



Genus *Hypericum*: General Properties, Chemical Contents and Biological Activities



Ghadir A. El-Chaghaby^{(1)#}, Falah S. Mohammed⁽²⁾, Sayed Rashad⁽¹⁾, Imran Uysal⁽³⁾, Oğuzhan Koçer⁽⁴⁾, Ömer Lekeziz⁽⁵⁾, Mehmet Doğan⁽³⁾, Ali E. Şabik⁽⁶⁾, Mustafa Sevindik⁽⁵⁾

⁽¹⁾Bioanalysis Laboratory, Regional Center for Food and Feed, Agricultural Research Center, Giza, Egypt; ⁽²⁾Department of Biology, Faculty of Science, University of Zakho, Duhok, 42001, Iraq; ⁽³⁾Department of Food Processing, Bahçe Vocational School, University of Osmaniye Korkut Ata, Osmaniye, 80000, Turkey; ⁽⁴⁾Department of Pharmacy Services, Vocational School of Health Services, University of Osmaniye Korkut Ata, Osmaniye, 80000, Turkey; ⁽⁵⁾Department of Biology, Faculty of Science and Literature, University of Osmaniye Korkut Ata, Osmaniye, 80000, Turkey; ⁽⁶⁾Department of Chemistry and Chemical Processing Technologies, Bahçe Vocational School, University of Osmaniye Korkut Ata, Osmaniye, 80000, Turkey.

PLANTS of the *Hypericum* L. genus are widely distributed with several identified species all over the world. In addition to their nutritional properties, plants of the *Hypericum* L. genus are also noteworthy for their pharmacological properties. These plants have long been a part of traditional medicine in many nations. The present work presents a brief review about *Hypericum* species; their general characteristics, bioactivities, and phytochemical composition as reported in the published literature. From the researches reviewed during the current work, it was confirmed that *Hypericum* species contain high levels of antioxidant, antimicrobial, and anticancer activities in terms of biological activity which enables the species to be commonly used in the fight against diseases. The plant species were also reported to contain appreciate concentrations of important minerals including iron, zinc, calcium and sodium. Many biological activities such as antihyperglycemic, anticancer, antimicrobial, anti-inflammatory, antioxidant, hepatoprotective activities, acetylcholinesterase and monoamine oxidase inhibitory properties are exhibited by *Hypericum* species. Additionally, it has been concluded that the most commonly reported chemical bioactive compounds found in *Hypericum* species are caryophyllene (1), caryophyllene oxide (2), germacrene-D (3), limonene (4), spathulenol (5), β -pinene (6), α -pinene (7), γ -muurolene (8), β -selinene (9), and δ -cadinene (10). Taking all of this information into account, it is clear that *Hypericum* plant species offer potential medicinal benefits in addition to their nutritional worth.

Keywords: Anticancer, Antimicrobial, Antioxidant, Complementary medicine, Goatweed, Kantaron, St. John's wort.

Introduction

The utilisation of natural products for therapeutic purposes dates back to the inception of human civilization on the planet (Sevindik et al., 2017). Presently, medicinal plants serve as the primary source of treatment for a significant proportion of the global populace. Numerous

natural materials are utilised within the scope of complementary and traditional medicine (Mohammed et al., 2020a; Korkmaz et al., 2021; Eisawi et al., 2022; Benabderrahmane et al., 2023). Within this context, humans have utilised various natural products like plants, animals and fungi in combating illnesses (Sevindik et al., 2018; Mohammed et al., 2021a; Bal et

#Corresponding author email: ghadiraly@yahoo.com

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<https://orcid.org/0000-0002-1836-7578>,

al., 2023). Plants are the most commonly used natural products within this context. Studies by many researchers have reported that plants have anti-inflammatory, antiallergic, antioxidant, anticancer, antiproliferative, anti-aging, hepatoprotective, DNA protective, antimicrobial activities (Guha et al., 2011; Mohammed et al., 2018; Ali et al., 2019; Mohammed et al., 2019; Çolak et al., 2020; Mohammed et al., 2021b; Bjørklund et al., 2022; Rashed et al., 2022; Unal et al., 2022; Mohammed et al., 2023a; Saleh et al., 2023; Uysal et al., 2023). In light of this, identifying the potentials of plants is highly significant in terms of their applications. In this review, the researches conducted on *Hypericum* species in the literature are discussed. In addition, the general characteristics, usage areas and chemical contents of *Hypericum* species were compiled.

