* 16(2017),58-63.

[162] C. Bitwell, SS. Indra, C. Luke, MK. Kakoma,A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants, *Scientific African,* 19(2023) e01585

[163] A. Ambrosini, LMP. Passaglia, Plant growth–promoting bacteria (PGPB): isolation and screening of PGP activities. *Curr. Prot. Plant Biol.* 2(2017)190–209.

[164] M Ghavam, Relationships of irrigation water and soil physical and chemical characteristics with yield, chemical composition and antimicrobial activity of Damask rose essential oil. *PLoS ONE* 16(2021) e0249363.

[165] JL.Rodriguez-Tudela, Method for determining minimum inhibitory concentration (MIC) by broth dilution of

fermentative yeasts. *Clinical Microbiology and Infection*, 9(2003) i-viii.

[166] BC. Nzeako, ZSN. Al-Kharousi, Z. Al-Mahrooqui, Antimicrobial activities of clove and thyme extracts. *Sultan Qaboos Univ. Med. J*. 6(2006) 33–39.

[167] M. Shahnama, S. Azami, M. Mohammadhosseini, Characterization of the Essential Oil and Evaluation of Antibacterial Activity of Methanolic Extract of Stachys lavandulifolia Vahl. *Int. J. Curr. Microbiol. App. Sci*. 4(2015)275-283.

[168] N. Thallaj, Evaluation of Antimicrobial Activities and Bioactive Compounds of Different Extracts Related to Syrian Traditional Products of Damask Rose (Rosa damascena). *Open Access Library Journal*, (2020)1-21.

[169] O. Borugă, C. Jianu, C. Mișcă, I. Goleț, AT. Gruia, FG. Horhat,Thymus vulgaris essential oil: chemical composition and antimicrobial activity. *Journal of medicine and life,* 7(2014)56-60.