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Review article

Exploring nature's hidden treasure: Unraveling the untapped phytochemical and pharmacological potentials of *Clinopodium vulgare* L. – A hidden gem in the Lamiaceae family

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ABSTRACT

Folk medicine, rooted in historical practice, has long been used for medicinal purposes, emphasizing the need to ensure the safety, quality, and efficacy of herbal medicines. This imperative has grown over time, prompting collaborative efforts to document historical records and preserve invaluable knowledge of medicinal plants. The Lamiaceae (Labiatae) family, renowned for its rich assortment of medicinal plants characterized by high concentrations of volatile oils, stands out in this regard. This review focuses on *Clinopodium vulgare* (*C. vulgare*) L., commonly known as wild basil or basil thyme, a significant species within the Lamiaceae family found across diverse global regions. *C. vulgare* boasts a storied history of application in treating various ailments, such as gastric ulcers, diabetes, and inflammation, dating back to ancient times. Rigorous research has substantiated its pharmacological properties, revealing its antioxidant, antiviral, antibacterial, anti-inflammatory, anticancer, antihypertensive, and enzyme-inhibitory effects. This comprehensive review provides an insightful overview of the Lamiaceae family, elucidates the extraction methods employed to obtain medicinal compounds, explores the phytoconstituents present in *C. vulgare*, and systematically details its diverse pharmacological properties. Additionally, the review delves into considerations of toxicity. By synthesizing this wealth of information, this study opens avenues for the potential therapeutic applications of *C. vulgare*. The practical value of this research lies in its contribution to the understanding of medicinal plants, mainly focusing on the pharmacological potential of *C. vulgare*. This exploration enriches our knowledge of traditional medicine and paves the way for innovative therapeutic

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approaches, offering promising prospects for future drug development. As the demand for natural remedies continues to increase, this work provides a valuable resource for researchers, practitioners, and stakeholders in herbal medicine and pharmacology.

Abbreviations

S. aureus	*Staphylococcus aureus*
E. coli	*Escherichia coli*
P. aeruginosa	*Pseudomonas aeruginosa*
B. subtilis	Bacillus subtilis
E. faecalis	*Enterococcus faecalis*
K. pneumoniae	*Klebsiella pneumoniae*
P. mirabilis	*Proteus mirabilis*
E. cloacae	*Enterobacter cloacae*
K. oxytoca	*Klebsiella oxytoca*
CUPRAC	Cupric ion reducing activity
DPPH	1,1-diphenyl-2-picrylhydrazyl
ABTS	2,2 Azino-bis (3-ethylbenzothiazloine-6-sulfonic acid)
FRAP	Ferric reducing antioxidant power
HRMS	High-resolution mass spectrometry
HPLC	High-performance liquid chromatography
GC	Gas chromatography

1. Introduction

Medicinal plant use is a time-honored practice that has grown and changed with human culture. Knowledge about these plants has passed from generation to generation, evolving with human knowledge, cultural norms, and scientific discoveries. Because of this slow but steady progression, a large body of information has been amassed, and it is ever-evolving as new information regarding the possible therapeutic effects of natural therapies is uncovered. Therefore, medicinal plant usage demonstrates the fruitful meeting point of ancient wisdom and cutting-edge research [1]. Medicinal plants serve as therapeutic sources in various cultural practices [2]. In modernized and developing nations, assurance of the safety, quality, and efficacy of herbal medicines and medicinal plants has emerged as a critical concern. By establishing a standard for assessing the effectiveness of plant-derived active compounds, herbal remedies could pave the way for novel healthcare approaches to address human illnesses in the coming years. A profound understanding of traditional knowledge and medicinal plants can contribute significantly to the exploration and utilization of natural plant resources. To ensure the preservation of this valuable knowledge of medicinal plants and their use for the benefit of humanity, it is essential to adopt a comprehensive approach and foster collaborative efforts toward documenting historical records. This must be done promptly before irreversible damage is caused to human health [3]. Throughout the ages, the medicinal properties of plants have been harnessed for their healing benefits, be it through the consumption of homemade herbal) teas or remedies or via the utilization of raw extracts and highly refined “enriched fractions” found in various pharmaceutical preparations, including but not limited to tinctures, powders, pills, and capsules [4–18]. Plant-based products have been used for medicinal purposes in various regions of the world for centuries. Many cultures have a long history of using plants for their medicinal properties, and these traditional practices have often been passed down through the generations [19]. In countries with middle and low incomes, the primary healthcare necessities of approximately 80 % of the population are met by medicinal plants [20].

Clinopodium L. (Lamiaceae) is a diverse group of flowering plants found across various regions, including southern and southeastern Europe, North America, Latin America, and Asia. The perennial aromatic plant C. *vulgare* L., or wild basil, has a wide range of ethnopharmacological uses that set it apart as a unique species [21]. This species exhibits variability and is distributed extensively across temperate regions in the Northern Hemisphere. The plant is spread across the mainland and various islands of Greece, inhabiting macchies and open woodlands at diverse elevations ranging from near sea level to approximately 2200 m above sea level [22]. The plant has square-shaped, erect, hairy stems and a rhizomatous growth pattern, with its leaves arranged in opposite pairs. Foliage displays the distinct feature of being covered in fine hairs, with a shape that can be either ovate or lanceolate, possessing either a short or nonexistent stalk, a wedge-shaped base, and margins that are bluntly toothed. The flowering structure at the tip of the plant stem forms a distinctive elongated cluster with multiple loosely arranged sets of flowers emerging from the leaf bases.

These blooms are adorned by four stamens, a lengthy style, and fused carpels. In the literature on botany in the German language, it is denoted by the term *calmintha,* whereas in the English language, it is referred to as *savory*. This particular plant tends to thrive in dry, sandy soil and can be found in scarce forests and amid shrubs at elevations not exceeding 1700 m in Europe and Asia [23]. Upon conducting a comprehensive literature search, it was found that certain studies exhibited a lack of connectivity and a limited number of

papers were obtained, such as a report published on the seed germination of *C. vulgare*. This study aimed to examine the impact of various treatments and to propose a method for effective seed germination. The highest germination rates and percentages were observed in wet and dry stratification, respectively [24]. Another study investigated seasonal effects on phenolic concentrations in leaves [22]. This review explores the various extraction methods, identified phytoconstituents, and their pharmacological properties. In addition, a toxicity study was conducted.

We conducted a thorough literature review, shedding light on the historical applications and pharmacological properties of *C. vulgare*. Notably, the review revealed critical research gaps, including challenges in standardization, limited toxicity studies, and the need to bridge traditional uses with modern healthcare practices. In response, this study endeavors to synthesize existing knowledge by offering a comprehensive overview of the Lamiaceae family, extraction methods, phytoconstituents, pharmacological properties, and toxicity of *C. vulgare*. The primary contributions highlight the practical implications of the diverse pharmacological properties of *C. vulgare*, leveraging its historical significance. Furthermore, this paper proposes future directions to address research gaps, advocating standardization, rigorous toxicity studies, and integration into modern medical practices. To augment the impact of research, discussions will also extend to emerging areas, such as artificial intelligence, exploring its potential role in optimizing extraction processes and predicting pharmacological effects, and telecommunications, considering novel ways to disseminate information about herbal medicines and share traditional knowledge. This integrated approach aims to enrich the overall contribution of this research and foster a more comprehensive understanding of the medicinal potential of *C. vulgare*.

