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Hypericum perforatum L. (Hypericaceae): Cultivation, diversity of biochemical composition, antimicrobial activities, active biomolecules and action mode-A review

Hajar Afqir[1,2,*], Saadia Belmalha[2], Jihane Laarifi[1], Ayoub Farihi[3,4], Soumaya Bataoui[1], Brahim Bourkhiss[5], Hassane Tahiri[6], Mohammed Ouhssine[1]

[1]*Laboratory of Natural Resources and Sustainable Development, Faculty of Science, Ibn Tofail University - Kenitra, Kingdom of Morocco.*
[2]*Department of Plant and Environment Protection, National School of Agriculture, BP S/40 50 000 Meknes, Morocco.*
[3]*Laboratory of Biology and Health, Biology Department, Ibn Tofail University, Faculty of Sciences, Morocco.*
[4]*Oriental Center for Water and Environmental Sciences and Technologies (COSTE), Mohammed Premier University, Oujda 60000, Morocco.*
[5]*Laboratory of Animal Plant Production and Agro-Industry, Department of Biology, Faculty of Sciences, Ibn Tofail University, B.P. 133, Kenitra 14000, Morocco.*
[6]*Faculty of Science, Department of Biology, Ibn Tofail University, Kenitra, Morocco.*

[*]**Corresponding author:** hajar.afq@gmail.com

Original Research

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Abstract:

This study analyses the knowledge on the cultivation, diversity, and variation of phytochemical constituents of essential oils and crude extracts from *Hypericum perforatum*. Equally, we presented a detailed discussion of the antimicrobial activities against pathogens and viruses, and the implicated biomolecules. A complete and organized literature search was carried out in the basic databases. According to the reviewed papers, *Hypericum perforatum* contains considerable amounts of chemical constituents, including phenolic, flavonoid, and terpene compounds, which are diverse and variable depending on the geography of plants, parts used, and extraction methods. These chemical constituents demonstrated serious inhibitory effects against fungi, bacteria, and viruses.

Keywords: Antimicrobial activities; Bioactive compounds; Essential oils; *Hypericum perforatum* L.; Hypericaceae; Mechanism; Phytochemical constituents

1. Introduction

The importance of herbal and therapeutic plants in human life and their distinct place in their lifestyles is obvious (Mohammadhosseini et al., 2021a; Sharif et al., 2024). A great deal of important natural chemicals has been isolated from various plant species as a result of the numerous scientific studies conducted on a broad range of herbal plants over the past few decades (Mohammadhosseini et al., 2021b). Medicinal plants are utilized in a variety of scientific fields, including the food industry, the fragrance and cosmetics industry, and many pharmaceutical and medical techniques (Mohammadhosseini et al., 2021b).

With its 484 species of trees, shrubs, and herbs, the among the family Hypericaceae is the significant genus *Hypericum* L. (Crockett et al., 2011; Venditti et al., 2018). The *Hypericum* grows in temperate areas and comprises many plant species with traditional values and is used as a medicinal

plant to treat eczema, burns, and wounds (Yazaki et al., 1994; Caprioli et al., 2016). Equally, numerous illnesses such as trauma, neuralgia, rheumatism, ulcers, gastroenteritis, hysteria, depression, and bedwetting are treated using *Hypericum* plants (Miller, 1998). Additionally, a number of Hypericum species have been employed for their sedative, antiseptic, and anti-inflammatory properties are these plant species and their derivatives (Baytop, 1984; Mukherjee et al., 2000; Ozturk et al., 2002). Hypericin, flavonoids, quercitrin, isoquercitrin, phenolic acids, chlorogenic acid, rutin, tannins, and hyperoside are the primary constituents of Hypericum plants (Barnes et al., 2001; Dall'Agnol et al., 2003). The anticancer (Agostinis et al., 2002), antioxidant (Cakir et al., 2003; Mandrone et al., 2015), antimicrobial (Jayasuriya et al., 1989; Dall'Agnol et al., 2003; Crockett, 2010), antifungal activities (Cakir et al., 2005; Fenner et al., 2005), cytotoxic (Jayasuriya et al., 1989), antidepressant (Butterweck et al., 2000), and antiviral effects (Meruelo et al., 1988; Esposito et al., 2013) are the most cited bioactivity properties of these plants. Furthermore, both GC/MS and GC, and have been extensively used to analyze the essential oils isolated from *Hypericum* plants growing in various parts of the world. For example, in Turkey, *H. scabrum* L. and *H. perforatum* L. were tested (Çakir et al., 1997; Erken et al., 2001), *H. scabrum* and *H. perforatum* in Uzbekistan (Baser et al., 2002), and *H. perforatum* and *H. olympicum* L. in Serbia (Gudžić et al., 2001).

Generally, the EO extracted from *Hypericum* species contains: (i) Hydrocarbons such as alkanols (C_{24}, C_{26}, and C_{28}), alkanes (C_{16}, and C_{29}), and *n*-decane (ii) Sesquiterpenes caryophyllene oxide and β-caryophyllene; (iii) Limonene, myrcene, and α-and β-pinene (Nahrstedt et al., 1997; Crockett, 2010). In another research, Ghasemi Pirbalouti et al. (2014) reported the β-caryophyllene and α-pinene as the principal constituents of essential oils extracted from flowers of *H. perforatum*, *H. hyssopifolium* Chaix, *H. scabrum*, and *H. helianthemoides* collected from Khorasan, located in the North-East of Iran. Further, Javidnia et al. (2008) recorded α-pinene as the major chemical in samples of *H. scabrum* collected from Fars, located in South Iran, while the β-caryophyllene with 23.3% and spathulenol with 17.4% were the main constituents recorded in *H. helianthemoides* (Spach) Boiss sampled from Fars in South Iran.

The biomolecules detected in *H. perforatum* were tested against a wide range of microorganisms, insects, and their larvae. Essential oils and crude extracts of *H. perforatum* were tested against bacteria, fungi, and viruses. For example, essential oils of *H. perforatum* were tested against bacteria, including *Bacillus cereus*, *Proteus vulgaris*, *Listeria monocytogenes*, and *Salmonella typhimurium*. Similarly, crude extracts from leaves were tested against fungi, including *Candida glabrata* (ATCC 28838), *Candida albicans* (ATCC 10231), and *Candida tropicalis* (ATCC 13801). The anti-bacterial effects showed huge variation depending on the used extracts, treated microorganism, used concentrations, treatment duration, and environment of the experiment (Couladis et al., 2003).

In this paper, we provide a review of the current understanding of *H. perforatum*'s chemistry and itemize its scientifically proven antimicrobial effects. Equally, we discussed the implicated chemical constituents in antimicrobial activities and the most investigated mode of action. Systematic reviews are crucial for efficiently integrating existing bibliographies and making data accessible for informed decision-making. The material included in this research will be extremely valuable in expanding the global databases on *H. perforatum*, a popular natural remedy for a variety of microbes.

