Zagazig Journal of Pharmaceutical Sciences

Journal homepage: https://zjps.journals.ekb.eg/

Print ISSN: 1110-5089 Online ISSN: 2356-9786

Phytochemistry and some biological activities of the Genus Hypericum

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ARTICLE INFO

Article History:
Received: 3 July 2023
Accepted: 17 Sept 2023
Published online: 25 Dec 2023

Key words:
Hypericum,
Hypericaceae,
chemical composition,
antibacterial,
antioxidant

ABSTRACT

Medicinal plants are the best source of medicine. Therefore, studies on these plants have increased because of the search for new active substances that can be used in the herbal pharmaceutical industries. Hypericum is a large genus of flowering plants, comprising many species, and presents an almost worldwide distribution. The importance of its species depends mainly on the presence of specialized secondary metabolites that display pharmaceutical and cosmetic properties. Hypericum species are known worldwide for their ethno-medicinal uses including treating infections and diseases. They are used as diuretics, cholagogues, antispasmodics, antiepileptics, and also for treating rheumatism, neuralgia, parasites, dyspepsia, diarrhea, etc. There are only few reports about the chemical composition of the genus Hypericum. The aim of the present study is to provide an overview of the importance of the genus Hypericum. A summary of the chemical composition, as well as the antibacterial and antioxidant activities of different Hypericum species.

1. Introduction

In developing countries, 70-95% of people depend on plants as their main method of treatment these days (Chassagne et al., 2021). According to the WHO, medicinal plants are the best source of medicines (Okmen and Balpınar, 2017). Some researchers believed that two-thirds of the world’s plants are medically beneficial (Krishnaiah et al., 2011). Therefore, research on medicinal plants has increased rapidly in order to find new active substances that can be used in herbal medicine industries (Okmen and Balpınar, 2017).

On the other hand, the problem of food preservation is becoming more complex, requiring a longer shelf life and greater protection from microbial spoilage and oxidative damage. Some statistics indicated that about 30% of people in industrialized countries suffer annually from foodborne diseases (Mimica-Dukića and Božin, 2007).

Medicinal plants are considered as powerful and easily available sources of antioxidants, due to the chemical compounds they contain that act individually or synergistically to treat diseases (Bhatt, Rawat, & Rawal, 2013). It has been reported that many phenolic compounds such as procyanidins, coumarins, flavonoids and tannins can scavenge radicals -in a dose-dependent manner- and are thus

DOI: 10.21608/ZJPS.2023.220695.1050
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considered as therapeutic medicines for free radical diseases (Zheleva-Dimitrova et al., 2010).

Medicinal plants also contain compounds that may inhibit the growth of viruses, protozoa, bacteria and fungi by various mechanisms and this can be of a significant clinical value in treating of resistant microbial strains (Vaou et al., 2021). These bioactive compounds are used as a starting point for the synthesis of antibiotics in order to treat infectious diseases (Kebede et al., 2021). In general, the extent of the antioxidant and antimicrobial effects of the extracts could be attributed to their phenolic compounds (Endes et al., 2015).

Hypericum is a large genus of flowering plants, including many species (Ion et al., 2022), and presents an almost worldwide distribution. The importance of its species depends mainly on the presence of specialized secondary metabolites that display pharmaceutical and cosmetic properties (Silva et al., 2021). Over the years, there has been a great interest in studying the different biological activities of Hypericum species (Ion et al., 2022). Therefore, the purpose of this study is to provide an overview of the importance of Hypericum. A summary of the typical essential oil constituents, as well as the antibacterial and antioxidant activities of different species belonging to the genus Hypericum.

2. The genus Hypericum

Hypericaceae family contains shrubs or herbaceous plants. They have glandular hairs that contains essential oils (EOs) (Gedik, 2022). This family includes nine genera, one of which is Hypericum (Rojas et al., 2013). Hypericum contains nearly 500 species (Maltas et al., 2013), perennial, herbaceous, or scrubby plants (Bejaoui et al., 2017), widely distributed in mountainous, tropical and temperate regions (Toiu et al., 2016). The genus received a great as it is a source of a variety of compounds with various biological effects (Bejaoui et al., 2017).

Hypericum species are globally recognised for their significant ethno-medicinal properties, which are utilised in the treatment of various infections and diseases (Saddiqe et al., 2016). These species exhibit a wide range of therapeutic effects, including diuretic, cholagogue, antispasmodic, antiepileptic, and antimigraine properties. Additionally, they are employed in the management of conditions such as rheumatism, neuralgia, parasitic infections, dyspepsia, sciatica, and diarrhea (Rojas et al., 2013)".

Hypericum plants have been included in Pharmacopoeias of many countries such as Germany, Czechoslovakia, Russia, Romania, Poland and France (Rouis, 2011). Various products containing Hypericum plants or their extracts have been developed as additives and many brands such as beverages and yogurts include these plants (Rouis, 2011).

The biological effects of the plants depend on their contents of secondary metabolites (Seyrekoglua et al., 2022). The chemical content of Hypericum plants is diverse with xanthones, glycosides, pyrones, flavonoids, tannins, anthraquinones, lactones, lipids, phloroglucinols, coumarins and EOs (Demirci and Baser, 2006).

The major phytomedicinal compounds of Hypericum species are naphthodianthrones (hypericin and pseudohypericin), phloroglucinol derivatives (adhyperforin and hyperforin), flavonoids (rutin, biapigenin, hyperoside, quercetin, quercitrin), chlorogenic acid and caffeic acid which possess many biological properties (Maltas et al., 2013).

Hypericum perforatum is one of the most widely used medicinal plants -among all species of the genus Hypericum- by the publics of both more industrialized and less developed countries (Caldeira et al., 2022). It is used as a mild antidepressant (Jaimand, 2013). This effect of H. perforatum is due to its main component hyperforin. The combined effect of the other components within the plant extract also contributes to its overall impact synergistically (Seyrekoglua et al., 2022).

3. Chemical Composition of the Essential Oils of Hypericum Species

The volatile substances in plants are generally analyzed through extraction steps, concentration, chromatography and detection steps (Balikci, 2020). Hypericum plants are generally known to be poor in essential oil (generally oil yield <1%, w/w) (Rouis, 2011).

***Table 1**. Chemical composition of Hypericum essential oils*

.

Species	Plant part	Main compounds	Ref.
H. elegans	AE	g-gurjunene, aromadendrene, and undecane	(Anna et al., 2013)
H. tetrapterum	AE	Copaene, α -longipinene, cadinene	
H. hirsutum	AE	caryophyllene oxide, phytol, α - caryophyllene and undecane	
H. perforatum	AE	ß – caryophyllene, caryophyllene oxide, α -pinene, ß -cadinene, and ß -pinene	
H. scabrum	AE	α-pinene, β-caryophyllene, myrcene, cadalene and β-pinene	(Çakir et al., 1998)
H. scabroides	AE	hexadecanoic acid, spathulenol, nonacosane, dodecanoic acid, baeckeol and γ-muurolene	(Özkan Demirci et al., 2013)
H. kotschyanum	AE	α-pinene, nonacosane, hexadecanoic acid, β-pinene, spathulenol and limonene	
H. salsugineum	AE	nonacosane, hexadecanoic acid and baeckeol	
H. thymopsis	AE	α-pinene, baeckeol, spathulenol, limonene and camphene	
H. uniglandulosum	AE	2,6-Dimethyl-3,5-heptadien-2-one, nonacosane, hexadecanoic acid and α-pinene	
H. uniglandulosum	AE	α-pinene, undecane, benzoic acid, cyclohexasiloxane	(Yüce-Babacan et al., 2017)
H. lydium	AE	α-pinene, ß-pinene, ß-myrcene	
H. thymopsis	AE	α-pinene, spathulenol, limonene	(Koç and Arabaci, 2021)
H. perforatum	AE	(germacrene D); ((E)-caryophyllene); (2-methyloctane); (α-pinene) and (bicyclogermacrene)	(Đorđević, 2015)
H. perforatum	FL	(E- ß –farnesene); (n-hexadecanal); (E-nerolidol)	(Jaimand, et al., 2012)
H. dogonbadanicum	FL	(phenyl ethyl octanoate); (terpin-4-ol); (α-phellandrene)	
	LE	ß-pinene, α-pinene and p-cymene	
H. helianthemoides	FL	α -pinene, Z- ß -ocimene and ß -pinene	
H. hyssopifolium	FL	α -pinene, ß -pinene and n-tetradecan	
	LE	E-nerolidol, n-tetradecane and α -himachalene	
H. lysimachioides	FL	α-pinene, Z- ß -ocimene and n-tetradecane	
H. triquetrifolium	FL	n-tetradecane, α -himachalene and α –pinene	
	LE	α -himachalen, n-tetradecane and n-pentadecane	
H. triquetrifolium	AE	Germacrene-D, ß -caryophyllene, δ -cadinene, trans- ß -farnesene, α -humulene, ß -selinene, γ-cadinene and trans-phytol	(Sajjadi et al., 2015)
H. richeri	AE	germacrene D, bicyclogermacrene, α-pinene, ß-pinene, decanoic acid, ß -caryophyllene, δ-cadinene, spathulenol and tetracosane	(Jerkovića, et al., 2013)
H. patulum	AE	β-pinene, α-pinene, limonene and α-humulene	(Morshedloo et al., 2014)
H. laricifolium	AE	and nonane *α*-pinene, verticiol, 3-methyl-nonane, 2-methyl-octane	(Rojas et al., 2013)
H. rumeliacum	AE	undecane, dodecanal, and germacrene D	(Radulović and Blagojević, 2012)
H. rumeliacum	AE	(E)-β-ocimene, β-pinene, (Z)-β-ocimene, dodecanal, germacrene D, myrcene	(Djordjevicet al., 2020)
H. rumeliacum	AE	α-pinene, ß-pinene, dehydro-aromadendrene, α-copaene	(Couladis et al., 2003)
H. lydium	AE	*α* -pinene, β-pinene and β-myrcene	(Yüce-Babacan and Bagci, 2017)

