

Phytochemistry and some biological activities of the Genus Hypericum

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ABSTRACT

Medicinal plants are the best source of medicines. 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.

Keywords : *Hypericum*, *Hypericaceae*, chemical composition, antibacterial, antioxidant.

Running title :An Overview of *Hypericum* Species

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 Balpinar, 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 Balpinar, 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 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*.

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 (Seyrekoglu 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 (Seyrekoglou et al., 2022).

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).

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 EO 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* EO. Spathuleneol was also identified in the EO of *H. pseudolaeve*, *H. thymbrifolium*, *H. kotschyanum*, *H. richeri*, *H. thymopsis*, *H. scabroides*. hexadecanoic acid was identified in

the EO of *H. scabroides*, *H. uniglandulosum*, *H. kotschyanum*, *H. salsugineum*.

Table 1. Chemical composition of *Hypericum* essential oils

Species	Plant part	Main compounds	Ref.
<i>H. elegans</i>	AE	g-gurjunene, aromadendrene, and undecane	(Anna et al., 2013)
<i>H. tetrapterum</i>	AE	Copaene, α -longipinene, cadinene	
<i>H. hirsutum</i>	AE	caryophyllene oxide, phytol, α -caryophyllene and undecane	
<i>H. perforatum</i>	AE	β -caryophyllene, caryophyllene oxide, α -pinene, β -cadinene, and β -pinene	
<i>H. scabrum</i>	AE	α -pinene, β -caryophyllene, myrcene, cadalene and β -pinene	(Çakir et al., 1998)
<i>H. scabroides</i>	AE	hexadecanoic acid, spathulenol, nonacosane, dodecanoic acid, baeckeol and γ -muurolene	(Özkan Demirci et al., 2013)
<i>H. kotschyanum</i>	AE	α -pinene, nonacosane, hexadecanoic acid, β -pinene, spathulenol and limonene	
<i>H. salsugineum</i>	AE	nonacosane, hexadecanoic acid and baeckeol	
<i>H. thymopsis</i>	AE	α -pinene, baeckeol, spathulenol, limonene and camphene	
<i>H. uniglandulosum</i>	AE	2,6-Dimethyl-3,5-heptadien-2-one, nonacosane, hexadecanoic acid and α -pinene	
<i>H. uniglandulosum</i>	AE	α -pinene, undecane, benzoic acid, cyclohexasiloxane	(Yüce-Babacan et al., 2017)

<i>H. lydium</i>	AE	α-pinene, β-pinene, β-myrcene		<i>H. patulum</i>	AE	β-pinene, α-pinene, limonene and α-humulene	(Morshedloo et al., 2014)
<i>H. thymopsis</i>	AE	α-pinene, spathulenol, limonene	(Koç and Arabaci, 2021)	<i>H. laricifolium</i>	AE	α-pinene, verticiol, 3-methyl-nonane, 2-methyl-octane and nonane	(Rojas et al., 2013)
<i>H. perforatum</i>	AE	(germacrene D); ((E)-caryophyllene); (2-methyloctane); (α-pinene) and (bicyclogermacrene)	(Đorđević, 2015)	<i>H. rumeliacum</i>	AE	undecane, dodecanal, and germacrene D	(Radulović and Blagojević, 2012)
<i>H. perforatum</i>	FL	(E- β - farnesene); (n-hexadecanal); (E-nerolidol)		<i>H. rumeliacum</i>	AE	(E)-β-ocimene, β-pinene, (Z)-β-ocimene, dodecanal, germacrene D, myrcene	(Đjordjević et al., 2020)
<i>H. dogonbadanicum</i>	FL	(phenyl ethyl octanoate); (terpin-4-ol); (α-phellandrene)		<i>H. rumeliacum</i>	AE	α-pinene, β-pinene, dehydro-aromadendrene, α-copaene	(Couladis et al., 2003)
	LE	β-pinene, α-pinene and p-cymene		<i>H. lydium</i>	AE	α -pinene, β -pinene and β -myrcene	(Yüce-Babacan and Bagci, 2017)
<i>H. helianthemoides</i>	FL	α -pinene, Z- β -ocimene and β -pinene		<i>H. ericoides</i>	AE	n-nonane, n-undecane, α-cubebene, α-pinene	(Rouis, et al., 2011)
<i>H. hyssopifolium</i>	FL	α -pinene, β -pinene and n-tetradecan		<i>H. androsaemum</i>	AE	longifolene, β-gurjunene, and γ-gurjunene	
	LE	E-nerolidol, n-tetradecane and α -himachalene		<i>H. apricum</i>	AE	cis-piperitol acetate, p-cymenene, α-pinene	
<i>H. lysimachioides</i>	FL	α -pinene, Z- β -ocimene and n-tetradecane		<i>H. armenum</i>	AE	γ -cadinene, longifolene, E-nerolidol	
<i>H. triquetrifolium</i>	FL	n-tetradecane, α -himachalene and α -pinene		<i>H. asperulum</i>	AE	α -muurolol, cis-sesquisabienen hydrate, germacrene B	
	LE	α -himachalen, n-tetradecane and n-pentadecane		<i>H. hirsutum</i>	AE	germacrene B, citronellyl propanoate, γ -gurjunene	
<i>H. triquetrifolium</i>	AE	Germacrene-D, β -caryophyllene, δ -cadinene, trans-β -farnesene, α -humulene, β -selinene, γ -cadinene and trans-phytol	(Sajjadi et al., 2015)	<i>H. linarioides</i>	AE	(E, E)-farnesyl acetate, cis-cadinene ether, 1-tridecene	
<i>H. richeri</i>	AE	germacrene D, bicyclogermacrene, α-pinene, β-pinene, decanoic acid, β -caryophyllene, δ -cadinene, spathulenol and tetracosane	(Jerkovića, et al., 2013)	<i>H. tetrapterum</i>	AE	trans-linalool oxide, p-cymenene, (E, E)-farnesyl acetate	
				<i>H. vermiculare</i>	AE	α -pinene, myrcyne, E- β -	