2. Methodology

2.1 Searching methodology and collection standards

The present review was prepared through the utilization of search engines, including MDPI, PubMed, Google Scholar, and Web of Science, to access and compile material (Muthu et al., 2025). During our investigation, we used two kinds of keywords. First, we used keywords related to the plant: *H. perforatum*, cultivation of *H. perforatum*, phytochemical profile of *H. perforatum*, essential oils of *H. perforatum*, bioactivity of essential oils extracted from *H. perforatum*, inhibitory capacity of *H. perforatum* essential oils, and biologically active constituents of *H. perforatum*. Second, we used keywords related to the chemical constituents recorded in the essential oils of the plant: Antimicrobial activity of thymol, inhibitory effects of pinene, limonene, and carvacrol. The papers were recorded from 1975 to 2023. We examined 450 publications in all, 100 of which were not subjected to peer review. To avoid any low-quality content, we eliminated the non-peer-reviewed research because this is the first review publication regarding the studied plant. To compile the current study, only 115 papers were chosen based on their scientific quality and applicability. Clear data on specific subjects is included in these articles. In addition, we created a geographic distribution map using the chosen articles as a basis.

The International Plant Names Index (IPNI) and the Plant List (www.plantlist.org) were used to verify the accuracy of the scientific name of the plant (Rivera et al., 2014; Dauncey et al., 2016) (see Fig. 1). According to Quattrocchi (2012), the names that are often used in English are listed. These were limited to plants that had traditionally been used to treat diabetes mellitus. The name of the plant and many word combinations were included in the search on the previously stated databases.

3. Cultivation of *H. perforatum*

H. perforatum L. (Fig. 2) is a medicinal herb used in traditional medicine for a long time in Eastern and Central Europe (Kwiecień et al., 2021). It has held a significant place in official medicine in EU nations for many years as a medicinal herb for both homeopathic and allopathic usage (Disler et al., 2014). *H. perforatum* is widely distributed in the wild throughout Europe, but because there is such a high demand for the raw material, its natural resources are swiftly depleted (Fig. 3). Because of this, it is successfully and widely grown commercially throughout the world, not just in European nations. Naturally, cultivation ensures that the raw material is under control and of good

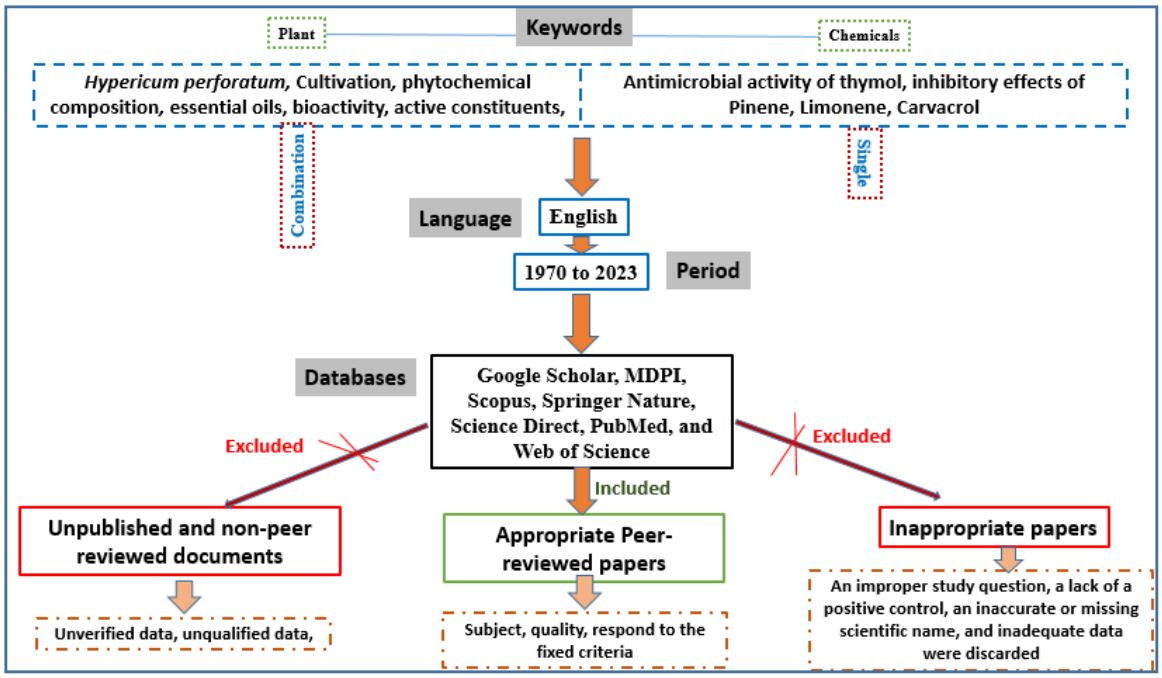

Figure 1. Research method followed to complete this review.

quality (Kwiecień et al., 2021). Typically, field cultivation is the most practical method for producing enough plant biomass when *Hypericum* is used for industrial applications. *H. perforatum* is highly relevant commercially, although the availability of raw materials is now quite limited. The main manufacturing centers in Europe are in Germany, Romania, and Italy (Crockett, 2010), although a sizable portion of the *Hypericum* supply is still sourced from wild populations.

It seems that farmers would benefit much from growing *Hypericum* for industrial use, *i.e.*, to produce consistent, high quantities of the necessary active metabolites. While several factors are recognized to have a major impact on the amount and production of active compounds in *Hypericum*, further investigation is still required to fully describe the specifics of field management strategies (Bruni et al., 2009). The available literature shows that not much research has been done to evaluate *H. perforatum*'s phytochemical and bio-agronomical responses to open field conditions. As a matter of fact, most of the articles that are now in print are based on wild plant samples or, in the case of cultivated plants, on individuals that were grown in small areas, mostly in vases and pots. Reproducibility is one of the numerous benefits of these kinds of studies, but there may also be some discrepancies between conditions in open fields and those in pots (Poorter et al., 2012), particularly for testing yield response, physiology, or chemistry using single-grown plants. This problem might have extremely serious repercussions, especially in Mediterranean regions where high levels of environmental and climatic variation are predicted to have a significant additional impact on the metabolisms of farmed plants.

Currently, Lazzara et al. (2021) cultivated three *Hypericum* genotypes, acquired from diverse areas of Italy: PFR-SI, from Siena, Tuscany; PFR-TN, from Trento province, Trentino; PFR-AG, from Sicily (Agrigento province). Mature seeds of the studied plant (*H. perforatum*) were ob-

Figure 2. General view of *H. perforatum* in the field.

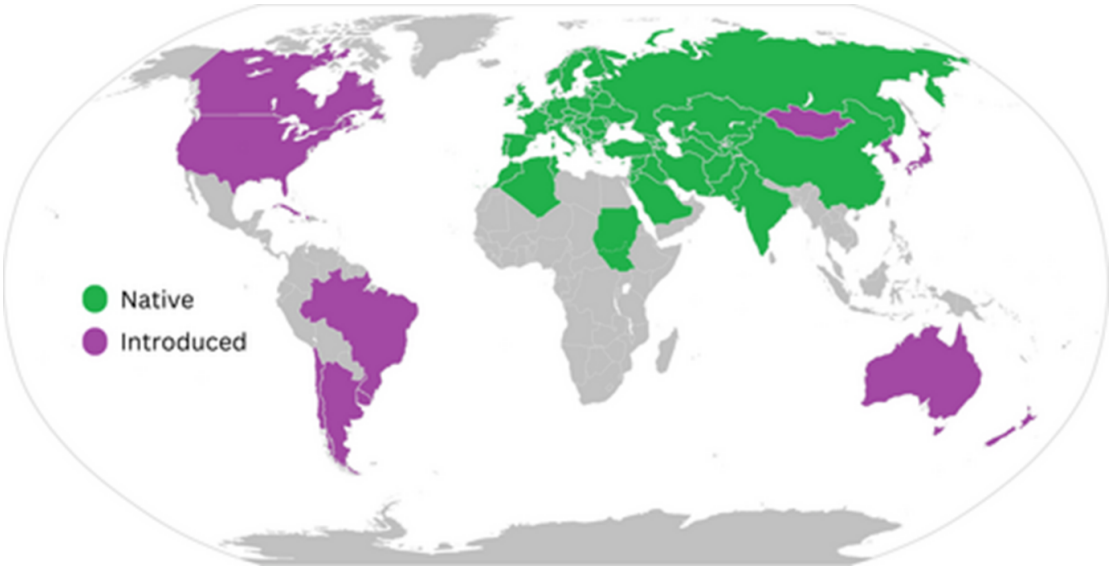

Figure 3. Distrubition of *H. perforatum* L. wordwide.