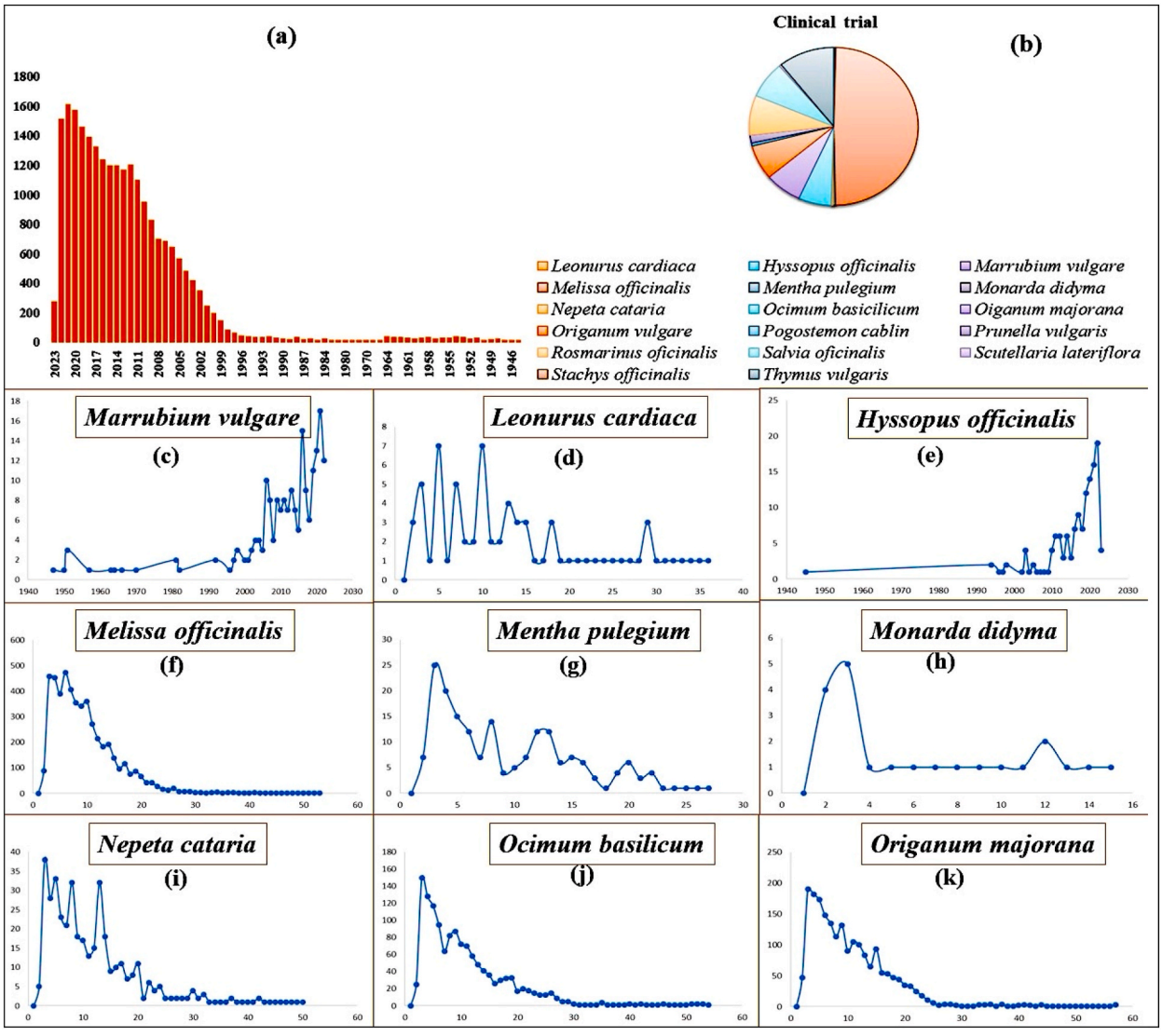

Fig. 1. Graphical representation of (**a**) Trends in PubMed for family Lamiaceae (**b**) Clinical trials in family Lamiaceae in PubMed (**c-k**) Trends in publications of some Lamiaceae species in PubMed.

2. Methodology

In this study, the Lamiaceae family was discussed with comprehensive and general information. Data were obtained from Google Scholar and PubMed searches for the present analyses. A query "Lamiaceae" was used to retrieve information on the pattern of literature published in the Lamiaceae family until 2023 in PubMed. However, the query terms "*Leonurus cardiaca*", "*Hyssopus officinalis*", "*Marrubium vulgare*", "*Melissa officinalis* (*M. officinalis*)", "*Mentha pulegium*", "*Monarda didyma* (*M. didyma*)", "*Nepeta cataria*", "*Ocimum basilicum* (*O. basilicum*)", "*Origanum majorana*", "*Origanum vulgare* (*O. vulgare*)", "*Pogostemon cablin*", "*Prunella vulgaris* (*P. vulgaris*)", "*Rosmarinus officinalis*", "*Salvia officinalis* (*S. officinalis*)", "*Scutellaria lateriflora*", "*Stachys officinalis*", "*Thymus vulgaris* (*T. vulgaris*)" were also used to retrieve information on the patterns of their literature published till 2023. The recovered data are graphically represented in Fig. 1. The figure shows trends in publications in PubMed for the Lamiaceae family (Fig. 1a). In addition, clinical trial investigations in the family Lamiaceae that appeared in PubMed have also been represented graphically (Fig. 1b), and patterns in publications of different Lamiaceae species in PubMed have also been depicted (Fig. 1, c-k) [25].

As the main focus of this review is on *C. vulgare*, inclusion and exclusion criteria were only used to gather information on *C. vulgare*, which was used to write the information on *C. vulgare.* However, for information on *C. vulgare*, a literature search was conducted on Google Scholar from January 1998 to May 2023, and inclusion and exclusion criteria were determined. The search query was "*C. vulgare*" only, and data from research papers, books, and abstracts of different kinds of literature were retrieved to compile this work. Only research and published works in English were considered in the analyses [25].

A total number of 9770 results were obtained, including research, reviews, abstracts, and citations by other studies, etc., using "*C. vulgare*" as a query. Out of 9,770, thirty-three items, including research articles, books, and abstracts, were included in this review. The exclusion of information was based on repetition of data, languages other than English, irrelevance to the data, very old data, and insufficient information. A literature search showed that the plant has not yet been studied widely but possesses immense potential as a prospect for future medicine. Hence, as mentioned in this review, only 33 articles were available for medicinal or other information. The focus was on summarizing the traditional uses of *C. vulgare*, extraction methods, phytoconstituents, elemental compositions, phytochelatins, and pharmacological activities. Four papers were found on its traditional uses, 18 on its extraction methods, 10 on its phytoconstituents, 2 on its elemental composition and phytochelatins, and 18 on its pharmacological activities. For pharmacological

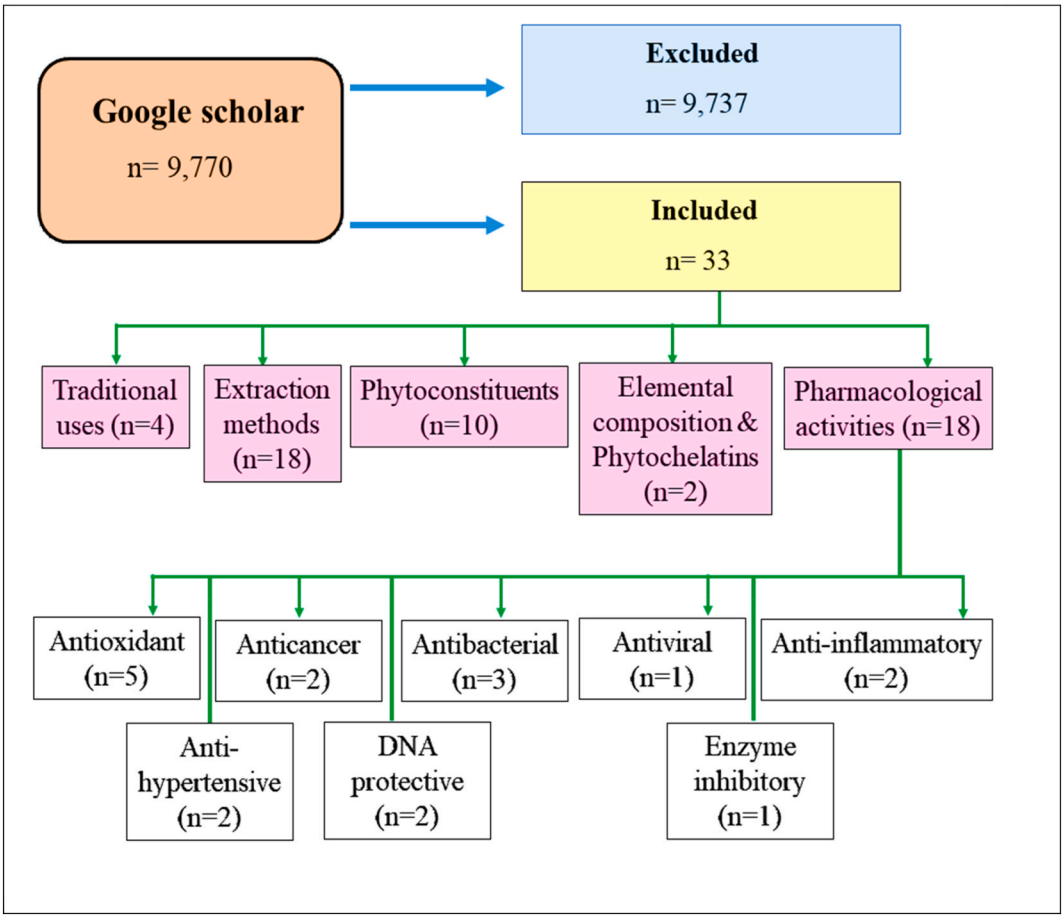

Fig. 2. Inclusion and exclusion criteria for *C. vulgare.*

activities, five were obtained for antioxidant, two for anticancer, three for antibacterial, one for antiviral, two for anti-inflammatory, two for antihypertensive, two for DNA protective, and one for enzyme inhibitory. The overall information of the retrieved data is schematically represented in Fig. 2 [25].

