



Evaluation of the Antimicrobial, Antioxidant, Anticholinesterase, and Antidiabetic Activities of *Matricaria chamomilla*, *Lavandula angustifolia*, *Hypericum perforatum*, *Salvia officinalis*, and *Foeniculum vulgare* Extracts

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ABSTRACT

This study evaluated and compared the antimicrobial, antioxidant, anticholinesterase, and antidiabetic activities of *Matricaria chamomilla* L. (chamomile), *Lavandula angustifolia* Mill. (lavender), *Hypericum perforatum* L. (St. John's wort), *Salvia officinalis* L. (sage), and *Foeniculum vulgare* Mill. (fennel) plants and their extracts. Antioxidant activity was assessed using DPPH and ABTS assays, while α -glucosidase and α -amylase inhibition assays determined antidiabetic potential. Acetylcholinesterase and butyrylcholinesterase inhibitory activities were measured via the Ellman method, and antimicrobial activity was evaluated using the micro-well dilution test. Among the tested extracts, *H. perforatum* extract and *H. perforatum* drug exhibited the most potent biological activities. In the α -glucosidase inhibition assay, *H. perforatum* extract displayed the highest inhibition (95.40%, $IC_{50} = 8 \mu\text{g/mL}$), followed by *H. perforatum* drug (94.71%, $IC_{50} = 27 \mu\text{g/mL}$). The strongest α -amylase inhibition was observed with the Soothing Complex Product (60.90%), following acarbose (74.61%). The highest ABTS radical scavenging activity was noted in *S. officinalis* drug (99.39%) and *H. perforatum* drug (99.32%), while the DPPH assay showed significant activity for *S. officinalis* extract (46.99%) and α -tocopherol (46.99%). Antimicrobial testing revealed moderate antibacterial effects of *F. vulgare* drug against *Staphylococcus aureus* and *Candida albicans* (MIC = 1250 $\mu\text{g/mL}$). Overall, *H. perforatum* extracts demonstrated strong enzyme inhibition and antioxidant properties, highlighting their potential for medicinal and dermocosmetic applications. These findings provide valuable insights into the bioactivity of herbal extracts, supporting their potential use in over-the-counter formulations and new plant-based therapeutic products.

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Introduction

Diabetes mellitus (DM) is a chronic condition characterized by hyperglycemia and can lead to a range of complications associated with various diseases. The most common type of DM is Type 2 diabetes mellitus (T2DM), which is a significant non-communicable disease with high mortality and a range of complications. One of the key risk factors associated with T2DM is postprandial hyperglycemia (PPHG), which refers to the rapid increase in blood glucose levels following meals. Controlling PPHG by reducing the digestion and absorption of carbohydrates is a strategy used in the prevention of diabetes. Additionally, the inhibition of enzymes such as α -amylase, α -glucosidase, and lipase plays a critical role in

the treatment of diabetes and obesity. Acarbose, commonly used in the treatment of hyperglycemia, prevents PPHG in diabetes by inhibiting α -glucosidase and α -amylase enzymes, which reduces the hydrolysis of carbohydrates (Schloesser et al., 2017; Hariftyani et al., 2021; Najibullah et al., 2021; Arslan & Çam, 2022).

Type 2 diabetes mellitus (T2DM) and Alzheimer's disease (AD) are both age-related conditions, with their incidence and prevalence increasing as individuals age. T2DM, one of the fastest growing epidemics, is characterized by insulin resistance in peripheral tissues, leading to hyperglycemia and hyperinsulinemia. AD, the most common neurodegenerative disorder, also becomes

more prevalent with age and is marked by neuronal loss, amyloid beta plaques, tau tangles, astrocyte proliferation, and microglial activation. Mitochondrial dysfunction and synaptic alterations further contribute to the disease. While the exact causes of AD remain unclear, the amyloid cascade hypothesis suggests that abnormal processing of amyloid-beta precursor protein and its accumulation may play a key role in its onset and progression (Barbagallo & Dominguez, 2014).

Matricaria chamomilla L., from the Asteraceae family, is an annual medicinal herb with thin, needle-like roots and an upright, highly branched stem (10–80 cm). Its long, narrow leaves are bipinnate or tripinnate. The golden-yellow tubular florets (1.5–2.5 mm) end in a glandular tube, while the 11–27 white ray florets (6–11 mm) are arranged concentrically. The flower receptacle (6–8 mm) is initially flat but becomes conical and is hollow, a key distinguishing feature. The fruit is a yellowish-brown achene (Gardiner, 1999; Singh et al., 2011). Chamomile exhibits significant antidiabetic, antioxidant, and antimicrobial properties supported by both traditional uses and scientific studies. Traditionally used as an infusion or decoction to manage diabetes, especially in Moroccan medicine, chamomile has been shown to reduce blood glucose levels and lipid peroxidation while enhancing antioxidant enzyme activities in diabetic models. Its antioxidant potential is attributed to a rich composition of flavonoids (e.g., luteolin, apigenin) and phenolic acids (e.g., chlorogenic, rosmarinic acids), with various extracts and essential oils demonstrating strong radical scavenging activity in DPPH, ABTS, and FRAP assays. Furthermore, chamomile essential oils and extracts possess notable antimicrobial effects, inhibiting a broad spectrum of Gram-positive and Gram-negative bacteria (including *Staphylococcus aureus* and *Pseudomonas aeruginosa*) and showing antifungal activity against *Candida* and *Aspergillus* species (El Mihyaoui et al., 2022).

Lavandula angustifolia Mill., also known as *L. officinalis*, is a highly aromatic shrub from the Lamiaceae family. Native to the Mediterranean region, it is an evergreen plant that grows up to 1–2 meters tall. Lavender thrives in diverse climates, preferring full sunlight and humus-rich soils with low organic matter. Its flowers and leaves are traditionally used for medicinal purposes, often in the form of essential oils or various extracts (Gilani et al., 2000; Méndez-Tovar et al., 2015; Niksic et al., 2016; Oskouie et al., 2018). *L. angustifolia* has been widely studied for its antidiabetic, antioxidant, and antimicrobial effects. Its antidiabetic potential has been demonstrated in various *in vivo* and *in vitro* models, with extracts showing significant hypoglycemic effects and protective activity against oxidative stress in diabetic conditions. The antioxidant activity is largely attributed to its rich phenolic content, including rosmarinic acid and flavonoids such as apigenin and kaempferol. Ethanol, aqueous ethanol, and methanol extracts have shown effective radical scavenging abilities and lipid peroxidation inhibition. In terms of antimicrobial properties, essential oils and extracts of *L. angustifolia* have exhibited inhibitory effects against a variety of pathogens, including *Staphylococcus aureus*, *Salmonella typhimurium*, *Candida albicans*, and *Candida glabrata*. The activity is linked to its major essential oil components, linalool and linalyl acetate, known for their antibacterial and antifungal potential (Üstüner, 2024).

H. perforatum, commonly known as St. John's Wort, is one of the most well-known species from the Hypericaceae family. It is a perennial plant widely found across Asia, Europe, and North Africa. Often used in herbal products and homeopathic preparations, St. John's Wort is also commonly used in food. The European Council has classified it as a natural food flavoring source, with restrictions based on its content of hypericin and xanthones (Zhang et al., 2020; Silva et al., 2021). *H. perforatum* exhibits strong antioxidant, antimicrobial, and antidiabetic activities that contribute to its therapeutic efficacy, particularly in wound healing. Its antioxidant effects are primarily due to its rich content of flavonoids (e.g., quercetin, hyperoside, rutin), phenolic acids (e.g., chlorogenic and caffeic acids), and naphthodianthrones (e.g., hypericin). These compounds effectively scavenge reactive oxygen species (ROS), reduce lipid peroxidation, and enhance antioxidant enzyme activities (e.g., catalase, superoxide dismutase, glutathione peroxidase), as shown in various *in vitro* assays such as DPPH and nitric oxide scavenging. The antimicrobial activity of *H. perforatum* is well-established, particularly against Gram-positive bacteria like *Staphylococcus aureus* and fungal strains such as *Candida albicans* and *Fusarium* spp. The most active components responsible are hypericin, hyperforin, and quercetin derivatives, which also reduce biofilm formation. Moreover, the plant's antidiabetic potential is supported by the presence of myricetin and quercetin (Farasati et al., 2024).

Salvia officinalis L., commonly known as sage, belongs to the Lamiaceae family and is recognized as an aromatic and medicinal plant. It is an evergreen, perennial shrub with a highly branched, woody stem and violet-colored flowers, reaching up to 60 cm in height. Native to the Mediterranean region, it is now cultivated worldwide. Among the *Salvia* species, *S. officinalis* has the highest yield of essential oils, up to 3%. This plant features glandular hairs and has a calyx that is 10–14 mm long, hairy, and toothed. The corolla is approximately 35 mm long and can be pink, violet-blue, or occasionally White (Tutin, 1972; Grdiša et al., 2015; Altindal & Altindal, 2016). *S. officinalis* exhibits a broad range of therapeutic activities, particularly antidiabetic, antioxidant, and antimicrobial effects, attributed to its rich phytochemical composition. Its antidiabetic activity has been demonstrated through the inhibition of α -amylase and α -glucosidase enzymes, which helps regulate postprandial glucose levels. The plant's antioxidant activity is primarily due to the presence of compounds such as rosmarinic acid, carnosic acid, and flavonoids, which efficiently scavenge free radicals and reduce oxidative stress—an important factor in chronic diseases like diabetes and neurodegeneration. In terms of antimicrobial activity, *S. officinalis* essential oils and extracts have shown effectiveness against various bacterial strains including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as antifungal activity against *Candida albicans*. These effects are largely attributed to bioactive constituents such as thujone, camphor, and 1,8-cineole, which exhibit bactericidal and fungistatic mechanisms (Miraj and Kiani, 2016).

Foeniculum vulgare Mill., commonly known as fennel, is a small, erect, and aromatic plant from the Apiaceae (Umbelliferae) family. Native to the Mediterranean and European regions, *F. vulgare* was originally endemic but is now widely cultivated in tropical and temperate climates worldwide. The plant has

bulbous leaves and yellow flowers, with green and white colors. Its double achenes are oval-shaped, veined, initially bluish and later turn brownish-gray. The bulb and seeds of fennel have a tuberous structure and a taste similar to licorice. The seeds, known for their essential oil, are particularly active. Fennel is a strong aromatic and spicy plant commonly used in cooking (Rizvi et al., 2007; Bukhari et al., 2014; Mehra et al., 2021). *F. vulgare* (fennel) demonstrates significant antidiabetic, antioxidant, and antimicrobial properties due to its diverse phytochemical composition, including essential oils (notably trans-anethole), flavonoids, phenolic acids, and coumarins. Its antidiabetic activity has been supported by studies on streptozotocin-induced diabetic rats, where both aqueous and methanol extracts lowered blood glucose and triglyceride levels while increasing glycogen storage in the liver and muscles. In terms of antioxidant effects, fennel is rich in polyphenols and flavonoids such as rosmarinic acid, quercetin, and caffeoylquinic acids, which contribute to strong radical scavenging activity measured by DPPH, FRAP, and hydrogen peroxide assays. Ethanolic and aqueous extracts showed dose-dependent antioxidant activity even higher than α -tocopherol at equivalent concentrations. Regarding antimicrobial activity, fennel exhibits strong effects against a wide range of bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, and *Helicobacter pylori*, with MIC values ranging from 5–80 mg/mL depending on the extract type. It also showed antifungal activity against *Candida albicans*, *Aspergillus niger*, and *Fusarium oxysporum*, largely attributed to constituents like anethole and dillapional (Kooti et al., 2015).