<i>H. asperulum</i>	AE	farnesene (α -pinene); (caryophyllene oxide); (E -caryophyllene) and (spathulenol)	(Khorshidi et al., 2020)	<i>H. heterophyllum</i>	AE	caryophyllene germacrene-D, bicyclogermacrene, d-cadinene, spathulenol, α -guaiene, and valencene	(Senkal and Uskutoglu, 2020)
<i>H. scabrum</i>	AE	(α -pinene); (β -pinene); (limonene) and (E -caryophyllene)		<i>H. amblysepalum</i>	AE	δ -3-carene, caryophyllene-oxide, cis-ocimene, β -caryophyllene, α -pinene	(Babacan, 2019)
<i>H. vermiculare</i>	AE	(α -pinene); (caryophyllene oxide); (E -caryophyllene) and (spathulenol)		<i>H. spectabile</i>	AE	β -caryophyllene, germacrene D, α -cadinol, caryophyllene oxide	
<i>H. pseudolaeve</i>	AE	(trans-caryophyllene); (δ -limonene); (α -cadinol); (caryophyllene oxide); (α -pinene); (spathulenol) and (β -selinene)	(Bagci and Babacan, 2013)	<i>H. helianthoides</i>	AE	α -pinene, δ -3-carene, d-limonene, cis-ocimene, undecane	(Demirci et al., 2005)
<i>H. thymbrifolium</i>	AE	α -pinene, undecane, germacrene D, β -pinene, β -myrcene, spathuleneol, naphthalane		<i>H. acmosepalum</i>	AE	(ar-curcumene); (β -selinene)	
<i>H. humifusum</i>	AE	(n-undecane); (α -pinene); (β -pinene); (limonene); (myrcene)	(Rouïs, et al., 2011)	<i>H. beanii</i>	AE	(γ -muurolene); (β -selinene); (caryophyllene oxide)	
<i>H. bupleuroides</i>	AE	(β -sesquiphellandrene); (β -caryophyllene); (selina-3,7(11)-diene); (γ -elemene); (undecane); (germacrene-B)		<i>H. calycinum</i>	AE	α -terpineol, P-pinene	
<i>H. gaitii</i>	AE	α -pinene, allo-aromadendrene, δ -cadinene, n-nonane, β -caryophyllene, α -selinene	(Grafakou et al., 2022)	<i>H. choisyanum</i>	AE	cis-eudesma-6,11-diene	(Bagci and Babacan, 2011)
<i>H. mexicanum</i>	AE	n-nonane, α -pinene		<i>H. forrestii</i>	AE	α -pinene, caryophyllene oxide	
<i>H. myricariifolium</i>	AE	α -pinene, β -caryophyllene	(Patiño-bayona et al., 2020)	<i>H. kouytchense</i>	AE	cis- β -guiaene, γ -muurolene	
<i>H. juniperinum</i>	AE	n-nonane, α -pinene, geranyl acetate, and β -		<i>H. lancasteri</i>	AE	β -selinene, eudesmadienone	
				<i>H. leschenaultii</i>	AE	(Cuparene) and (γ -muurolene)	
				<i>H. monogynum</i>	AE	Tricosane, myrcene	
				<i>H. patulum</i>	AE	β -selinene	
				<i>H. pseudohenryi</i>	AE	β -selinene	
				<i>H. X moserianum</i>	AE	γ -muurolene, δ -cadinene	
				<i>H. salsolifolium</i>	AE	α -pinene, limonene, spathulenol, β -pinene, germacrene D	
				<i>H. retusum</i>	AE	α -pinene, limonene, spathulenol, β -pinene,	

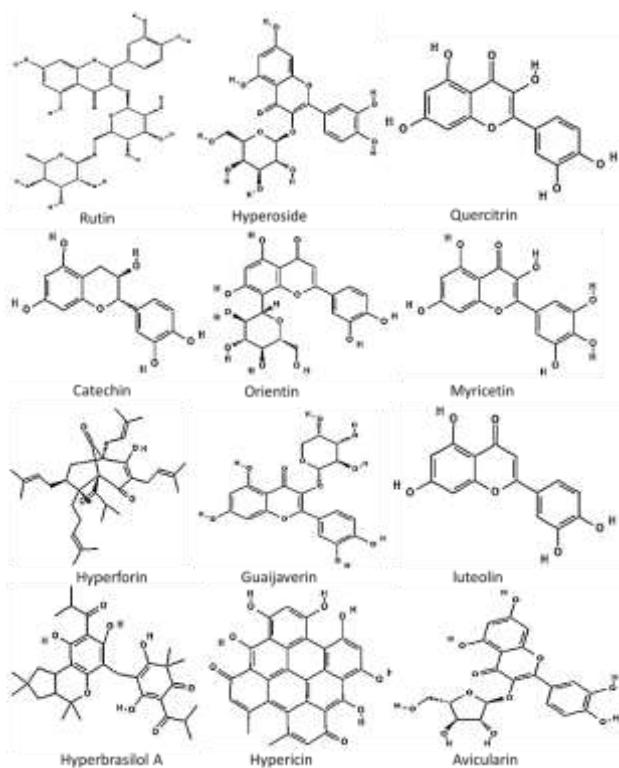
		germacrene D	
<i>H. maculatum</i>	-	β -farnesene, n-undecane, β -caryophyllene, δ -cadinene, muurolene	(Gudžić et al., 2002)
<i>H. foliosum</i>	-	n-nonane, limonene, terpinolene, β -caryophyllene, β -pinene	(Santos et al., 1999)
<i>H. brasiliense</i>	WP	β -Caryophyllene, α -Humulene, Caryophyllene oxide, Cubenol, aromadendrene	(Abreu et al., 2004)

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

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, environment, ontogeny, season, analytical method (Hajdari, et al., 2014), geographical distribution, type of glands and phenological cycle (Jerković et al., 2013).

Figure 1:Chemical structure of some compounds isolated from *Hypericum* species



For instance, the *H. perforatum* EO extracted from aerial parts obtained from the Republic of Moldova contained β -caryophyllene, caryophyllene oxide, α -pinene, β -cadinene, and β -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, β -pinene and p-cymene as its main compounds.