tained in 2012 during the spring and summer. Before planting, *H. perforatum* seeds were exposed to a vernalization phase of 1 week at T = 4 °C, because *Hypericum* seeds are typically thought to be "recalcitrant" to germinate (Cirak, 2007). Afterward, plantlets (germinated seeds) were transplanted to bigger (approximately 5 cm diameter) pots of plastic, packed with a mixed substrate of sand-perlite (1:1) to ensure the development of roots during the 2nd week of August. After, seeds were implanted in 104-hole extended polystyrene trays (Fascella et al., 2017). Three months later (after sowing), prepared samples were moved into larger pots (diameter of 18 cm), packed with a growth substrate built from a mixture of 60% peat, 30% sand, and 10% vermiculite. Further, in one-half of the samples, the remaining samples were relocated to an open field on the trial farm. In total, there were 70 samples of each selected biotype of transplanted plant. The soil was constituted from vertic-xerofluvent (NRCS, 2003) and characterized by a separate clayey texture with the addition of slight organic material and nitrogen.

All the prepared plants were cut down to the ground during the flowering stage between 2013 and 2016 (from mid-May to the beginning of June in the field and mid-June in containers) to promote rapid regrowth next year. Information on the number of stems, weight, and height for each sample for five plants was recorded for each treatment. Subsequently, all stems of the prepared plants were categorized into flowering and vegetative shoots, with stems classified as flowering if they had at least one fully developed flower (without petals). Additionally, flowers were hand-picked and weighed.

In the first year of culture, there was no difference in plant height between the two treatments, but there were significant variations between the biotypes, with the AG biotype having the highest mean height (67.8 cm) and the other two having incredibly low heights (around 30 cm). In the second year, higher values were seen, but the fundamental trend remained. In general, plants grown in pots outperformed those in open fields, with the biotype from AG reaching the greatest height value of the entire experiment (85.0 cm). Plant height seemed to stabilize at roughly constant levels in the final two trial years, whereas plants grown in pots displayed a general drop in mean height, even if this decline was not statistically significant (Lazzara et al., 2021). The different management techniques significantly affected the total number of stems per plant (vegetative + flowered) in all years and in each specific biotype. This result allows for some general reflection on the plants' response over the course of multiple years and environmental circumstances, together with the observation of the mean YxMxB interactions.

It is important to keep in mind that pots in 2015 allowed for both the maximum (27.5 stems/plant, biotype TN) and minimum (7.2 stems/plant, biotype SI) of the entire experiment, even if the ANOVA did not reveal any significant changes in the interactions. However, from 2014 to 2016, the average number of stems per plant rose in the field, while in containers the number of stems fell. A substantial three-factor interaction was revealed by the ANOVA of the weight of stems per plant, highlighting the notable behavioral variations among the three biotypes due to the experimental conditions under consideration. All experimental factors significantly altered the total aerial plant biomass (flowers plus stems) in each of the four trial years, and in all but one example (2016), the interaction was also significant.

These findings show that the effects of management measures differ within each year and among the biotypes under study. The overall reduced plant size was influenced by reductions in height, biomass weight, and stem count numbers during the first year. However, depending on the biotype and cultural management, the overall trend's strength changed. The second trial year (2014) yielded the highest plant biomass for plants grown in open fields; on the other hand, the third trial year (2015) yielded a higher plant biomass for plants cultivated in pots. However, different genotypes of *H. perforatum* have been associated with different response patterns (Pluhár et al., 2002), and this intrinsic variability might explain the different results obtained when the same genotype is cultivated under different growth con-

trol techniques. Other authors have already observed higher herbage yields of *Hypericum* in the second year after sowing (Kizil et al., 2013). Furthermore, all three biotypes got the maximum value of total aerial biomass in field culture, except for the TN biotype growing in conditions of the pots. It should be mentioned that during the experiment, the TN biotype showed the greatest mean values of plant biomass estimated at 170.7 g/plant in pots in 2014 and the lowest value was estimated at 8.8 g/plant in open field in 2013. This suggests that the TN biotype was most susceptible to different cropping environments.

Except for the SI biotype grown in a potplant, most experimental settings had a drop in biomass during the most recent trial year (2016), with values resembling those from the first year. Expectations were that flower yields would be comparable to the total aerial biomass, with a general decrease in the first year and an increase in the second year. Flower yields decreased throughout the course of the next two years and eventually recovered to levels comparable to those of the first year. However, relevant outliers may be found, as demonstrated by the very significant MxB interactions throughout all trial years. The AG biotype grown in an open field yielded the highest yields (7.8 g fresh flowers/plant) in the second trial year (2014); in most cases, open field conditions allowed for the highest flower yields in 2014, but the same biotypes grown in pots yielded the highest flower yields the following year.

The total phenolic compound content was notably higher in 2015 compared to 2014 due to the aging of the plants, leading to significant alterations in their phytochemical composition. The two non-native biotypes showed better performance in pots, while the local genotype was generally more suitable for field cultivation. Performance varied across different genotypes. Additionally, the phytochemical profile of plants grown in pots differed significantly compared to that of plants grown in open fields. Therefore, precise quality inspections of the harvested material are essential when the cultivation is for industrial purposes.

4. Diversity of biochemical composition

The chemical composition of *H. perforatum* L. is widely investigated in fruits, leaves, and other parts of the plant (Table 1) (Newall et al., 1996; Nahrstedt et al., 1997). However, the richness of chemical components varies depending on the type of extract, geographical location, climate conditions, and the examined part of the plant (Schepetkin et al., 2020). In samples from Asia (Iran and Syria), decane (27.7 – 59.60%), 2,6-dimethyl-heptane (6.2 – 36.1%), dodecane (12.9%), β-selinenol (18.1%), α-pinene (12.5%), and menthol (8.9%) were the predominant constituents. In

Table 1. Variation of chemical constituents in essential oils of *H. perforatum* L. depending on geographical location, used parts of the plant, and extraction methods.