This study aims to evaluate and compare the antimicrobial, antioxidant, anticholinesterase, and antidiabetic effects of five medicinal plants—*M. chamomilla*, *L. angustifolia*, *H. perforatum*, *S. officinalis*, and *F. vulgare*—which are included in Greenext's commercial formulation, "Soothing Complex." These species were selected based on their widespread traditional use and well-documented individual biological activities. However, there is a lack of comparative data evaluating their combined and individual effects across different extract types. The study investigates four sample types: ethanol extracts prepared by the company, the final ready-made mixture, methanol extracts of dried plant materials, and an equal-proportion mixture of these extracts. By examining their activity profiles side-by-side, this research aims to determine whether the combination of these extracts yields enhanced or unique biological effects. In doing so, the study addresses a gap in the literature and contributes to the scientific basis for the development of new over-the-counter (OTC) herbal products with potential therapeutic and dermocosmetic applications.

Material and Method

Plant material

M. chamomilla (MC, chamomile, flowers), *L. angustifolia* (LA, lavender, flowers), *H. perforatum* (HP, St. John's wort, aerial parts), *S. officinalis* (SO, sage,

leaves), and *F. vulgare* (FV, fennel, fruits) plants used in this research were obtained from the medicinal and aromatic plant plantation field conducted at Atatürk University Plant Production Application and Research Center (AUPPARC), while the extracts were supplied by Laber Kimya Organik and Greenext. Additionally, the Soothing Complex product used in the analyses was also provided by the company. The full names and corresponding abbreviations of the samples used in this study were defined and applied consistently throughout the manuscript to ensure clarity. The abbreviation SCP refers to Soothing Complex Product. FDM stands for Five Drug Mixture (prepared by us). DRUG (D) refers to extracts from company and EXTRACT (E) refers to extracts prepared by us in our laboratory. SOD and SOE refer to samples of *S. officinalis*. MCD and MCE represent the samples of *M. chamomilla*. FVD and FVE correspond to samples of *F. vulgare*. HPD and HPE indicate the samples of *H. perforatum*. Lastly, LAD and LAE refer to the samples of *L. angustifolia*.

Extraction

The crude plant materials sent by the AUPPARC were weighed using a precise balance, with approximately 10–20 grams of each sample transferred into a round-bottom flask. To each flask, 90 mL of methanol was added, and the mixtures were subjected to maceration in a shaking water bath at 40°C and 100 RPM for 3 days. After extraction, the plant material was filtered through filter paper and a regular funnel into a separate flask, and the remaining plant residue was removed from the solvent. The filtrates were then concentrated in a rotary evaporator at 40°C and 120 RPM until dryness. The concentrated extracts were dissolved in a small amount of methanol and transferred into small jars. Additionally, the solvents of the ethanol extracts sent by the company were evaporated in the rotary evaporator. Finally, the quantities and yield percentages of the obtained extracts were calculated. Equal amounts of each extract were then combined to prepare a homogeneous mixture. As a result of these procedures, the obtained extracts were left on a heated plate for 3 days to completely evaporate any remaining methanol. Afterward, the extracts were dried and prepared for weighing before proceeding with the activity assays. The yield (%) was calculated as:

$$\% \text{ Yield} = \frac{\text{The extract weight (g)}}{\text{The crude material (g)}} \times 100$$

The soothing complex product and the plant ethanol extracts were supplied ready-made by the company and were used in the activity determinations.

α -Glucosidase Inhibitor Activity Assay

The α -glucosidase inhibitory activity was evaluated following a modified version of the method described by Bachhawat et al. (2021). In this assay, a 96-well microplate was used, where 50 μ L of phosphate buffer (50 mM, pH 6.9) was combined with 10 μ L of α -glucosidase enzyme solution (1 U/mL) and 20 μ L of plant extract at varying concentrations (1–5000 μ g/mL). The mixture was incubated at 37°C for 5 minutes. After incubation, 20 μ L of 3 mM *p*-nitrophenyl- α -D-glucopyranoside (pNPG) was

introduced as the substrate, and the reaction proceeded for another 30 minutes at the same temperature. To halt the reaction, 50 μ L of 0.1 M sodium carbonate was added. Acarbose served as the reference inhibitor. The release of *p*-nitrophenol (pNP) was quantified by measuring absorbance at 405 nm. All experiments were performed in triplicate, and the percentage of enzyme inhibition was determined using the formula:

$$\% \text{ Inhibition} = [(A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}}] \times 100$$

IC₅₀ values were determined using the linear equation ($y = mx + n$) derived from the dose–response curve plotting concentration against percent inhibition.

***α*-Amylase Inhibitory Activity Assay**

The α -amylase inhibitory activity was assessed based on a modified version of the method described by Nampoothiri et al. (2011). In this assay, 100 μ L of the test sample, prepared at various concentrations (1–5000 μ g/mL), was mixed with an equal volume of 1% starch solution in 20 mM sodium phosphate buffer (containing 6 mM sodium chloride, pH 6.9). The mixture was incubated at 25°C for 10 minutes in a microplate. Following this, 100 μ L of porcine pancreatic α -amylase solution (0.5 mg/mL) was introduced into each well, and incubation continued under the same conditions for another 10 minutes. To terminate the reaction, 200 μ L of dinitrosalicylic acid (DNS) reagent was added, and the samples were heated at 100°C for 5 minutes. After cooling to room temperature, 50 μ L of each reaction mixture was transferred to a 96-well microplate, and 200 μ L of distilled water was added for dilution. The absorbance was then recorded at 540 nm, with acarbose serving as the reference inhibitor. Each experiment was conducted in triplicate, and the percentage inhibition was calculated using the following formula:

$$\% \text{ Inhibition} = [(A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}}] \times 100$$

Determination of DPPH Radical Scavenging Capacity

The antioxidant capacity of the prepared extracts was assessed using the DPPH $\cdot$ radical scavenging assay, following a modified version of the method described by Blois (1958). α -Tocopherol and Trolox were selected as reference antioxidants, and a 1 mM DPPH $\cdot$ solution was utilized to evaluate their free radical scavenging potential. The inhibition percentages of the standards were determined across various concentrations (1–100 μ g/mL) to establish a suitable concentration range for testing the extracts. For the assay, extract dilutions ranging from 10 to 100 μ g/mL were prepared and reacted with a 1 mM DPPH $\cdot$ solution. Absorbance measurements were taken at 517 nm against a blank containing 99% ethanol. Each experiment was conducted in triplicate. The DPPH $\cdot$ radical scavenging activity of the extracts was calculated using the following formula:

$$\% \text{ Scavenging Capacity} = [(A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}}] \times 100$$

Determination of ABTS Radical Scavenging Capacity

The antioxidant potential of the extracts was evaluated using the ABTS $^{+\cdot}$ radical scavenging assay, following a modified version of the method established by Re et al. (1999). α -Tocopherol and Trolox were used as reference

antioxidants, and a 2 mM ABTS $^{+\cdot}$ solution served as the oxidative agent for assessing their free radical scavenging activity. The inhibition percentages of the standards were determined across a concentration range of 1–100 μ g/mL to establish an appropriate range for testing the extracts. Dilutions of the extracts (10–100 μ g/mL) were prepared and reacted with a 2 mM ABTS $^{+\cdot}$ solution. Absorbance was measured at 734 nm using a phosphate-buffered blank as the reference. Each experiment was performed in triplicate. The ABTS $^{+\cdot}$ radical scavenging activity of the extracts was calculated using the following equation:

$$\% \text{ Scavenging Capacity} = [(A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}}] \times 100$$

Acetylcholinesterase (AChE) and Butyrylcholinesterase (BChE) Inhibitory Activities

The inhibitory activities of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) were evaluated using a modified version of the method described by Ingkaninan et al. (2000). The assay was conducted in a 96-well microplate, where a reaction mixture was prepared by adding 125 μ L of 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB, 3 mM; Ellman's reagent), 25 μ L of the respective substrate (15 mM acetylthiocholine iodide for AChE or butyrylthiocholine iodide for BChE), 50 μ L of Tris-HCl buffer (50 mM, pH 8), and 25 μ L of the test sample. To initiate the reaction, 25 μ L of the enzyme (AChE or BChE) was added, followed by incubation at room temperature for 10 minutes for AChE assays and 15 minutes for BChE assays. The enzymatic activity was quantified by measuring absorbance at 405 nm using a spectrophotometer. Donepezil was used as the reference inhibitor. Each assay was performed in triplicate, and the percentage of enzyme inhibition was calculated using the following formula:

$$\% \text{ Inhibition} = [(A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}}] \times 100$$

Determination of Antimicrobial Activity

The antimicrobial activity of the extracts was tested against *Staphylococcus aureus* ATCC 6538, *Pseudomonas aeruginosa* ATCC 9027, and *Candida albicans* ATCC 10231 using a modified microdilution method. The procedure followed the Clinical Laboratory Standards Institute (CLSI) guidelines for aerobic bacteria (M-7-A7) and fungi (M-27-A3). Initially, bacterial cultures were grown on Mueller-Hinton agar (MHA) and fungal cultures on Potato Dextrose Agar (PDA), followed by incubation at 37°C for 24 hours. After incubation, individual colonies were transferred into tubes containing Mueller-Hinton broth (MHB) for bacteria and RPMI medium for *Candida* species, with further incubation at 37°C for 24 hours. Microbial suspensions were then adjusted to match the McFarland No. 0.5 standard, corresponding to approximately 10⁸ CFU/mL for bacteria and 10⁶ CFU/mL for yeast. The assay was performed in 96-well U-bottom microplates, where the test extracts, microbial suspensions, and antimicrobial controls were added. The plates were sealed and incubated at 37°C for 16–20 hours. To assess microbial growth, 20 μ L of 0.01% resazurin solution was introduced into each well. Following an additional 1–2 hours of incubation at 37°C, color changes were recorded, with viable cells reducing resazurin (blue) to resorufin (pink), indicating microbial growth. The antimicrobial

efficacy of the extracts was evaluated against *Candida* species, as well as Gram-positive and Gram-negative bacterial strains. Each experiment was performed in triplicate, and the mean minimum inhibitory concentration (MIC) values were determined (Göger et al., 2018).

Statistical Analysis

All statistical analyses and graphical visualizations were conducted using the R programming language within the RStudio environment (v2024.12.0+467). Data processing and analysis were performed using the tidyverse, ggplot2, stats, and multcompView packages. Antioxidant capacity data (ABTS^{•+}, DPPH[•]) and cholinesterase inhibition results were first evaluated by one-way analysis of variance (ANOVA); where significant differences were detected, Tukey's Honest Significant Difference (HSD) post-hoc test was applied. A significance level of $p < 0.05$ was considered statistically significant. To explore the overall variation structure within the dataset, Principal Component Analysis (PCA) was performed, and the first two principal components explaining the majority of the variance were presented as biplot graphics.