H. ericoides	AE	n-nonane, n-undecane, α-cubebene, α-pinene	(Rouis, et al., 2011)
H. androsaemum	AE	longifolene, ß-gurjunene, and γ-gurjunene	(Jaimand, et al., 2013)
H. apricum	AE	cis-piperitol acetate, p-cymenene, α-pinene	
H. armenum	AE	γ -cadinene, longifolene, E-nerolidol	
H. asperulum	AE	α -muurolol, cis-sesquisabienen hydrate, germacrene B	
H. hirsutum	AE	germacrene B, citronellyl propanoate, γ –gurjunene	
H.linarioides	AE	(E, E)-farnesyl acetate, cis-cadinene ether, 1-tridecene	
H. tetrapterum	AE	trans-linalool oxide, p-cymenene, (E, E)-farnesyl acetate	
H. vermiculare	AE	α -pinene, myrcyne, E- ß -farnesene	
H. asperulum	AE	(α-pinene); (caryophyllene oxide); (E-caryophyllene) and (spathulenol)	(Khorshidi et al., 2020)
H. scabrum	AE	(α-pinene); (β-pinene); (limonene) and (E-caryophyllene)	
H. vermiculare	AE	(α-pinene); (caryophyllene oxide); (E-caryophyllene) and (spathulenol)	
H. pseudolaeve	AE	(trans-caryophyllene); (δ-limonene); (α-cadinol); (caryophyllene oxide); (α-pinene); (spathulenol) and (β-selinene)	(Bagci and Babacan, 2013)
H. thymbrifolium	AE	α-pinene, undecane, germacrene D, β-pinene, β-myrcene, spathuleneol, naphthalane	
H. humifusum	AE	(n-undecane); (α-pinene); (β-pinene); (limonene); (myrcene)	(Rouis, et al., 2011)
H. bupleuroides	AE	(β-sesquiphellandrene); (β-caryophyllene); (selina-3,7(11)-diene); (γ-elemene); (undecane); (germacrene-B)	(Demirci and Baser, 2006)
H. gaitii	AE	α-pinene, allo-aromadendrene, δ-cadinene, n-nonane, β-caryophyllene, α-selinene	(Grafakou et al., 2022)
H. mexicanum	AE	n-nonane, α-pinene	(Patiño-bayona et al., 2020)
H. myricariifolium	AE	α-pinene, β-caryophyllene	
H. juniperinum	AE	n-nonane, α-pinene, geranyl acetate, and β-caryophyllene	
H. heterophyllum	AE	germacrene-D, bicyclogermacrene, d-cadinene, spathulenol, a-guaiene, and valencene	(Senkal and Uskutoglu, 2020)
H. amblysepalum	AE	δ -3-carene, caryophyllene-oxide, cis-ocimene, ß-caryophyllene, α-pinene	(Babacan, 2019)
H. spectabile	AE	ß - caryophyllene, germacrene D, α-cadinol, caryophyllene oxide	
H. helianthemoides	AE	α-pinene, δ -3-carene, d-limonene, cis-ocimene, undecane	
H. acmosepalum	AE	(ar-curcumene); (β-selinene)	(Demirci et al., 2005)
H. beanii	AE	(γ-muurolene); (β-selinene); (caryophyllene oxide)	
H. calycinum	AE	α-terpineol, P-pinene	
H. choisyanum	AE	cis-eudesma-6,11-diene	
H. forrestii	AE	a-pinene, caryophyllene oxide	
H. kouytchense	AE	cis-β-guiaene, γ-muurolene	
H. lancasteri	AE	β-selinene, eudesmadienone	
H. leschenaultii	AE	(Cuparene) and (γ-muurolene)	
H. monogynum	AE	Tricosane, myrcene	
H. patulum	AE	β-selinene	
H. pseudohenryi	AE	β-selinene	
H. X moserianum	AE	γ-muurolene, δ-cadinene	
H.salsolifolium	AE	α-pinene, limonene, spathulenol, β-pinene, germacrene D	(Bagci and Babacan, 2011)
H.retusum	AE	α-pinene, limonene, spathulenol, β-pinene, germacrene D	
H. maculatum	-	β-farnesene, n-undecane, β-caryophyllene, δ-cadinene, muurolene	(Gudžić et al., 2002)
H. foliosum	-	n-nonane, limonene, terpinolene, β–caryophyllene, β-pinene	(Santos et al., 1999)
H. brasiliense	WP	ß-Caryophyllene, α-Humulene, Caryophyllene oxide, Cubenol, aromadendrene	(Abreu et al., 2004)

AE: Aerial parts; FL: flower; LE: leaf; WP: whole plant

The essential oil (EO) composition of about 50 different Hypericum species have so far been identified (Özkan et al., 2013). The main components of some Hypericum species EOs are presented in Table 1. Some components were detected in more than one species, such as α –pinene was identified in the EO of H. vermiculare, H. pseudolaeve, H. thymbrifolium, H. humifusum, H. ericoides, H. apricum, H. laricifolium, H. lydium, H. richeri, H. patulum, H. lysimachioides, H. triquetrifolium, H. dogonbadanicum, H. helianthemoides, H. hyssopifolium, H. uniglandulosum, H. kotschyanum, H. thymopsis, H. perforatum, H. scabrum. Whereas β-Pinene was identified in the EO of H. humifusum, H. lydium, H. richeri, H. patulum, H. thymbrifolium, H. dogonbadanicum, H. helianthemoides, H. hyssopifolium, H. kotschyanum, H. perforatum, H. scabrum. Undecane was also introduced as one of the main compounds of H. bupleuroides, H. thymbrifolium, H. humifusum, H. ericoides, H. hirsutum, H. rumeliacum, H. elegans EOs. Spathuleneol was also identified in the EOs of H. pseudolaeve, H. thymbrifolium, H. kotschyanum, H. richeri, H. thymopsis, H. scabroides. hexadecanoic acid was identified in the EOs of H. scabroides, H. uniglandulosum, H. kotschyanum, H. salsugineum.

In contrast, some compounds were detected as main constituents in the unique species, such as copaene in the EO of H. tetrapterum, α-muurolol in the EO of H. asperulum, cis-piperitol acetate in the EO of H. apricum and verticiol in the EO of H. laricifolium.

Previous investigations on the EO composition of Hypericum plants did not give homogenous results. These studies have shown that this variance depends on genetics and environment, ontogeny, season, analytical method (Hajdari, et al., 2014), geographical distribution, type of glands and phenological cycle (Jerkovića et al., 2013).

For instance, the H. perforatum EO extracted from aerial parts obtained from the Republic of Moldova contained ß–caryophyllene, caryophyllene oxide, α–pinene, ß–cadinene, and ß– pinene in the following percentages (12.175%,12.119%, 8.574%, 4.155%, 3.216%), respectively (Anna, Maria, Veaceslav, Ion, & Anatolie, 2013), while another H. perforatum EO extracted from aerial parts obtained from southeastern Serbia showed germacrene D, (E)-caryophyllene, 2-methyloctane, α-pinene, bicyclogermacrene and (E)-β-ocimene as main volatile constituents in the following percentages (18.6%, 11.2%, 9.5%, 6.5%, 5.0%, 4.6%), respectively (Đorđević, 2015).

The variability of the EOs composition depend also on the part analyzed (Hajdari, et al., 2014). For instance, the flowers oil of H. dogonbadanicum was dominated by phenyl ethyl octanoate, terpin-4-ol, and α-phellandrene, whereas the oil from the leaves of the same plant had α-pinene, ß-pinene and p-cymene as its main compounds .

The flowers oil of H. hyssopifolium was quite different from the leaves oil. α -pinene, ß -pinene and n-tetradecan were the main compounds of the flowers oil, where the leaves contained E-nerolidol, n-tetradecane and α -himachalene.

4. Chemical Composition

This review summarizes the chemical constituents from the genus Hypericum which are mainly responsible for its pharmacological benefits. We documented about 100 different natural products and 34 different plant species as sources for these natural products (Table 2). Most of the chemical constituents were mainly isolated from the aerial parts and a few from roots and fruits. The isolated compounds are in the class of phenolic compounds, flavonoids and its glycosides, phloroglucinols, triterpenoid, benzophenones, naphthodianthrone. Flavonoids were the most abundant among the isolated compounds. Hypericum species were also characterized by containing several compounds of the xanthones class .

According to this survey, quercitin, rutin, hypericin, isoquercitrin, quercetrin, chlorogenic acid, pseudohypericin and I3–II8 Biapigenin are the most abundant among secondary metabolites isolated from Hypericum species. The pharmacological researches mainly focus on flavonoids such as rutin, hyperoside, and quercetin, and naphthodianthrones such as hypericin.

Table 2. *Compounds isolated from Hypericum species*

Compound	Plant species	Plant part	Ref.
Phenolic compounds			
3-geranyl-1-(2'-methylbutanoyl) phloroglucinol	*H. scruglii*	AE	(Sanna et al., 2018)
	H. empetrifolium	FR	(Crockett et al.,
3-geranyl-1-(2'-methylpropanoyl) phloroglucinol	*H. scruglii*	AE	(Sanna et al., 2018)
	H. empetrifolium	FR	(Crockett et al., 2008)
3-(13-hydroxygeranyl)-1-(2'-methylbutanoyl) phloroglucinol	*H. scruglii*	AE	(Sanna et al., 2018)
adhyperfoliatin	*H. trichocaulon*	AE	(Daskalaki et al., 2022)
(E)-chlorogenic acid	*H. trichocaulon*	AE	
procyanidin A2	*H. trichocaulon*	AE	
Uliginosin B	*H. caprifoliatum*	AE	(Bridia et al., 2022)
	H. denudatum	AE	
	H. polyanthemum	AE	
Uliginosin A	*H. brasiliense*	LE - FL	(Rocha et al., 1995)
Isouliginosin B	*H. denudatum*	AE	(Bridia et al., 2022)
	H. polyanthemum	AE	
	H. brasiliense	LE - FL	(Rocha et al., 1995)
Hyperbrasilol B	*H. austrobrasiliense*	AE	(Bridia et al., 2022)
	H. caprifoliatum	AE	
	H. pedersenii	AE	
Hyperbrasilol A	*H. brasiliense*	LE - FL	(Rocha et al., 1995)
	H. denudatum	AE	(Bridia et al., 2022)
Isohyperbrasilol B	*H. caprifoliatum*	AE	
	H. pedersenii	AE	
Austrobrasilol B	*H. austrobrasiliense*	AE	
	H. caprifoliatum	AE	
	H. pedersenii	AE	
Isoaustrobrasilol B	*H. austrobrasiliense*	AE	
Austrobrasilol A	*H. austrobrasiliense*	AE	
	H. caprifoliatum	AE	
	H. pedersenii	AE	
	H. denudatum	AE	
Denudatin A	*H. denudatum*	AE	
Japonicine A	*H. caprifoliatum*	AE	
	H. pedersenii	AE	
	H. brasiliense	LE - FL	(Rocha et al., 1995)