Genus *Hypericum*

Hypericum (Hypericaceae) are flowering plants that are considered to be invasive and harmful weeds that spread almost everywhere except for polar areas, deserts, and tropical lowlands. The species of *Hypericum* are plants with a highly variable structure, including trees, shrubs, annuals, and perennials. Many species of woody plants have multiple stems originating from a single base. Shrub forms have erect or spreading stems. Most of the *Hypericum* species are apomictic. Some of them have simple single rows, while others have long and thin feathers of the *Hypericum* species (Crockett & Robson, 2011). The majority of *Hypericum* members exhibit opposite and alternate leaf arrangements. With the exception of some species, most of them lack stipules on their leaves and have either sessile or short-stalked leaves. Typically, leaves are shaped in an elongated oval form that tapers towards a straight edge. Typically, there are four or five sepals present. The majority of *Hypericum* species have yellow flowers. Furthermore, there are colour variations that transition from a pale lemon hue to a deep orange-yellow shade. The seeds of *Hypericum* species are small. The colours range from yellowish-brown to dark purplish-brown. The seeds are cylindrical or elliptical in shape (Ernst, 2003; Saddiqe et al., 2010).

Species belonging to *Hypericum* are named with local names in different countries around the world. These are known as **Arabic**: جون سانت نبتة; **Chinese**: 圣约翰草; **English**: St. John's

Wort, goatweed; **French**: Millepertuis; **German**: Johanniskraut; **Greek**: Βαλσαμόχορτο; **India**: सेंट जॉन का पौधा; **Italian**: Erba di San Giovanni; **Russian**: Зверобой; **Spanish**: Hierba de San Juan; **Turkish**: Kantaron.

Since ancient times, the *Hypericum* species has been one of the most popular species used for treating numerous illnesses both in conventional medicine and contemporary medicine systems. In numerous parts of the world, dried or fresh forms of *Hypericum* species are used for treating some general diseases, to support the immune system and to be used as a traditional treatment method, as well as for negative complications in humans. It is also used as a dietary supplement (Medina et al., 2006; Çırak, 2006, Schepetkin et al., 2020; Jakubczyk et al., 2021). *Hypericum*, which has a wide distribution in many countries, was widely used in the ancient Greek civilization for the treatment of many diseases such as sedative, wound healing, depression treatment and burn healing. (Klemow et al., 2011). Generally, it is used for treating diseases such as colds and bronchitis, which are usually seen in the upper respiratory tract, for treating diseases in the excretory system such as bladder disorders, constipation and the treatment of parasites in the intestines, for treating ulcers, migraines and diabetes. It is also seen that it is used for treating various burns (WHO, 1999; Vakili et al., 2018). The above-ground parts are dried and powdered, and a healing effect is provided because of direct application to cut or burn wounds. *Hypericum*, which can be consumed in the form of tea, is also used for treating haemorrhoids and for treating diseases such as ulcers and gastritis (Honda et al., 1998). The essential oils originating from its leaves are extensively used for in dermatological skin problems (Asan, 2019). *Hypericum* is used in industrial areas and in treatment of diseases. Some of the *Hypericum* species are also used to dye fabric yellow in the textile dye industry with dyes obtained from flower parts (Baytop, 1999). Some species are used to benefit from their antiseptic and sedative effects (Apaydın et al., 1999).

Mineral contents of *Hypericum* Species

Plants contain many elements. With these properties, they can be a source in terms of elements in their use. The mineral contents of *Hypericum* species in the literature researches are shown in Table 1.

TABLE 1. Mineral contents of different parts of *Hypericum* species based on dry weight