Results

Table 1 showed the extract amounts and yield percentages of the five plant species. *L. angustifolia* had the highest extraction yield (13.25%), followed by *H. perforatum* (12.57%), *S. officinalis* (11.88%), *F. vulgare* (7.59%), and *M. chamomilla* (7.95%).

The α -glucosidase inhibitory activity results were presented in Table 2. Among all tested samples, *H. perforatum* extract (HPE) showed the most potent inhibition (95.40%, $IC_{50} = 8 \mu\text{g/mL}$), followed by *H. perforatum* drug (HPD) and *S. officinalis* extract (SOE). Several samples, such as *M. chamomilla* extract (MCE) and *L. angustifolia* extract (LAE), exhibited negligible inhibition at the tested concentration.

In the α -amylase inhibition assay (Table 3), the Soothing Complex Product (SCP) showed the highest inhibition (60.90%), followed by *M. chamomilla* drug (MCD), *F. vulgare* drug (FVD), and *F. vulgare* extract (FVE). The reference compound acarbose exhibited 74.61% inhibition.

Table 4 summarized the antioxidant activity determined by ABTS^{•+} and DPPH[•] radical scavenging assays. *H. perforatum* and *S. officinalis* samples demonstrated strong ABTS^{•+} activity (over 99%), comparable to trolox. DPPH[•] scavenging was highest in *S. officinalis* extract (46.99%), similar to α -tocopherol.

According to Table 5, antimicrobial evaluation showed moderate activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* in several samples. *S. officinalis* drug, *L. angustifolia* drug, and *S. officinalis* extract were among the most active samples with MIC values ranging from 625 to 1250 $\mu\text{g/mL}$.

Table 6 presented the anticholinesterase activity results. *H. perforatum* drug had the highest acetylcholinesterase inhibition (26.39%), while *M. chamomilla* extract showed the highest butyrylcholinesterase inhibition (40.16%). Overall, moderate inhibition was observed across most samples.

Table 1. Yield Calculations of Extracts Obtained from Extraction Processes

Plant Species	Extract Amount (g)	Yield (%)
<i>Matricaria chamomilla</i> L.	0.6373	7.945
<i>Lavandula angustifolia</i> Mill.	1.3264	13.248
<i>Hypericum perforatum</i> L.	1.2616	12.572
<i>Salvia officinalis</i> L.	1.1883	11.880
<i>Foeniculum vulgare</i> Mill.	1.5231	7.5928

Table 2. α -Glucosidase Enzyme Inhibitory Effect inhibition values of samples at a concentration of 750 $\mu\text{g/mL}$

Samples	Concentration (750 $\mu\text{g/mL}$) % Inhibition (mean $\pm$ standard deviation)	IC_{50} ($\mu\text{g/mL}$)
SCP	nd	nd
FDM	86.72 $\pm$ 1.84	460
SOD	21.61 $\pm$ 7.37	2263
SOE	81.49 $\pm$ 0.44	417
MCD	nd	nd
MCE	nd	nd
FVD	nd	nd
FVE	59.14 $\pm$ 5.48	659
HPD	94.71 $\pm$ 0.24	27
HPE	95.40 $\pm$ 0.17	8
LAD	nd	nd
LAE	4.38 $\pm$ 0.57	4609
Acarbose	18.04 $\pm$ 1.57	3248

SCP: Soothing Complex product, FDM: Five drug mixture, SOD: *Salvia officinalis* drug, SOE: *Salvia officinalis* extract, MCD: *Matricaria chamomilla* drug, MCE: *Matricaria chamomilla* extract, FVD: *Foeniculum vulgare* drug, FVE: *Foeniculum vulgare* extract, HPD: *Hypericum perforatum* drug, HPE: *Hypericum perforatum* extract, LAD: *Lavandula angustifolia* drug, LAE: *Lavandula angustifolia* extract. nd: Not detected; the inhibitory activity could not be measured or was not significant under the test conditions.

Table 3. α -Amylase Enzyme Inhibitory Effect inhibition values of samples at a concentration of 5000 $\mu\text{g/mL}$

Samples	Concentration (5000 $\mu\text{g/mL}$)
	% Inhibition (mean $\pm$ standard deviation)
SCP	60.90 $\pm$ 2.03
FDM	40.66 $\pm$ 1.23
SOD	36.95 $\pm$ 3.67
SOE	45.26 $\pm$ 0.56
MCD	53.95 $\pm$ 2.87
MCE	46.09 $\pm$ 3.45
FVD	53.49 $\pm$ 4.34
FVE	53.13 $\pm$ 1.78
HPD	26.95 $\pm$ 2.34
HPE	29.52 $\pm$ 1.20
LAD	44.53 $\pm$ 4.56
LAE	42.81 $\pm$ 0.78
Acarbose	74.61 $\pm$ 3.12

Table 4. Comparison of the ABTS^{•+} and DPPH[•] radical scavenging capacities of the samples

Samples	ABTS ^{•+} radical scavenging capacity (100 $\mu\text{g/mL}$ % inhibition $\pm$ standard deviation)	DPPH [•] radical scavenging capacity (50 $\mu\text{g/mL}$ % inhibition $\pm$ standard deviation)
α -Tocopherol	53.877 $\pm$ 0.0027 c	46.989 $\pm$ 0.0064 b
Trolox	99.679 $\pm$ 0.0048 a	91.327 $\pm$ 0.0013 a
SCP	4.243 $\pm$ 0.0069 i	3.554 $\pm$ 0.0700 ij
FDM	47.964 $\pm$ 0.0125 d	15.729 $\pm$ 0.0085 f
SOD	99.394 $\pm$ 0.0006 a	26.536 $\pm$ 0.0441 e
SOE	80.325 $\pm$ 0.0122 b	46.989 $\pm$ 0.0064 b
MCD	35.600 $\pm$ 0.0305 g	30.649 $\pm$ 0.0048 d
MCE	40.287 $\pm$ 0.0143 f	8.711 $\pm$ 0.0052 g
FVD	6.097 $\pm$ 0.0124 h	5.769 $\pm$ 0.0350 gh
FVE	3.453 $\pm$ 0.0122 hi	0.422 $\pm$ 0.0178 j
HPD	99.316 $\pm$ 0.0004 a	31.731 $\pm$ 0.0393 cd
HPE	99.1730 $\pm$ 0.0013 a	33.557 $\pm$ 0.0253 c
LAD	42.708 $\pm$ 0.0142 e	15.573 $\pm$ 0.0314 f
LAE	5.919 $\pm$ 0.0094 hi	5.490 $\pm$ 0.1467 hi

SCP: Soothing Complex product, FDM: Five drug mixture, SOD: *Salvia officinalis* drug, SOE: *Salvia officinalis* extract, MCD: *Matricaria chamomilla* drug, MCE: *Matricaria chamomilla* extract, FVD: *Foeniculum vulgare* drug, FVE: *Foeniculum vulgare* extract, HPD: *Hypericum perforatum* drug, HPE: *Hypericum perforatum* extract, LAD: *Lavandula angustifolia* drug, LAE: *Lavandula angustifolia* extract. Different lowercase letters within each column indicate statistically significant differences between the samples ($p < 0.05$).

Table 5. MIC values of the samples against *S. aureus* ATCC 6538, *P. aeruginosa* ATCC 9027, and *C. albicans* ATCC 10231

Samples	<i>S. aureus</i> ATCC 6538	<i>P. aeruginosa</i> ATCC 9027	<i>C. albicans</i> ATCC 10231
SCP	>2500	>2500	2500
FDM	1250	>2500	2500
SOD	625	1250	625
SOE	1250	2500	625
MCD	2500	2500	1250
MCE	2500	>2500	2500
FVD	1250	2500	1250
FVE	1250	2500	1250
HPD	1250	2500	1250
HPE	1250	2500	1250
LAD	625	1250	625
LAE	2500	>2500	625
Ampicillin	0.125>	4	-
Ciprofloxacin	0.125>	0.125>	-
Fluconazole	-	-	32

SCP: Soothing Complex product, FDM: Five drug mixture, SOD: *Salvia officinalis* drug, SOE: *Salvia officinalis* extract, MCD: *Matricaria chamomilla* drug, MCE: *Matricaria chamomilla* extract, FVD: *Foeniculum vulgare* drug, FVE: *Foeniculum vulgare* extract, HPD: *Hypericum perforatum* drug, HPE: *Hypericum perforatum* extract, LAD: *Lavandula angustifolia* drug, LAE: *Lavandula angustifolia* extract.

Table 6. The percentage inhibition of the anticholinesterase enzyme by the extracts and the standard compound

Samples	Acetylcholinesterase 100 µg/ml % Inhibition (mean ± sd)	Butyrylcholinesterase 1000 µg/mL % Inhibition (mean ± sd)
SCP	25.71 ± 4.13 b	27.99 ± 1.46 def
FDM	21.98 ± 2.17 cd	32.83 ± 0.42 c
SOD	18.57 ± 1.64 e	36.83 ± 1.49 b
SOE	20.65 ± 2.14 cde	35.74 ± 1.93 b
MCD	17.90 ± 1.96 e	33.60 ± 0.81 c
MCE	19.60 ± 0.67 de	40.16 ± 0.99 b
FVD	16.71 ± 1.92 e	27.12 ± 0.78 f
FVE	20.02 ± 1.15 cde	38.15 ± 2.49 b
HPD	26.39 ± 0.86 b	30.78 ± 0.84 cde
HPE	23.19 ± 1.29 bc	31.75 ± 2.11 cde
LAD	19.13 ± 0.60 de	31.75 ± 2.11 cd
LAE	19.91 ± 1.69 cde	27.70 ± 1.36 ef
Donepezil	101.33 ± 1.12 a	99.47 ± 0.17 a

SCP: Soothing Complex product, FDM: Five drug mixture, SOD: *Salvia officinalis* drug, SOE: *Salvia officinalis* extract, MCD: *Matricaria chamomilla* drug, MCE: *Matricaria chamomilla* extract, FVD: *Foeniculum vulgare* drug, FVE: *Foeniculum vulgare* extract, HPD: *Hypericum perforatum* drug, HPE: *Hypericum perforatum* extract, LAD: *Lavandula angustifolia* drug, LAE: *Lavandula angustifolia* extract. Different lowercase letters within each column indicate statistically significant differences between the samples ($p < 0.05$).