DOI: 10.21608/ZJPS.2023.220695.1050
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hengshanols A	*H. hengshanense*	AE	(Han et al., 2022)
Hyperforin	*H. perforatum*	-	(Cossuta et al., 2011)
	H. perforatum	FLS	(Tusevski et al., 2018)
	H. humifusum	AE	(Béjaoui et al., 2017)
	H. confertum	FL	(Camas et al., 2014)
	H. pruinatum	FL	
	H. lydium	FL	
adhyperforin	*H. confertum*	FL	
	H. pruinatum	FL	
	H. lydium	FL	
1-(6-hydroxy-2,4-dimethoxyphenyl)-2-methyl-1-propanone	*H. cistifolium*	AE	(Crockett et al., 2016)
hydroquinone	*H. lanceolatum*	STB	(Kowa et al., 2020)
3-O-Caffeoylquinic acid (chlorogenic acid)	*H. richeri*	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. hirsutum	AE	
	H. androsaemum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	LE- FL	
	H. perforatum	FLS	(Tusevski et al., 2018)
4-O-Caffeoylquinic acid	*H. barbatum*	AE	(Zdunica et al., 2017)
5-O-Caffeoylquinic acid	*H. richeri*	AE	
	H. barbatum	AE	
	H. perforatum	AE	
	H. hirsutum	AE	
	H. androsaemum	AE	
	H. acutum	AE	

Neochlorogenic acid	*H. confertum*	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	LE- FL	
	H. lydium	ST- LE- FL	
caffeic acid	*H. confertum*	LE- FL	
	H. thymifolium	FL	
	H. linarioides	FL	
	H. pruinatum	LE- FL	
2,4-dihydroxybenzoic acid	*H. confertum*	ST- LE- FL	
	H. thymifolium	LE- FL	
	H. linarioides	LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	FL	
	H. scabrum	LE- FL	
	H. lydium	FL	
3,4-dihydroxybenzoic acid	*H. scruglii*	*AE*	(Sanna et al., 2018)
Quinic acid	*H. perforatum*	FLS	(Tusevski et al., 2018)
3-p-Coumaroylquinic acid	*H. perforatum*	FLS	
3-Feruloylquinic acid	*H. perforatum*	FLS	
Flavonoids			
amentoflavone	*H. confertum*	LE- FL	(Camas et al., 2014)
	H. thymifolium	FL	
	H. linarioides	LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	LE- FL	
	H. scabrum	FL	
	H. lydium	LE- FL	
Rutin (quercetin 3-O-rutinoside)	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. triquetrifolium	AE	(Alzoubi et al., 2020)

	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum		
	H. hirsutum		
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	ST- LE- FL	
	H. trichocaulon	AE	(Daskalaki et al., 2022)
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Hyperoside (quercetin 3-O-galactoside)	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. trichocaulon	AE	(Daskalaki et al., 2022)
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. hirsutum	AE	
	H. androsaemum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. brasiliense	LE - FL	(Rocha et al., 1995)
	H. ternum	-	(Bernardi et al., 2007)
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	ST- LE- FL	
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)

Quercitrin (quercetin 3-O-rhamnoside)	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	LE	
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. trichocaulon	AE	(Daskalaki et al., 2022)
	H. brasiliense	LE - FL	(Rocha et al., 1995)
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Isoquercitrin	*H. richeri*	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. hirsutum	AE	
	H. androsaemum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. ternum	-	(Bernardi et al., 2007)
	H. brasiliense	LE - FL	(Rocha et al., 1995)
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	

	H. lydium	ST- LE- FL	
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Quercetin	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. hyssopifolium	AE	(Cakir et al., 2003)
	H. confertum	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	ST- LE- FL	
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. hirsutum	AE	
	H. androsaemum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. brasiliense	LE - FL	(Rocha et al., 1995)
	H. laricifolium	AE	(Miguel et al., 2018)
	H. lanceolatum	FL	(Nguemo et al., 2020)
	H. coadunatum	AE	(Díaz, 2022)
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Quercetin 3-methyl ether	*H. ternum*	-	(Bernardi et al., 2007)
3,7-dimethyl ether Quercetin	*H. ternum*	-	
arabinofuranoside Quercetin-3-O-α-l	*H. hyssopifolium*	AE	(Cakir et al., 2003)
Quercetin-3-O-ß-d-galactopyranoside	*H. hyssopifolium*	AE	
Quercetin-3-O-ß-d-galactopyranoside-7-O-ß-d-glucopyranoside	*H. hyssopifolium*	AE	

Avicularin	*H. confertum*	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE	
	H. linarioides	ST- LE- FL	
	H. pruinatum	LE- FL	
	H. olivieri	FL	
	H. scabrum	FL	
	H. lydium	FL	
Catechin	*H. confertum*	ST- LE- FL	
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	ST- LE- FL	
	H. perforatum	FLS	(Tusevski et al., 2018)
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Epicatechin	*H. confertum*	ST- LE- FL	(Camas et al., 2014)
	H. thymifolium	ST- LE- FL	
	H. linarioides	ST- LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	ST- LE- FL	
	H. scabrum	ST- LE- FL	
	H. lydium	ST- LE- FL	
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
	H. perforatum	FLS	(Tusevski et al., 2018)
Amentoflavone	*H. perforatum*	FLS	
	H. confertum	LE- FL	(Camas et al., 2014)
Cyanidin 3-O-glycoside	*H. perforatum*	FLS	(Tusevski et al., 2018)
Cyanidin 3-O-rhamnoside	*H. perforatum*	FLS	
miquelianin	*H. calycinum*	-	(Kırmızıbekmeza et al., 2009)
myricitrin	*H. trichocaulon*	AE	(Daskalaki et al., 2022)

myricetin	*H. lanceolatum*	FL	(Nguemo et al., 2020)
orientin	*H. coadunatum*	AE	(Díaz, 2022)
	H. hirsutum	AE	(Zdunica et al., 2017)
2"-O-Acetyl-orientin	*H. hirsutum*	AE	
I3–II8 Biapigenin	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. hirsutum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. lanceolatum	FL	(Nguemo et al., 2020)
	H. hyssopifolium	AE	(Cakir et al., 2003)
	H. trichocaulon	AE	(Daskalaki et al., 2022)
	H. ternum	-	(Bernardi et al., 2007)
	H. calycinum	-	(Kırmızıbekmeza et al., 2009)
Myricetin 3-O-rutinoside	*H. richeri*	AE	(Zdunica et al., 2017)
Myricetin 3-O-galactoside	*H. richeri*	AE	
Myricetin 3-O-glucoside	*H. richeri*	AE	
luteolin	*H. brasiliense*	LE - FL	(Rocha et al., 1995)
Kaempferol 3-O-rutinoside	*H. perforatum*	FLS	(Tusevski et al., 2018)
kaempferol-3-O-β-Dglucopyranoside	*H. lanceolatum*	FL	(Nguemo et al., 2020)
kaempferol	*H. brasiliense*	LE - FL	(Rocha et al., 1995)
friedelanone	*H. lanceolatum*	FL	(Nguemo et al., 2020)
friedelan-3-β-ol	*H. lanceolatum*	FL	
B-type procyanidin dimer	*H. perforatum*	FLS	(Tusevski et al., 2018)
	H. perforatum	FLS	
	H. perforatum	FLS	
Procyanidin trimer	*H. perforatum*	FLS	

8-C- β-L- arabinopiranosylapigenin	*H. coadunatum*	AE	(Díaz, 2022)
guaijaverin	*H. coadunatum*	AE	
	H. ternum	-	(Bernardi et al., 2007)
	H. brasiliense	LE - FL	(Rocha et al., 1995)
Hovetrichoside C	*H. coadunatum*	AE	(Díaz, 2022)
Naphthodianthrone			
Hypericin	*H. triquetrifolium*	AE	(Alzoubi et al., 2020)
	H. perforatum	FLS	(Tusevski et al., 2018)
	H. perforatum	-	(Cossuta et al., 2011)
	H. humifusum	AE	(Béjaoui et al., 2017)
	H. confertum	LE- FL	(Camas et al., 2014)
	H. thymifolium	LE- FL	
	H. linarioides	LE- FL	
	H. pruinatum	LE- FL	
	H. olivieri	LE- FL	
	H. scabrum	FL	
	H. lydium	LE- FL	
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. hirsutum	AE	
	H. acutum	AE	
	H. maculatum	AE	
	H. hyssopifolium	AE	(Cakir et al., 2003)
Protopseudohypericin	*H. perforatum*	FLS	(Tusevski et al., 2018)
Pseudohypericin	*H. perforatum*	FLS	
	H. confertum	LE- FL	(Camas et al., 2014)
	H. thymifolium	LE- FL	
	H. linarioides	LE- FL	
	H. pruinatum	ST- LE- FL	
	H. olivieri	LE- FL	