Continent	Origin of samples	Principal chemical compounds of essential oils	References
	Country	Compounds	
Asia	Iran	Decane (59.6%), dodecane (12.9%), ethyl cyclohexane (6.8%), 5-methyl nonane (4.7%), and 3-methyl nonane (4.3%)	(Parchin et al., 2016)
		Eudesma-4 (15%), 7-dien-1β-ol (7.5 to 8.1%), thymol (7.0 to 7.2%), 1,4-*trans*-1 and 7-*trans*-acorenone (5.2 to 5.5%)	(Morshedloo et al., 2017)
		α-Pinene (21.9%), nonane (9.8%), *n*-octane (9.1%), and dodecanol (6.8%)	(Ghasemi Pirbalouti et al., 2014)
		α-Pinene (12.5%), β-pinene (8.3), (*E*)-β-ocimene (4.4%), 2-methyl decane (4.00%), undecane (7.0%), germacrene D (6.9%), and α-selinene (4.2%)	(Ghasemi Pirbalouti et al., 2014)
	Syria	β-Selinenol, followed by elemol, and β-elemene (18.1%,12.8%, and 10.7%, respectively)	(Saleh, 2019)
Europe	Turkey	β-Selinene (19.4%), bicyclogermacrene (15.3%), tetradecene (8.2%), and α-amorphene (8.1%)	(Yüce, 2016)
	Serbia	Germacrene D (18.6%), β-caryophyllene (11.2%), 2-methyl octane (9.5%), α-pinene (6.5%), bicyclogermacrene (5%), and (*E*)-β-ocimene (4.6%)	(Dordević, 2015)
	Greece	β-Selinene (14.7%), α-selinene (14.6%), (*E*)-β-caryophyllene (10.3%), α-pinene (7.5%), and germacrene D (5.5%),	(Zeliou et al., 2020)
	France	Germacrene D (17.8%), β-caryophyllene (14.8%, *ar*-curcumene (13%), and (*E*)-β-farnesene (7.1%)	(Schwob et al., 2002)
	Italy	2-Methyloctane (21.1%), germacrene D (17.6%), and α-pinene (15.8%)	(Pintore et al., 2005)

samples from Europe (Greece and Serbia), germacrene D (5.5 – 18.6%), followed by β-selinene (14.70%), and α-selinene (at 14.6%), β-caryophyllene (at 11.2%), and (*E*)-β-caryophyllene (10.3%) were the supreme leading chemicals in essential oils of *H. perforatum*. In samples from Africa (Tunisia), β-selinene (8.9 – 14.7%), α-pinene (5.4%), and α-selinene (5.00%) were the most recorded elements in essential oils of the plant.

The chemical composition of *H. perforatum* is dominated by several well-characterized bioactive compounds with distinct chemical structures. The naphthodianthrones hypericin and pseudohypericin are polycyclic anthraquinone derivatives with a perylene quinone backbone, responsible for the plant's red pigmentation and photodynamic activity (Nahrstedt et al., 1997). The phloroglucinols, primarily hyperforin and adhyperforin, are prenylated acylphloroglucinols characterized by a highly lipophilic and thermolabile structure, known for their role in inhibiting neurotransmitter reuptake (Chatterjee et al., 1998). The plant also contains numerous flavonoids, such as quercetin, rutin, hyperoside, and isoquercitrin, which share the C6–C3–C6 flavonoid backbone, often glycosylated, conferring antioxidant and anti-inflammatory activities (Barnes et al., 2001). Other secondary metabolites include phenolic acids, such as chlorogenic acid (Fig. 4) and caffeic acid derivatives, as well as xanthones, including kielcorin and tetrahydroxyxanthones, all of which contribute to antimicrobial and antioxidant properties (Avato et al., 2004). These structurally diverse compounds collectively explain the wide spectrum of pharmacological effects attributed to *H. perforatum*.

According to Nahrstedt et al. (1997) and Dordević (2015), additional physiologically active substances, such as flavonoids and tannins, also exist, and the main active chemicals are assumed to be hypericin, naphthodianthrone, hyperforin, and prenylated phloroglucinol. Fresh material of the plant contains the biosynthetic precursors of pseudohypericin, hypericin, proto-pseudohypericin, and proto-hypericin, as well as hypericin, isohypericin, and pseudohypericin. Additionally, analogs of anthraquinones, such as naphthodianthrones, as well as cyclopseudohypericin are recorded. According to (Vanhaelen et al., 1983), hypericin content, which ranges from 0.1 to 0.15%, is considered to comprise both hypericin and pseudohypericin. This is why the term "total hypericins" is occasionally used.

In terms of the relationship between chemicals and the examined parts of the plant, Dordević (2015) investigated the biomolecules of the aerial parts of *H. perforatum* L. by GC and GC/MS. In total, 134 chemical composites were recognized, accounting for 98.7% of the total oil. Germacrene D, at 18.6%, and β-caryophyllene, at 11.2%, made up most of the essential oil's composition. Then 2-methyloctane, at 9.5%, α-pinene, at 6.5%, bicyclogermacrene, at 5.0%, and (*E*)-ocimene, at 4.6%. Sesquiterepenoids, particularly sesquiterepene hydrocarbons at 48.7%, made up a significant portion of the volatile profile of *H. perforatum* at 57.7%. Hydrocarbons made up the majority of monoterpenoids at 22.4% as well as 21.4%. The percentage of nonterpenoid chemicals in the whole essential oil was 18.1%.

Currently, Schepetkin et al. (2020) have investigated the chemical composition of the flower (HEO_{Fl}) and leaf (HEO_{Lv}) of *H. perforatum* based on gas chromatography-mass spectrometry. Monoterpenes made up the majority of HEO_{Fl} (52.8%), with a high concentration of oxygenated monoterpenes, including *cis-p*-menth-3-en-1,2-diol with 9.10%, followed by α-terpineol with 6.10%, terpinen-4-ol with 7.40%, and limonen-4-ol with 3.2%, while sesquiterpenes were only present in small levels. While sesquiterpenes made up the majority of HEO_{Lv} (63.2%), like germacrene D and β-caryophyllene with 25.7% and 9.5%, respectively.

4.1 Flavonoids

The flavonoids of *H. perforatum* are widely examined (Table 2). They varied both qualitatively and quantitatively,

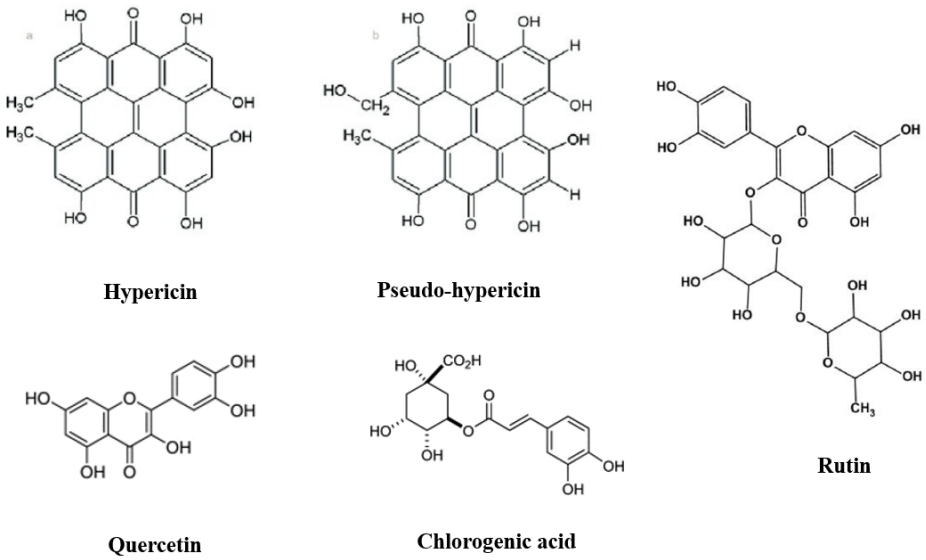

Figure 4. Structure of the main chemical compounds found in *H. perforatum*.