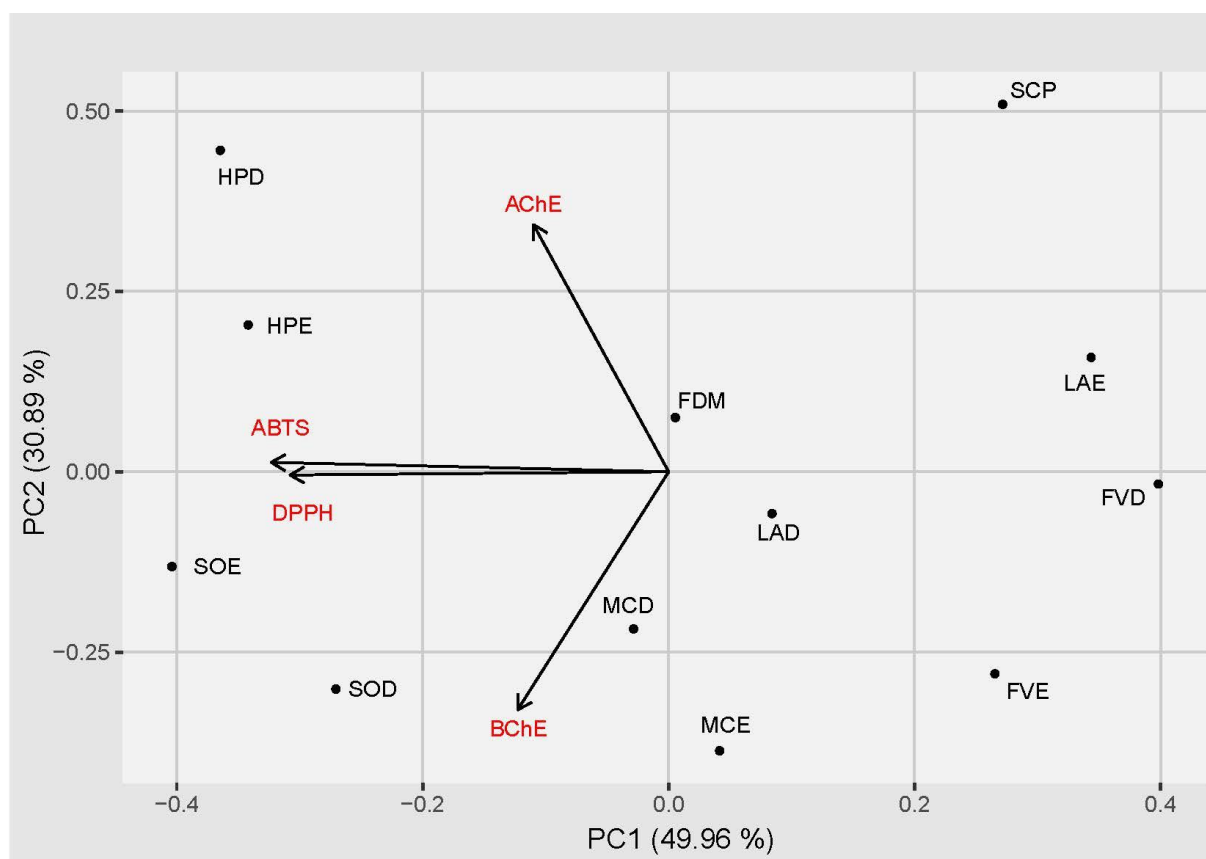


Figure 1. PCA biplot of antioxidant capacities and cholinesterase inhibition activities of the samples

Principal Component Analysis (PCA) was performed to evaluate the relationships between various herbal products and their biological activities, including antioxidant capacity (DPPH and ABTS) and cholinesterase inhibitory effects (AChE and BChE) (Figure 1). The first two principal components (PC1 and PC2) accounted for 49.96% and 30.89% of the total variance, respectively, cumulatively explaining 80.85% of the dataset's variability. The biplot revealed a clear separation of the samples based on their bioactivity profiles. Samples such as *Hypericum perforatum* drug and extract (HPD and HPE), as well as *Salvia officinalis* drug and extract (SOD and SOE), were positioned on the left side of the plot,

correlating strongly with the antioxidant parameters (DPPH and ABTS), suggesting high radical scavenging activity. In contrast, samples including the Soothing Complex Product (SCP), *Lavandula angustifolia* extract (LAE), and *Foeniculum vulgare* drug and extract (FVD and FVE) were distributed towards the right quadrant, where the vectors for AChE and BChE were directed, indicating a higher potential for cholinesterase inhibition. Other samples, such as the *Matricaria chamomilla* drug and extract (MCD and MCE), were located near the origin, implying moderate or nonspecific bioactivity with respect to the studied parameters.

Discussion

Previous studies have emphasized that the α -glucosidase inhibition capacity of plants is a significant strategy in diabetes treatment. For instance, the α -glucosidase inhibition capacity of the essential oil of *L. angustifolia* has been reported to be higher compared to the standard inhibitor acarbose. According to the study, the IC_{50} value of *L. angustifolia* for α -glucosidase was reported as 609.44 μ g/mL. In our study, however, the percentage inhibition of the *L. angustifolia* methanol extract was found to be lower, with an IC_{50} value calculated as 4609 μ g/mL. This result shows a lower inhibitory activity compared to the values reported in the literature. The discrepancy may arise from differences in the plant parts used, extraction methods, environmental conditions under which the plant was grown, and experimental procedures (Najibullah et al., 2021).

The essential oil (EO) of *L. angustifolia* was evaluated for its *in vitro* antidiabetic potential by inhibiting the activities of pancreatic α -amylase and intestinal α -glucosidase enzymes. The EO exhibited significant inhibitory effects on both enzymes, comparable to the standard drug acarbose. Specifically, the IC_{50} value for α -amylase inhibition was 3.20 ± 0.01 mg/mL, while the IC_{50} value for α -glucosidase inhibition was 2.78 ± 0.007 mg/mL. In comparison, acarbose showed IC_{50} values of 3.06 ± 0.03 mg/mL for α -amylase and 2.81 ± 0.02 mg/mL for α -glucosidase. At a concentration of 1 mg/mL, *L. angustifolia* EO inhibited α -amylase by approximately 84% and α -glucosidase by around 80.2%, demonstrating inhibitory activities very close to those of acarbose (83% and 86.16%, respectively) (Jeddi et al., 2023).

The ethanol extract (La1) and ethyl acetate fraction (La2) of *L. angustifolia* were evaluated for their inhibitory effects on α -glucosidase and α -amylase. La1 showed stronger inhibition with IC_{50} values of 0.82 ± 0.01 mg/mL for α -amylase and 0.51 ± 0.01 mg/mL for α -glucosidase, compared to La2 which exhibited IC_{50} values of 1.56 ± 0.02 mg/mL and 0.68 ± 0.01 mg/mL, respectively. The significant activity was attributed to compounds like rosmarinic acid and luteolin-7-O-glucoside (Tundis et al., 2023).

In a study, methanol extracts of *H. perforatum* were evaluated for their potential antidiabetic effects by measuring their inhibitory activities against two key carbohydrate-hydrolyzing enzymes: α -glucosidase and α -amylase. The results revealed that *H. perforatum* exhibited α -glucosidase inhibition at a level of 3.88 mmol acarbose equivalents (ACEs)/g extract, and α -amylase inhibition at 0.73 mmol ACEs/g extract. Although these activities were moderate compared to *H. humifusum*, the presence of bioactive compounds such as hypericin and hyperforin in *H. perforatum*—quantified at 60 mg/g and 8.5 mg/g of dry extract, respectively—suggests that these constituents may contribute to the observed enzymatic inhibition (Béjaoui et al., 2017).

In another study, aqueous extracts of *H. perforatum* sourced from Turkey (Domestic, DHPE) and from abroad (Imported, IHPE) were compared in terms of their α -glucosidase and α -amylase inhibitory activities. Both extracts exhibited strong inhibition against these key carbohydrate-hydrolyzing enzymes, surpassing the

standard drug acarbose. For α -glucosidase inhibition, DHPE and IHPE showed IC_{50} values of 16.35 ± 0.07 μ g/mL and 15.05 ± 1.36 μ g/mL, respectively, while acarbose exhibited a higher IC_{50} of 30.62 ± 2.07 μ g/mL, indicating weaker inhibition. In the α -amylase assay, DHPE had a stronger effect ($IC_{50} = 22.24 \pm 1.79$ μ g/mL) than IHPE ($IC_{50} = 54.35 \pm 0.35$ μ g/mL), and both outperformed acarbose ($IC_{50} = 59.01 \pm 1.04$ μ g/mL) (Marah et al., 2022).

A study investigated the enzyme inhibitory effects of methanolic extracts from roots (RO), flower shoots (FS), and non-flower shoots (NFS) of *H. perforatum* collected from wild populations in Macedonia. Among the tested plant parts, the root extracts (RO) exhibited the strongest inhibitory activity against both α -glucosidase and α -amylase, enzymes crucial for postprandial glucose metabolism. At the highest tested concentration (250 μ g/mL), RO extracts inhibited α -glucosidase by 94.1%, significantly outperforming FS (70.4%) and NFS (67.2%), and approaching the inhibition level of the standard drug acarbose (96%). Similarly, for α -amylase inhibition, RO extracts showed a maximum inhibition of 27%, slightly higher than FS (about 27%) and clearly stronger than NFS (21.4%). At lower concentrations (50 and 150 μ g/mL), RO still maintained superior enzyme inhibition compared to the aerial parts (Tusevski et al., 2018).

In a study, the ethanol extract of *H. perforatum* collected from various locations in Ordu Province, Turkey, was evaluated for its enzyme inhibitory properties. At a concentration of 0.2 mg/mL, the extract exhibited α -glucosidase inhibition of 45%, which is significantly higher than that of the reference compound acarbose (6% at 0.014 mg/mL). The study did not provide specific α -amylase inhibition data, but it supports the hypothesis that inhibition of both α -glucosidase and α -amylase enzymes is a viable strategy for managing type 2 diabetes. The extract's antidiabetic potential is attributed to its rich phenolic content and the presence of compounds like hyperforin, quercetin, rutin, and chlorogenic acid (Ayvaz et al., 2023).

In a study, the α -glucosidase and α -amylase inhibitory effects of both native and enzymatically modified aqueous infusions of *M. chamomilla* were evaluated. The enzymatic modification was carried out using a combination of hesperidinase and β -galactosidase, which resulted in the hydrolysis of glycosylated flavonoids and the enhancement of bioactive aglycones like apigenin, luteolin, and esculetin. The modified infusion showed a significantly stronger α -glucosidase inhibitory activity ($56.9 \pm 3.7\%$) compared to the native infusion ($37.4 \pm 5.6\%$) at 60 mM concentration, indicating enhanced potential for postprandial blood glucose regulation. However, the α -amylase inhibitory activity of both native and modified infusions remained low, with no statistically significant difference between them (around 10–12% inhibition) (Franco et al., 2020).

A study evaluated the antidiabetic effects of *M. chamomilla* essential oil (MCEO), chamomile honey, and their 1:1 mixture by assessing their ability to inhibit the digestive enzymes α -glucosidase and α -amylase. Among the tested samples, MCEO showed the strongest inhibitory

effects, with an IC_{50} of $265.57 \pm 0.03 \mu\text{g/mL}$ for α -glucosidase and $121.44 \pm 0.05 \mu\text{g/mL}$ for α -amylase. Notably, the α -amylase inhibition by MCEO was more effective than the standard drug acarbose ($IC_{50} = 396.42 \pm 5.16 \mu\text{g/mL}$), although its α -glucosidase inhibition was slightly lower than that of acarbose ($IC_{50} = 199.53 \pm 1.12 \mu\text{g/mL}$). The honey and mixture samples also demonstrated enzyme inhibition but with significantly higher IC_{50} values, indicating weaker activity. The potent inhibitory effect of MCEO is attributed to its major volatile constituents such as camphor, 3-carene, β -myrcene, and α -phellandrene, which are known to exert bioactivity against carbohydrate-metabolizing enzymes (Qasem et al., 2022).