	H. scabrum	FL	
	H. lydium	LE- FL	
	H. richeri	AE	(Zdunica et al., 2017)
	H. perforatum	AE	
	H. barbatum	AE	
	H. acutum	AE	
	H. maculatum	AE	
Terpenoid derivatives			
2-benzoyl-3,3-dimethyl-4R,6S-bis-(3-methylbut-2-enyl)-cyclohexanone	*H. galioides*	AE	(Crockett et al., 2016)
2-benzoyl-3,3-dimethyl-4*S*,6*R*-bis-(3-methylbut-2-enyl)-cyclohexanone	*H. galioides*	AE	
betulinic acid	*H. lanceolatum*	STB	(Zofou et al., 2011)
	H. lanceolatum	STB - TW	(Happi et al., 2023)
ursolic acid	*H. lanceolatum*	STB - TW	
Benzophenones			
2,2',5,6'-tetrahydroxybenzophenone	*H. lanceolatum*	STB	(Zofou et al., 2011)
isogarcinol	*H. lanceolatum*	FL	(Nguemo et al., 2020)
Hyperibone	*H. coadunatum*	AE	(Díaz, 2022)
Xanthone			
5-hydroxy-3-methoxyxanthone	*H. lanceolatum*	STB	(Zofou et al., 2011)
6,7-dihydroxy-1,3-dimethoxyxanthone	*H. lanceolatum*	STB	(Kowa et al., 2020)
1,3,5,6-tetrahydroxy-4-prenylxanthone	*H. lanceolatum*	STB	
3-hydroxy-5-methoxyxanthone	*H. lanceolatum*	STB	(Zofou et al., 2011)
	H. lanceolatum	STB	(Kowa et al., 2020)
1,6-dihydroxyxanthone	*H. lanceolatum*	STB - TW	(Happi et al., 2023)
euxanthone	*H. lanceolatum*	FL	(Nguemo et al., 2020)
norathyriol	*H. lanceolatum*	STB - TW	(Happi et al., 2023)

1,7-dihydroxyxanthone	*H. laricifolium*	AE	(Miguel et al., 2018)
1,3,8-trihydroxy-2-methoxyxanthone	*H. laricifolium*	AE	
1,3-dihydroxy-2-methoxyxanthone	*H. laricifolium*	AE	
1,3-dihydroxy-6-methoxy-xanthone	*H. laricifolium*	AE	(Ramírez-gonzález et al., 2013)
2,8-dihydroxy-1-methoxyxanthone	*H. laricifolium*	AE	(Miguel et al., 2018)
3,8-dihydroxy-1,2-dimethoxyxanthone	*H. laricifolium*	AE	
1-hydroxy-7-methoxyxanthone	*H. laricifolium*	AE	(Ramírez-gonzález et al., 2013)
2-hydroxy-xanthone	*H. laricifolium*	AE	
6-deoxyisojacareubin	*H. laricifolium*	AE	
1,5,6-trihydroxy-7-methoxy-xanthone	*H. laricifolium*	AE	
hyperixanthone A	*H. trichocaulon*	AE	(Daskalaki et al., 2022)
5-O-methyl-2-deprenylrheediaxanthone B	*H. roeperanum*	RO	(Rath et al., 1996)
5-O-methylisojacareubin	*H. roeperanum*	RO	
5-O-demethylpaxanthonin	*H. roeperanum*	RO	
roeperanone	*H. roeperanum*	RO	
Dimethylmangiferin	*H. perforatum*	FLS	(Tusevski et al., 2018)
3,6-Dihydroxy-1,5,7-trimethoxy-xanthone	*H. perforatum*	RO	
Cadensin C	*H. perforatum*	RO	
Cadensin C isomer	*H. perforatum*	RO	
γ-Mangostin	*H. perforatum*	RO	
5-O-Methyl-2-deprenylrheediaxanthone B	*H. perforatum*	RO	
Cadensin G	*H. perforatum*	RO	
Garcinone C	*H. perforatum*	RO	

AE: Aerial parts; ST: Stem; FL: flowers; LE: leaves; FR: Fruits; TW: twigs; RO: roots; STB: stem bark; FLS: Flower shoot.

5. Antimicrobial activity of *Hypericum* species

Microorganisms are present in the environment. Therefore, they can easily access food (Gonelimali, 2018). These days, drug-resistant bacteria are rapidly emerging all over the world and pose a threat to the efficiency of antibiotics (Özkan et al., 2019). Along with the problem of developing resistance, other problems such as high cost and side effects motivated researchers to look for alternative sources of antimicrobial agents, especially plants and plant products (Anusha et al., 2015). The genus *Hypericum* has been found to produce compounds that have antimicrobial properties (Bejaoui et al., 2017). Many studies have been conducted in many countries showing the antibacterial effect of this genus (table 3).

Methanolic extracts of six *Hypericum* species (*H. perforatum, H. neurocalycinum, H. spectabile, H. thymbrifolium, H. malatyanum* and *H. pseudolaeve*) were screened for antibacterial effect against many microorganisms. All extracts displayed antibacterial effect against *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis* ATCC 12228 and Methicillin-resistant *Staphylococcus aureus* ATCC33591, with MIC values ranged from 4.8 µg/ml to 156 µg/ml.

Boga et al., (2016) evaluated the antibacterial effect of many extracts of the whole plant of *H. capitatum* var. *capitatum* against *Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC 25922, *Streptococcus pyogenes* ATCC19615, and *Pseudomonas aeruginosa* ATCC27853. The acetone and methanolic extracts were active on all tested microorganisms. The methanolic extract showed highest effect against *Escherichia coli* with an MIC value of 10 µg/ml (Boga et al., 2016).

Tchakam et al., (2012) investigated the antibacterial effect of the methanolic extract of *H. lanceolatum* leaves. The extract showed antimicrobial activity against *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumonia* ATCC 13883, *Salmonella typhi* ATCC 6539, *Enterococcus faecalis* ATCC 10541, with MIC values ranged from 32 µg/ml to 64 µg/ml (Tchakam, et al., 2012). According to the published literature, the antibacterial activity varies according to the plant part. This is because the concentration of secondary metabolites accumulated in the plant cells varies according to the plant parts (Selvamohan et al., 2012). Antimicrobial activity of different parts (leaf, stem and flower) of *H. montbretii* and *H. bupleuroides* was determined using disc diffusion methods against several microbial species (*Bacillus subtilis* ATCC 6633, *Staphylococcus epidermidis* ATCC 12228, *Escherichia coli* ATCC 25922, and *Staphylococcus aureus* ATCC 25923). The results showed that the extracts displayed good-moderate antimicrobial effect, with MIC values ranged between (0.20-100)µg/ml.

Table 3. *Antibacterial effect of some Hypericum Species against various bacterial strains*

Species	Extract/ plant part	Micro-organisms	MIC (mg/ml)	Ref.
H. perforatum	Total methanol / AE	*S. aureus* (ATCC 6538)	0.0048	(Özkan et al., 2019)
		Methicillin-resistant S. aureus (ATCC33591)	0.039	
		S. epidermidis (ATCC 12228)	0.078	
H. spectabile	Total methanol / AE	*S. aureus* (ATCC 6538)	0.0048	
		Methicillin-resistant S. aureus (ATCC33591)	0.0048	
		S. epidermidis (ATCC 12228)	0.039	
H. pseudolaeve	Total methanol / AE	*S. aureus* (ATCC 6538)	0.019	
		Methicillin-resistant S. aureus (ATCC33591)	0.156	
		S. epidermidis (ATCC 12228)	0.078	
H. thymbrifolium	Total methanol / AE	*S. aureus* (ATCC 6538)	0.039	
		Methicillin-resistant S. aureus (ATCC33591)	0.0048	
		S. epidermidis (ATCC 12228)	0.0048	
H. neurocalycinum	Total methanol / AE	*S. aureus* (ATCC 6538)	0.0048	
		Methicillin-resistant S. aureus (ATCC33591)	0.0048	
		S. epidermidis (ATCC 12228)	0.0048	
H. malatyanum	Total methanol / AE	*S. aureus* (ATCC 6538)	0.0048	
		Methicillin-resistant S. aureus (ATCC33591	0.0048	
		S. epidermidis (ATCC 12228)	0.0048	
H. jovis	EO/	*B. cereus* (human isolate)	0.0075	(Grafakou et al.,

	AE	*S. aureus* (ATCC 11632)	0.015	2020)
		E. coli (ATCC 25922)	0.0015	
		P. aeruginosa (ATCC 27853)	0.0015	
H. empetrifolium	EO/ AE	*B. cereus* (human isolate)	0.015	
		S. aureus (ATCC 11632)	0.030	
		E. coli (ATCC 25922)	0.010	
		P. aeruginosa (ATCC 27853)	0.005	
H. amblycalyx	EO/ AE	*B. cereus* (human isolate)	0.0025	
		S. aureus (ATCC 11632)	0.015	
		E. coli (ATCC 25922)	0.0025	
		P. aeruginosa (ATCC 27853)	0.0025	
H. androsaemum	Methanol (100%)/ AE	*S. aureus* (NCIMB 8625)	0.1	(Saddiqe et al., 2020)
		B. subtilis (NCIMB 1026)	0.1	
		E. coli (B 81)	0.1	
		P. aeruginosa (NCIMB 1039)	0.1	
		(ATCC 13048) *E. aerogenes*	0.1	
H. ericoides	Methanol (100%)/ AE	*S. aureus* (NCIMB 8625)	0.1	
		B. subtilis (NCIMB 1026)	0.1	
		E. coli (B 81)	0.1	
		P. aeruginosa (NCIMB 1039)	0.1	
		(ATCC 13048) *E. aerogenes*	0.1	
H. xmoserianum	Methanol (100%)/ AE	*S. aureus* (NCIMB 8625)	0.1	
		B. subtilis (NCIMB 1026)	0.1	
		E. coli (B 81)	0.1	
		P. aeruginosa (NCIMB 1039)	0.1	
		(ATCC 13048) *E. aerogenes*	0.1	
H. olympicum	Methanol (100%)/ AE	*S. aureus* (NCIMB 8625)	0.025	
		B. subtilis (NCIMB 1026)	0.025	
		E. coli (B 81)	0.025	
		P. aeruginosa (NCIMB 1039)	0.05	
		(ATCC 13048) *E. aerogenes*	0.05	
H. scabrum	EO/ AE	*P. aeruginosa* (CIP 82118)	> 0.512	(Fahed et al., 2021)
		S. aureus (ATCC 29213)	> 0.512	
H. lanceolatum	Methanol /LE	*K. pneumonia* (ATCC 13883)	0.064	(Tchakamet al., 2012)
		P. aeruginosa (ATCC 27853)	0.064	
		S. typhi (ATCC 6539)	0.032	
		E. faecalis (ATCC 10541)	0.064	
H. humifusum	Ethanol/ AE	*S. aureus* (ATCC 49444)	0.078	(Toiu et al., 2016)
		L. monocytogenes (ATCC 19114)	0.078	
		B. cereus (ATCC 11778)	0.62	
		P. aeruginosa (ATCC 27853)	0.62	
		S. typhimurium (ATCC 14028)	1.25	
		E. coli (ATCC 25922)	0.62	
H.bupleuroides	Methanol/ LE	*B. subtilis* (ATCC 6633)	0.00156	(Ceylan et al., 2020)
		S. aureus (ATCC 25923)	0.00125	
		S. epidermidis (ATCC 12228)	0.0125	
		E. coli (ATCC 25922)	0.1	
	Methanol/ FL	*B. subtilis* (ATCC 6633)	0.0002	
		S. aureus (ATCC 25923)	0.025	
		S. epidermidis (ATCC 12228)	0.0125	
		E. coli (ATCC 25922)	0.1	
H. montbretii	Methanol/ LE	*B. subtilis* (ATCC 6633)	0.0002	
		S. epidermidis (ATCC 12228)	0.00625	
	Methanol ST	*B. subtilis* (ATCC 6633)	0.0002	
		E. coli (ATCC 25922)	0.1	
Hypericum capitatum var.	Petroleum ether/ WP	*S. pyogenes* (ATCC 19615)	2	(Boga et al., 2016)
		S. aureus (ATCC 25923)	-	