The present literature review used the scientific name *C. vulgare* for wild basil; however, other synonyms for this plant were also used. To maintain the clarity of the names, only *C. vulgare* was used throughout the paper. Fig. 3 depicts the trend in research articles on *C. vulgare* in PubMed using the "*Clinopodium vulgare*" query [25].

3. Lamiaceae family

Lamiaceae (also known as Labiatae) is an exceptionally varied and prevalent group of plants, particularly regarding their use in ethnomedicine. The potency of their medicinal properties is attributed to the high concentration of volatile oils found in them [26,27]. Lamiaceae botanical clans are one of the most extensive families of dicotyledons, encompassing a plethora of species that exude powerful fragrances. This aroma is attributed to the external glandular structures present in these plants, which synthesize volatile oils [27,28]. The significance of this particular oil is noteworthy in various industries, such as pharmaceuticals, flavoring, pesticides, fragrance, perfumery, and cosmetics [27,28]. The Lamiaceae family, commonly known as mints, comprises a group of taxonomically distinct blooming plants. Historically, they have been recognized to have a close relationship with the Verbenaceae family [27].

During the 1990s, research on the evolutionary relationships of plants indicated that numerous genera previously categorized under Verbenaceae were part of Lamiaceae. It is possible that the present understanding of Verbenaceae classification suggests no stronger association with Lamiaceae than with certain other families within the order Lamiales. The closest relatives of Lamiaceae within the Lamiaceae family remain unknown. The plants exhibit a common characteristic of emitting fragrant scents throughout their various components and encompass a multitude of popular herbs utilized in cooking, comprising mint, rosemary, basil, sage, marjoram, thyme, orthosiphon, ocimum, lavandula, leucas, anisomeles, coleus, hyptis, colebrookea (oregano) brunella, lamium, teucrium, scutellaria, and perilla. Many family members grow extensively because of their distinctive fragrance and effortless propagation through stem cuttings, making them one of the most uncomplicated plants for cultivation. Apart from being cultivated for their edible leaves, certain plants, such as the *Coleus* plant, are also grown for their ornamental foliage. The Lamiaceae family has expanded significantly and now comprises approximately 236 different genera, housing a staggering 6900–7200 distinct species. Within the Lamiaceae family, notable for its diversity, the genus *Salvia* stands out, with an impressive 900 species. Other significant genera include *Scutellaria, Coleus, Plectranthus, Hyptis, Teucrium, Thymus,* and *Nepeta,* each comprising between 200 and 360 species, contributing to the rich variety within this botanical family [27].

Some genera of this family have been widely studied, and some are yet to be studied and explored. *Conradina* A. Gray (belonging to the Lamiaceae family) is a rare group of shrubs found only in the southeastern region of the United States. These plants are easily identifiable because of their unique narrow leaves and minor fragrances. The distinguishing features of *Conradina* species include an abundance of fine hairs on the underside of their leaves as well as a distinctly angled corolla tube in their blossoms [29].

Stachys L., commonly known as woundwort, encompasses around 300 species, making it one of the most extensive genera in the Lamiaceae family. It has a near-global distribution, with most of its species thriving in the temperate, balmy areas of the Mediterranean and Southwest Asia. While North and South America and Southern Africa serve as secondary centers for the genus, they are absent in Australia and New Zealand [30]. The *Hyptis* genus, belonging to the Lamiaceae family, is of significant importance, as it is the second most crucial genus found in the Americas. Comprising more than 290 species, these plants are exclusively found in the Neotropical region. The distinguishing feature of this genus is its glandular trichomes that produce essential oils (EOs), which are highly sought after in rural areas of Latin America. The local population consumes it as an infusion to treat respiratory and gastrointestinal issues and skin ailments [31]. The genus *Salvia* is a member of the extensive Lamiaceae family, which includes approximately 252 genera and

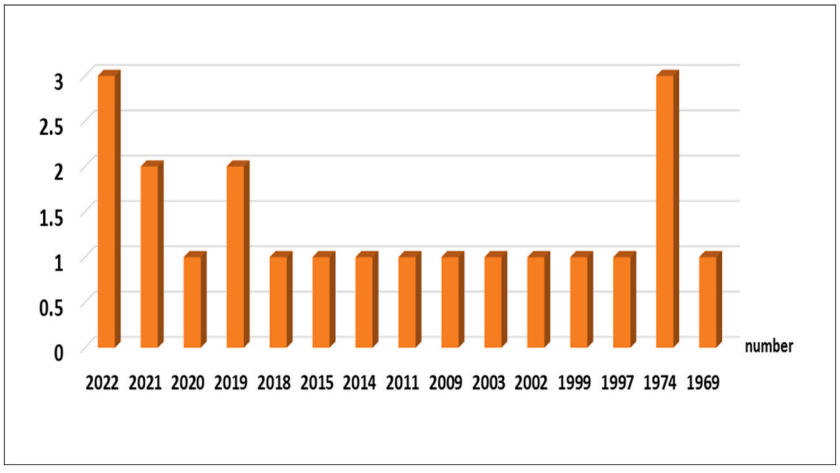

Fig. 3. Trends of research articles on *C. vulgare* in PubMed.

7200 species of flowering plants. *Salvia* encompasses various species grown for their fragrant properties and are utilized as seasoning agents, food additives, cosmetic and perfume ingredients, and traditional remedies [32]. Information on some medicinally important species of the Lamiaceae family is provided in Tables 1–2.

4. Traditional uses

C. vulgare has been used to treat gastric ulcers, diabetes, mastitis, skin irritation, prostatitis, swelling, and skin irritation [21,55]. It has been utilized as a curative medicinal plant in folk medicine for wart treatment and wound healing in Bulgaria [4]. Additionally, it has been used to treat skin irritation and as a cat foot in Bulgaria [56].

5. Extraction methods and phytochemistry

Different methods can be used to extract phytochemicals from plants, including maceration, Soxhlet extraction, steam distillation, supercritical fluid extraction, and ultrasound-assisted extraction. However, the extraction method depends on many factors, such as

Table 1
Comprehensive information on some species of the Lamiaceae family.

Plant	Part used	Pharmacological properties	Significance	Reference
O. basilicum	Aerial	Spermatogenic	*O. basilicum* extract improved sperm parameters in rats	[33]
	Leaves and stalks	Antihypertensive	Reduced blood pressure and cardiac hypertrophy in renovascular hypertensive rats	[34]
	Leaves	Anti-inflammatory	*O. basilicum* L. leaf and callus extracts showed anti-inflammatory activity on LPS-stimulated macrophages, potential benefits in preventing pathological inflammation	[35]
M. officinalis	Aerial	Ant depressive	The hydro-alcoholic extract is effective in preventing anxiety and depression	[36]
	Leaves	Neuroprotective	Effective in protection against 3, 4-methylenedioxymethamphetamine induced apoptosis in primary neurons	[37]
	Aerial	Cardiovascular effects	Improved glycemic control, lipid profile, and inflammation reduction and safe to use	[38]
	Leaves	Cytotoxic	Ethanolic extract (50 %) exhibited an anti-proliferative effect on HCT-116 cancer cells, and rosmarinic acid from the extract showed cytotoxic activity against the cancer cells	[39]
	Leaves	Hypoglycemic and antihyperlipidemic	Showed hypoglycemic properties by activating peroxisome proliferator-activated receptors (PPARs)	[40]
M. didyma	Aerial	Anti-inflammatory and antioxidant	EO of *M. didyma* L. showed antioxidant and anti-inflammatory activity, dominated by the presence of carvacrol, *p*-cymene, and thymol	[41]
	Aerial	Phytotoxic	*M. didyma* EO and thymol solution (59.3 %) exposure on weed seeds increased malondialdehyde (MDA) and hydrogen peroxide (H_2O_2) levels and markers of oxidative stress	[42]
	Leaves and inflorescences	Antifungal	*EO from M. didyma* showed high antifungal properties against *Botrytis cinerea*.	[43]
O. vulgare	Flowered aerial part	Antioxidant	*O. vulgare* showed enhanced antioxidant activity, and the formulation maintained the antioxidant potential	[44]
	Aerial	Antimicrobial, antioxidant, and enzyme inhibitory	EO from *O. vulgare* subsp. showed strong antimicrobial, antioxidant, and enzyme inhibitory action against butyrylcholinesterase, acetylcholinesterase, α-amylase, tyrosinase and α-glucosidase	[45]
	Leaves	Learning and memory enhancers	*O. vulgare* aqueous extract containing high levels of antioxidants may potentially enhance passive avoidance learning in male Wistar rats.	[46]
T. vulgaris	Aerial	Antimicrobial	*T. vulgaris* essential oil (TVEO) can be used as an effective and safe alternative to synthetic drugs for multidrug-resistant bacteria.	[47]
	Whole	Antioxidant	Steam distillation resulted in more diverse and slightly higher antioxidant activity than non-polar solvent extraction. Both samples exhibited antioxidant activity because of volatile and non-volatile compounds	[48]
	Aerial	Antinoniceptive	Thyme syrup and tincture showed pain-relieving effects in mice; this could be due to changes in the metabolic pathways of the drugs	[49]
S. officinalis	Aerial	Antispasmodic and antidiarrheal	Crude extract showed antispasmodic and antidiarrheal activities, probably due to the activation of voltage-dependent K+ channels	[50]
	Leaves	Neuro receptors modulations	The extract showed modulation of neuro-receptors and serotonin transporters, providing a base for its effectiveness in treating menopausal symptoms	[51]
	Aerial	Antifungal	Results showed antifungal activity against *Candida* species. Carnosol and 12-methoxy-trans-carnosic acid (more effective against biofilm formation) were the two main phytocompounds identified	[52]
P. vulgaris	Flower	Antibacterial	*P. vulgaris* flower extract showed strong antibacterial activity against different pathogens and possessed rosmarinic acid, including the potential therapeutic and pharmacological significance	[53]
	Ground vegetable	Antiulcer	*P. vulgaris* showed antiulcer properties due to its polyphenol content in rats with phenylbutazone-induced ulcer	[54]