Another study investigated the *in vitro* hypoglycemic potential of *M. chamomilla* extracts and essential oils collected from six different districts of Diyarbakır, Türkiye. Various solvent extracts—petroleum ether (PE), ethyl acetate (EA), methanol (MeOH), infusion (INF)—and essential oils (EO) were evaluated for their α -glucosidase inhibitory activity. The ethyl acetate extracts of samples M1 (95.34%), M2 (95.27%), and M3 (98.05%) showed the highest inhibitory activities, comparable to that of the standard drug acarbose (97.59%). Among essential oils, the sample from M2 (Sur) displayed the strongest inhibition (92.22%) at a lower concentration (0.5 mg/mL), also approaching acarbose in potency. The inhibition trend generally followed the polarity of the solvents used, with mid-polarity EA extracts outperforming both non-polar (PE) and highly polar (INF) counterparts. Infusion extracts consistently showed the weakest activity (Şahin et al., 2023).

A study investigated the antidiabetic potential of hydro-methanol extract and its phenolic-enriched fractions (ethyl acetate and *n*-butanol) from the aerial parts (leaves and stems) of *S. officinalis*. The ethyl acetate fraction exhibited the strongest enzyme inhibitory activities, with IC_{50} values of $46.52 \pm 2.68 \mu\text{g/mL}$ for α -amylase and $104.58 \pm 0.06 \mu\text{g/mL}$ for α -glucosidase. While these values were higher (i.e., less potent) than the standard drug acarbose (IC_{50} of $26.84 \mu\text{g/mL}$ for α -amylase and $42.52 \mu\text{g/mL}$ for α -glucosidase), they still indicated substantial activity. The *n*-butanol fraction showed weaker inhibition with IC_{50} values of $98.49 \mu\text{g/mL}$ and $376.15 \mu\text{g/mL}$, respectively. The hydro-methanol extract also displayed moderate inhibitory effects. A strong positive correlation was found between phenolic/flavonoid content and enzyme inhibition, suggesting that these phytochemicals play a central role in the observed activity (Mahdi et al., 2020).

A comparative study evaluated the α -glucosidase inhibitory effects of ethanolic extracts from seven wild-growing *Salvia* species in the Mediterranean region, including *S. officinalis*. Among the tested species, *S. officinalis* exhibited notable α -glucosidase inhibition, though it was not the most active. The study found that *S. glutinosa* showed the highest inhibition, while *S. officinalis* and *S. fruticosa* displayed moderate inhibitory effects. The results suggest that although *S. officinalis* does not have the strongest α -glucosidase inhibition among its genus, it still contributes meaningful antidiabetic potential. The activity was positively correlated with total phenolic and tannin contents, especially rosmarinic acid, which was the

predominant compound in *S. officinalis* (38,800 $\mu\text{g/g}$) (Mervić et al., 2022).

Another study investigated the ability of *S. officinalis* decoctions to inhibit key metabolic enzymes related to diabetes and obesity, particularly α -glucosidase and α -amylase. The decoction of *S. officinalis* exhibited a notable inhibitory effect on α -glucosidase, with an EC_{50} value of $71.2 \pm 5.0 \mu\text{g/mL}$, which was significantly more potent than the reference drug acarbose ($EC_{50} = 357.8 \pm 12.3 \mu\text{g/mL}$). This suggests a 4-fold stronger activity than acarbose in inhibiting this enzyme. However, *S. officinalis* showed no substantial inhibitory effect against α -amylase, even at a concentration of 0.5 mg/mL. The observed α -glucosidase inhibition was attributed to the plant's high content of rosmarinic acid, apigenin-glucuronide, and scutellarein glycosides, which have previously been reported as effective inhibitors of carbohydrate-metabolizing enzymes (Pereira et al., 2018).

A study assessed the ability of *S. officinalis* extracts to inhibit α -amylase activity, a key enzyme in carbohydrate digestion. Both dichloromethane and methanolic extracts were tested *in vitro*. The methanol extract of *S. officinalis* showed a strong inhibitory effect, with an IC_{50} value of $54.9 \pm 5.7 \mu\text{g/mL}$, while the dichloromethane extract exhibited slightly weaker activity ($IC_{50} = 71.2 \pm 14.4 \mu\text{g/mL}$). Although both values were higher than that of the standard drug acarbose ($IC_{50} = 42.9 \pm 3.9 \mu\text{g/mL}$), the difference was not statistically significant ($p > 0.05$). These results support the antidiabetic potential of *S. officinalis*, likely attributed to its rich content of polyphenols and terpenoids such as rosmarinic acid and carnosol, which are known to interfere with carbohydrate-hydrolyzing enzymes (Javid et al., 2022).

A study investigated the *in vitro* inhibitory effects of three different extracts (ethyl acetate, *n*-butanol, and benzene) of *F. vulgare* seeds on α -glucosidase and α -amylase enzymes. All three extracts showed high α -glucosidase inhibitory activity, with levels comparable to or exceeding the reference drug acarbose. In contrast, α -amylase inhibition was moderate, with ethyl acetate and benzene extracts displaying notable effects, while the *n*-butanol extract exhibited negligible activity. The presence of flavonoids, saponins, terpenoids, tannins, and phenolic compounds in all extracts is believed to be responsible for the observed enzyme inhibition (Godavari et al., 2018).

Another study evaluated the antidiabetic potential of ethanolic leaf extract of *F. vulgare* (FVEE) by assessing its inhibitory effects on α -amylase and α -glucosidase. The extract was tested at five concentrations (125–1000 $\mu\text{g/mL}$). At the highest dose (1000 $\mu\text{g/mL}$), FVEE showed a strong inhibitory effect, with 87.14% inhibition of α -amylase and 85.20% inhibition of α -glucosidase, which was comparable to the standard drug acarbose (88.13% and 87.19%, respectively). The results indicate that FVEE has a significant enzyme-inhibitory effect, potentially due to the presence of bioactive secondary metabolites such as flavonoids, alkaloids, saponins, triterpenoids, tannins, and phenols, as confirmed by phytochemical screening (Kumar and Subramanayaan, 2022).

A study investigated the inhibitory effects of phenolic-rich extracts from the aerial parts of *F. vulgare* under different extraction conditions (varying time, temperature, and solvents) on key digestive enzymes. Among the tested

conditions, the methanol extract at 25°C for 8 hours exhibited the strongest inhibitory effects, achieving 82.26% inhibition of α -glucosidase and 82.43% inhibition of α -amylase. These values were comparable to those reported for standard inhibitors like acarbose. The results also showed that enzyme inhibition correlated positively with total phenolic content, which peaked at 15.2 mg GAE/g under the same extraction conditions. Conversely, lower enzyme inhibition was observed with shorter extraction times and alternative solvent systems (Abu-Zaiton et al., 2015).

Another study compared the aqueous extracts of the leaf (FVLE) and rootstock (FVRE) of *F. vulgare* in terms of their chemical composition and *in vitro* antidiabetic effects. Both extracts showed dose-dependent inhibitory effects on α -glucosidase and α -amylase, with the rootstock extract demonstrating significantly higher activity. Specifically, FVRE inhibited α -glucosidase with an IC_{50} of 165.90 ± 1.2 μ g/mL and α -amylase with an IC_{50} of 194.30 ± 4.8 μ g/mL, which was even more potent than the reference drug acarbose for α -amylase (IC_{50} = 311.20 ± 1.38 μ g/mL). In contrast, the leaf extract (FVLE) showed lower enzyme inhibition, with IC_{50} values of 203.80 ± 1.3 μ g/mL for α -glucosidase and 1026.50 ± 6.5 μ g/mL for α -amylase. The superior activity of the rootstock extract was attributed to its distinct phenolic profile, particularly higher levels of quinic acid, gallic acid, and chlorogenic acid, which are known to inhibit carbohydrate-hydrolyzing enzymes (Sayah et al., 2020).

In our study, *H. perforatum* exhibited the strongest α -glucosidase inhibitory activity (IC_{50} = 8 μ g/mL), outperforming the standard drug acarbose and aligning with previous studies reporting potent enzyme inhibition for *H. perforatum* extracts (Marah et al., 2022; Tusevski et al., 2018). *S. officinalis* also showed notable α -glucosidase inhibition (81.49%), consistent with literature highlighting its phenolic-rich fractions as effective inhibitors (Mahdi et al., 2020; Pereira et al., 2018). In contrast, *M. chamomilla* exhibited weak α -glucosidase and moderate α -amylase inhibition, agreeing with reports suggesting generally low to moderate antidiabetic potential depending on extraction type (Franco et al., 2020; Qasem et al., 2022). *L. angustifolia* displayed limited inhibition, which is consistent with findings where significant activity was observed mainly for essential oils rather than methanol extracts (Jeddi et al., 2023; Tundis et al., 2023). *F. vulgare* showed moderate α -amylase and weaker α -glucosidase inhibition compared to previous studies that reported stronger effects for phenolic-rich extracts (Godavari et al., 2018; Abu-Zaiton et al., 2015). Overall, our results confirm the superior antidiabetic potential of *H. perforatum* and *S. officinalis*, while indicating limited but still noteworthy activities for *M. chamomilla*, *L. angustifolia*, and *F. vulgare*.

Although acarbose is a widely used reference drug for inhibiting carbohydrate-hydrolyzing enzymes, several plant extracts have demonstrated comparable or even stronger inhibitory activities in various studies. For instance, *H. perforatum* extracts showed α -glucosidase IC_{50} values as low as 8 μ g/mL in our study, which is markedly lower than that of acarbose (IC_{50} = 3248 μ g/mL). Similarly, aqueous extracts of *H. perforatum* reported by

Marah et al. (2022) exhibited IC_{50} values around 15–16 μ g/mL, significantly surpassing acarbose's inhibitory effect. Moreover, decoctions of *S. officinalis* were found to inhibit α -glucosidase with an EC_{50} value of 71.2 ± 5.0 μ g/mL, showing stronger activity than acarbose (EC_{50} = 357.8 ± 12.3 μ g/mL) (Pereira et al., 2018). These findings suggest that certain plant extracts, owing to their rich phenolic and flavonoid compositions, can inhibit carbohydrate-digesting enzymes more effectively than synthetic drugs like acarbose, providing a scientific rationale for their potential use in managing postprandial hyperglycemia.