capitatum		*P. aeruginosa* (ATCC 27853)	2.2	
		E. coli (ATCC 25922)	-	
	Acetone/ WP	*S. pyogenes* (ATCC 19615)	0.28	
		S. aureus (ATCC 25923)	0.25	
		P. aeruginosa (ATCC 27853)	0.3	
		E. coli (ATCC 25922)	0.015	
	Methanol/ WP	*S. pyogenes* (ATCC19615)	0.25	
		S. aureus (ATCC 25923)	0.3	
		P. aeruginosa (ATCC 27853)	0.26	
		E. coli (ATCC 25922)	0.01	

AE: Aerial parts; ST: Stem; FL: flower; LE: leaf; WP: whole plant; *S. aureus: Staphylococcus aureus; S. epidermidis: Staphylococcus epidermidis; E. coli: Escherichia coli; P. aeruginosa: Pseudomonas aeruginosa; S. pyogenes: Streptococcus pyogenes; B. subtilis: Bacillus subtilis; B. cereus: Bacillus cereus; E. aerogenes*: *Enterobacter aerogenes; K. pneumonia: Klebsiella pneumonia; S. typhimurium: Salmonella typhimurium; S. typhi: Salmonella typhi; E. faecalis: Enterococcus faecalis; L. monocytogenes: Listeria monocytogenes.*

6. Antioxidant activity of *Hypericum* species

Oxidative stress is the main cause of many diseases such as atherosclerosis, arthritis, cancer, as well as neurodegenerative diseases (Saddiqeet al., 2016).

Because some synthetic antioxidants such as BHA and BHT are now suspected of being harmful to human health (El Ouariachi et al., 2014), extensive research is being done to isolate phytochemicals that can act as antioxidants (Saddiqe et al., 2016). Many herbs used in complementary medicine have antioxidant potential (Mohammed et al., 2020). *Hypericum* species have been reported to contain many phenolic compounds and are good sources of antioxidants, making them possible to use in ethnomedicine (Ozkana et al., 2018).

The antioxidant capacity of *Hypericum* species has been well documented (Table 4). The antioxidant effect of the whole plant extracts of *H. capitatum* var. *capitatum* was tested. The results indicated that the methanolic and water extracts displayed moderate lipid peroxidation inhibitory effect in β-carotene bleaching test and strong inhibition in ABTS test. The methanolic extract also displayed stronger effect than α-Toc and BHT standards in DPPH test (Boga et al., 2016).

The antioxidant capacities of the methanolic extracts of three *Hypericum* species (*H. aviculariifolium, H. salsugineum, H. perforatum*) were evaluated. The methanolic extract of *H. salsugineum* showed the highest antioxidant effect (DPPH inhibition=88.29%) among the extracts (Maltas et al., 2013).

The antioxidant effect of *H. scabrum* and *H. origanifolium* aerial parts extracts was tested. The species showed stronger activities in DPPH test than ascorbic acid and butylated hydroxytoluene standards (Seyrekoglua et al., 2022).

When testing the antioxidant activity of any plant extract, one should take into account that this activity varies according to the plant part. Methanolic extracts of different plant parts of *H. hookerianum* (leaf, flower and aerial parts) were tested for antioxidant effect using different methods. The extract from leaf had the strongest antioxidant activity in comparison with the extracts from flowering tops and aerial parts (Chandrashekhara et al., 2009).

Table 4. *Antioxidant activity of some Hypericum species*

Species	extract/ plant part	Technique	Concentration (mg/ml)	Results	Ref.
H. perforatum	Methanol (FL)	DPPH	-	scavenging %=32	(Okmen and Balpınar, 2017)
H. perforatum	Methanol	DPPH	0.5	scavenging %=81.21 ±0.58	(Maltas, et al., 2013)
H. salsugineum	Methanol	DPPH	0.5	scavenging %=88.29 ±0.96	

H. aviculariifolium subsp. *depilatum* var. *depilatum*	Methanol	DPPH	0.5	scavenging % =86.88 ±0.87	
H. spectabile	Ethanol (AE)	DPPH	2	scavenging %=86.74	(Mohammed et al., 2020)
H. spectabile	Methanol (AE)	DPPH	-	mg/ml 0.028 0.567 ± EC50=	(Ozkan et al., 2018)
		FRAP	5	reducing power= 2.66 ± 0.031 mM Fe 2+	
H. pseudolaeve	Methanol (AE)	DPPH	-	0.036 mg/ml EC50=0.916 ±	
		FRAP	5	reducing power= 2.21 ± 0.015 mM Fe 2+	
H. thymbrifolium	Methanol (AE)	DPPH	-	EC50=0.622 ± 0.051 mg/ml	
		FRAP	5	0.036 reducing power= 2.58 ± mM Fe 2+	
H. neurocalycinum	Methanol (AE)	Anti-LPO	-	EC50= 2.49 ± 0.09 mg/ml	(Ozkan et al., 2018)
		DPPH	-	EC50= 0.251 ± 0.01 mg/ml	
		Superoxide anion	-	EC50= 0.613 ± 0.05 mg/ml	
		FRAP	5	FRAP value= 2.39 ± 0.039 mM Fe 2+	
H. malatyanum	Methanol (AE)	Anti-LPO	-	EC50= 4.82 ± 0.03 mg/ml	
		DPPH	-	EC50= 1.54 ± 0.04 mg/ml	
		Superoxide anion	-	EC50= 0.802 ± 0.03 mg/ml	
		FRAP	5	FRAP value= 2.23 ± 0.013 mM Fe 2+	
H. hookerianum	Methanol (LE)	ABTS	-	IC50= 5.60±0.30 µg/ml	(Chandrashekhar et al., 2009)
		DPPH	-	IC50= 3.30±0.05 µg/ml	
		Hydrogen peroxide	-	IC50= 58.06±1.95 µg/ml	
		Lipid per oxidation	-	IC50= 58.00±1.42 µg/ml	
	Methanol (FLT)	ABTS	-	IC50= 7.65±0.26 µg/ml	
		DPPH	-	IC50= 5.10±0.12 µg/ml	
		Hydrogen peroxide	-	IC50=117.64±5.14 µg/ml	
		Lipid per oxidation	-	IC50= 295.00±11.2 µg/ml	
	Methanol (AE)	ABTS	-	IC50= 10.90±0.32	
		DPPH	-	IC50= 5.25±0.11 µg/ml	
		Hydrogen peroxide	-	IC50= 74.14±3.82 µg/ml	
		Lipid per oxidation	-	IC50= 850.00±28.4 µg/ml	
H. androsaemum	Methanol (AE)	DPPH	-	IC50= 92.70±2.85 µg/ml	(Saddiqe et al., 2016)
		anion (super oxide)	0.5	Anion Scavenging%=33.20±1.22	
		anti-lipid peroxidation	0.5	Anti-lipid peroxidation%= 11.13±1.02	
H. androsaemum	Methanol (AE)	DPPH	-	IC50= 0.093 mg/ml	(Saddiqe et al., 2020)
H. ericoides	Ethyl acetate (AE)	DPPH	-	IC50= 0.295 mg/ml	
H. x moserianum	Ethyl acetate	DPPH	-	IC50= 0.13 mg/ml	