Table 2
Botanical classification of the plant described in this study.

Kingdom	*Plantae*
Subkingdom	*Tracheobionta*
Super division	*Spermatophyta*
Division	*Magnoliophyta*
Class	*Magnoliopsida*
Subclass	*Asteridae*
Order	*Lamiales*
Family	Lamiaceae
Genus	Clinopodium
Species	vulgare L.

the plant material used, the specific compounds of interest, and the purpose of the crude extract. Some of these methods are described in this section.

a) **Maceration:** Maceration involves immersing the plant material in a solvent for a specific time to allow soluble compounds to dissolve, followed by filtration and drying to obtain the extract [57].
b) **Soxhlet Extraction:** In Soxhlet extraction, a small amount of solvent is continuously boiled and passed through a solid matrix to extract the desired compounds. This cycle continues until the desired level of the extract is achieved [58].
c) **Steam Distillation:** Steam distillation involves the use of steam to extract the volatile compounds. The plant material is exposed to steam, followed by the separation of the compounds and steam through the condensation process [59].
d) **Supercritical Fluid Extraction:** Supercritical fluid extraction employs a compressed substance, usually carbon dioxide, with both liquid and gas properties to effectively dissolve a broad range of compounds for extraction [60].
e) **Ultrasound-assisted Extraction:** Ultrasound-assisted extraction involves the use of ultrasound waves to disrupt plant cells and extract compounds, followed by solvent immersion and filtration [61].

Different extraction procedures were used to extract the ingredients from the *C. vulgare* plant. Its leaves, stems, flowers, roots, etc., have also been extracted, characterized, and used in different studies. A distillation process using a Clevenger-type apparatus was used to isolate EOs from the air-dried and ground aerial parts. The plant parts were air-dried, ground, and subjected to water distillation for 3 h. This process resulted in an EO yield of 0.75 % (v/w). It was then carefully dried using anhydrous sodium sulfate and filtered. The final product was stored in a cool environment at a temperature of +4 °C until further testing and analysis. The EOs were analyzed using gas chromatography-mass spectrometry (GC-MS), which identified 40 compounds that confirmed 99.4 % oil, of which the main compounds were thymol (38.9 %), γ-terpinene (29.6 %), and 9.1 % was *p*-cymene (9.1 %) [62]. In another study, an aqueous extract of *C. vulgare* was prepared, and the effects of solvent, time, and temperature on its biological activity were observed. First, it was boiled for 5, 10, and 15 min at 100 °C, followed by chromatography (Silica gel 60 column/Sephadex G 10 column) and eluted with chloroform, chloroform: methanol (9:1 v/v), ethyl acetate, and acetone/water. However, another batch extraction was performed using different solvents at different temperatures [4]. In another study, various extracts of *C. vulgare,* including acidified, alkalized, and

Table 3
Extraction techniques for *C. vulgare* phytochemicals.

Plant part	Extract type	Extraction/Separation Method	Result	Reference
Aerial	Aqueous	Distillation	Whole *C. vulgare* e.o. was found to possess better antioxidant activity than individual phytochemicals	[62]
Aerial	Methanolic	Ultrasonic assisted	Most abundant signals were obtained for chlorogenic acid, caffeic acid, and catechin	[68]
Aerial	Aqueous	Ultrasound-assisted/UHPLC-HRMS	Different types of flavonoids, saponins, and caffeic acid oligomers were identified. Rosmarinic acid was abundantly present.	[21]
Aerial	Acetone, methanol, and water	Soxhlet/RP-HPLC	Methanolic and water extracts were rich in phenolic and flavonoid compounds, respectively.	[45]
Aerial	Ether	GC	Phenolcarboxylic acids were isolated	[69]
Aerial	–	GC-MS solid phase microextraction,	Subsp. Arundanum was highly rich in EOs	[67]
Aerial	–	Hydrodistillation, GC, GC-MS	β-caryophyllene, germacrene-D, and β-caryophyllene oxide were present as main consituents.	[63]
Aerial	–	HPLC	Phenolcarbonic Acid and flavonoids were isolated	[66]
Aerial	–	Hydrodistillation, GC, GC-MS	Major components were santolinyl acetate, vulgarone B, 14-hydroxy-a-muurolene	[64]
Aerial	Aqueous	GC-MS, UH-HPLC-HRMS	low content of GC-compatible components and high content of triterpene saponins	[70]
Aerial	Aqueous	Ultrasonic-assisted, UH-HPLC-HRMS, MS/MS	Three new phytocompounds from active CV3 extract were identified	[65]

lipophilic extracts, were prepared. To extract the plant material, powdered plant material consisting of stems, leaves, flowers, and total plant material was mixed with HPLC-grade water and gently agitated until it reached room temperature. Three different extraction methods were used: water alkalization using ammonia, water acidification using formic acid, and pure water up to its natural pH. After extraction, the aqueous extracts were frozen at −50 °C and subjected to centrifugation, filtration, and lyophilization. Additionally, the aerial parts of the plant were exposed to supercritical fluid extraction employing CO_2 to obtain a lipid fraction that was soluble in DMSO [55]. Methanol, acetone, and water extracts were obtained from the aerial parts of *C. vulgare* L., including the leaves, flowers, and buds. The Soxhlet extraction method was used with methanol, acetone, and water [45]. Another study reported hydrodistillation extraction using a Clevenger-type apparatus [63,64] and ultrasonic extraction [65].

Phytochemical isolations are generally performed using HPLC [66], GC-FID and GC-MS [63,67], UH-HPLC-HRMS, and MS/MS [65]. From the study, different phytocompounds, including EOs, flavonoids, phenols, etc., were identified, such as ferulic acid, benzoic acid, rutin, rosmarinic acid, apigenin, lauric acid, myristic acid, pentadecanoic acid, palmitic acid, germacrene-D, *β*-caryophyllene and *β*-caryophyllene oxide, kaempferol, catechin, choline, etc. The list of extraction procedures and phytoconstituents is given in Table 3 and Table 4, respectively, and some chemical structures are given in Figs. 4–5.

Table 4
Phytoconstituents identified in different studies of *C. vulgare*.