Overall, the antioxidant capacities of the plant extracts used in our study are consistent with the findings reported in the literature. Notably, *H. perforatum* and *S. officinalis* exhibited high antioxidant activity in both ABTS and DPPH assays. The strong antioxidant properties of these plants suggest that they may have potential therapeutic applications in the treatment of diseases associated with oxidative stress (Altun et al., 2013; Alahmad et al., 2022). A flavonoid-rich extract of *H. perforatum* (FEHP) was prepared and evaluated for its antioxidant properties through various *in vitro* assays. FEHP showed strong DPPH radical scavenging activity with an IC_{50} of 10.63 μ g/mL and superoxide radical scavenging with an IC_{50} of 54.3 μ g/mL. It demonstrated a concentration-dependent increase in reducing power (r^2 = 0.9991) and significantly inhibited lipid peroxidation in both linoleic acid and liposome models. Additionally, FEHP exhibited effective metal ion chelation, particularly evident in the site-specific deoxyribose degradation assay (Zou et al., 2004). The total ethanolic extract (TE) of *H. perforatum* and its fractions were phytochemically characterized and evaluated for antioxidant activity. HPLC–DAD–MS/MS analysis revealed the presence of flavonoids, caffeoylquinic acids, hyperforins, and hypericins, with flavonoids being the major contributors. TE exhibited strong DPPH free radical-scavenging activity with an EC_{50} of 21 μ g dry weight biomass (dwb)/mL and effectively inhibited lipid peroxidation in rat cortical synaptosomes with an EC_{50} of 26 μ g dwb/mL. Fractions rich in flavonoid aglycones (V5) and flavonol glycosides (V4, V6) showed the most potent antioxidant effects, while hyperforin and hypericin fractions had negligible activity (Silva et al., 2005).

The antioxidant activities of polyphenols from *S. officinalis* (sage), including flavone glycosides and various rosmarinic acid derivatives, were systematically evaluated. Rosmarinic acid derivatives showed potent antioxidant effects across three assays: DPPH radical scavenging, superoxide anion scavenging, and phosphomolybdenum reduction. Their superoxide scavenging activities ranged from 220 to 300 SOD units/mg, approximately 15–20 times greater than that of trolox. DPPH scavenging activities were similarly strong, with rosmarinic acid derivatives scavenging about 90% of radicals, significantly outperforming trolox. In contrast, flavonoid glycosides showed weaker to moderate antioxidant activities, with compounds containing catechol groups (like luteolin glycosides) being more active (Lu and Foo, 2001).

On the other hand, the low antioxidant capacity of *F. vulgare* is inconsistent with the high activity reported in the literature. In a study, the water and ethanol extracts of *F. vulgare* (fennel) seeds were evaluated for their antioxidant

activities through multiple *in vitro* assays. Both extracts exhibited strong total antioxidant activity, with the water extract inhibiting 91.6% and the ethanol extract 98.6% of lipid peroxidation at 100 mg concentration, outperforming α -tocopherol (36.9%) but slightly lower than BHA (94.3%) and BHT (97.8%). Both extracts showed significant reducing power and effective scavenging activities against DPPH radicals, superoxide anions, and hydrogen peroxide. At 250 μ g/mL, water and ethanol extracts showed 47.49% and 36.46% DPPH scavenging, respectively. Superoxide scavenging activity reached 96.6% for water and 94.0% for ethanol extracts. Metal chelating activities were moderate, with the water extract achieving 30.7% and the ethanol extract 26.5% inhibition at 250 μ g/mL. The antioxidant activities were generally concentration-dependent and attributed partly to the phenolic contents (21.25 mg GAE/g for water extract and 90.00 mg GAE/g for ethanol extract) (Oktay et al., 2003). A study systematically evaluated the antioxidant potential of different parts of *F. vulgare* (fennel) collected in Portugal, including shoots, leaves, stems, and inflorescences. Shoots exhibited the strongest antioxidant activities across all assays, with EC₅₀ values of 1.34 ± 0.07 mg/mL for DPPH scavenging, 0.48 ± 0.02 mg/mL for reducing power, 0.49 ± 0.03 mg/mL for β -carotene bleaching inhibition, and 0.13 ± 0.03 mg/mL for lipid peroxidation inhibition. Shoots also contained the highest levels of phenolics (65.85 ± 0.74 mg/g extract), ascorbic acid (570.89 ± 0.01 μ g/g dry weight), and tocopherols (34.54 ± 1.28 μ g/g dry weight), and were the only part to contain flavonoids. In contrast, stems exhibited the lowest antioxidant potential and the lowest content of bioactive compounds (Barros et al., 2009).

In another study, the essential oils and extracts of *F. vulgare* (fennel) and *M. chamomilla* (chamomile) were evaluated for their antioxidant activities using the DPPH• radical scavenging assay. Methanol extracts exhibited the highest antioxidant potential among all tested solvents. The EC₅₀ value for chamomile methanol extract was 0.0022 ± 0.0005 , corresponding to an antiradical power (ARP) of 455, while fennel methanol extract had an EC₅₀ of 0.0031 ± 0.0008 and an ARP of 323. The total phenolic contents were also highest in methanol extracts, with chamomile at 3.7 mg GAE/g and fennel at 3.4 mg GAE/g. Essential oils of both plants contained major compounds like trans-anethole (fennel) and α -bisabolol oxide A (chamomile), contributing to their antioxidant effects. Overall, chamomile methanol extract demonstrated superior free radical scavenging ability compared to fennel extracts and oils (Roby et al., 2013).

A study evaluated the antioxidant activity of *M. chamomilla* (chamomile) extracts obtained by different extraction methods. Essential oil was isolated by steam distillation and steam distillation-extraction (SDE), yielding approximately 0.07%. GC-MS analysis identified 88 compounds, with chamazulene (19.9%), α -bisabolol (20.9%), and bisabolol oxide A (21.6%) as the main constituents. Flavonoid-rich extracts were prepared using ethanol-water solutions of various concentrations. Antioxidant activity was measured using the DPPH radical scavenging assay. Extracts obtained through cold and warm ethanol extractions showed significant antioxidant activity, with average DPPH reaction rates ranging from 0.2 to 9.0 μ M/s. The highest antioxidant activities were

observed in extracts obtained with 60% and 20% ethanol, while extracts from stems, roots, and water extracts showed lower activity. Additionally, β -cyclodextrin encapsulation of the essential oil achieved about 60% yield, confirmed by TG-DTG and DSC analyses (Costescu et al., 2008).

A study compared the antioxidant activities of *L. angustifolia* plants grown under field conditions and propagated *in vitro*. Extracts from *in vitro* plants demonstrated significantly higher antioxidant activity than field-grown plants across all assays (DPPH, FRAP, and ABTS). *In vitro* propagated plants exhibited stronger DPPH radical scavenging, higher ferric reducing antioxidant power (FRAP), and greater ABTS radical scavenging capacity. The enhanced antioxidant potential was attributed to higher polyphenol contents in *in vitro* plants, suggesting that tissue culture techniques can enhance the biological activities of lavender extracts (Andrys et al., 2013). Another study evaluated the phytochemical profile and antioxidant activities of extracts from three *L. angustifolia* (Betty's Blue, Elizabeth, Hidcote) and two *Lavandula* $\times$ *intermedia* (Grosso, Gros Bleu) cultivars obtained through maceration, decoction, and ultrasound-assisted extraction (UAE). HPLC analysis revealed the presence of major compounds such as rosmarinic acid (2.52–10.82 mg/g), ferulic acid glucoside (2.94–8.67 mg/g), caffeic acid (1.70–3.10 mg/g), morin (1.02–13.63 mg/g), coumarin (1.01–5.97 mg/g), and herniarin (1.05–8.02 mg/g). Antioxidant activities assessed by DPPH and FRAP assays ranged from 104.58–206.77 μ mol Trolox/g d.w. and 79.21–203.06 μ mol Trolox/g d.w., respectively. UAE extracts consistently showed the highest antioxidant activities and polyphenolic contents. The study concluded that both the cultivar type and extraction method significantly influenced the antioxidant potential, with ultrasound-assisted extraction yielding the best results (Dobros et al., 2022).

In our study, *Hypericum perforatum* and *Salvia officinalis* exhibited the highest antioxidant activities, particularly in the ABTS assay, consistent with previous reports emphasizing their strong radical scavenging capacities due to high flavonoid and phenolic acid content (Silva et al., 2005; Lu and Foo, 2001). *Matricaria chamomilla* demonstrated moderate antioxidant activity, aligning with studies indicating variable efficacy depending on extraction methods (Roby et al., 2013). *Lavandula angustifolia* showed relatively low antioxidant activity, corroborating earlier findings that highlight significant variation based on cultivation and extraction conditions (Andrys et al., 2013). In contrast, *Foeniculum vulgare* exhibited weaker antioxidant effects than expected, differing from literature where strong activity was observed under optimized extraction protocols (Oktay et al., 2003; Barros et al., 2009). These results emphasize the influence of extraction methods and phytochemical profiles on the antioxidant performance of plant extracts.

In a study, the antimicrobial properties of ethanol extracts from the leaves and flowers of *L. angustifolia* cultivated in southern Poland were evaluated. The extracts demonstrated significant antibacterial and antifungal activities. Both flower and leaf extracts inhibited the viability of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*, with noticeable effects observed at low concentrations (0.31%). Additionally, the

extracts effectively suppressed the growth of mold fungi, particularly *Trichoderma viride* and *Chaetomium globosum*. Leaf extracts showed slightly stronger antifungal effects compared to flower extracts. Control tests confirmed that ethanol at the concentrations used did not contribute to microbial inhibition (Betlej et al., 2023). Another study investigated the phenolic content and antimicrobial activity of *L. angustifolia* flower macerates prepared with methanol (M1) and a methanol:water (1:1) mixture (M2). The hydro-alcoholic macerate (M2) exhibited a higher total phenolic content (3520 mg/100g d.w.) compared to the alcoholic macerate (M1, 2860 mg/100g d.w.). HPLC-DAD analysis revealed six phenolic compounds in M2 and four in M1, with notable amounts of gallic acid, chlorogenic acid, and ellagic acid. Both macerates demonstrated moderate antimicrobial activity against bacterial and *Candida* strains, with M2 generally showing stronger effects (Stanciu et al., 2019). The essential oil (EO) of *L. angustifolia* demonstrated significant antimicrobial activity against various Gram-positive and Gram-negative bacteria, as well as fungal strains. The highest antibacterial effect was observed against *Micrococcus luteus* (19.1 ± 1.0 mm inhibition zone), followed by *Bacillus cereus* and *Staphylococcus aureus*. Among Gram-negative bacteria, *Salmonella enterica* was the most sensitive. Remarkable antifungal activity was also noted against *Candida tropicalis* (24.1 ± 0.9 mm) and *Candida albicans* (19.05 ± 1.03 mm). The essential oil exhibited low MIC, MBC, and MFC values (0.125–1.0% for bacteria and 0.25–2.0% for fungi), indicating potent bactericidal and fungicidal effects (Jeddi et al., 2023).