depending on the origin of the plants, the parts used, and the extraction conditions. For example, Ollivier et al. (1985) and Hoelzl et al. (1987) revealed flavonol constituents such as quercetin and kaempferol in *H. perforatum*. In parallel, avones such as luteolin, biavonoids such as biapigenin and amentoavone, which are an avone derived from biapigenin, were also mentioned. Other constituents like glycosides (*i.e.*, hyperoside, quercitrin, isoquercitrin, and rutin), and catechins were recorded. In terms of quantities, Dorossiev (1985) evaluated three types of flavonoids, namely isoquercitrin, hyperoside, and rutin, and their concentrations were 0.3%, 0.9%, and 1.6%, respectively. Currently, Kwiecień et al. (2018) analysed quantitatively 21 flavonoids in methanolic extracts from three cultivars of *H. perforatum* by high-performance liquid chromatography. The obtained results showed that three types of glycosides, including rutoside, quercitrin, and hyperoside, as well as three types of aglycones, such as kaempferol, quercetin, and luteolin, were identified in all tested extracts. The whole quantities of the estimated constituents augmented between 1.18 and 21.66-fold on variants of LS media and between 1.52 and 17.34-fold on variants of MS media. Further, quercetin was the main metabolite with a maximum quantity of 210.55 mg per 100 g^{-1} dry weight [DW]. Further, Germ et al. (2010) investigated the tannin contents in leaves and flowers of *H. perforatum* plants developed under three treatments of radiation (UV-B) with spectrophotometry using $AlCl_3$ reagent. The concentration of flavonoids in leaves varies between 6.31 and 9.0/100 g of dry matter (DM). The concentration of flavonoids in the leaves increased with increasing UV-B radiation dosage. Because UV-B radiation causes the production of important enzymes for the phenylpropanoid pathway, plants often increase the de novo synthesis of flavonoids when UV-B radiation is increased (Searles et al., 2001; Rozema et al., 2002). The concentration of flavonoids in *H. perforatum* flowers fluctuated depending on treatment; however, it did not shadow the variation of UV-B dose. Compared to leaves, flowers had a lower quantity of flavonoids. Bayram et al. (2022) evaluated the total flavonoid compounds in deep eutectic solvents extracts of *H. perforatum* using LC-MS/MS. Further, the total phenolic compounds were estimated between 0.02 ± 0.00 and 12.29 ± 0.30 mg QE/g.

4.2 Phenols and volatile oils

The polyphenols of *H. perforatum* are varied qualitatively and quantitatively depending on the origin of plants, parts used, and extraction conditions (Table 2). The essential oils of *H. perforatum* were found to have 94 different components. 3-methoxy-2,3-dimethylcyclobutene (9.8%), *cis*-*p*-menth-3-en-1,2-diol (9.1%), terpinen-4-ol (7.4%), α-terpineol (6.1%), *trans*-ascaridol glycol (4.6%), 4-hydroxy-4-methyl-cyclohex-2-enone (3.4%), limonen-4-ol (3.2%), *p*-cymen-8-ol (2.9%), myrtenol (2.7%), and α-pinene (2.2%) are the principal constituents. There were twenty more chemicals present in amounts less than 2.0%. Overall, there were notable variations in the essential oil composition of *H. perforatum* leaves and flowers. Sesquiterpene hydrocarbons (52.9%), including extremely high concentrations of germacrene D (25.7%), made up the majority of the leaf's constituents, while oxygenated monoterpenes (49.2%) made up most of the flowers.

Table 2. Diversity of polyphenols and flavonoids in extracts of *Hypericum perforatum* L. depending on origin, used organs, and extraction solvents.

	Origin	Organs	Crude extracts	Ethanol	Ethanol-water	Methanol	Water	dimethyl sulfoxide (DMSO)	*H. perforatum* olive oil macerate	Deep eutectic solvents	References
TPC	Morocco	Dried plant	-	-	-	5.50±1.13 mg GAE/g	15.26±1.30 mg GAE/g	-	-	-	(Afqir et al., 2024)
TPC	Greece	Plant	86±13.34 mg GAE/g dry plant material	-	-	-	-	-	-	-	(Kakouri et al., 2023)
TPC	Poland	Air-dried Flowers	-	245±26 mg GAE/g	371±49 mg GAE/g	-	-	-	-	-	(Makarova et al., 2021)
TPC		lyophilized flowers	-	152±13 mg GAE/g	238±26 mg GAE/g	-	-	-	-	-	
TPC	Turkey	Plant	-	23.02±1.58 mg GA/g	-	28.68±1.85 mg GA/g	4.28±0.25 mg GA/g	-	-	3-.10±0.86-16.64±2.09 mg GA/g	(Bayram et al., 2022)
TPC	Turkey	flowers and leaves	-	-	-	-	-	417.75±9.63 µg GAE/mL extract	79.43±0.63 µg GAE/mL extract	-	(Eroglu et al., 2021)
TPC	Turkey	Aerial parts	-	-	265.43±0.378-233.83±0.028 g/kg GAE	-	-	-	-	-	(Seyrekoğlu et al., 2020)
TPC	Montenegro	Wild-growing plants	-	13.5 mgGAE/gDW	-	16.66 mgGAE/gDW	-	-	-	-	(Sladjana et al., 2021)
TFC	Poland	Air-dried Flowers	-	122±4 mg CAE/g	160±7 mg CAE/g	-	-	-	-	-	(Makarova et al., 2021)
TFC		lyophilized flowers	-	80±7 mg CAE/g	107±16 mg CAE/g	-	-	-	-	-	
TFC	Morocco	Dried plant	-	-	-	10.65±0.49	8.25±1.08	-	-	-	(Afqir et al., 2024)
TFC	Turkey	Plant	-	0.08±0.00 mg QE/g	-	0.10±0.01 mg QE/g	2.49±0.09 mg QE/g	-	-	0.02±0.00-12.29±0.30 mg QE/g	(Bayram et al., 2022)
TFC	Montenegro	Wild-growing plant	-	4.54 mgQE/gDW	-	6.91 mgQE/gDW	-	-	-	-	(Sladjana et al., 2021)
TFC	Greece	Plant	0.21±0.14 mg RE/g dry plant material	-	-	-	-	-	-	-	(Kakouri et al., 2023)