	(AE)				
H. olympicum	Methanol (AE)	DPPH	-	IC50= 0.098 mg/ml	
H. origanifolium	Ethyl acetate (LE)	DPPH	-	IC50= 3.37 ± 0.26 µg/ml	(Öztürk et al., 2009)
H. origanifolium	Ethanol-water (AE)	DPPH	-	IC50= 3.79 ± 0.27 µg/ml	(Seyrekoglua et al., 2022)
H. scabrum	Ethanol-water (AE)	DPPH	-	IC50= 3.65±0.40 µg/ml	
H. aucheri	Methanol (AE)	DPPH	0.01	scavenging %=58.2 ± 0.1	(Zheleva-Dimitrova et al., 2010)
		ABTS	0.01	scavenging %=65.6 ± 0.2	
H. barbatum	Methanol (AE)	DPPH	0.01	scavenging %= 31.9 ± 0.1	
		ABTS	0.01	scavenging %= 34.5 ± 0.2	
H. cerastoides	Methanol (AE)	DPPH	0.01	scavenging %=84.2 ± 0.3	
		ABTS	0.01	scavenging %=90.2 ± 0.1	
H. elegans	Methanol (AE)	DPPH	0.01	scavenging %=25.9 ± 0.1	
		ABTS	0.01	scavenging %=31.9 ± 0.2	
H. linarioides	Methanol (AE)	DPPH	0.01	scavenging %=54.2 ± 0.1	
		ABTS	0.01	scavenging %=57.8 ± 0.4	
H. maculatum	Methanol (AE)	DPPH	0.01	scavenging %=56.2 ± 0.2	
		ABTS	0.01	scavenging %=61.9 ± 0.2	
H. richeri	Methanol (AE)	DPPH	0.01	scavenging %= 49.9 ± 0.1	
		ABTS	0.01	scavenging %=55.7 ± 0.2	
H. rumeliacum	Methanol (AE)	DPPH	0.01	scavenging %= 58.9 ± 0.2	
		ABTS	0.01	scavenging %=65.2 ± 0.1	
H. tetrapterum	Methanol (AE)	DPPH	0.01	scavenging %=61.8 ± 0.2	
		ABTS	0.01	scavenging activity%=68.3 ± 0.2	
H. umbellatum	Methanol (AE)	DPPH	0.01	scavenging activity%= 49.1 ± 0.2	
		ABTS	0.01	scavenging activity%=55.9 ± 0.2	
H. humifusum	Ethanol (AE)	DPPH	-	IC50=18.51 ± 4.94 µg/ml	(Toiu et al., 2016)
H.bupleuroides	Methanol (LE)	DPPH	-	IC50=0.06 mg/ml	(Ceylan et al., 2020)
H. montbretii	Methanol (LE)			IC50=0.06 mg/ml	
H. capitatum var. *capitatum*	petroleum ether (WP)	Lipid peroxidation	-	IC50= >200 µg/ml	(Boga et al., 2016)
		DPPH	-	IC50= >200 µg/ml	
		ABTS	-	IC50= >200 µg/ml	
	acetone (WP)	Lipid peroxidation	-	IC50= >200 µg/ml	
		DPPH	-	IC50= >200 µg/ml	
		ABTS	-	IC50= 88.84 ± 1.40 µg/ml	
	methanol (WP)	Lipid peroxidation	-	IC50= 41.69 ± 1.29 µg/ml	
		DPPH	-	IC50= 16.82 ± 0.58 µg/ml	
		ABTS	-	IC50= 9.24 ± 0.28 µg/ml	
	water (WP)	Lipid peroxidation	-	IC50= 92.85 ± 1.05 µg/ml	
		DPPH	-	IC50= >200 µg/ml	
		ABTS	-	IC50=9.76 ± 0.14 µg/ml	

AE: Aerial parts; ST: Stem; FL: flower; LE: leaf; WP: whole plant; FLT: Flowering tops; Dw: dry weight

7. Conclusions

There are only few reports about the chemical composition of the genus *Hypericum*. In the current study, we compared the chemical composition of EOs isolated from different *Hypericum* species. This comparison can contribute to the addition of new criteria for chemotaxonomy to distinguish between *Hypericum* species. We have also reviewed several studies that included the isolation of chemical compounds from *Hypericum* species. We documented and classified about 100 different natural products isolated from *Hypericum* species. The isolated compounds are in the class of phenolic compounds, flavonoids and its glycosides, phloroglucinols, triterpenoid, benzophenones, naphthodianthrone and xanthones. Antibacterial and antioxidant activities of the genus have also been reviewed. There may be a need for other studies to accurately determine the components responsible for these biological activities, and to determine how to isolate and prepare them.

Conflict of Interest

There is no conflict of interest.

Author contribution

The author was responsible for conception and design of the study, acquisition of data, analysis and interpretation of data, in addition to drafting and revising the manuscript and approving it for submission

References

Abreu IN, Reis MG, Marsaioli AJ, Mazzafera P. (2004) Essential oil composition of *Hypericum brasiliense* choise. Flavour Fragr J. 19:80–82.

Alzoubi K, Abdel-Hafiz L, Khabour O, El-Elimat T, Alzubi M, Alali F. (2020) Evaluation of the Effect of *Hypericum triquetrifolium* Turra on Memory Impairment Induced by Chronic Psychosocial Stress in Rats: Role of BDNF, 14:5299-5314.

Anna, B., Maria, G., Veaceslav, K. Ion, D., and Anatolie, N., (2013) Essential Oil Chemical Composition Biodiversity in The *Hypericum* L. Species from The Spontaneous Flora of the Republic of Moldova, Muzeul Olteniei Craiova. *Oltenia. Studii si comunicari. Stiintele Naturii*, 29(2):47–52.

Anusha, K., Ganashree, N., Kruthika, G., Poojashree, R., Sushmitha, K., and Prashith, T. R. (2015) Antimicrobial and antioxidant activity of leaf and flower of *Hypericum mysorense*, *Journal of Chemical and Pharmaceutical Research*, 7(5):981–987.

Babacan EY. (2019) Volatile oils composition of *Hypericum amblysepalum* Hochst., *Hypericum spectabile* Jaub. & Spach. and *Hypericum helianthemoides* (Spach) Boiss. growing in Turkey. Pharm Chem J. 6(6):114–20.

Bagci, E., and Babacan, E. (2013) The Essential Oils of the Aerial Parts of Two *Hypericum* (H. pseudolaeve Robson and *H. thymbrifolium* Boiss. & Noë) (Guttiferae) Species from Turkey, *Journal of essential oil-bearing plants*, 13(4):390-397. DOI:10.1080/0972060X.2010.10643840.

Bagci, E., and Babacan, E. (2011) Composition of the essential oil of *Hypericum salsolifolium* Hand.- Mazz. and *Hypericum retusum* Aucher from Turkey, Acta Botanica Gallica, 158:2, 169-173, DOI: 10.1080/12538078.2011.10516264.

Balikci, N., Sarimahmut, M., Ari, F., Aztopal, N., Özel, M., Ulukaya, E., Celikler, S., (2020) Toxicity assessment of *Hypericum olympicum* subsp. *olympicum* L. on human lymphocytes and breast cancer cell lines, *Journal of Applied Biomedicine*. 18(1), 1–8. doi:10.32725/jab.2020.002.

Béjaoui A, Salem I, Rokbeni N, M'rabet Y, Boussaid M, and Boulila A. (2017) Bioactive compounds from *Hypericum humifusum* and *Hypericum perfoliatum*: inhibition potential of polyphenols with acetylcholinesterase and key enzymes linked to type-2 diabetes, Pharm Biol. 55(1):906–911. doi: 10.1080/13880209.2016.1270973.

Bejaoui, A., Salem, I., Rokbeni, N., M'rabet, Y., Boussaida M., and Boulila A., (2017) Bioactive compounds from *Hypericum humifusum* and *Hypericum perfoliatum*: inhibition potential of polyphenols with acetylcholinesterase and key enzymes linked to type-2 diabetes, Pharmaceutical Biology, 55(1):906–911. doi.org/10.1080/13880209.2016.1270973.

Bernardi A, López-Alarcón C, Aspee A, Rech S, Von Poser G.L, Bride R, and Lissp E. (2007). Antioxidant activity of flavonoids isolated from *Hypericum ternum*. Journal of the Chilean Chemical Society, 52(4), 1326-1329. dx.doi.org/10.4067/S0717-97072007000400013.

DOI: 10.21608/ZJPS.2023.220695.1050
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Bhatt, I. D., Rawat, S. and Rawal, R. (2013) Antioxidants in Medicinal Plants. Chapter 13, 295-299. doi: 10.1007/978-3-642-29974-2.

Boga, M., Ertas, A., Eroglu-Ozkan, E., Kizil, M., Ceken, B., and Topcu, G. (2016) Phytochemical analysis, antioxidant, antimicrobial, anticholinesterase and DNA protective effects of *Hypericum capitatum* var. *capitatum* extracts, South *African Journal of Botany*. 104:249–257. doi: 10.1016/j.sajb.2016.02.204.

Bridia H, Pustay A, Bordignonc S, Picoli S, Poser G, and Ferraz A. (2022) Antimicrobial activity of dimeric acylphloroglucinols isolated from southern Brazilian *Hypericum* species against to resistant bacterial, 36(24):6448-6452. DOI: 10.1080/14786419.2022.2038596.

Cakir A, Mavi A, Yıldırım A, Durub M, Harmandarb M, and Kazaz C. (2003) Isolation and characterization of antioxidant phenolic compounds from the aerial parts of Hypericum hyssopifolium L. by activity-guided fractionation. Journal of Ethnopharmacology, 87:73–83. doi:10.1016/S0378-8741(03)00112-0.

Çakir, A., Duru, M., Harmandar, M., Ciriminna, R., Passannanti, S., and Piozzi, F. (1998) Comparison of the volatile oils of *Hypericum scabrum* L. and *Hypericum perforatum* L. from Turkey, *Flavour and Fragrance Journal,* 12(4), 285-287. doi.org/10.1002/(SICI)1099-1026(199707).

Caldeira, G., Gouveia, L., Serrano, R. and Silva, O. (2022) *Hypericum* Genus as a Natural Source for Biologically Active Compounds, *Plants*, 11, 2509, 1–16. doi.org/10.3390/plants11192509.

Camas N, Radusiene J, Ivanauskas L, Jakstas V, Kayikci S, and Cirak C. (2014) Chemical composition of *Hypericum* species from the Taeniocarpium and Drosanthe sections. Plant Syst Evol. 300:953–960. DOI 10.1007/s00606-013-0934-3.

Ceylan, S., Harşit, B., Saral, Ö., Özcan, M., and Demir, I. (2020) Comparison of antioxidant and antimicrobial activities of plant extracts Centaury (*Hypericum montbretii* and *Hypericum bupleuroides*) and Blackthorn (*Paliurus spina-christi* Mill) in Artvin, Giresun region of Turkey, *Journal of Forestry Faculty*, 21(1):13–20. doi:10.17474/artvinofd.579494.

Chandrashekhar, H., Venkatesh, P., Ponnusankar, S., and Vijayan, P. (2009) Antioxidant activity of *Hypericum hookerianum* Wight and Arn, *Natural Product Research*, 23(13), 1240–1251. doi: 10.1080/14786410902885070.