Phytoconstituents	Technique	Reference
α-thujene, *α*-pinene, camphene, sabinene, *β*-pinene, *β*-myrcene, *α*-phelladrene, *p*-mentha-1(7), 8-diene, *α*-terpinene, *p*-cymene, (z)-*β*-ocimene, (e)-*β*-ocimene, *γ*-terpinene, *cis*-sabinene hydrate, terpinolene, *trans*-sabinene hydrate, borneol, terpinen-4-ol, *α*-terpineol, pulegone, carvacrol methyl ether, *cis*-piperitone epoxide, isopulegone, *trans*-piperitone epoxide, thymol, carvacrol, piperitenone, thymol acetate, piperitenone oxide, *β*-caryophyllene, *β*-copaene, aromadendrene, *α*-caryophyllene, *γ*-muurolene, germacrene D, bicyclogermacrene, *β*-bisabolene, *γ*-cadinene, *δ*-cadinene, spathulenol	GC-MS	[62]
Caffeic acid, chlorogenic acid, rosmarinic acid, apigenin, kaempferol, catechin, choline, adenine, inositol, acetic acid, formic acid, fumaric acid, malic acid, citric acid, alanine, glutamine, glutamate, valine, *α*-glucose, *β*-glucose, sucrose	HPLC, ^{1}H and 2D-NMR,	[68]
Clinopodic acid K, followed by salvianolic acid a and salvianolic acid L	UH-HPLC-HRMS, MS/MS	[65]
Saikogenin F-3-*O*-(hexosyl-[O-hexosyl-*O*-hexosyl-Ohexosyl]-deoxyhexoside (clinoposaponin V)), apigenin-7-*O*-glucoside, luteolin-8-C-glucoside (orientin), luteolin-7-*O*-glucoside, naringenin-*O*-hexouronide, quercetin-3-*O*-glucoside (isoquercitrine), luteolin-*O*-neohesperidoside, isosakuranetin-7-*O*-neohesperidoside, salvianic acid A (danshensu), caffeic acid, salvianolic acid F, clinopodic acid A, salvianolic acid G, rosmarinic acid, clinopodic acid B, salvianolic acid D isomer, salvianolic acid D, salvianolic acid C isomer, isosalvianolic acid C, salvianolic acid C, isosalvianolic acid C isomer, salvianolic acid A, salvianolic acid A isomer, salvianolic acid A isomer, salvianolic acid A isomer, salvianolic acid T/U, salvianolic acid J/clinopodic acid C/E, salvianolic acid H/I, salvianolic acid H/I, lithospermic acid A/clinopodic acid J/N, methoxy-lithospermic acid/clinopodic acid D/F, methoxy-salvianolic acid H/I, salvianolic acid K isomer, salvianolic acid K isomer, salvianolic acid K isomer, salvianolic acid K, yunnaneic acid E isomer, yunnaneic acid E, yunnaneic acid E isomer, clinopodic acid Q, salvianolic acid E, yunnaneic acid G, salvianolic acid L, isosalvianolic acid B/salvianolic acid B/lithospermic acid B/clinopodic acid I, isosalvianolic acid B/salvianolic acid B/lithospermic acid B/clinopodic acid I, sagerinic acid, clinopodic acid K, clinopodic acid O, yunnaneic acid A, saikogenin F-3-*O*-hexosyl-*O*-deoxyhexoside (clinoposaponin XV), saikogenin F–*O*-Hex, dHex, Pent, clinoposaponin XVIII, saikogenin F-3-*O*-(hexosyl-[O-hexosyl]-deoxyhexoside (buddlejasaponin IV)), saikogenin F-3-*O*-(hexosyl-[O-hexosyl-*O*-hexosyl-Ohexosyl]-deoxyhexoside (clinoposaponin V))	UHPLC-HRMS	[21]
α-pinene, camphene, *β*-pinene, myrcene, limonene, (z)-*β*-ocimene, (e)-*β*-ocimene, *υ*-terpinene, camphor, isoborneol, terpinen-4-ol, *α*-terpineol, myrtenal, carvenone, piperitone oxide, thymol, bornyl acetate, carvacrol, piperitenone oxide, *β*-bourbonene, *β*-elemene, *β*-caryophyllene, *β*-farnesene, *α*-humulene, *υ*-muurolene, germacrene-d, *υ*-elemene, unknown, *α*-farnesene, *υ*-cadinene, ***δ***-cadinene, unknown, nerolidol isomer, spathulenol, *β*-caryophyllene oxide, globulol, humulene oxide, *t*-muurolol, *α*-cadinol	GC, GC-MS	[63]
Cis-cinnamic acid, *trans*-cinnamic acid, *p*-coumaric acid, ferulic acid	GC	[69]
Germacrene-D, *β*-caryophyllene and *β*-caryophyllene oxide	GC, GC-MS	[63]
α-thujene, *α*-pinene, camphene, sabinene, *β*-pinene, *β*-mrycene, *α*-terpinene, *α*-phelladrene, limonene, *p*-cymene, *β*-ocimene, 1,3,6-octatriene, *γ*-terpinene, *trans*-sabinene hydrate, linalool, terpineol-4-ol, camphor, borneol, pulegone, *α*-terpinolene, thymol, carvacrol, *α*-copaene, *β*-caryophyllene, *β*-cubebene, aromadendrene, *α*-humulene, germacrene, piperitenone, *β*-bisabolene, bicyclogermacrene, *δ*-cadinene, spathulenol, caryophyllene oxide, *α*-muurolene, hexadecanoic acide	GC-MS	[67]
Chlorogenic acid, kafainic acid, *p*-cumarinic acid, faurulic acid, hesperidin, hyperoside, rutin, quercetin, luteolin, kaempferol, apigenin, acacetin	HPLC	[66]
α-pinene, *β*-pinene, 1,8-cineole, santolina alcohol, camphor, *trans*-dihydro- *α*-terpineol, santolinyl acetate, decanal, dihydroedulan II, tridecane, presilphiperfol-7-ene, 7-*epi*-silphiperfol-5-ene, silphiperfol-4,7(14)-diene, *α*-copaene, *β*-bourbonene, *β*-longipinene, (e)-*β*-damascone, *β*-caryophyllene, *α*-humulene, germacrene D, 10-*epi*-cubenol, germacrene d-4-ol, caryophyllene oxide, globulol, presilphiperfolan-8-ol, *α*-acorenol, allo-aromadendrene epoxide, vulgarone b, *β*-eudesmol, selin-11-en-4 α-ol, *β*-acoradienol, 14-hydroxy-9-*epi*-(*b*)-caryophyllene, guaia-3,10(14)-dien-11-ol, 4-oxo-β-ionone, 14-hydroxy-α-muurolene, *β*-bisabolenol, *β*-eudesmol acetate, *α*-eudesmol acetate, octadecane, 6,10,14-trimethyl-2-pentadecanone, hexadecanol, nonadecane, eicosane, heneicosane, docosane, tricosane, tetracosane, pentacosane, hexacosane, heptacosane, octacosane, nonacosane	GC, GC-MS	[64]
Quinic acid, shikimic acid, citric acid, 3-(3,4-dihydroxyphenyl) lactic acid, chlorogenic acid, protocatechuic acid, *p*-hydroxybenzoic acid, 3,4-dihydroxyphenyl propionic acid/4-hydroxyphenyl acetic acid, *trans*-cinnamic acid (traces), caffeic acid, rosmarinic acid, *p*-coumaric acid, ferulic acid, *m*-coumaric acid, *o*-hydroxybenzoic acid, kaempferol, quercetin, apigenin, naringenin, betulinic acid, ursolic acid, botulin	GC-MS, UH-HPLC-HRMS	[70]