The flowers oil of *H. hyssopifolium* was quite different from the leaves oil. α -Pinene, β -

pinene and n-tetradecan were the main compounds of the flowers oil, where the leaves contained E-nerolidol, n-tetradecane and α -himachalene.

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.

Table 2. Compounds isolated from Hypericum species

Compound	Plant species	Plant part	Ref.
Phenolic compounds			
β -geranyl-1-(2'-methylbutanoyl) phloroglucinol	<i>H. ascyron</i>	AE	(Sanna et al., 2018)
β -geranyl-1-(2'-acetylbutanoyl) phloroglucinol	<i>H. ascyron</i>	FR	(Crockett et al., 2018)
β -geranyl-1-(2'-acetylpropanoyl) phloroglucinol	<i>H. ascyron</i>	AE	(Sanna et al., 2018)
3-(1,3-bis(2-hydroxy-3- β -methylbutanoyl) phloroglucinol)	<i>H. ascyron</i>	FR	(Crockett et al., 2018)
α -chlorogenic acid	<i>H. ascyron</i>	AE	
β -chlorogenic acid	<i>H. ascyron</i>	AE	(Dakalaki et al., 2022)
Quercetin B	<i>H. ascyron</i>	AE	
Quercetin A	<i>H. ascyron</i>	AE	
Luteolin B	<i>H. ascyron</i>	AE	
Luteolin A	<i>H. ascyron</i>	LE - FL	(Rocha et al., 1995)
Hyperinsol B			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Hyperinsol B			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Hyperinsol A			
<i>H. ascyron</i>	LE - FL		(Bodda et al., 1955)
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Isotropetransol B			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Antrobaanol B			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Isotrobaanol B			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Antrobaanol A			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		
Benzodrol A			
<i>H. ascyron</i>	AE		
Tapozicole A			
<i>H. ascyron</i>	AE		
<i>H. ascyron</i>	AE		

	<i>H. brasiliense</i>	LE - FL	(Rocha et al., 1993)
hesperidin A	<i>H. brasiliense</i>	AE	(Bian et al., 2022)
<i>H. pedunculatum</i>		-	(Camara et al., 2011)
<i>H. pedunculatum</i>		PLS	(Tsuwaki et al., 2018)
Hyperforin	<i>H. brasiliense</i>	AE	(Bian et al., 2017)
<i>H. canariense</i>		FL	
<i>H. pyrenaicum</i>		FL	
<i>H. dolomiticum</i>		FL	
affroforin	<i>H. canariense</i>	FL	
<i>H. pyrenaicum</i>		FL	
<i>H. dolomiticum</i>		FL	
3-(6-hydroxy-2,4-dimethoxyphenyl)-2-methyl-3- β -propanone	<i>H. canariense</i>	AE	(Crockett et al., 2016)
hydroquinone	<i>H. canariense</i>	STB	(Kame et al., 2020)
3-O-Caffeoylquinic acid (chlorogenic acid)	<i>H. nobilis</i>	AE	
<i>H. pedunculatum</i>		AE	
<i>H. brasiliense</i>		AE	
<i>H. canariense</i>		AE	
<i>H. pyrenaicum</i>		AE	
<i>H. dolomiticum</i>		AE	
<i>H. confertum</i>		ST- LE- FL	
<i>H. pyrenaicum</i>		ST- LE- FL	
<i>H. brasiliense</i>		ST- LE- FL	
<i>H. gracilescens</i>		ST- LE- FL	
<i>H. pedunculatum</i>		ST- LE- FL	
<i>H. pilosum</i>		LE- FL	
<i>H. ascyron</i>		ST- LE- FL	
<i>H. lycium</i>		LE- FL	
<i>H. pedunculatum</i>		PLS	(Tsuwaki et al., 2018)
4-O-Caffeoylquinic acid	<i>H. barbatum</i>	AE	
<i>H. nobilis</i>		AE	
5-O-Caffeoylquinic acid	<i>H. barbatum</i>	AE	
<i>H. pedunculatum</i>		AE	
Neochlorogenic acid	<i>H. brasiliense</i>	AE	
<i>H. confertum</i>		ST- LE- FL	
<i>H. pyrenaicum</i>		ST- LE- FL	
<i>H. brasiliense</i>		ST- LE- FL	
<i>H. canariense</i>		ST- LE- FL	
<i>H. pyrenaicum</i>		ST- LE- FL	
<i>H. dolomiticum</i>		ST- LE- FL	
<i>H. confertum</i>		LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. lycium</i>		LE- FL	
<i>H. confertum</i>		LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. dolomiticum</i>		LE- FL	
<i>H. confertum</i>		LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. lycium</i>		LE- FL	
Caffeic acid	<i>H. confertum</i>	LE- FL	
<i>H. pyrenaicum</i>		FL	
<i>H. brasiliense</i>		FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. confertum</i>		ST- LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. lycium</i>		LE- FL	
2,4-dihydroxybenzoic acid	<i>H. confertum</i>	ST- LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. pyrenaicum</i>		ST- LE- FL	
<i>H. dolomiticum</i>		FL	
<i>H. confertum</i>		LE- FL	
<i>H. pyrenaicum</i>		LE- FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. lycium</i>		LE- FL	
3,4-dihydroxybenzoic acid	<i>H. ascyron</i>	AE	(Sanna et al., 2018)
Quinic acid	<i>H. pedunculatum</i>	PLS	
3-p-Coumaroylquinic acid	<i>H. pedunculatum</i>	PLS	(Tsuwaki et al., 2018)
3-Feruloylquinic acid	<i>H. pedunculatum</i>	PLS	
Triterpenoids			
amurensin	<i>H. confertum</i>	LE- FL	
<i>H. pyrenaicum</i>		FL	
<i>H. brasiliense</i>		LE- FL	
<i>H. pyrenaicum</i>		ST- LE- FL	
<i>H. dolomiticum</i>		LE- FL	