Chassagne, F., Samarakoon, T., Porras, G., Lyles, J. T., Dettweiler, M., Marquez, L., Salam, A., Shabih, S., Farrokhi, D., and Quave, C., (2021) A Systematic Review of Plants with Antibacterial Activities: A Taxonomic and Phylogenetic Perspective, Frontiers in Pharmacology, 11, 1–29. doi: 10.3389/fphar.2020.586548.

Cossuta D, Vatai T, Báthori M, Hohmann J, Keve T, Simándi B. (2011) Extraction of Hyperforin and Hypericin from ST. John's Wort (*Hypericum Perforatum* L.) With Different Solvents, Journal of Food Process Engineering, 35(2):222-235. DOI: 10.1111/j.1745-4530.2010.00583.x.

Couladis M, Chinou I, Tzakou O, Petrakis P V, Cooperation G. (2003) Composition and Antimicrobial Activity of the Essential Oil of Hypericum rumeliacum subsp .apollinis (Boiss. & Heldr.). Phyther Res.17:152–154.

Crockett S, Wenzig E, Kunert O, and Bauer R. (2008) Anti-inflammatory phloroglucinol derivatives from *Hypericum empetrifolium*, Phytochemistry Letters, 1(1):37-43. doi.org/10.1016/j.phytol.2007.12.003.

Crockett SL, Kunert O, Pferschy-Wenzig E-M, Jacob M, Schuehly W and Bauer R (2016) Phloroglucinol and Terpenoid Derivatives *from Hypericum cistifolium* and *H. galioides* (Hypericaceae). Front. Plant Sci. 7:961. doi: 10.3389/fpls.2016.00961.

Daskalaki A, Grafakou M, Barda C, Kypriotakis Z, Heilmann J, Skaltsa H. (2021) Secondary metabolites from *Hypericum trichocaulon* Boiss. & Heldr., growing wild in the island of crete, 1-5. doi.org/10.1016/j.bse.2021.104294.

Demirci B, Can Baser H, Crockett S, Khan I. (2005) Analysis of the Volatile Constituents of Asian *Hypericum* L. (Clusiaceae, Hyperidoideae) Species, Journal of Essential Oil Research, 17(6):659-663.

Demirci, F., and Baser, K., (2006) Volatiles of *Hypericum bupleuroides* Griseb., *Journal of Essential Oil Research*, 18, 650–651.

Díaz JG. (2022) Chemical Composition of *Hypericum Coadunatum* Chr. from the Canary Islands. J Mol Struct. 1248:1–13. doi.org/10.1016/j.molstruc.2021.131447.

Djordjevic A, Mitic V, Stankov-Jovanovic V, and Stojanovic G. (2020) Chemical Composition, Antimicrobial Activity and Chemotaxonomy of Essential Oil of Aerial Parts of *Hypericum* *rumeliacum* Boiss. Species, Journal of Essential Oil Bearing Plants, 23(2):246-254.

Đorđević, A., (2015) Chemical Composition of *Hypericum perforatum* L. Essential Oil, *Advanced technologies*, 4(1):64–68.

El Ouariachi, E., Lahhit, N., Bouyanzer, A., Hammouti, B., Paolini, J., Majidi, L., et al. (2014) Chemical composition and antioxidant activity of essential oils and solvent extracts of *Foeniculum vulgare* Mill. from Morocco. *Journal of Chemical Pharmaceutical Research*,6(4):743–748.

Endes, Z., Uslu, N., Gümüşcü, A., and Özcan, M. (2015) Antioxidant activity of some traditionally medicinal plants from Turkey, *Journal of Agroalimentary Processes and Technologies*, 21(3):213–215.-

Fahed, L., Beyrouthy, M., Ouaini, N., Eparvier, V., Stien, D., Vitalini, S., and Iriti, M. (2021) Antimicrobial Activity and Synergy Investigation of *Hypericum scabrum* Essential Oil with Antifungal Drugs. *Molecules,* 26, 6545, 1-8. doi.org/10.3390/molecules26216545.

Gedik, O., (2022) Fixed and essential oil composition of *Hypericum venustum*, *Hypericum scabrum* and *Hypericum spectabile* species, *Progress in Nutrition*, 24(2):1–8. doi:10.23751/pn.v24i2.12172.

Gonelimali, F., Lin, J., Miao, W., Xuan, J., Charles, F., Chen, M., and Hatab, S. (2018) Antimicrobial Properties and Mechanism of Action of Some Plant Extracts Against Food Pathogens and Spoilage Microorganisms. *Frontiers in Microbiology*. 9(1639):1-9. doi:10.3389/fmicb.2018.01639.

Grafakou M, Barda C, Karikas GA, Skaltsa H. (2022) *Hypericum* Essential Oils-Composition and Bioactivities: An Update (2012–2022). molecules. 27(5246):1–21.

Grafakou, M., Diamanti, A., Antaloudaki, E., Kypriotakis, Z., ´Ciri´c, A., Sokovi´c, M., and Skaltsa, H. (2020) Chemical Composition and Antimicrobial Activity of the Essential Oils of Three Closely Related *Hypericum* Species Growing Wild on the Island of Crete, Greece, *Applied sciences*, 10, 2823:1–12. doi:10.3390/app10082823.

Gudžić B, Djokovic D, Vajs V, Palić R, Stojanovic G. (2002) Composition and antimicrobial activity of the essential oil of *Hypericum maculatum* Crantz, Flavour and Fragrance Journal, 17(5):392 -394.

Hajdari, A., Mustafa, B., Nebija, D., Kashtanjeva, A., Widelski, J., Glowniak, K., and Novak, J., (2014) Essential oil composition and variability of *Hypericum perforatum* L. from wild population in Kosovo, *Current Issues in Pharmacy and Medical Sciences*, 27(1), 51–54.doi: 10.2478/cipms-2014-0013.

Han Q, Shu G,_Cheng H, Wang S, Zhou T, et al. (2022) New Aclyphloroglucinols and geranyl-α-pyrones from *Hypericum hengshanense*, Fitoterapia, 162. doi.org/10.1016/j.fitote.2022.105253.

Happi GM, Ahmed SA, Kemayou G, Salau S, Dzouemo LC, et al. (2023) Bioassay-Guided Isolation of Antiplasmodial Compounds from Hypericum lanceolatum Lam. (Hypericaceae) and Their Cytotoxicity and Molecular Docking. Biomed Res Int. 1–9. https://doi.org/10.1155/2023/4693765.

Ion, V., Ielciu, I., Cârje A., Muntean, D., Crisan, G., and Păltinean, R., (2022) *Hypericum* spp. -An Overview of the Extraction Methods and Analysis of Compounds, *Separations,* 9, 17:1–21. doi.org/10.3390/separations9010017.

Jaimand, K., Rezaee, M., Mirza M., Naderi M., Mozaffrian V., Azadi R., Golipoor M., and Karimi S., (2013) Essential Oil Composition of Eight *Hypericum* species (Hypericaceae) from Iran: Part II, *Journal of Medicinal Plants and By-products*, 1:61–68.

Jaimand, K., Rezaee, M., Naderi, M., Mozaffrian, V., Azadi, R., Karimi, S., and Gholipoor, M. (2012) Chemical Composition of the Essential Oils of Six *Hypericum* Species (Hypericaceae) from Iran, *Journal of Medicinal Plants and By-products*, 1:7–11.

Jerkovića, I., Marasovića, M., Marijanovićb, Z., Pilepićc, K., Malešc, Ž., and Miloša, M., (2013) Chemical Composition of *Hypericum richeri* subsp. *grisebachii* Essential Oil from Croatia, *Natural Product Communications*, 8(2):231–233. doi:10.1177/1934578X1300800226.

Joujeh, R. (2020) Phytochemical and Biological Study of *Centaurea Cineraria* L. Cultivated in Syria, *Bulletin of Pharmaceutical Sciences*, 43(2):141-147.

Kebede, T., Gadisa, E., and Tufa, A. (2021) Antimicrobial activities evaluation and phytochemical screening of some selected medicinal plants: A possible alternative in the treatment of multidrug-resistant microbes. *Plos One*, 16(3):1–16. doi: 10.1371/journal.pone.0249253.

Khorshidi J, Morshedloo M, Moradi S. Essential oil composition of three Iranian *Hypericum* species collected from different habitat conditions, Biocatalysis and Agricultural Biotechnology, 2020;28: 101755.

Kırmızıbekmeza H, Bassarellob C, Piacenteb S, Celepa E, Ataya I, Mercanoğluc G and Yeşilada E. (2009) Phenolic Compounds from *Hypericum calycinum* and Their Antioxidant Activity. Nat Prod Commun. 4(4):531–534.

Koç E, Arabaci T. (2021) Antioxidant Capacity and Essential Oil Composition of *Hypericum thymopsis* Boiss. (Hypericaceae) from Turkey. Hacettepe J Biol Chem. 49(4):385–390.

Kowa TK, Tchokouaha LRY, Nyemb JN, Wabo HK, Tchinda AT, Appiah-opong R, et al. (2020) Antipromastigote and cytotoxic activities of some chemical constituents of *Hypericum lanceolatum* Lam. (Guttifereae). J Appl Pharm Sci. 10(1):26–32. DOI: 10.7324/JAPS.2020.101004.

Krishnaiah, D., Sarbatly, R., and Nithyanandam, R. (2011) A review of the antioxidant potential of medicinal plant species, *Food and Bioproducts Processing*, 8 9:217–233. doi: 10.1016/j.fbp.2010.04.008.

Maltas, E., Uysal, A., Yildiztugay, E., Aladag, M., Yildiz, S., and Kucukoduk, M., (2013) Investigation of Antioxidant and Antibacterial Activities of Some *Hypericum* Species, *Fresenius Environmental Bulletin*, 22, 3a, 862–869.

Miguel M, Moisela M, Brel O, Bourdy G, Cruza M, Dionicio I, Carraz M, Jullian V. (2018) Xanthones from *Hypericum laricifolium* Juss., and Their Antiproliferative Activity Against HEP3B Cells. Rev Soc Quím Perú. 84(4):428–435.