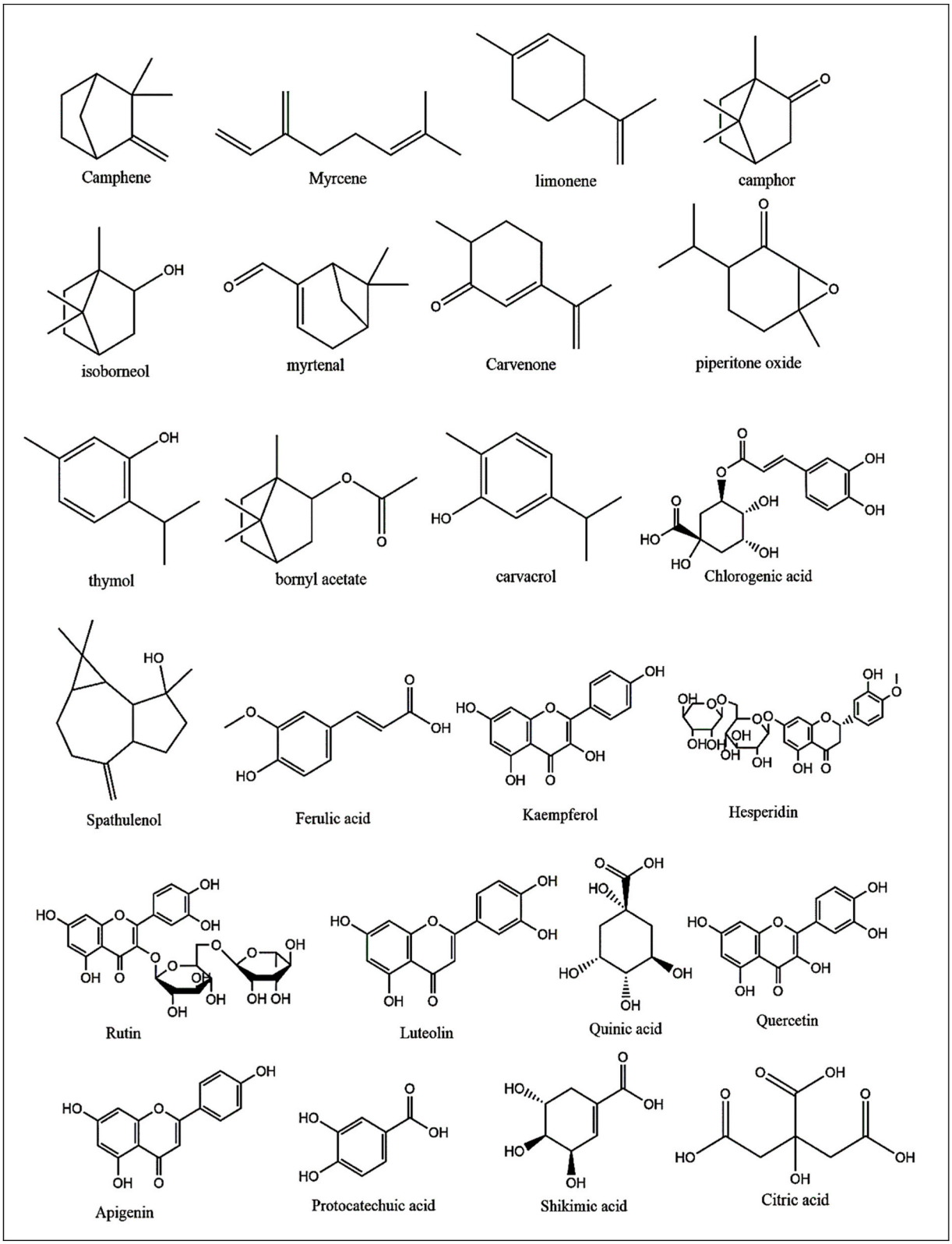

Fig. 4. Structures of some phytoconstituents present in *C. vulgare.*

6. Elemental composition and phytochelatins

The difference in the elemental composition has been investigated in a study from different Bulgarian regions, where cadmium was found to be the most toxic element, with a concentration of up to 95 % in water infusions of leaves. The leaves contained high concentrations of various elements in the following order: Ca > K > Mg > Al > Fe > Na > Zn > Mn > B > Sr > Cu > Cr > Ni > Pb > Ce > La > Cd [71]. Another study for determining phytochelatins evaluated glutathione, PC2, PC3, PC4, and PC5 [72]. Another study investigated the phytochelatin dynamics of *C. vulgare* organs, including shoots, leaves, and roots, under cadmium stress. The results showed that the synthesis of phytochelatins increased when the concentration of cadmium increased (as stress). These studies confirm the phytochelatin properties of this plant [72].

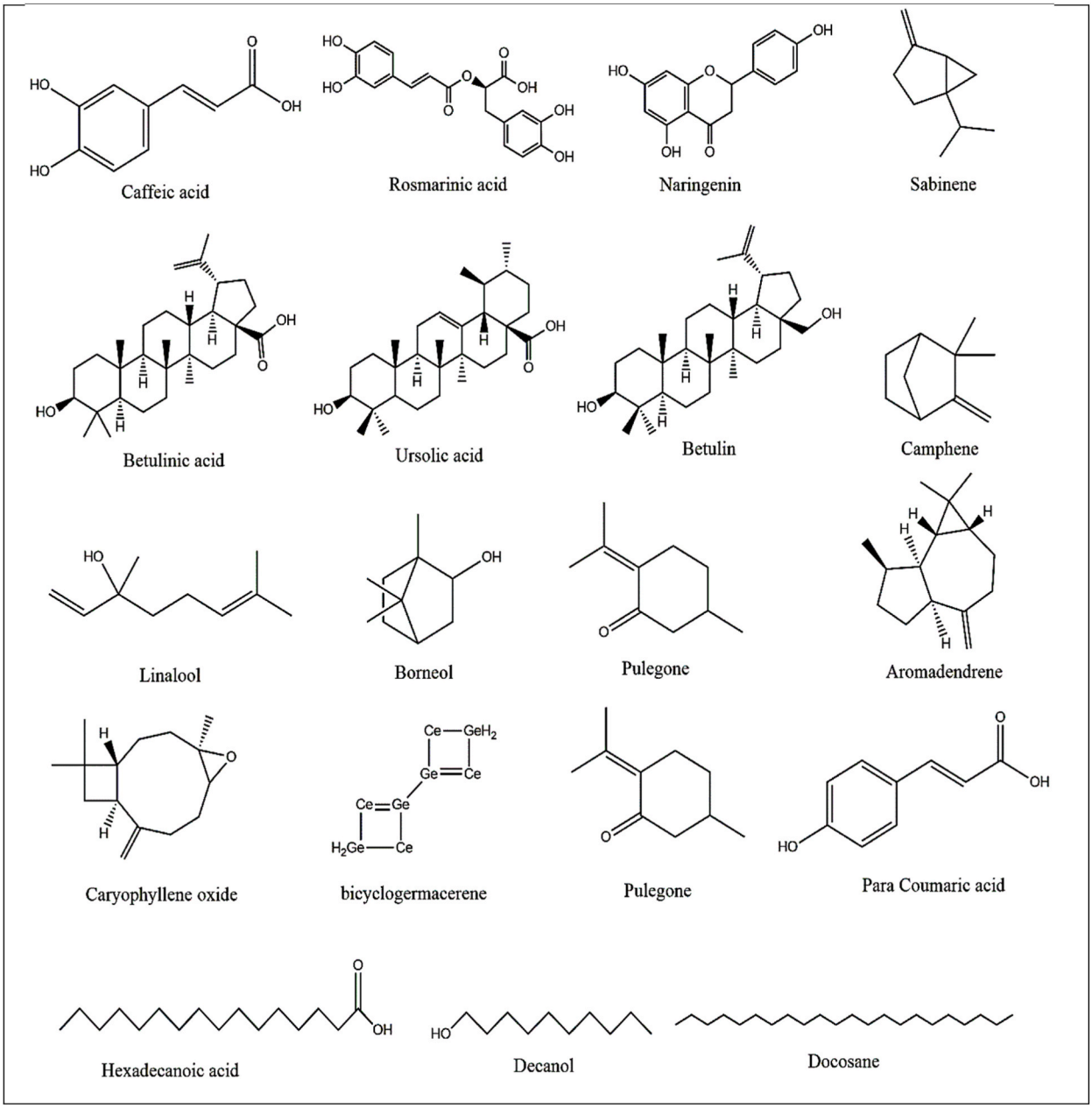

Fig. 5. Structures of some phytoconstituents present in *C. vulgare*.

7. Pharmacology

C. vulgare has been studied for its medicinal properties. Different types of biological actions, such as antioxidant, antiviral, antibacterial, anti-inflammatory, anticancer, antihypertensive, and enzyme inhibitory activities, have been confirmed. A short overview of the pharmacological activities of *C. vulgare* is presented in Table 5 and Fig. 6.

7.1. Antimicrobial activity

Several studies have examined the potential antibacterial activity of *C. vulgare* [23]. These results indicated that the extracts from this plant exhibited potent antibacterial effects against different pathogenic bacterial species. The antibacterial activities of organic solvent extracts were found to be selective, with the efficacy varying based on both the concentration of extract used and the bacterial species and type. The acetone and ethyl acetate extracts showed better antibacterial activity than the ethanol extract. The minimum inhibitory concentration (MIC) values of *C. vulgare* extracts were found to be between 0.625 and 20 mg/ml (acetone), 0.625 and 10 mg/ml (ethyl acetate), and 1.25 to greater than 20 mg/ml (ethanol). However, a combined effect was noted for *Bacillus subtilis* and *Klebsiella pneumoniae* [23]. The presence of extracts at concentrations lower than the inhibitory level (1/4 and 1/8 MIC) showed a significant increase of up to 16 times in the efficacy of gentamicin and cephalexin [73].

Similarly, another study examined the effects of 5 % (v/v) ethanolic and propylene glycol extracts of *C. vulgare* on Gram-positive and Gram-negative bacteria. This study revealed a significant impact on the concentrations of both Gram-positive and Gram-negative bacteria [76]. The extracts also showed similar efficacy against microorganisms with multi-drug resistance obtained from uroculture samples under laboratory conditions [23]. Another study reported the antibacterial activity of *C. vulgare* and showed good results [77]. The antifungal properties of this particular species have not been documented; however, there have been claims regarding the antifungal capabilities of other species within the same genus.

Table 5
Pharmacological activities of *C. vulgare* as reported in several studies.