	<i>H. acutum</i>	PL	
	<i>H. dolium</i>	LE - PL	
Rhamn (quercitin 3-O-galactoside)	<i>H. perforatum</i>	PLS	(Tuneski et al., 2018)
	<i>H. ligustrinifolium</i>	AE	(Alrooki et al., 2020)
	<i>H. richeri</i>		
	<i>H. perforatum</i>	AE	(Zdunica et al., 2017)
	<i>H. acutum</i>		
	<i>H. corymbosum</i>	ST - LE - PL	
	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. dolium</i>	ST - LE - PL	
	<i>H. trichocalyx</i>	AE	(Baskalaki et al., 2022)
	<i>H. corymbosum</i>	-	(Kumazaki et al., 2009)
Hippocrate (quercitin 3-O-galactoside)	<i>H. perforatum</i>	PLS	(Tuneski et al., 2018)
	<i>H. trichocalyx</i>	AE	(Baskalaki et al., 2022)
	<i>H. richeri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. ligustrinifolium</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. perforatum</i>	LE - PL	(Rocha et al., 1995)
	<i>H. acutum</i>	-	(Bernardi et al., 2007)
	<i>H. confertum</i>	ST - LE - PL	(Camara et al., 2014)
Quercitin (quercitin 3-O-galactoside)	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	
	<i>H. glaucum</i>	ST - LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. dolium</i>	ST - LE - PL	
	<i>H. calycinum</i>	-	(Kumazaki et al., 2009)
	<i>H. perforatum</i>	PLS	(Tuneski et al., 2018)
	<i>H. confertum</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	PL	
	<i>H. perforatum</i>	ST - LE - PL	
	<i>H. glaucum</i>	LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. dolium</i>	LE	
Quercitin (quercitin 3-O-dimethylsides)	<i>H. richeri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. ligustrinifolium</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. trichocalyx</i>	AE	(Baskalaki et al., 2022)
	<i>H. perforatum</i>	LE - PL	(Rocha et al., 1995)
	<i>H. calycinum</i>	-	(Kumazaki et al., 2009)
Inquinatina	<i>H. richeri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. ligustrinifolium</i>	AE	
	<i>H. ligustrinifolium</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. perforatum</i>	LE	
	<i>H. calycinum</i>	-	(Kumazaki et al., 2009)

	<i>H. acutum</i>	-	(Bernardi et al., 2007)
	<i>H. brevifoliae</i>	LE - PL	(Rocha et al., 1995)
	<i>H. confertum</i>	ST - LE - PL	
	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	(Camara et al., 2014)
	<i>H. glaucum</i>	ST - LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	-	(Kumazaki et al., 2009)
Quercetin	<i>H. perforatum</i>	PLS	(Tuneski et al., 2018)
	<i>H. ligustrinifolium</i>	AE	(Gakis et al., 2003)
	<i>H. confertum</i>	ST - LE - PL	
	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	(Camara et al., 2014)
	<i>H. glaucum</i>	ST - LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	-	(Rocha et al., 1995)
	<i>H. ligustrinifolium</i>	AE	(Miguel et al., 2018)
	<i>H. richeri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. barbata</i>	AE	
	<i>H. ligustrinifolium</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. perforatum</i>	LE - PL	
	<i>H. ligustrinifolium</i>	AE	
Quercetin 3-anethol ether	<i>H. acutum</i>	-	(Zdunica et al., 2017)
Quercetin 3,7-dimethyl ether	<i>H. acutum</i>	-	(Bernardi et al., 2007)
Quercetin-3-O- <i>o</i> -methylflavanone	<i>H. ligustrinifolium</i>	AE	
Quercetin-3-O- <i>B</i> -d-galactopyranoside	<i>H. ligustrinifolium</i>	AE	(Gakis et al., 2003)
Quercetin-3-O- <i>O</i> - <i>d</i> -galactopyranoside- <i>7</i> - <i>O</i> - <i>B</i> -d-glucopyranoside	<i>H. ligustrinifolium</i>	AE	
Aviculam	<i>H. confertum</i>	ST - LE - PL	
	<i>H. dumosifolium</i>	ST - LE	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	LE - PL	
	<i>H. glaucum</i>	PL	
	<i>H. acutum</i>	PL	
	<i>H. ligustrinifolium</i>	PL	
	<i>H. confertum</i>	ST - LE - PL	
Cacectan	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	
	<i>H. glaucum</i>	ST - LE - PL	
	<i>H. acutum</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	PLS	(Tuneski et al., 2018)
	<i>H. calycinum</i>	-	(Kumazaki et al., 2009)
Epicatexio	<i>H. confertum</i>	ST - LE - PL	
	<i>H. dumosifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. perforatum</i>	ST - LE - PL	(Camara et al., 2014)
	<i>H. ligustrinifolium</i>	ST - LE - PL	
	<i>H. ligustrinifolium</i>	ST - LE - PL	