Furthermore, Ghasemi Pirbalouti et al. (2014) compared the bioactivity and biochemical profile of essential oils of three Hypericum species, namely *H. perforatum*, *H. helianthemoides*, and *H. scabrum*. As a result, 48 volatile chemical constituents expressing 89% were recognized in *H. perforatum* compared to 31 and 33 constituents in the essential oils of BOTH *H. scabrum* and *H. helianthemoides*, representing 95% and 96%, respectively. Moreover, α-pinene with 12.5 ± 1.0%, followed by β-pinene with 8.3 ± 1.7%, undecane with 7.0 ± 0.5%, and germacrene D (6.9 ± 0.1%) were the main chemical biomolecules in the volatile oil of *H. perforatum*. Similar results were documented in the volatile oils of this plant by Crockett (2010). An additional research, Tamfu et al. (2022) explored the phenolic composition in *H. perforatum* with the Ultrasound-Assisted Extraction method using ethanol: water at 70% as solvent. The most recorded phenolic constituents were *p*-coumaric, *p*-hydroxy-benzoic acids, chlorogenic, ferulic, caffeic, and vanillic. In terms of quantities, quercetin at 43.71 ± 0.68 µg/g, followed by rutin at 29.23 (± 0.43) µg/g, and coumarin at 17.40 (± 0.28) µg/g were the highest evaluated phenolic constituents. Bayram et al. (2022) evaluated the total phenolic compounds in deep eutectic solvent extracts of *H. perforatum* by LC-MS/MS. Total phenolic contents were estimated between 3.10 ± 0.86 and 16.64 ± 2.09 mg GA/g. In terms of essential oils, methyl-2-octane, followed by a saturated hydrocarbon, makes up most of the phenolic compounds with nearly 30%, along with *n*-nonane, geraniol, α-terpineol, and α- and β-pinene. In parallel, minor quantities of monoterpenes like limonene and myrcene, humulene (sesquiterpenes), and lastly, caryophyllene were mentioned in this plant (Mathis et al., 1964a; Ghasemi Pirbalouti et al., 2014; Schepetkin et al., 2020).

4.3 Prenylated phloroglucinols

The investigation of prenylated phloroglucinols in this plant is limited. Brondz et al. (1983), Ollivier et al. (1985), Ayuga et al. (1986), and Upton et al. (1997) detected the presence of hyperforin with estimated quantities ranging from 2.0 to 4.5%, and adhyperforin with quantities ranging from 0.2 to 1.9%. In other studies, Trifunović et al. (1998) and Verotta et al. (1999) and Verotta et al. (2000), described the existence of oxygenated analogs of hyperforin in the essential oils extracted from *H. perforatum*.

4.4 Tannins

The first recorded tannins in the essential oils extracted from *H. perforatum* were proanthocyanidins, as mentioned by Bisset (1994). Furthermore, Germ et al. (2010) investigated the tannin contents in leaves and flowers of *H. perforatum* plants cultivated under three treatments of UV-B radiation spectrophotometrically using vanillin-HCl reagent. The results obtained showed superior quantities of tannins in leaves compared to flowers. The concentration of tannins in leaves varies between 26.6 and 31.4/100 g in DM. In comparison to plants cultivated at lower UV-B radiation levels, leaves under ambient or improved UV-B radiation treatment had higher tannin concentrations. Tannins serve several crucial roles. They significantly contribute to the anti-oxidative action in numerous plant species, and they effectively protect plants from herbivores by lowering their palatability and digestibility (Oszmianski et al., 2007; Gu et al., 2008). Green tea tannins have a role in the tannin-protein combination and affect the infusion's sensual qualities (Lu et al., 2009).

4.5 Other chemical components

In addition to principal chemical constituents such as flavonoids, phenols, and tannins, other constituents were reported in essential oils and extracts of *H. perforatum* plants. These constituents include Acids, saturated hydrocarbons, pectin, carotenoids, and alcohols (Mathis et al., 1964b; Brondz et al., 1983; Assadzadeh et al., 2021). The most recorded acids were isovaleric, nicotinic, palmitic, stearic, and myristic. The most recorded alcohols were C24, C26, and C28, while C16 and C30 straight-chain were the most saturated hydrocarbons in the studied plant. Other elements of trace, such as β-sitosterol, nicotinamide, and choline, were recorded (Mathis et al., 1964b; Brondz et al., 1983; Assadzadeh et al., 2021).

5. Inhibition activity against microorganisms and viruses

5.1 Inhibition against bacteria, fungi, and viruses

5.1.1 Effects of essential oils

The inhibition capacity of *H. perforatum* essential oils was tested against a wide variety of bacteria, viruses, and fungi. The inhibitory rates were variable depending on the concentrations used and the tested pathogens (see Table 3). Ghasemi Pirbalouti et al. (2014) tested the antibacterial activity of essential oils extracted from *H. perforatum* against four pathogens. Consequently, the MCI and MBC were 250 and 500 mg/mL against *Bacillus cereus*, 250 and 500 mg/mL against *Listeria monocytogenes*, 250 and 500 mg/mL against *Pseudomonas aeruginosa*, and 250 and 500 mg/mL against *Salmonella typhimurium*. In another study, different volumes (1, 2.5, and 5 µL) of essential oils extracted from the study plant were applied on TLC plates (Kieselgel 60 F254, Merck, Art. 57212), then scattered on bacterial suspensions of *Micrococcus luteus* (ATCC 9341), *Escherichia coli* (ATCC 35218), *Pseudomonas tolaasii*, *Candida albicans*, *Salmonella typhimurium* (ATCC 13311), *Salmonella enteritidis* (ATCC 13076), *Staphylococcus aureus* (ATCC 6538), and *S. epidermidis* (ATCC 12228) (Rančić et al., 2005). Thus, the oils showed a strong antimicrobial activity against *S. epidermidis*, *S. aureus*, *P. tolaasii*, *Salmonella typhimurium*, *Micrococcus luteus*, *Salmonella enteritidis*, and *E. coli*. Further, the oil showed strong inhibition areas even at the lowest concentrations. In another study, volatile essential oils (500 µg/mL) of wild *H. perforatum* from Chongqing, Wuxi County, were tested against *Salmonella enterica* ssp. enterica (ATCC 14028), *Pseudomonas aeruginosa* (ATCC 27853), *E. coli* (ATCC 25922), and *Staphylococcus aureus* ssp. *aureus* (ATCC 29213) (Ji et al., 2021). The inhibitory level varied between 1.2 and 32% for *Salmonella enterica* ssp. *enterica*, 8.1 to 32% for *Escherichia coli*, and between 16.9 and 27.8% against *P. aeruginosa* when matched to positive controls. The highest inhibition rate was 62.00 ± 2.76% against *Staphylococcus*

Table 3. Antimicrobial activity of *H. perforatum* derivatives (essential oils, crude extracts, and others) against fungi and viruses.

Group	Name of pathogens	Type of extract	Concentration	Impact	References
Fungi	*Candida albicans*	Volatile oils	500 µg/mL	Resistant	(Ji et al., 2021))
	Aspergillus flavus (ATCC 9170), *A. niger* (ATCC 6275), *Penicillium funiculosum* (ATCC 10509), and *Cladosporium cladosporioides* (ATCC 13276), and *Trichoderma viride* (IAM 5061)	Essential oils	0.5, 2.5, and 5 µL	Minimal fungicidal concentration: 15 – 30 µg/mL,	(Rančić et al., 2005)
Viruses	Influenza virus	Fractions	-	Suppression	(Mishenkova et al., 1975)
	Herpes simplex virus (types 1 and 2) and HIV-1	Hypericin and pseudo-hypericin	-	Suppression	(Hudson et al. (1991); Lavie et al. (1989); Lopez-Bazzocchi et al. (1991); Meruelo et al. (1988))
	Sindbis virus and murine cytomegalovirus (MCMV)	Hypericin	-	Suppression	(Hudson et al., 1991)
	Hepatitis C and HIV	Hypericin	-	Resistant	(Anon, 1995; Anon, 1995)
	HIV-positive	Extracts- synthetic hypericin	0.5 mg kg daily, 0.25 mg kg three times weekly, or 0.25 mg kg twice weekly	Suppression	(Cooper et al. (1990); Steinbeck-Klose et al. (1993))
	Bronchitis virus (IBV)	Crude extract and fractions	-	-	(Chen et al., 2019)
	SARS-CoV-2	Extract			(Mohamed et al., 2022)

aureus subsp. aureus, while the lowest was 1.20 ± 1.35% against *Salmonella enterica subsp. enterica*. The value of MIC_{50} in *Hypericum* volatile oil counter *S. aureus* subsp. aureus was estimated at 441.32 ± 2.75 (µg/mL) (Ji et al., 2021).