Extract type	Extraction method	Type of activity	*In vitro*/*In vivo* assay	Result	Reference
Aqueous	Maceration, Chromatography	Anticancer	A2058, HEp-2 and L5178Y cells	The highest activity was observed in HEp-2 cells	[4]
Acidified, alkalized, and lipophilic	Supercritical	Anticancer	CaOV, HeLa, HT-29, and FL cells	Acidified and lipophilic extracts showed better activity in CaOV and HeLa cells than other cell types	[55]
Ethanol, ethyl acetate and acetone	Maceration	Antibacterial	*S. aureus, E. coli, P. aeruginosa* Clinical isolates: *S. aureus, B. subtilis, E. faecalis, K. pneumoniae, E. coli, P. aeruginosa, P. mirabilis*	Most sensitive bacteria were Gram- positive (*S. aureus* ATCC 25923 and *B. subtilis*). Synergism were detected in *B. subtilis* and *K. pneumoniae*	[73]
Acetone, methanol, and water	Soxhlet	Enzyme inhibitory	α-glucosidase, butyrylcholinesterasE, α-amylase, and tyrosinase tests	Different *C. vulgare* extracts were found to possess very strong enzyme inhibitory activity. However, the levels were different	[45]
Methanolic	Ultrasonic assisted	Anti-inflammatory	Neutrophils (cells), ICR mice (female, 6 week-old, 25–26 g), i.p.	CVE could affect neutrophil functions but may vary by inflammation, cell state, and chlorogenic/caffeic acid content	[68]
Ethanol and propylene glycol	Maceration	Antibacterial	*S. aureus* 209 P, *K. pneumoniae* 52145, *E. cloacae, P. mirabilis, K. Oxytoca, E. coli*	Very good activity against Gram-positive and Gram-negative bacteria and similar action against multi-drug resistant bacteria	[23]
Aqueous, butanolic	–	DNA protective	*DNA topology*	The extract was found to be protective against DNA damage	[74]
Aqueous	Simple aqueous extraction	Anti-inflammatory	RAW 264.7 murine macrophages	*C. vulgare* was found to be effective in the suppression of lipopolysaccharide-induced inflammatory responses	[75]
Aqueous, butanolic	–	Antioxidant	DPPH	Due to the antioxidant activity, the extract caused no DNA damage	[74]
Aerial	Ultrasonic-assisted	Antioxidant	Clinopodic acid K, followed by salvianolic acid A and salvianolic acid L	CV3 fraction was found to be a strong antioxidant, and moderately α-glucosidase and α-amylase enzyme inhibitory were	[65]
Aqueous	Simple aqueous extraction	Antioxidant	DPPH	The extract showed strong antioxidant activity	[75]
–	*C. vulgare* tea and decoction	Antiviral	–	The warts were healed, and no inflammation or recurrence was observed	[56]
Acetone, methanol, and water	Soxhlet	Antioxidant	DPPH, ABTS, CUPRAC, FRAP, phosphomolybdenum assay, chelating effect	Different *C. vulgare* extracts were found to possess strong antioxidant activity, but the variations in different tests were observed	[45]

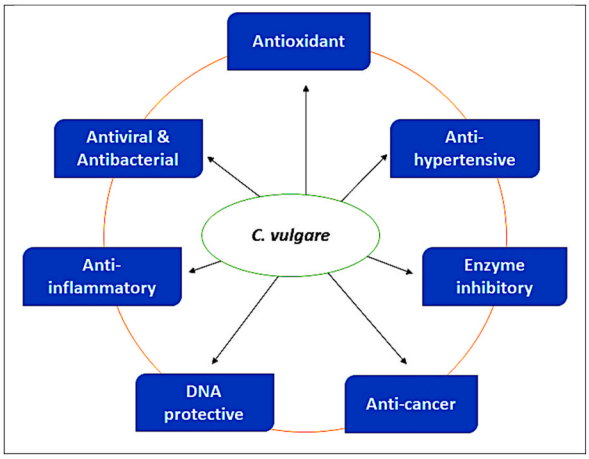

Fig. 6. Various biological and pharmacological properties of *C. vulgare*.

7.2. Antiviral activity

Common warts include skin infections caused by human papillomavirus. A study was conducted to evaluate its antiviral activity. The research was performed on two groups. One group was prescribed a dose of a cup of *C. vulgare* tea thrice a day, and another group was defined with topical application of thick decoction of *C. vulgare* thrice a day for two weeks in addition to drinking the tea three times a day. In the first group, the hand warts disappeared within three months. However, in group two, it disappeared within one month. In addition, no side effects, inflammation, or recurrence was observed. This study confirmed its antiviral properties, especially in common warts [56].

7.3. Antioxidant activity

Studies on antioxidant activity showed that all essential oils of *C. vulgare* were superior in reducing oxidants compared to the individual compounds. Antioxidant activity was assessed using the DPPH assay and β-carotene/linoleic acid system. *C. vulgare* EOs as a whole showed IC_{50} (μg/ml) to be 63.0 ± 2.71, and thymol and γ-terpinene were 162 ± 1.3, 122 ± 2.5, respectively, in the DPPH assay. In addition, *p*-cymene did not exhibit any antioxidant activity in the DPPH assay. In the *β*-carotene/linoleic acid system, *C. vulgare* whole EO showed 52.3 ± 1.19 % inhibition of linoleic acid. Simultaneously, thymol and γ-terpinene exhibited 56.7 ± 1.49 % and 79.2 ± 1.23 %, respectively. *p*-cymene was found to be ineffective in linoleic acid oxidation [62]. Antioxidant activity was also assessed by the phosphomolybdenum assay and chelating effect with DPPH, FRAP, and ABTS assays in one study. In the phosphomolybdenum assay, methanol exhibited the highest activity, followed by water and acetone. In the chelating effect test, the acetone extract exhibited the highest activity. The DPPH assay showed the highest activity in water, followed by methanol, and the lowest activity in the acetone extract. However, ABTS, CUPRAC, and FRAP studies showed maximum activity in the methanolic extract, followed by water, and least activity in acetone [45]. Other studies involving antioxidant studies on *C. vulgare* extract were also performed; the plant showed good results [75]. Another study based on DPPH, ABTS, and FRAP assays was also performed to determine the antioxidant activity of *C. vulgare* extracts and their different fractions. CV3 fraction showed the highest antioxidant activity with IC_{50} 0.02 mg/ml (DPPH), 0.0002 mg/ml (ABTS), and 0.89 mM TE/mg dw (FRAP) [65]. Other studies have also used the DPPH assay [74].

7.4. Anticancer activity

Few studies have investigated the anticancer properties of *C. vulgare* [4,68]. Studies have shown that different extracts of *C. vulgare* possess effective anticancer activities against various cancer cell types. *In vitro* studies of different aqueous extracts of *C. vulgare* on different cancer cell lines exhibited very good antitumor activity, such as human metastatic melanoma (A2058), human larynx epidermoid carcinoma (HEp-2), wild-type mouse lymphoma cells (L5178Y), human normal amniotic cells (FL), and mouse embryonic fibroblast (3T3) cells [4]. A significant reduction in the number of surviving cancer cells was observed, including permanent physical alterations such as cytoplasmic vacuolization, nuclear disintegration, and cellular lysis [4]. These transformations led to cell death, which commenced within a few hours of treatment initiation. The IC_{50} values obtained for growth inhibition of A2058, HEp-2, and L5178Y cells by the aqueous extract were determined to be 20, 10, and 17.8 mg/ml, respectively. However, its chloroform extract was also slightly cytotoxic and contained ursolic acid and gentriacontan [4]. Another study revealed that two acidified and lipophilic extracts showed distinct dose-dependent cytotoxic effects on HeLa and CaOV cells. CaOV cells were significantly more susceptible to the toxic effects of the extracts than HeLa cells, with IC_{50} values of 260.86 μg/ml for (acidified extract) and 225 μg/ml for (lipophilic extract). However, the alkalized extract decreased the survival rate of HeLa and CaOV cells by approximately 20 % and 28 %, respectively. At the highest concentration (400 μg/ml), all the studied extracts caused only a minimal reduction in the viability

(ranging from 6 to 18 %) of HT-29 and FL cells [55].