Mineral	concentration ($\mu\text{g/g}$)	References
Na	83-4900	Dastagir et al. (2016), Sekeroglu et al. (2018)
Zn	20.12-80	Helmja et al. (2011), Dastagir et al. (2016), Sekeroglu et al. (2018)
Ca	2500-10390	Dastagir et al. (2016), Sekeroglu et al. (2018)
Co	102-175	Helmja et al. (2011)
Cu	6.7-26	Dastagir et al. (2016), Sekeroglu et al. (2018)
Ni	1.481-1.765	Dastagir et al. (2016), Sekeroglu et al. (2018)
Cd	0.0278-0.0405	Dastagir et al. (2016), Sekeroglu et al. (2018)
Cr	3.57-243	Helmja et al. (2011), Sekeroglu et al. (2018)
P	1346-2880	Sekeroglu et al. (2018)
S	1222-2476	Sekeroglu et al. (2018)
Pb	4.807-220	Helmja et al. (2011) Sekeroglu et al. (2018)
Mg	790-2234	Helmja et al. (2011), Sekeroglu et al. (2018)
K	9471-15161	Helmja et al. (2011)
Fe	108.9-5000	Dastagir et al. (2016), Sekeroglu et al. (2018)
Mn	8.6-85	Helmja et al. (2011), Dastagir et al. (2016), Sekeroglu et al. (2018)
B	20-25.1	Sekeroglu et al. (2018)
Mo	0.12-0.73	Sekeroglu et al. (2018)

According to literature data, there are varying amounts of Na, Zn, Ca, Co, Cu, Ni, Cd, Cr, P, S, Pb, Mg, K, Fe, Mn, B and Mo contents in the stem, leaf, flower and fruit parts of different *Hypericum* species (Helmja et al., 2011; Dastagir et al., 2016; Sekeroglu et al., 2018). Therefore, it is thought that *Hypericum* species can be recommended as a natural mineral source based on these literature data.

Phytochemical compounds in Hypericum Species

It is known that plants have many different pharmacological effects owing to their phytochemical composition (Bal et al., 2017; Islek et al., 2021). In the current study, phytochemical compounds reported in different parts of *Hypericum* species in the literature were compiled. Table 2 displays the outcomes that were attained.

As a result of literature research, the 10 most common compounds reported in different *Hypericum* species are caryophyllene (1), caryophyllene oxide (2), germacrene-D (3), limonene (4), spathulenol (5), α -pinene (6), β -pinene (7), β -selinene (8), γ -muurolene (9), and δ -cadinene (10). The formulas of these compounds are shown in Fig. 1.

In this case, it is assumed that it might be

a natural source for the chemicals based on information found in the literature.

Biological activities of Hypericum Species

Plants are very important natural resources in terms of biological activities (Mohammed et al., 2020b). Many different plant species are known to have biological activities (Mohammed et al., 2021c). In the published literature, it has been reported that species belonging to the genus *Hypericum* have many biological activities. As a result of the literature research, it has been seen that many studies on *Hypericum* species originate from Turkey. The main reason for this is thought to be due to the fact that 100 of the 490 *Hypericum* species distributed in the world are distributed in Turkey. In addition, 45 of these species are endemic to Turkey (Aköz, 2013). In addition, different researchers from different countries have studies on *Hypericum* species. A summary of the species, biological activities, solvent or essential oil used, and references reported according to literature data are shown in Table 3.

In the next sections of this review, the previously published studies concerning different types of bioactivities reported for *Hypericum* species will be discussed.

TABLE 2. Phytochemical compounds recorded in different *Hypericum* species

<i>Hypericum</i> species	Used parts	Regions	Phytochemical compound	References
<i>aemosepalum</i>	Aerial parts	China	ar-curcumene β-selinene caryophyllene oxide	Demirci et al. (2005)
<i>aegypticum</i> ssp. <i>aegypticum</i>	Aerial parts	Africa	ishwarane	Crockett et al. (2007)
<i>aegypticum</i> ssp. <i>marrocanum</i>	Aerial parts	Africa	Caryophyllene oxide Caryophyllene Caryophylladienol-II	Crockett et al. (2007)
<i>androsaemum</i>	Fresh leaves	Portugal	(E)-Caryophyllene γ-Elemene β-Gurjunene curcumene	Guedes et al. (2004)
<i>aviculariifolium</i> subsp. <i>depilatum</i> var. <i>depilatum</i>	aerial parts	Türkiye	α-Pinene Germacrene D β-Pinene	Yuce & Bagci (2012)
<i>balearicum</i>	aerial parts	Africa	α-pinene, β-pinene, and β-eudesmol	Crockett et al. (2007)
<i>barbatum</i>	aerial parts	Serbia	(-)-α-pinene (-)-β-pinene (-)-limonene (-)-(E)-caryophyllene (-)-caryophyllene oxide	Saroğlu et al. (2007)
<i>beanii</i>	aerial parts	China	γ-muurolene β-selinene caryophyllene oxide	Demirci et al. (2005)
<i>brasiliense</i>	aerial parts	Brasil	betulinic acid	Aberu et al. (2004)
<i>calycinum</i>	aerial parts	China	α-terpineol β-pinene	Demirci et al. (2005)
<i>canariense</i>			n-nonane (E)-caryophyllene β-pinene	Zorzetto et al. (2015)
<i>choisyanum</i>	aerial parts	China	cis-eudesma-6,11-diene	Demirci et al. (2005)
<i>delphicum</i>	aerial parts	Africa	caryophyllene oxide, β-caryophyllene and undecane	Crockett et al. (2007)
<i>elongatum</i>			α-pinene β-pinene γ-terpinene	Ghasemi et al. (2007)