Equally, the essential oils of *H. perforatum* showed significant inhibitory effects against a wide range of fungi, including pathogens to human health, animals, and plants. Ji et al. (2021) tested the inhibitory capacity of the volatile oils extracted from *H. perforatum* gathered from two areas, Chongqing (Wuxi County) and Chongqing (Wushan County), against *Candida albicans*. Therefore, the fungus was resistant to the treatment used on both plants. In another study, Microdilution tests were conducted on *Cladosporium cladosporioides* (ATCC 13276), *A. flavus* (ATCC 9170), *Aspergillus niger* (ATCC 6275), *Trichoderma viride* (IAM 5061), and *Penicillium funiculosum* (ATCC 10509), using three concentrations (0.5, 2.5, and 5 µL) of *H. perforatum* essential oils (Rančić et al., 2005).

Therefore, the highest minimal fungicidal concentration (mg/mL) was 30 µg/mL in all tested fungi, except *Cladosporium cladosporioides* where the minimal fungicidal concentration was only 15 mg/mL. The minimal inhibition concentration was 15 mg/mL for all tested fungi.

5.1.2 Effects of extracts

Various studies have tested the antibacterial activities of different extracts and their derivatives against bacterial strains. For example, Bahmani et al. (2019) tested the antibacterial effects of hydroalcoholic extracts from *H. perforatum* against *Staphylococcus aureus*. The smallest inhibitory concentration (MIC) was 10000 µg/mL, the smallest bactericidal quantity (MBC) was 2500 µg/mL, and the disc diffusion method (DDM) was 384 µg/mL. Additionally, flower extracts of *H. perforatum* were tested against five coagulase-negative *Staphylococci* (CNS) and two *S. aureus* (Okmen et al., 2017). The tested extracts repressed the development of the bacteria, and the formed inhibition zones against bacteria have ranged between 13 and 17 mm. The maximum inhibition zone was recorded in both CNS-33 and CNS-37, and its diameter was around 17 mm. CNS-22 revealed the lowest susceptibility to the extract of methanol with 812.5 µg/mL. Similarly, flower extracts of *H. perforatum* with concentrations of 25000 and 12500 µg plate were tested against *Salmonella typhimurium* (TA100) and *Salmonella typhimurium* (TA98) (Okmen et al., 2017). In results, the inhibition rate was superior against *Salmonella typhimurium* (TA98) with 64.6% compared to 49.7% against *Salmonella typhimurium* (TA100) in the first concentration. Similarly, in 12500 µg /plate concentration, the inhibition rate was 39.1% against *Salmonella typhimurium* (TA100) and 58.4% against *Salmonella Typhimurium* (TA98). Alahmad et al. (2022) verified the antibacterial effect of green synthesis of silver nanoparticles (AgNPs) based on *H. perforatum* L. water extract against clinical and food pathogens including the *Staphylococcus aureus* (ATCC 43300), *Bacillus cereus* (ATCC 11778), and *Bacillus subtilis* (ATCC 6633) (Gram-positive bacteria), and the Gram-negative bacteria like β-lactamase *K. pneumoniae* (clinical isolate), *P. aeruginosa* (ATCC 13048), *E. coli* (ATCC 25922), and expanded-spectrum β-lactamase *E. coli* (ESBL, clinical isolate). AgNPs exposed antibacterial effects against both experienced Gram-negative and Gram-positive bacterial strains, producing the formation of inhibition zones estimated at 13

to 32 mm with MIC values from 6.25 to 12.5 µg/mL; strains of *E. coli* were resistant to experienced AgNPs. Moreover, the growing rate of *S. aureus* was considerably decreased due to the tested AgNPs at concentrations superior to 1/2 MIC.

5.2 Antiviral effects

Flavonoids and catechin-containing fractions of *H. perforatum* have demonstrated effectiveness against the virus of influenza (Mishenkova et al., 1975). Then, pseudo-hypericin and Hypericin have been proven to suppress Herpes simplex virus types 1 and 2, as well as Human Immunodeficiency Virus (HIV)-1 in *in vitro* tests (Meruelo et al., 1988; Lavie et al., 1989; Hudson et al., 1991; Lopez-Bazzocchi et al., 1991). Additionally, it has been demonstrated that hypericin renders Sindbis virus and murine cytomegalovirus (MCMV) inactive (Hudson et al., 1991). Furthermore, the antiviral effect of hypericin seems to include a mechanism of photoactivation (Hudson et al., 1991; Upton et al., 1997).

Both hepatitis C and HIV have been demonstrated to be resistant to hypericin's antiviral effects (Anon, 1995; Anon, 1995). *H. perforatum* extract showed great capacity to offer immunologic and clinical advantages in HIV-positive people, such as rises in CD4 cell sums in certain patients, in controlled investigations (Cooper et al., 1990; Steinbeck-Klose et al., 1993). Further, 30 patients of HIV-positive (with CD4 cell counts) of 350 cells/mm^3 received intravenous or oral synthetic hypericin at three doses (successive) of 0.5, 0.25 (three times weekly), or 0.25 mg kg (twice weekly) in a stage I dosage-escalating test (Gulick et al., 1999). Due to side effects, 16 patients had to terminate their treatments early, while phototoxicity prevented many additional patients from finishing their dose increase. Indicators of antiretroviral action, such as the HIV titter, HIV p24 antigen rate, HIV RNA replicas, and CD4 cell counts did not change appreciably.

Currently, the antiviral effects of *H. perforatum* have been tested on the virus of infectious bronchitis (IBV) in both *in vitro* and *in vivo* experiments (Chen et al., 2019). The findings of both experiments defined that the crude extract and their related fractions from *H. perforatum* were effective in suppressing the IBV. In the last year, Mohamed et al. (2022) tested for the first time the anti-viral activity of the studied plant against SARS-CoV-2, that presents a significant threat to human health, especially given the dearth of effective antivirals to combat the virus during routine therapy procedures. The authors confirmed the capacity of *H. perforatum* extract (*i.e.*, HP1) to inhibit the infection of the tested cells by the pseudo-typed VSV SARS-CoV-2 S-protein-d21-carrying virus (Mohamed et al., 2022).