In a study, the essential oil and methanol extract of *M. chamomilla* from Djibouti were evaluated for their antimicrobial activities. Using the disc diffusion method, both extracts exhibited inhibition against a range of bacterial and fungal strains. The essential oil showed stronger antimicrobial activity than the methanol extract, with inhibition zones ranging from 14 to 30 mm for bacteria, particularly against *Pseudomonas aeruginosa* and *Shigella dysenteriae*. Minimum inhibitory concentration (MIC) values for the essential oil ranged between 1–4 µg/mL for most bacterial strains, indicating potent bactericidal effects. The essential oil and methanol extract also demonstrated antifungal activity against *Candida albicans* and *Aspergillus* species, often exceeding the effects of standard antifungal agents like benomyl and griseofulvin (Abdoul-Latif et al., 2011). A study evaluated the antimicrobial and toxicity profiles of *M. recutita* (chamomile) essential oil, both alone and in combination with standard antimicrobial agents (ampicillin, cefuroxime, tetracycline, fluconazole, and nystatin). The essential oil, rich in α -bisabolol oxide A (47.7%) and (E)- β -farnesene (21.5%), was fractionated and tested against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* strains. While the essential oil alone showed moderate antimicrobial activity, its combination with fluconazole and nystatin exhibited synergistic and additive effects, especially against *C. albicans*. Cytotoxicity tests on WS1 cells and toxicity assays on *Aliivibrio fischeri* confirmed that these combinations were not significantly toxic at antimicrobial concentrations (Göger et al., 2018). Another study analyzed the chemical composition,

antioxidant, and antimicrobial activities of the essential oil obtained from *M. chamomilla* flowers by hydrodistillation. GC-MS and GC-FID analysis identified 52 compounds, accounting for 93.9% of the oil, with (E)- β -farnesene (29.8%), (E,E)- α -farnesene (9.3%), α -bisabolol oxide A (7%), chamazulene (6.4%), and germacrene D (6.2%) as major components. The essential oil exhibited moderate antioxidant activity, with an EC₅₀ value of 2.07 mg/mL after 90 minutes of incubation. Antimicrobial testing via the agar diffusion method showed strong activity against *S. aureus* (40.00 mm inhibition zone) and moderate effects against *E. coli*, *Listeria monocytogenes*, and *Salmonella enterica*, but no activity against *Pseudomonas aeruginosa* (Stanojevic et al., 2016).

A study investigated the antibacterial activity and phytochemical composition of *H. perforatum* extracts against multi-drug-resistant (MDR) clinical bacterial strains. Methanol extract and its solvent fractions (*n*-hexane, ethyl acetate, chloroform, aqueous) were tested against MRSA, *Enterococcus faecalis*, *E. coli*, *Klebsiella pneumoniae*, *P. aeruginosa*, *Acinetobacter baumannii*, and *Proteus mirabilis*. The total methanol extract exhibited the strongest antibacterial activity, with inhibition zones ranging from 17.9 to 27.9 mm and low MIC values (e.g., 3.9 µg/mL against *K. pneumoniae* and *E. faecalis*). TEM analysis revealed significant ultrastructural damage in treated *K. pneumoniae* cells. Phytochemical analysis using LC-ESI-MS/MS identified flavonoids, anthraquinones, and phenolic acids as major compounds. The extracts also showed strong antioxidant activity and low cytotoxicity (Sherif et al., 2023). Another study evaluated the antimicrobial effects of the ethanol extract (HP-EtOH) and various sub-extracts (*n*-hexane, chloroform, ethyl acetate, *n*-butanol, and water) of *H. perforatum* against oral pathogens including *Streptococcus mutans*, *Streptococcus sobrinus*, *Lactobacillus plantarum*, and *Enterococcus faecalis*. The water extract (HP-H₂O) demonstrated the strongest antibacterial activity, with MIC values of 8–32 mg/mL, particularly effective against *S. sobrinus* and *L. plantarum*. Other sub-extracts showed moderate antimicrobial activity. The extracts also inhibited biofilm formation, with IC₅₀ values ranging from 7.23 to 29.91 mg/mL (Süntar et al., 2016). A *in vitro* study investigated the antimicrobial and anti-biofilm effects of *H. perforatum* oil against common periodontitis-associated pathogens, including *S. aureus*, *S. mutans*, *E. coli*, *Enterococcus faecalis*, and *Porphyromonas gingivalis*. Antimicrobial activities were assessed by disk diffusion, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC) methods. The oil exhibited antibacterial effects comparable to standard antibiotics, with MIC values ranging from 32 to 256 µg/mL and MBC values from 128 to 512 µg/mL. Strong anti-biofilm activity was observed, with minimum biofilm inhibitory concentrations (MBICs) between 256 and 512 µg/mL. Time-kill assays confirmed the bactericidal effect of the oil (Bagheri et al., 2022).

In a study, it was evaluated the chemical composition and antimicrobial activity of *S. officinalis* essential oil collected from two different altitudes (100 m and 500 m) along the Syrian coastline. Gas chromatography analysis revealed that the major components of the oil were 1,8-cineole, camphor, borneol, α -pinene, β -pinene, camphene,

β -myrcene, and caryophyllene, with variations in their percentages depending on altitude. Antimicrobial testing using the disc diffusion method showed that the essential oil exhibited strong antibacterial activity against Gram-positive bacteria (*S. aureus* and *Streptococcus* group D) and *C. albicans*, achieving complete inhibition at 20 μ L/mL concentration. Against Gram-negative bacteria (*E. coli*, *Salmonella typhi*, and *P. aeruginosa*), the essential oil showed a temporary bacteriostatic effect (Khalil and Li, 2011). A study compared the chemical composition and antimicrobial activity of ethanol extracts obtained from the flowers, leaves, and stems of *S. officinalis* collected from southeastern Serbia. GC-FID and GC-MS analyses identified manool (9.0–11.1%) as the major component, along with other typical sage constituents such as α -pinene, camphene, limonene, 1,8-cineole, thujones, camphor, and borneol. Antimicrobial activity was assessed using modified diffusion and dilution methods. The leaf extract demonstrated stronger antimicrobial effects compared to flower and stem extracts, especially against *Bacillus subtilis*, *S. aureus*, *Sarcina lutea*, and *Aspergillus niger*. However, the extracts showed little to no inhibitory effect on *E. coli*, *Salmonella enteritidis*, *P. aeruginosa*, *C. albicans*, and *Saccharomyces cerevisiae* (Veličković et al., 2003). The essential oil of *S. officinalis* exhibited notable antibacterial and antifungal activities. Among the tested microorganisms, Gram-positive bacteria were generally more sensitive than Gram-negative bacteria. However, a remarkable sensitivity was also observed among Gram-negative strains, including multiresistant *E. coli*, *S. typhi*, and *Shigella sonnei*. The essential oil showed significant inhibition zones, comparable or superior to penicillin in some cases. Additionally, *S. officinalis* essential oil demonstrated fungistatic and fungicidal effects against several dermatomycetes and *C. albicans*, although it was less effective than rosemary oil (Bozin et al., 2007).

A study analyzed the chemical composition and antimicrobial activity of the essential oil and seed extracts of *F. vulgare* (fennel). GC-MS analysis identified 31 components in the essential oil, with trans-anethole (70.1%) as the dominant compound. The methanolic and ethanolic seed extracts mainly contained linoleic acid (56%) along with smaller amounts of palmitic and oleic acids. Antimicrobial activity was evaluated using disk diffusion and MIC methods. The essential oil showed strong antimicrobial activity against several bacterial strains (*Bacillus cereus*, *B. magisterium*, *B. subtilis*, *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas putida*) and *C. albicans*, with inhibition zones up to 31 mm and MIC values as low as 0.4% (v/v) against *C. albicans*. Essential oil generally exhibited stronger antimicrobial effects than the seed extracts (Gulfraz et al., 2008). The essential oil of *F. vulgare* seeds exhibited considerable antimicrobial activity, particularly against Gram-positive bacteria and pathogenic fungi. Using the disc diffusion method, the essential oil showed strong inhibition zones, with *Bacillus subtilis* (29 mm) and *Aspergillus niger* (28 mm) being the most sensitive microorganisms. The lowest minimum inhibitory concentration (MIC) values were observed for *B. subtilis* (62.6 μ g/mL) and *A. niger* (80.6 μ g/mL). In contrast, *E. coli* exhibited the least sensitivity with a smaller inhibition zone (14 mm) and higher MIC value (259.3 μ g/mL). The methanol and ethanol seed extracts

showed no antimicrobial activity (Anwar et al., 2009). Another study focused on the phytochemical analysis and antimicrobial evaluation of the aerial parts of *F. vulgare* collected from Algeria. Seven oxygenated monoterpenes were isolated and structurally characterized for the first time from this species using 1D/2D NMR and mass spectrometry. The antimicrobial activity of the crude $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:1) extract was tested against six bacterial and three fungal strains using the agar diffusion method. The extract showed inhibitory effects against all tested microorganisms, with the highest activity observed against *Proteus vulgaris* (inhibition zone up to 15 mm) and strong antifungal activity, particularly against *Aspergillus* species. In general, the extract exhibited stronger antifungal than antibacterial activity (Zellagui et al., 2011).

In our study, *S. officinalis* drug and extract exhibited the strongest antimicrobial effects, particularly against *S. aureus*, *P. aeruginosa*, and *C. albicans*, with MIC values between 625–1250 μ g/mL. These findings align with literature reports where *S. officinalis* essential oils and extracts demonstrated potent antibacterial and antifungal activities, often attributed to monoterpenoids like 1,8-cineole and camphor (Bozin et al., 2007; Khalil and Li, 2011). *L. angustifolia* samples also showed moderate antimicrobial activity, consistent with previous studies reporting significant inhibition of both bacterial and fungal strains, particularly with ethanol extracts and essential oils (Betlej et al., 2023; Jeddi et al., 2023). *H. perforatum* exhibited notable activity against Gram-positive bacteria and *Candida* species, supporting literature that highlights its strong antibacterial properties related to hyperforin and hypericin content (Sherif et al., 2023; Süntar et al., 2016). In contrast, *M. chamomilla* and *F. vulgare* samples demonstrated weaker antimicrobial effects in our study, differing from some reports that emphasized stronger activities depending on extraction methods and plant parts (Abdoul-Latif et al., 2011; Gulfraz et al., 2008). Overall, our findings confirm the prominent antimicrobial potential of *S. officinalis* and *H. perforatum*, while suggesting more moderate activities for *L. angustifolia*, *M. chamomilla*, and *F. vulgare*.

In a study, the hydroalcoholic extract of *M. chamomilla* demonstrated significant anticholinesterase activity in a scopolamine-induced memory impairment model in rats. Scopolamine administration significantly increased acetylcholinesterase (AChE) activity in the hippocampus, while treatment with *M. chamomilla* extract (at both 25 and 75 mg/kg doses) markedly reduced this elevated AChE activity, suggesting a protective effect on cholinergic neurotransmission. This inhibitory effect on AChE is believed to contribute to the observed improvements in cognitive performance, as lower AChE activity helps maintain acetylcholine levels, supporting synaptic function and memory processes (Ionita et al., 2018). The study investigated the acetylcholinesterase (AChE) inhibitory effects of polyphenolic compounds extracted from *M. recutita* (commonly known as chamomile). Utilizing in vitro assays, the researchers identified several phenolic constituents, including apigenin, luteolin, and their glycosides, which exhibited significant AChE inhibitory activity (Qader et al., 2020). The study evaluated the acetylcholinesterase (AChE) inhibitory activity of specialized metabolites isolated from *Chamaemelum*

nobile (Roman chamomile). Among the 15 isolated compounds, apigenin 7-O-rutinoside exhibited the strongest AChE inhibition with an IC_{50} value of 181.58 μ M, followed by a newly tested flavonoid derivative (compound 15) with an IC_{50} of 189.82 μ M. Coumarin derivative scopolin and several germacrane-type sesquiterpene lactones also showed notable inhibitory activity, with IC_{50} values ranging between 224.78 and 303.71 μ M. Specifically, 11,13-dihydro-8-tigloylhydroxyisobornil demonstrated an IC_{50} of 244.74 μ M (Polcaro et al., 2025).