	<i>H. jordanicum</i>	ST- LE- FL	
	<i>H. galileeum</i>	ST- LE- FL	
	<i>H. zeyheri</i>	ST- LE- FL	
	<i>H. luteum</i>	ST- LE- FL	
	<i>H. cylindrum</i>	-	(Kumamoto et al., 2009)
	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
Amarilla/avene	<i>H. confertum</i>	LE- FL	(Camaras et al., 2014)
	<i>H. perforatum</i>	FLS	
Cyanidin 3-O-glycoside	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
Cyanidin 3-O-dammoside	<i>H. perforatum</i>	FLS	
miquelianin	<i>H. calycinum</i>	-	(Kumamoto et al., 2009)
myricetin	<i>H. trichosodon</i>	AE	(Dankalaki et al., 2022)
myricetin	<i>H. lancifolium</i>	FL	(Gigueme et al., 2020)
orientin	<i>H. confertum</i>	AE	(Diaz, 2022)
	<i>H. Alpinum</i>	AE	(Zdzienica et al., 2017)
2'-O-Acetyl-orientin	<i>H. Alpinum</i>	AE	
D-III Flavonoids	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
	<i>H. richieri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. barbatum</i>	AE	
	<i>H. gracilem</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. lanceolatum</i>	FL	(Gigueme et al., 2020)
	<i>H. hyperosideum</i>	AE	(Cakir et al., 2005)
D-IV Flavonoids	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
	<i>H. richieri</i>	AE	
	<i>H. perforatum</i>	AE	
	<i>H. barbatum</i>	AE	
	<i>H. gracilem</i>	AE	
	<i>H. acutum</i>	AE	
	<i>H. maculatum</i>	AE	
	<i>H. lanceolatum</i>	FL	(Gigueme et al., 2020)
	<i>H. hyperosideum</i>	AE	(Cakir et al., 2005)
D-V Flavonoids	<i>H. perforatum</i>	AE	(Dankalaki et al., 2022)
	<i>H. galileeum</i>	-	(Bernardi et al., 2007)
	<i>H. calycinum</i>	-	(Kumamoto et al., 2009)
Mycetin 3-O-rutinoside	<i>H. richieri</i>	AE	
Mycetin 3-O-galactoside	<i>H. richieri</i>	AE	(Zdzienica et al., 2017)
Mycetin 3-O-glucoside	<i>H. richieri</i>	AE	
luteolin	<i>H. brunnescens</i>	LE - FL	(Rocha et al., 1995)
Kaempferol 3-O-rutinoside	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
Kaempferol 3-O-D-glucopyranoside	<i>H. lancifolium</i>	FL	(Gigueme et al., 2020)
kaempferol	<i>H. brunnescens</i>	LE - FL	(Rocha et al., 1995)
friedmannone	<i>H. lancifolium</i>	FL	(Gigueme et al., 2020)
friedmann-3-O-ol	<i>H. lancifolium</i>	FL	
B-type procyanidin dimer	<i>H. perforatum</i>	FLS	
	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
	<i>H. perforatum</i>	FLS	
Procyandin dimer	<i>H. perforatum</i>	FLS	
S-C- β-L- arabinopyranosylapigenin	<i>H. confertum</i>	AE	(Diaz, 2022)
	<i>H. confertum</i>	AE	
	<i>H. luteum</i>	LE - FL	(Rocha et al., 1995)
Hesychiaside C	<i>H. confertum</i>	AE	(Diaz, 2022)
	Naphthoanthrone		
Hesychia	<i>H. trigonophyllum</i>	AE	(Akroush et al., 2020)
	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)
	<i>H. perforatum</i>	-	(Camaras et al., 2011)
	<i>H. barbatum</i>	AE	(Edgerton et al., 2017)
	<i>H. confertum</i>	LE- FL	(Camaras et al., 2014)
	<i>H. hyperosideum</i>	LE- FL	

	<i>H. hyperosideum</i>	LE- FL		
	<i>H. gracilem</i>	LE- FL		
	<i>H. galileeum</i>	LE- FL		
	<i>H. gracilem</i>	FL		
	<i>H. galileeum</i>	LE- FL		
	<i>H. richieri</i>	AE		
	<i>H. perforatum</i>	AE		
	<i>H. barbatum</i>	AE		
	<i>H. Alpinum</i>	AE		
	<i>H. maculatum</i>	AE		
	<i>H. hyperosideum</i>	AE	(Cakir et al., 2005)	
Hesychia	<i>H. perforatum</i>	FLS	(Tasevski et al., 2018)	
	<i>H. perforatum</i>	FLS		
	<i>H. hyperosideum</i>	LE- FL		
	<i>H. gracilem</i>	LE- FL		
	<i>H. gracilem</i>	LE- FL		
	<i>H. gracilem</i>	FL		
Hesychia	<i>H. gracilem</i>	AE	(Zdzienica et al., 2017)	
	<i>H. gracilem</i>	AE		
	<i>H. gracilem</i>	AE		
	<i>H. gracilem</i>	AE		
	<i>H. gracilem</i>	AE		
	<i>H. gracilem</i>	AE		
Terpenoid derivatives	<i>H. galileeum</i>	AE		
	<i>H. galileeum</i>	AE		
	2-benzyl-3,3-dimethyl-9H,9H-bis(3-methylbut-2-enyl)-cyclohexanone	<i>H. galileeum</i>	(Cordell et al., 2016)	
	2-benzyl-3,3-dimethyl-4H,4H-bis(3-methylbut-2-enyl)-cyclohexanone	<i>H. galileeum</i>		
		<i>H. galileeum</i>		
		<i>H. galileeum</i>		
betulinic acid	<i>H. lanceolatum</i>	STB	(Zofou et al., 2011)	
	<i>H. lanceolatum</i>	STB - TW	(Happi et al., 2023)	
usolic acid	<i>H. lanceolatum</i>	STB - TW		
	<i>H. lanceolatum</i>			
Benzophenones	2,2',5,5-tetrahydroxybenzophenone	<i>H. lanceolatum</i>	STB	(Zofou et al., 2011)
	usonicid	<i>H. lanceolatum</i>	FL	(Gigueme et al., 2020)
	Hyperosine	<i>H. confertum</i>	AE	(Diaz, 2022)
Xanthone	3-hydroxy-3-methoxyxanthone	<i>H. lanceolatum</i>	STB	(Zofou et al., 2011)
	6,7-dihydroxy-1,3-dimethoxyxanthone	<i>H. lanceolatum</i>	STB	
	1,3,3,6-tetrahydroxy-4-prenylxanthone	<i>H. lanceolatum</i>	STB	(Koya et al., 2020)
	3-hydroxy-3-methoxyxanthone	<i>H. lanceolatum</i>	STB	(Zofou et al., 2011)
	<i>H. lanceolatum</i>	STB	(Koya et al., 2020)	
	1,8-dihydroxanthone	<i>H. lanceolatum</i>	STB - TW	(Happi et al., 2023)
xanthone	<i>H. lanceolatum</i>	FL	(Gigueme et al., 2020)	
	<i>H. lanceolatum</i>	STB - TW	(Happi et al., 2023)	
Hesychia	usathinal	<i>H. lanceolatum</i>	STB - TW	(Happi et al., 2023)
	1,7-dihydroxanthone	<i>H. lanceolatum</i>	AE	
	1,3,3-tri-hydroxy-2-methoxyxanthone	<i>H. lanceolatum</i>	AE	(Miguel et al., 2018)
	1,3-dihydroxy-2-methoxyxanthone	<i>H. lanceolatum</i>	AE	
	1,3-dihydroxy-6-methoxy-xanthone	<i>H. lanceolatum</i>	AE	(Ramirez-gonzales et al., 2013)
	2,3-dihydroxy-1-methoxyxanthone	<i>H. lanceolatum</i>	AE	(Miguel et al., 2018)
Hesychia	3,8-dihydroxy-1,2-dimethoxyxanthone	<i>H. lanceolatum</i>	AE	
	1-hydroxy-7-methoxyxanthone	<i>H. lanceolatum</i>	AE	(Ramirez-gonzales et al., 2013)
Hesychia	2-hydroxy-xanthone	<i>H. lanceolatum</i>	AE	
		<i>H. lanceolatum</i>		