7.5. Anti-inflammatory activity

Developing novel and selective anti-inflammatory drugs has focused on COX-2, a promising molecular target. Recent research on the anti-inflammatory activity of *C. vulgare* has shown promising results, particularly in the context of targeting COX-2, a key enzyme in the inflammatory process [78]. Noteworthy findings include.

a) **Inhibition of COX-2 Expression:** Studies have demonstrated that caffeic acid, chlorogenic acid, and *C. vulgare* extracts can inhibit COX-2 expression induced by zymosan in neutrophils. This indicates the potential of *C. vulgare* to modulate neutrophil function, which is crucial for the inflammatory response of the body [79].
b) **Modulation of Neutrophil Function:** The influence of *C. vulgare* on neutrophil activity depends on various factors, such as the state of the cells, the inflammatory environment, and the concentration of active compounds such as chlorogenic and caffeic acid in the extract [79].
c) **Response to Lipopolysaccharide-induced Inflammation:** The aqueous extract of *C. vulgare* was shown to be effective in responding to lipopolysaccharide-induced inflammatory reactions. This includes inhibition of Iκ-B phosphorylation, thus impeding the activation of NF-κB, a protein complex that plays a crucial role in inflammatory responses [80,81].
d) **Reduction in Inflammatory Markers:** The extract was found to reduce the production of nitric oxide (NO) by downregulating iNOS expression and inhibiting MMP-9 activation. It also minimally affects COX-2 protein concentration and decreases the release of PGE2, both of which are significant markers of inflammation [82].
e) **Impact on Cytokines and Oxidative Stress:** A significant reduction in the levels of IL-10 and IL-1, which are key inflammatory cytokines, was observed. The extract also inhibits xanthine oxidase, contributing to the reduction of reactive oxygen species (ROS), thereby addressing oxidative stress, which is often associated with inflammation [80,83].

In summary, the anti-inflammatory potential of *C. vulgare*, particularly through the modulation of COX-2 expression and other inflammatory pathways, makes it a potential candidate for the development of novel anti-inflammatory drugs.

7.6. Antihypertensive activity

This plant has also been found to be antihypertensive [84,85]. One study reported an antihypertensive effect in Sprague-Dawley rats [84,85]. *In vitro* and *in vivo* pharmacological methodologies were used to test the crude extract and *C. vulgaris* fraction in rats. *C. vulgaris* fractions and the crude extract showed a fall in mean arterial pressure in high salt-induced hypertensive and normotensive rats for different doses, in which chloroform was the most effective and aqueous was the least effective. The antihypertensive effect of *C. vulgaris* could be due to vasodilation mediated through a combination of muscarinic receptor-linked NO, activation of prostacyclin, TEA-sensitive K^+ channels, and Ca^{+2} antagonism. These results indicated the presence of quercetin and rutin in the extract [85].

7.7. DNA protective activity

C. vulgare has been investigated for its property to protect DNA. The aerial parts, including flowers, stems, and leaves, were used for aqueous and butanol extraction. A DNA topology assay was performed, and no DNA damage was observed in any of the extracts. In addition, a DNA-protective effect was detected. It was found that even at the lowest concentration, leaf and total aqueous extracts were the most protective against plasmid DNA (10 μg/ml). However, other extracts were protective at higher concentrations (500–1000 μg/ml) [74]. Another study investigated the effect of *C. vulgare* on the repair capacity of *Saccharomyces cerevisiae* and showed that its combination with zeocin protects DNA from double-strand breaks [86].

7.8. Enzyme inhibitory activity

C. vulgare had enzyme inhibitory activity. One study evaluated the acetone and water-methanol extracts against α-glucosidase, butyrylcholinesterase, α-amylase, and tyrosinase. The methanolic and water extracts were found to be unreactive against butyrylcholinesterase and tyrosinase. The acetone extract was highly inhibitory against butyrylcholinesterase, acetylcholine, esterase, and tyrosinase activity. The methanolic extract showed the highest α-amylase inhibitory activity. At the same time, the aqueous extract exhibited the highest α-glucosidase inhibitory activity. Another research group has studied its inhibitory activity against α-glucosidase, acetylcholinesterase, and α-amylase enzymes. The results showed moderate inhibition of α-glucosidase and α-amylase by the CV3 fraction of *C. vulgare* [65].

8. Quality based control and standardization

Plant quality control encompasses a broad range of procedures and strategies designed to ensure the safety, consistency, and efficacy of plant-derived products. It involves a systematic assessment of critical factors, including the identification, potency, purity, and composition of plant materials through various evaluations and tests. Key measures in quality control include botanical authentication, phytochemical analysis, determination of bioactive constituents, detection of impurities, assessment of physical

characteristics, and adherence to stringent good manufacturing practice (GMP) guidelines. These practices are implemented to uphold product quality, enhance safety, comply with regulatory standards, and provide consumers with reliable, standardized plant-based products. However, based on the literature search conducted, the analysis of quality control for *C. vulgare* is limited to aspects such as phytochemical analysis, heavy metals, elemental composition, phytochelatins, extraction, processing, formulation, and biological activity, as mentioned in the manuscript. Further information is required to fully understand the quality control and standardization of *C. vulgare* [87].

9. Toxicity study

Evaluating the toxicity of a substance is crucial for determining the appropriate dosage for medicinal purposes, identifying potential adverse effects, and providing essential information to regulatory bodies. Despite the numerous pharmacological effects of *C. vulgare*, its potential toxicity has not been thoroughly investigated. Several studies have assessed the acute and subacute toxicity of *C. vulgare* water extract through *in vivo* experiments in mice and rats. These studies used intraperitoneal and oral administration methods. The LD_{50} (i.p.) dose of *C. vulgare* was found to be 675 mg/kg in mice and 500 mg/kg in rats, resulting in central nervous system toxicity when administered intraperitoneally. In contrast, the oral LD_{50} of both rats and mice was greater than 2000 mg/kg. In subacute oral administration, no detrimental effects were observed on urine chemistry, blood parameters, hematology, or histomorphology of the liver, pancreas, kidney, and spleen [21].

10. Conclusion and future perspectives

This review article provides a brief overview of the Lamiaceae family, with a focus on the selected species. It offers a thorough examination of *C. vulgare*, a notable member of the Lamiaceae family. This study delves into the historical use of *C. vulgare*, detailing its extraction techniques, phytochemical composition, pharmacological benefits, and potential toxicity. Highlighting existing research gaps, this study underscores the importance of standardized methodologies and in-depth toxicity analysis to better integrate *C. vulgare* in traditional medicinal applications. The long-standing medicinal use of this plant lays the groundwork for further scientific investigation. Despite its array of health benefits, *C. vulgare* has not been studied extensively. Given its purported health advantages, *C. vulgare* has emerged as a promising and safe herbal remedy for various health conditions. This review is the first to extensively cover these facets of *C. vulgare*. It aims to provide readers with a holistic understanding of the diverse attributes of the plant and its potential utility in the medical field.

Several recommendations have been proposed to pave the way for future research.

a) **Collaboration:** Researchers, herbalists, and healthcare practitioners should collaborate to establish standardized protocols for the extraction and preparation of *C. vulgare*-derived remedies.
b) **Comprehensive Toxicity Assessments:** Future studies should prioritize thorough toxicity assessments to determine the safety profile of *C. vulgare*, ensuring its suitability for therapeutic use.
c) **Modern Analytical Techniques:** Integration of advanced analytical techniques, such as chromatography and spectroscopy, can enhance the identification and quantification of key phytoconstituents in *C. vulgare*.
d) **Synergies with Emerging Technologies:** Researchers are encouraged to explore potential synergies between *C. vulgare* and emerging technologies, particularly artificial intelligence, to optimize extraction processes and predict pharmacological effects.
e) **Telecommunications:** Leveraging telecommunications can help disseminate information about herbal medicines and facilitate knowledge exchange among traditional practitioners, researchers, and wider communities.

This comprehensive overview and the proposed recommendations aim to promote further research and utilization of *C. vulgare* in the field of herbal medicine and healthcare [88].

Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Data availability statement

No supplementary data or supporting data were utilized or presented in this manuscript.

CRediT authorship contribution statement

Kamal Ahmad Qureshi: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Adil Parvez:** Writing – review & editing, Data curation. **Mohd Masih Uzzaman Khan:** Writing – review & editing, Data curation,

Conceptualization. **Ashok Aspatwar:** Writing – review & editing, Data curation. **Akhtar Atiya:** Writing – review & editing, Funding acquisition, Data curation. **Gamal Osman Elhassan:** Writing – review & editing, Data curation. **Riyaz Ahmed Khan:** Writing – review & editing. **Shakkeela Yusuf Erattil Ahammed:** Writing – review & editing, Data curation. **Wasi Uzzaman Khan:** Writing – review & editing, Data curation. **Mariusz Jaremko:** Writing – review & editing, Funding acquisition, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Mariusz Jaremko reports article publishing charges and writing assistance were provided by King Abdullah University of Science and Technology (KAUST), Thuwal, Saudi Arabia. Akhtar Atiya reports financial support and writing assistance were provided by Deanship of Scientific Research at King Khalid University, Abha, Saudi Arabia, through the Large Group Research Project under grant number RGP.2/14/1444. Other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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