A study investigated the acetylcholinesterase (AChE) inhibitory activities of essential oil (EO) and various solvent extracts of *L. angustifolia* cultivated in Bosnia and Herzegovina. The EO, rich in linalool (27.72%) and linalyl acetate (22.82%), was obtained by steam distillation and characterized by GC-FID/MS analysis. Extracts were prepared using ultrasonic extraction with solvents of differing polarities, and total phenolic content was highest in water (45.30 mg GAE/g) and ethanol (14.40 mg GAE/g) extracts. In terms of acetylcholinesterase inhibition, the essential oil demonstrated significant inhibitory activity, achieving over 50% inhibition at concentrations of 5–10 mg/mL, while the extracts showed comparatively weak inhibition (Talić et al., 2023). Another study evaluated the acetylcholinesterase (AChE) inhibitory activity of *L. officinalis* essential oil across different phenological stages. The essential oil obtained during the full flowering phase demonstrated the strongest AChE inhibitory activity, with an IC_{50} value of 0.18 mg/mL, indicating potent enzyme inhibition. A moderate inhibitory effect was also observed during the early flowering stage (IC_{50} = 0.46 mg/mL). The strong AChE inhibition is attributed to major constituents such as 1,8-cineole, linalool, and camphor, compounds previously associated with neuroprotective properties (Lahmar et al., 2025).

In a study, it was evaluated the acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activities of ethyl acetate, methanol, and water extracts of *H. perforatum* (St. John's wort) collected from Turkey. The methanol extract exhibited the strongest acetylcholinesterase inhibition, with $49.54 \pm 4.44\%$ inhibition at 200 μ g/mL concentration, while the ethyl acetate extract showed the highest butyrylcholinesterase inhibition at $50.79 \pm 3.07\%$ (Altun et al., 2013). A study assessed the anticholinesterase activity of aqueous, ethanol, and water-ethanol (1:1) extracts of St. John's wort prepared via water bath extraction at 60°C. The ethanol extract exhibited the strongest acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activities, with inhibition rates of 65% for AChE and 75% for BChE. The water-ethanol extract showed moderate inhibition (59% for AChE and 66% for BChE), while the aqueous extract demonstrated weaker activity, particularly for BChE inhibition (16%) (Dincel et al., 2025). Another study isolated six new and seven known polycyclic polyprenylated acylphloroglucinols (PPAPs) from the aerial parts of *H. perforatum* and evaluated their acetylcholinesterase (AChE) inhibitory activities. Among the isolated compounds, hyperfol F (compound 4) and uralone K (compound 12) exhibited moderate AChE inhibition, with IC_{50} values of 20.32 ± 0.68 μ M and 27.37 ± 1.21 μ M, respectively. Other compounds such as

hyperfol C (1), hyphenrone T (10), and hyphenrone U (11) showed weaker inhibitory effects with IC_{50} values ranging from 37.51 to 47.23 μ M (Lou et al., 2020).

A study evaluated the cholinesterase inhibitory properties of *Salvia officinalis* (sage) and its effects on mood, anxiety, and cognitive performance in healthy young adults. An ethanolic extract of dried *S. officinalis* leaf demonstrated dose-dependent inhibition of both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), with stronger inhibition observed for BuChE (IC_{50} = 0.054 mg/mL) compared to AChE (IC_{50} = 0.365 mg/mL). In the clinical trial, participants receiving sage extracts (300 mg or 600 mg) showed improved mood parameters, such as increased alertness, calmness, and contentedness, particularly at the higher dose. Cognitive performance improvements were also observed, especially after administration of the 600 mg dose (Kennedy et al., 2006). Another study evaluated the *in vitro* acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activities of 56 different extracts (prepared using petroleum ether, chloroform, ethyl acetate, and methanol) from 14 Turkish *Salvia* species, including *Salvia officinalis*. Anticholinesterase activities were determined using the Ellman method. The results showed that most nonpolar extracts (especially petroleum ether and chloroform extracts) exhibited significant inhibition, particularly against BChE. Although *S. officinalis* was referenced based on previous literature for its well-known AChE inhibitory properties linked to its essential oil constituents like α -pinene, 1,8-cineole, and camphor, this study primarily focused on other Turkish *Salvia* species. In general, petroleum ether and chloroform extracts showed stronger anticholinesterase effects compared to ethyl acetate and methanol extracts (Orhan et al., 2007). Another study investigated the chemical composition and biological activities of *S. officinalis* essential oil (EO) from Tunisia, focusing particularly on its anti-acetylcholinesterase (AChE) activity. The essential oil, predominantly composed of camphor (33.61%), 1,8-cineole (22.22%), and α -thujone (21.43%), exhibited strong AChE inhibitory activity, with an IC_{50} value of 38.71 ± 2.09 mg/L. The significant inhibition is attributed mainly to the presence of monoterpenes like 1,8-cineole, α -pinene, camphor, and β -caryophyllene, known for their cholinesterase inhibitory properties (El Euch et al., 2019).

A study evaluated the acetylcholinesterase (AChE) inhibitory activity of essential oils, ethanol extracts, and water extracts of five aromatic herbs traditionally used as food spices in Portugal, including *F. vulgare*, *Mentha spicata*, *Mentha pulegium*, *Rosmarinus officinalis*, and *Thymus serpyllum*. Among the tested samples, the essential oil of *R. officinalis* exhibited the strongest AChE inhibitory effect with an IC_{50} value of 69.8 ± 0.1 μ g/mL. The essential oil of *F. vulgare* also demonstrated notable AChE inhibitory activity with an IC_{50} value of 252 ± 0.1 μ g/mL, while its ethanol and water extracts showed weaker inhibition (IC_{50} values of 308 ± 0.1 μ g/mL and 1490 ± 0.3 μ g/mL, respectively). Although the major component of *F. vulgare* essential oil, (E)-anethole (70.2%), showed poor inhibitory activity individually, the moderate activity of the whole oil may result from the combined effect of other minor constituents such as (Z)-anethole. Overall, essential oils exhibited stronger inhibition compared to ethanol and

water extracts (Mata et al., 2007). Another study assessed the antiamnesic and anticholinesterase potential of *F. vulgare* (fennel) methanolic fruit extract in mice. Using behavioral models such as the Elevated Plus Maze and Passive Avoidance Paradigm, researchers evaluated both short-term and long-term memory. Pretreatment with the fennel extract for eight consecutive days significantly ameliorated scopolamine-induced (0.4 mg/kg) and age-related memory deficits. The extract notably reduced transfer latencies in both young and aged mice and increased step-down latency, indicating improved memory retention. Biochemical analyses revealed that the fennel extract significantly inhibited whole-brain acetylcholinesterase activity, suggesting enhanced central cholinergic function (Joshi and Parle, 2007).

In our study, *H. perforatum* drug showed the highest acetylcholinesterase (AChE) inhibition (26.39%), followed by *M. chamomilla* extract, which exhibited the strongest butyrylcholinesterase (BChE) inhibition (40.16%). These findings are consistent with previous studies reporting moderate to strong cholinesterase inhibitory activities for *H. perforatum*, attributed to hyperforin, quercetin, and related phenolic compounds (Sherif et al., 2023; Silva et al., 2005). Similarly, the moderate BChE inhibition observed for *M. chamomilla* aligns with earlier reports highlighting flavonoid-rich extracts as contributors to cholinesterase inhibition (Abdoul-Latif et al., 2011; Franco et al., 2020). *S. officinalis* demonstrated relatively low cholinesterase inhibition in our study, which is consistent with some reports showing variability depending on extract type and phenolic composition (Bozin et al., 2007; Javid et al., 2022). *L. angustifolia* and *F. vulgare* samples exhibited weak cholinesterase inhibition, corroborating findings that suggest essential oils rather than methanol extracts are primarily responsible for significant inhibitory activity in these species (Jeddi et al., 2023; Godavari et al., 2018). Overall, our results support the notable anticholinesterase potential of *H. perforatum* and *M. chamomilla*, while indicating lower activity for *S. officinalis*, *L. angustifolia*, and *F. vulgare* compared to some literature values.

Conclusion

This study comprehensively evaluated the biological activities of extracts from *M. chamomilla*, *L. angustifolia*, *H. perforatum*, *S. officinalis*, and *F. vulgare*, along with the Soothing Complex product and their formulated mixtures. Among the tested samples, *H. perforatum* extract exhibited the strongest α -glucosidase inhibitory activity, with an IC_{50} value of 8 μ g/mL, indicating its promising antidiabetic potential. The *S. officinalis* extract also showed notable enzyme inhibition, particularly in antioxidant and anticholinesterase assays. Antioxidant evaluations revealed that *H. perforatum* drug, *S. officinalis* drug, and extract forms possess significant ABTS and DPPH radical scavenging activities, comparable to or exceeding those of standard antioxidants such as trolox and α -tocopherol. The antimicrobial analysis showed moderate to good activity in several samples, with *S. officinalis* and *L. angustifolia* extracts demonstrating lower MIC values, especially against *Staphylococcus aureus* and *Candida albicans*. These results emphasize the therapeutic potential of these

plant species, particularly *H. perforatum* and *S. officinalis*, for the development of new phytotherapeutic and dermocosmetic formulations, including over-the-counter products. Future studies may focus on *in vivo* validation, detailed phytochemical profiling, and formulation development to support clinical translation.

Declarations

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval

This study did not require ethical approval. Peer-review: Externally peer-reviewed.

Authors Contribution

Meryem Uğurlu, Hafize Yuca, Furkan Çoban, and Songül Karakaya conceptualized and designed the study. The supervision and execution of the study were carried out by Hafize Yuca, Furkan Çoban, and Songül Karakaya. The materials used in the study were provided by Meryem Uğurlu, Hafize Yuca, and Furkan Çoban. Data collection and processing were conducted by Meryem Uğurlu, Bilge Aydın, Gamze Göger, Furkan Çoban, and Songül Karakaya, while the analysis and interpretation of the data were performed by Meryem Uğurlu, Bilge Aydın, and Gamze Göger. The literature review was carried out by Meryem Uğurlu, Bilge Aydın, Gamze Göger, and Hafize Yuca. The manuscript was written by Hafize Yuca, Furkan Çoban, and Songül Karakaya, and the critical review and final revisions were also completed by the same authors.

Conflict of Interest

The authors have no conflict of interest to declare.

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