6-deoxyhyperacetin	<i>H. hyperosideum</i>	AE	
1,3,6-trihydroxy-7-methoxy-xanthone	<i>H. hyperosideum</i>	AE	
Hyperanthane A	<i>H. hyperosideum</i>	AE	(Daskalakis et al., 2022)
5-O-methyl-2-deoxytheodoxanthone B	<i>H. hyperosideum</i>	RO	
3-O-methylisoquercetin	<i>H. hyperosideum</i>	RO	(Rath et al., 1998)
3-O-demethylxanthone	<i>H. hyperosideum</i>	RO	
isopunicetin	<i>H. hyperosideum</i>	RO	
Demethylisoquercetin	<i>H. hyperosideum</i>	FLS	
3,6-dihydroxy-1,5,7-trimethoxy-xanthone	<i>H. hyperosideum</i>	RO	
Catechin C	<i>H. hyperosideum</i>	RO	
Catechin C isomer	<i>H. hyperosideum</i>	RO	(Tuncerko et al., 2018)
γ -Mangostin	<i>H. hyperosideum</i>	RO	
5-O-Methyl-1,2-deoxytheodoxanthone B	<i>H. hyperosideum</i>	RO	
Catechin D	<i>H. hyperosideum</i>	RO	
Gallocatein C	<i>H. hyperosideum</i>	RO	

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

According to this survey, quercetin, rutin, hypericin, isoquercitrin, quercetin, 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.

Antimicrobial activity of Hypericum species
Microorganisms are widespread in nature and are beneficial to life, but some can cause serious harm

(Maraz and Khan, 2021). Microorganisms can easily access food (Gonelimali, 2018). Currently, 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).

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) μ g/ml.

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

Species	Extracts/ plant part	Micro-organisms	MIC (mg/ml)	Ref.
<i>H. perforatum</i>	Total methanol AE	<i>S. enterica</i> (ATCC 8758) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. aureus</i> (ATCC 6538) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>S. enterica</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.0048 0.028 0.018 0.0048 0.0048 0.039 0.019	
<i>H. spissifolium</i>	Total methanol AE	<i>S. enterica</i> (ATCC 12228) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.078 0.038	
<i>H. montbretii</i>	Total methanol AE	<i>S. enterica</i> (ATCC 12228) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.0048 0.0048 0.0048	
<i>H. macrocarpum</i>	Total methanol AE	<i>S. enterica</i> (ATCC 12228) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.156 0.016 0.0048	
<i>H. perforatum</i>	Total methanol AE	<i>S. enterica</i> (ATCC 12228) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.078 0.038 0.0048 0.0048	(Ozkan et al., 2019)
<i>H. perforatum</i>	Total methanol AE	<i>S. enterica</i> (ATCC 12228) <i>Methicillin-resistant S. aureus</i> (ATCC33591) <i>E. coli</i> (ATCC 12228) <i>S. enterica</i> (ATCC 8738)	0.0048 0.0048 0.0048 0.0048	
<i>H. perforatum</i>	EO AE	<i>S. cerevisiae</i> (bakers yeast) <i>S. griseus</i> (ATCC 11832) <i>E. coli</i> (ATCC 25922)	0.0075 0.033 0.0013	
<i>H. perforatum</i>	EO AE	<i>S. cerevisiae</i> (ATCC 25922) <i>E. coli</i> (ATCC 11832) <i>P. aeruginosa</i> (ATCC 2733)	0.030 0.010 0.0013	(Grafakos et al., 2010)
<i>H. amblyodon</i>	EO AE	<i>S. cerevisiae</i> (bakers yeast) <i>S. griseus</i> (ATCC 11832) <i>E. coli</i> (ATCC 25922) <i>P. aeruginosa</i> (ATCC 2733) <i>B. subtilis</i> (ATCC 11571) <i>E. coli</i> (ATCC 25922) <i>P. aeruginosa</i> (ATCC 2733)	0.0025 0.015 0.0023 0.0023	
<i>H. annuum</i>	EO AE	<i>S. cerevisiae</i> (bakers yeast) <i>S. griseus</i> (ATCC 11832) <i>E. coli</i> (ATCC 25922)	0.0075 0.013 0.0013	
<i>H. amplexicaule</i>	EO AE	<i>S. cerevisiae</i> (bakers yeast) <i>S. griseus</i> (ATCC 11832) <i>E. coli</i> (ATCC 25922) <i>P. aeruginosa</i> (ATCC 2733)	0.0015 0.038 0.0013	
<i>H. androsaemum</i>	Methanol(10%) AE	<i>S. cerevisiae</i> (NCIMB 5623) <i>E. faecalis</i> (NCIMB 1024) <i>E. coli</i> (B 81) <i>P. aeruginosa</i> (NCIMB 1038)	0.1 0.1 0.1	
<i>H. ericoides</i>	Methanol(10%) AE	<i>E. aerogenes</i> (ATCC 13048) <i>S. enterica</i> (NCIMB 8625) <i>E. faecalis</i> (NCIMB 1024) <i>E. coli</i> (B 81) <i>P. aeruginosa</i> (NCIMB 1038) <i>S. enterica</i> (ATCC 13048) <i>S. enterica</i> (NCIMB 8625)	0.1 0.1 0.1 0.1 0.1 0.1 0.1	(Gaddipati et al., 2020)
<i>H. lucidum</i>	Methanol(10%)	<i>S. enterica</i> (NCIMB 8625)	0.1	