6. Implicated biomolecules in antimicrobial activities

As mentioned earlier, the *H. perforatum* is rich in dozens of bioactive molecules that confer its antimicrobial activities (Table 1 and Table 2). Germacrene-D and α-Pinene that were mentioned as main elements in samples from Iran were tested against a wide range of microorganisms including: i) bacteria: two Gram-positive *Staphylococcus epidermidis* (ATCC 12228) and *S. aureus* (ATCC 25923), four Gram-negative *Escherichia coli* (ATCC 25922), *Enterobacter cloacae* (ATCC 13047), *Pseudomonas aeruginosa* (ATCC 227853), and *Klebsiella pneumoniae* (ATCC 13883); and ii) fungi: *Candida tropicalis* (ATCC 13801), *C. glabrata* (ATCC 28838), and *C. albicans* (ATCC 10231) (Couladis et al., 2003). The tested molecules displayed a restrained *in vitro* action against the six Gram-positive and negative bacteria, and a stronger effect counter the three-examined fungi. In another study, the thymol recorded in Iranian samples of the *H. perforatum* was tested against *Staphylococcus aureus*, *Salmonella typhimurium*, and *Vibrio parahaemolyticus* (Karapinar et al., 1987). As a result, thymol was effective against all tested bacteria. Similarly, El Atki et al. (2019) explored the antibacterial capacity of thymol against *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumonia* (Gram-negative bacteria) and *Staphylococcus aureus* (Gram-positive) (108 CFU/mL) (El Atki et al., 2019). As result, thymol exhibited the highest antibacterial effect against *S. aureus* and *E. coli* with an assessed MIC rate of 0.35 mg/mL. In another study, Szostek et al. (2022) explored the anti-bacterial action of ciprofloxacin thymol derivatives counter *S. aureus* T 5591, *S. aureus* T 5595, *S. pasteuri* KR 4358, *S. epidermidis* KR 4243, *E. coli* 510, *E. coli* 600, *E. coli* 520, and *P. aeruginosa* 659. Therefore, all studied composites were relatively inactive against strains of *P. aeruginosa* 659 and *E. coli* 510. Furthermore, the thymol group revealed similar effectiveness towards *E. coli* 600 and 520, with MIC values ranging between 4 and 64 µg/mL. In another investigation, Mohamed et al. (2022) proved the capacity of quercitrin, hyperoside, pseudohypericin, quercetin, and hypericin extracted from *H. perforatum* via chromatography/electrospray of high-performance and liquid ionization-mass spectroscopy, to inhibit SARS-CoV-2.

7. Mechanisms

The complexity and composition of EOs from *H. perforatum* suggest that their biological effects are caused by a variety of pathways, many of which are summarized in Table 2. Several different sorts of mechanisms of action were found in the studied literature, which are discussed below.

First, the chemical constituents of *H. perforatum* act by the modification of the cytoplasmic membrane because via their interaction with their hydrophobic elements (Vuuren et al., 2007). For example, with scanning electron microscopy, Chauhan et al. (2014) have shown the capacity of thymol (recorded in essential oils of the study plant) to disrupt the membrane reparation in cells of *Salmonella ser. Typhimurium*. In addition, thymol and limonene showed a great capacity to inhibit *Pseudomonas fluorescens*, *Salmonella enterica serovar typhimurium*, *Staphylococcus aureus*, *Escherichia coli*, and *Brochothrix thermosphacta* via variations in the configuration of membrane fatty acids of microbial cells (Di Pasqua et al., 2006). Considerable changes were also detected on the long chain of unsaturated fatty acids when *Salmonella* and *E. coli* strains rose in the incidence with limonene. Similarly, the cyclic monoterpenes

limonene and α-pinene pierce the membrane of bacterial cells and increase their permeability (Melkina et al., 2021). According to research of (Cai et al., 2019; Salehi et al., 2019), the lack of an outer membrane in Gram-positive bacteria facilitates the direct interaction of the EOs with the cellular membrane, which can either inactivate the bacterial enzymes or alter the permeability of the membrane and cause intracellular content to leak out.

In an *in vitro* study, Wang et al. (2017) examined the inhibition action of β-galactosidase via cinnamaldehyde, unaccompanied and in mixture with thymol and carvacrol. Consequently, the mixtures of cinnamaldehyde, thymol, and carvacrol exposure exhibited synergistic properties on the suppression of β-galactosidase. Further, using 3-D spectroscopy and circular dichroism, it was demonstrated that the conformation of β-galactosidase and the surrounding microenvironment of tryptophan and tyrosine residues changed when the combined compounds bound to the enzyme. The combination under test was inserted into the β-galactosidase dynamic pocket site and bonded with amino acid residues, including Trp999, Trp568, Phe601, and Met502 (Wang et al., 2017). Furthermore, atomic force microscopy demonstrated that binding with an experienced combination resulted in a significant weakening of the β-galactosidase's normal conformation, such as larger dimensions and morphological modifications of the β-galactosidase particle.

Constituents of essential oils of *H. perforatum* lead to the degradation of internal macromolecules of bacteria. For example, cyclic monoterpenes like α-pinene and limonene (abundant in *H. perforatum*) were tested against genetically modified *Escherichia coli* bioluminescent bacteria (Melkina et al., 2021). According to the findings of this report, limonene activates the PkatG and PsoxS promoters by forming oxidative species, which damages proteins and DNA (SOSresponse) by heat shock. In cells of *E. coli*, the activity of limonene at high concentrations and over an extended period renders degrading processes irreversible. The action of α-pinene is significantly weaker; all it causes in the bacteria is heat shock (Melkina et al., 2021).

The antiviral element of *H. perforatum* was the ethyl acetate extraction section against SARS-CoV-2 (HPE) (Mohamed et al., 2022). In cells of chicken embryo kidney (CEK), the management with HPE dramatically decreased the relative messenger ribonucleic acid (mRNA) expression and virus titter of IBV, as well as the positive signal of green immunofluorescence in IBV. Additionally, IBV-prompted damage to the kidney and trachea was lessened by HPE treatment at dosages between 120 and 480 mg/kg for a period of five days. In addition, expression levels of IBV mRNA in the kidney and trachea were decreased. Tumor necrosis factor-alpha (TNF-alpha), nuclear factor-kappa and beta (NF-B), and IL-6 mRNA manifestation levels considerably decreased, whereas melanoma differentiation-associated protein 5 (MDA5), interferon alpha (IFN-alpha), antiviral signaling gene of mitochondria, and levels of interferon-beta (IFN-beta) mRNA considerably augmented *in vivo* and *in vitro*. These proved that HPE had important anti-IBV properties *in vivo* and *in vitro*. In addition, it is possible owing through the MDA5 signaling pathway to upregulate the expression of mRNA in type I interferon and downregulate mRNA expression of TNF-α and IL-6 by the NF-κB signaling pathway (Mohamed et al., 2022).

8. Concluding remarks

One of the most effective medicinal herbs is *H. perforatum*, which is frequently used to treat a wide variety of infections and serious medical disorders. This plant is still poorly studied in African countries, where it is widely used in commercial forms, despite its remarkable place in the international pharmacopeia as a natural source with multiple functional activities accounting for antimicrobial, antioxidant, antidiabetic, anti-dyslipidemia, anti-inflammatory, and anticancer effects. The variety of chemicals included in *H. perforatum*, such as phenols, flavonoids, terpenes, etc., may be responsible for its antibacterial qualities. These substances have a synergistic interaction among several bioactive molecules, which allows us to know their biological effects. To learn more about novel chemical ingredients, their biological characteristics, and how environmental factors affect *H. perforatum* synthesis, additional comparative research is necessary. It is also necessary to look at how climate change affects adaptation, geographic distribution, and chemical makeup to choose appropriate conservation methods.

Authors contributions

H.A., S.B. and M.O. designed the paper and conceived the idea. H.T., H.A., J.L. and A.F. was responsible for writing and editing the manuscript, and B.B. and S.B. provided technical support. All authors discussed and revised the manuscript.

Availability of data and materials

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

Conflict of interests

The author 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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