Mimica-Dukića, N., and Božin, B., (2007) Natural Product Communications Essential Oils from Lamiaceae Species as Promising Antioxidant and Antimicrobial Agents, *Natural Product Communications*., 2(4), 445-452.

Mohammed, F. S., Şabik, A., Dogan, M., Selamoglu, Z., and Sevindik, M. (2020) Antioxidant Potential of *Hypericum spectabile* JAUB. ET SPACH, *Bulletin of Biotechnology*, 1(2):43–45.

Morshedloo, M., Yazdani, D., and Aghayi, F. (2014) Chemical Composition of the Essential Oil from *Hypericum patulum* Thunb. Cultivated in Iran, *Journal of Essential Oil Bearing Plants*, 17(1), 131-135. doi.org/10.1080/0972060X.2013.862076.

Nguemo RBT, Njouendou AJ, Mpetga JDS, Kengne IC, Nago RDT, Fobofou SAT, et al. (2020) Antimicrobial activities of chemical constituents from the flowers of *Hypericum lanceolatum* Lam. (Hypericaceae). Int J Appl Microbiol Biotechnol Res. 8:66–72. doi.org/10.33500/ ijambr.2020.08.007.

Okmen, G., and Balpınar, N. (2017) The Biological Activities of *Hypericum perforatum* L., *African Journal of Traditional, Complementary and Alternative Medicines*, 14(1):213–218. doi: 10.21010/ajtcam.v14i1.23.

Özkan E., Demirci, B, Gürer, Ç., Kültür, Ş, Mat, A., and Başer, K., (2013) Essential Oil Composition of Five Endemic *Hypericum* Species from Turkey. *Medicinal & Aromatic Plants*, 2:121, 1-4. doi:10.4172/2167-0412.1000121.

Özkan, E., ÇelİK, B., and Mat, A., (2019) Antimicrobial activities of five endemic Hypericum species from Anatolia compared with *Hypericum perforatum*, *Journal of Research in Pharmacy*, 23(1):114–119. doi.org/10.12991/jrp.2018.115.

Ozkan, E., Ozden, T., Ozsoy, N., and Mat, A. (2018) Evaluation of chemical composition, antioxidant and anti-acetylcholinesterase activities of *Hypericum neurocalycinum* and *Hypericum malatyanum*, *South African Journal of Botany*, 114, 104-110. doi.org/10.1016/j.sajb.2017.10.022.

Ozkan, E., Ozsoy, N., Ozden, T., Ozhan, G., and Mat, A. (2018) Evaluation of Chemical Composition and In-vitro Biological Activities of Three Endemic *Hypericum* Species from Anatolia (*H. thymbrifolium*, *H. spectabile* and *H. pseudolaeve*), *Iranian Journal of Pharmaceutical Research*, 17(3), 1036–1046.

Öztürk, N., Tunçel M., and Potoğlu-Erkara, İ. (2009) Phenolic compounds and antioxidant activities of some *Hypericum* species: A comparative study with *H. perforatum*, *Pharmaceutical Biology*, 47(2), 120–127. doi:10.1080/13880200802437073.

Patiño-bayona WR, Plazas E, Bustos-cortes J, Prieto-rodríguez JA, Patiño-Ladino O. Essential Oils of Three *Hypericum* Species from Colombia: Chemical Composition, Insecticidal and Repellent Activity Against Sitophilus zeamais Motsch. (Coleoptera: Curculionidae). Rec Nat Prod. 2020;1–11.

Radulović, N., and Blagojević P. (2012) Chemical Composition of Hypericum rumeliacum Boiss. Essential Oil. A New Chemotype of This Pharmacologically Valuable Species?, *Chemistry and Biodiversity*, 9(10), 2324-2341. doi.org/10.1002/cbdv.201200139.

Ramírez-gonzález I, Amaro-luis JM, and Bahsas A. (2013) Xanthones from aerial parts of *Hypericum laricifolium* Juss. Nat Prod Commun. 8(12):1731–2. doi.org/10.1177/1934578X1300801218.

Rocha L, Marston A, Potterat O, Kaplan M, Stoeckli-Evans H, and Hostettmann K. (1995) Antibacterial phloroglucinols and flavonoids from *Hypericum brasiliense,* Phytochemistry, 40(5):1447-1452. https://doi.org/10.1016/0031-9422(95)00507-4.

Rojas, J., Buitrago, A., Rojas, L., and Morales, A., (2013) Chemical Composition of *Hypericum laricifolium* Juss. Essential Oil Collected from Mérida-Venezuela. *Medicinal & Aromatic Plants*, 2:132. doi:10.4172/2167-0412.1000132.

Rouis, Z., Elaissi, A., Abid, N., Lassoued, M., Cioni, P., Flamini, G., and Aouni, M., (2011) Volatile Components of *Hypericum humifusum*, *Hypericum Perfoliatum* and *Hypericum ericoides* by HS-SPME-GC and HS-SPME-GCMS Using NANO Scale Injection Techniques, *Digest Journal of Nanomaterials and Biostructures*, 6(4):1919–1928.

Rath G, Potterat O, Mavi S, Hostettmann K. (1996) Xanthones from *Hypericum roeperanum*, Phytochemistry, 43(2):513-520. doi.org/10.1016/0031-9422(96)00284-1.

Saddiqe, Z., Maimoona, A., Abbas, G., Naeem, I., and Shahzad, M., (2016) Pharmacological screening of *Hypericum androsaemum* extracts for antioxidant, anti-lipid peroxidation, antiglycation and cytotoxicity activity, *Pakistan Journal of Pharmaceutical Sciences*, 29(2):397–405.

Saddiqe, Z., Naeem, I., Hellio, C., Patel, A., and Abbas, G. (2020) Phytochemical profile, antioxidant and antibacterial activity of four *Hypericum* species from the UK, *South African Journal of Botany*, 133(3):45-53. doi.org/10.1016/j.sajb.2020.05.018.

Sajjadi, S., Mehregan, I. and Taheri, M. (2015) Essential oil composition of *Hypericum triquetrifolium* Turra growing wild in Iran, *Research in Pharmaceutical Sciences*, 10(1):90–94.

Sanna C, Scognamiglio M, Fiorentino A, Corona A, Graziani V, Caredda A, et al. (2018) Prenylated phloroglucinols from Hypericum scruglii, an endemic species of Sardinia (Italy), as new dual HIV-1 inhibitors effective on HIV-1 replication. PLoS ONE 13(3): e0195168. doi.org/10.1371/journal.pone.0195168

Santos P, Figueiredo A, Barroso J, Pedro L, Scheffer J. Composition of the essential oil of *Hypericum foliosum* Aiton from five Azorean islands, Flavour and Fragrance Journal, 1999;14(5):283-286.

Selvamohan, T., Ramadas V., and Kishore, S. (2012) Antimicrobial activity of selected medicinal plants against some selected human pathogenic bacteria, *Advances in Applied Science Research*, 3(5):3374–3381.

Senkal B, Uskutoglu T. Investigation of the change in essential oil components with the composition of fatty acids from *Hypericum heterophyllum* Vent., an endemic species in Turkey, *Authorea*. 2020.

Seyrekoglua, F., Temizb, H., Esera, F., and Yildirim, C., (2022) Comparison of the antioxidant activities and major constituents of three Hypericum species (*H. perforatum*, *H. scabrum* and *H. origanifolium*) from Turkey, *South African Journal of Botany*, 146:723–727. doi:10.1016/j.sajb.2021.12.012.

Silva, A., Taofiq, O., Ferreira, I., and Barros, L., (2021) Hypericum genus cosmeceutical application–A decade comprehensive review on its multifunctional biological properties, *Industrial Crops and Products*, 159, doi.org/10.1016/j.indcrop.2020.113053.

Tchakam, P., Lunga, P., Kowa, T., Lonfouo, A., Wabo, H., Tapondjou, L., Tane, P., and Kuiate, J., (2012) Antimicrobial and antioxidant activities of the extracts and compounds from the leaves of *Psorospermum aurantiacum* Engl. and *Hypericum lanceolatum* Lam., *BMC Complementary and Alternative Medicine*, 12, 136:1–8. doi:10.1186/1472-6882-12-136.

Toiu, A., Vlase, L., Drăgoi, C., Vodnar, D., and Oniga, I., (2016) Phytochemical Analysis, Antioxidant and Antibacterial Activities of *Hypericum humifusum* L. (Hypericaceae), *FARMACIA*, 64(5):663–667.

Tusevski O, Krstikj M, Stanoeva JP, Stefova M, Simic SG. (2018) Phenolic profile and biological activity of *Hypericum perforatum* L.: Can roots be considered as a new source of natural compounds? South African J Bot. 117:301–310. https://doi.org/10.1016/j.sajb.2018.05.030.

Vaou, N., Stavropoulou, E., Voidarou, C., Tsigalou, C., and Bezirtzoglou, E. (2021) Towards Advances in Medicinal Plant Antimicrobial Activity: A Review Study on Challenges and Future Perspectives, *Microorganisms*, 9(10), 2041. doi:10.3390/microorganisms9102041.

Yüce-Babacan, and E., Bagci, E., (2017) Essential oil composition of *Hypericum uniglandulosum* Hausskn. ex Bornm. and *Hypericum lydium* Boiss. from Turkey, *International Journal of Nature and Life Sciences*, 1(1): 12–16.

Zdunica G, Godjevacb D, Savikina K and Petrovicc S. (2017) Comparative Analysis of Phenolic Compounds in Seven Hypericum Species and Their Antioxidant Properties. Nat Prod Commun. 12(11):1805–1811.

Zheleva-Dimitrova, D., Nedialkov, P., and Kitanov, G. (2010) Radical scavenging and antioxidant activities of methanolic extracts from *Hypericum* species growing in Bulgaria, *Pharmacognosy Magazine*, 6(22):74–78. doi: 10.4103/0973-1296.62889.

Zofou D, Kowa T.K, Wabo H.K. *et al. Hypericum lanceolatum* (Hypericaceae) as a potential source of new anti-malarial agents: a bioassay-guided fractionation of the stem bark. *Malar J* 10, 167 (2011). https://doi.org/10.1186/1475-2875-10-167.