<i>H. hamatum</i>	Ethanol AE	<i>S. aureus</i> (ATCC 49444)	0.078	(Tobu et al., 2016)
		<i>E. coli</i> (ATCC 35142)	0.078	
		<i>B. cereus</i> (ATCC 11781)	0.02	
		<i>P. aeruginosa</i> (ATCC 27333)	0.02	
		<i>S. enteritidis</i> (ATCC 14028)	0.29	
		<i>K. pneumoniae</i> (ATCC 35221)	0.02	
<i>H. hypericoides</i>	Methanol LE	<i>B. subtilis</i> (ATCC 66153)	0.00156	(Ceyhan et al., 2020)
		<i>S. aureus</i> (ATCC 25923)	0.00125	
		<i>E. coli</i> (ATCC 25923)	0.0125	
	Methanol FL	<i>B. subtilis</i> (ATCC 66153)	0.0002	
		<i>S. aureus</i> (ATCC 25923)	0.025	
		<i>E. coli</i> (ATCC 25923)	0.0125	
<i>H. moscheutos</i>	Methanol LE	<i>B. subtilis</i> (ATCC 66153)	0.0002	(Boga et al., 2016)
		<i>S. enteritidis</i> (ATCC 14028)	0.00425	
		<i>B. subtilis</i> (ATCC 66153)	0.0002	
	Methanol ST	<i>E. coli</i> (ATCC 25923)	0.1	
		<i>S. pyogenes</i> (ATCC 19615)	2	
		<i>S. aureus</i> (ATCC 25923)	-	
<i>Hypericum capitatum var. capitatum</i>	Petroleum ether WP	<i>P. aeruginosa</i> (ATCC 27333)	0.25	(Boga et al., 2016)
		<i>E. coli</i> (ATCC 25923)	-	
		<i>S. aureus</i> (ATCC 19615)	0.25	
	Acetone WP	<i>P. aeruginosa</i> (ATCC 27333)	0.25	
		<i>E. coli</i> (ATCC 25923)	0.015	
		<i>S. pyogenes</i> (ATCC 19615)	0.25	
	Methanol WP	<i>S. aureus</i> (ATCC 19615)	0.25	
		<i>P. aeruginosa</i> (ATCC 27333)	0.25	
		<i>E. coli</i> (ATCC 25923)	0.015	

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*.

Antioxidant activity of Hypericum species

Oxidative stress is the main cause of many diseases such as atherosclerosis, arthritis, cancer, as well as neurodegenerative diseases (Saddiqe et 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. avicularifolium*, *H. salsugineum*, *H. perforatum*) were evaluated. The methanolic extract of *H. salsugineum* showed the highest antioxidant effect (DPPH inhibition=88.29%) among the extracts (Malatas et al., 2013).

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

It is important to consider that the antioxidant activity of a plant extract can differ depending on the specific part of the plant being tested. 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 (Chandrashekara et al., 2009).

Table 4. Antioxidant activity of some *Hypericum* species

Species	extract/ plant part	Technique	Concentra- tion (mg/ml)	Results	Ref.
<i>H. perforatum</i>	Methanol (FL)	DPPH	-	scavenging %=12	(Gümüş and Balgınat, 2017)
<i>H. perforatum</i>	Methanol	DPPH	0.5	scavenging %=11.21 ± 0.18	
<i>H. perforatum</i>	Methanol	DPPH	0.5	scavenging %=11.29 ± 0.06	(Maltais, et al., 2013)
<i>H. perforatum</i> var. <i>Ascyronum</i> <i>var. decoloratum</i>	Methanol	DPPH	0.5	scavenging % = 86.88 ± 0.17	
<i>H. perforatum</i>	Ethanol (AE)	DPPH	2	scavenging %=6.74	(Mehman and et al., 2020)
<i>H. perforatum</i>	Methanol (AE)	DPPH	-	EC50=0.567 ± 0.028 mg/ml reducing power= 2.66 ± 0.031 mM Fe 2+	
<i>H. perforatum</i>	Methanol (AE)	F2AF	-	EC50=0.916 ± 0.036 mg/ml reducing power= 2.21 ± 0.013 mM Fe 2+	(Ozkan e al., 2018)
<i>H. perforatum</i>	Methanol (AE)	DPPH	-	EC50=0.622 ± 0.031 mg/ml reducing power= 2.58 ± 0.036 mM Fe 2+	
<i>H. perforatum</i>	Methanol (AE)	F2AF	2	FRAP value= 2.59 ± 0.039 μM Fe 2+	(Ozkan e al., 2018)
<i>H. perforatum</i>	Methanol (AE)	Auto-LPO	-	EC50= 2.49 ± 0.09 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	DPPH	-	EC50= 0.271 ± 0.03 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	Superoxide anion	-	EC50= 0.633 ± 0.05 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	F2AF	2	FRAP value= 2.59 ± 0.039 μM Fe 2+	
<i>H. perforatum</i>	Methanol (AE)	Auto-LPO	-	EC50= 4.42 ± 0.03 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	DPPH	-	EC50= 1.14 ± 0.03 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	Superoxide anion	-	EC50= 0.802 ± 0.01 mg/ml	
<i>H. perforatum</i>	Methanol (AE)	F2AF	2	FRAP value= 2.23 ± 0.031 μM Fe 2+	

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

CONCLUSION

There are only few reports about the chemical composition of the genus Hypericum. In the current review, the chemical composition of the essential oils isolated from different Hypericum species was compared, which may contribute to adding new criteria for chemotaxonomy of these species. In addition, about 100 different natural products isolated from Hypericum species were documented and classified, and these compounds were found to be 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.

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<i>H. perforatum</i>	Methanol (LE)	ABTS	-	IC50= 5.60 ± 0.38 μg/ml	(Chandra Shukla et al., 2009)	
	Methanol (LE)	DPPH	-	IC50= 3.30 ± 0.03 μg/ml		
	Methanol (LE)	Hydrogen peroxide	-	IC50= 58.06 ± 1.93 μg/ml		
	Methanol (LE)	Lipid per oxidation	-	IC50= 58.00 ± 1.42 μg/ml		
	Methanol (FL)	ABTS	-	IC50= 7.65 ± 0.26 μg/ml		
	Methanol (FL)	DPPH	-	IC50= 3.10 ± 0.12 μg/ml		
	Methanol (FL)	Hydrogen peroxide	-	IC50= 117.64 ± 5.14 μg/ml		
	Methanol (FL)	Lipid per oxidation	-	IC50= 295.00 ± 11.2 μg/ml		
	Methanol (AE)	ABTS	-	IC50= 16.95 ± 0.33		
	Methanol (AE)	DPPH	-	IC50= 5.25 ± 0.11 μg/ml		
<i>H. perforatum</i>	Methanol (AE)	Hydrogen peroxide	-	IC50= 74.14 ± 3.82 μg/ml	(Saddiq et al., 2016)	
	Methanol (AE)	Lipid per oxidation	-	IC50= 339.09 ± 28.4 μg/ml		
	Methanol (AE)	DPPH	-	IC50= 92.70 ± 2.85 μg/ml		
	Methanol (AE)	Antioxidant capacity	0.5	Anton Scavenging% = 11.20 ± 1.22		
	Methanol (AE)	Anti-lipid peroxidation	0.5	Anti-lipid peroxidation% = 11.13 ± 1.02		
	<i>H. austro-africanum</i>	Methanol	DPPH	-	IC50= 0.983 mg/ml	
	<i>H. austro-africanum</i>	Ethyl acetate	DPPH	-	IC50= 0.293 mg/ml	
	<i>H. austro-africanum</i>	Ethyl acetate	DPPH	-	IC50= 0.11 mg/ml	
	<i>H. austro-africanum</i>	Methanol	DPPH	-	IC50= 0.098 mg/ml	
	<i>H. austro-africanum</i>	Ethyl acetate (LE)	DPPH	-	IC50= 3.37 ± 0.26 μg/ml	
<i>H. negundinum</i>	Ethanol-water	DPPH	-	IC50= 3.79 ± 0.27 μg/ml	(Grynska et al., 2022)	
	Ethanol-water	DPPH	-	IC50= 3.79 ± 0.27 μg/ml		
	Ethanol-water	DPPH	-	IC50= 3.83 ± 0.49 μg/ml		
	<i>H. austriacum</i>	Methanol (AE)	DPPH	0.01	scavenging %= 58.2 ± 0.1	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 83.0 ± 0.2	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 33.8 ± 0.1	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 34.5 ± 0.2	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 84.2 ± 0.3	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 31.9 ± 0.1	
	<i>H. austriacum</i>	Methanol (AE)	ABTS	0.01	scavenging %= 31.2 ± 0.1	
<i>H. capitatum</i>	Methanol	DPPH	-	IC50= 0.983 mg/ml	(Carrá et al., 2016)	
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
	Methanol	ABTS	-	IC50= 0.983 mg/ml		
<i>H. capitatum</i>	Petroleum ether (WP)	Lipid peroxidation	-	IC50> 200 μg/ml	(Giga et al., 2010)	
	Petroleum ether (WP)	DPPH	-	IC50> 200 μg/ml		
	Petroleum ether (WP)	ABTS	-	IC50> 200 μg/ml		
	Acetone (WP)	Lipid peroxidation	-	IC50> 200 μg/ml		
	Acetone (WP)	DPPH	-	IC50> 200 μg/ml		
	Acetone (WP)	ABTS	-	IC50> 200 μg/ml		
	Methanol (WP)	Lipid peroxidation	-	IC50= 41.68 ± 1.29 μg/ml		
	Methanol (WP)	DPPH	-	IC50= 16.82 ± 0.38 μg/ml		
	Methanol (WP)	ABTS	-	IC50= 9.14 ± 0.26 μg/ml		
	water (WP)	Lipid peroxidation	-	IC50= 92.13 ± 1.05 μg/ml		
	water (WP)	DPPH	-	IC50> 200 μg/ml		
	water (WP)	ABTS	-	IC50= 0.78 ± 0.14 μg/ml		

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التركيب الكيميائي، وبعض الفعاليات الحيوية لجنس *Hypericum*

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*دكتوراه في علم الحياة النباتية، محاضر في كلية الزراعة، جامعة حلب، **دكتوراه في هندسة التقانات الحيوية، مدرس في كلية الهندسة التقنية، جامعة حلب

النباتات الطبيعية هي أفضل مصدر للأدوية، لذلك زادت الدراسات على هذه النباتات بهدف البحث عن مواد فعالة جديدة يمكن استخدامها في الصناعات الدوائية العشبية. الجنس *Hypericum* هو جنس كبير من النباتات الزهرية، ويضم العديد من الأنواع المنتشرة عالمياً، تعتمد أهمية أنواع الجنس بشكل أساسي على وجود مستقبلات ثانوية تبدي خصائصاً صيدلانية وجميلية. تشتهر أنواع الجنس *Hypericum* في جميع أنحاء العالم بأهميتها الطبية وتستخدم لعلاج الالتهابات والأمراض، كعوامل مدرة للبول، ومدرة للصفراء، ومضادات التشنج، ومضادات الصرع، وكذلك للروماتيزم ، والألم العصبي، والطفيليات، وعسر الهضم، والإسهال، وما إلى ذلك. يوجد فقط تقارير قليلة عن التركيب الكيميائي لأنواع جنس *Hypericum*. تهدف الدراسة الحالية إلى تقديم لمحة عامة عن أهمية جنس *Hypericum* ، ملخص عن التركيب الكيميائي، وكذلك الفعاليات المضادة للبكتيريا والمضادة للأكسدة لأنواع مختلفة من الجنس.

الكلمات المفتاحية: التركيب الكيميائي، Hypericaceae، *Hypericum*، مضاد جرثومي، مضاد أكسدة.