TABLE 2. Cont.

<i>Hypericum</i> species	Used parts	Regions	Phytochemical compound	References
<i>empetrifolium</i>	aerial parts	Greece	n-nonan; α -pinen; Camphene; verbenen; β -pinen; 6-metil-5-hepten-2-on; mirsen; n-dekan; α -fellandren; α -terpinen; osimen; (E)-karyofillen; p-simen; limonen; 1,8-sineol; (Z)- β -osimen; (E)- β - osimen; γ -terpinen; 2-metil-dekan; terpinolen; linalol; nundekan; n-nonanal; endo-fenkol; ekzo-fenkol; α -kamfolenal; trans-pinokarveol; kamfor; kamfen hidrat; (E)- β - ionon; izoborneol; borneol; terpinen-4-ol; naftalen; α -terpineol; mirtenol; trans-karveol; sitronellol; geraniol; α -Terpinen-7-al; 2-undekanon; α -kubeben; α -longipinen; siklosativen; α -ylangen; α -kopaen; β -patchulen; β -elemen; α -sedren; β -sedren; aromadendren; α -humulen; (E)- β -farnesen; allo-aromadendren; γ -guryunen; γ -muurolen; γ -kurkumen; germakren-D; β -selinen; valensen; viridifloren; α -selinen; bisiklogermakren; α -muurolen; α -kamigren; trans- β -guayen; α -bulnesen; (E,E)- α -Farnesen; γ -kadinen; 7-epi- α -selinen; cis- kalamen; δ -kadinen; karyofillen oksit; 1transkalamen; kadina-1,4-dien; α -kalakoren; karyofillen alkol; (Z)- 3-hekzenil-benzoat; spatulenol; -epikubenol; kubenol; α -muurolol; α -kadinol; valerianol; β -bisabolol; bulnesol; kadalen; kusinol; benzil benzoat; akorenon	Petrakis et al. (2005)
<i>ericoides</i>	aerial parts	Tunusia	n-octane α -pinene pulegone acetophenone	Hosni et al. (2011)
<i>forrestii</i>	aerial parts	China	α -pinene caryophyllene oxide	Demirci et al. (2005)
<i>grandifolium</i>			n-Nonane (E)-caryophyllene	Zorzetto et al. (2015)
<i>heterophyllum</i>	aerial parts	Türkiye	isocaryophyllene α -pinene δ -cadinene γ -muurolene n-decane γ -cadinene β -caryophyllene	Cakir et al. (2004)
<i>hirsutum</i>	aerial parts	Serbia	nonane undecane (-)-(E)-caryophyllene (-)-caryophyllene oxide	Saroğlu et al. (2007)
<i>hyssopifolium</i>	aerial parts	Türkiye	α -Pinene β -Pinene Limonene α -phellandrene	Cakir et al. (2004)

TABLE 2. Cont.

<i>Hypericum</i> species	Used parts	Regions	Phytochemical compound	References
<i>kouytchense</i>	aerial parts	China	cis- β -guaiaene γ -muurolene	Demirci et al. (2005)
<i>lancasteri</i>	aerial parts	China	β -selinene eudesmadienone	Demirci et al. (2005)
<i>leschenaultii</i>	aerial parts	China	cuparene γ -muurolene	Demirci et al. (2005)
<i>maculatum</i>	aerial parts	Serbia	spathulenol globulol	Saroğlu et al. (2007)
<i>monogynum</i>	aerial parts	China	tricosane myrcene	Demirci et al. (2005)
<i>patulum</i>	aerial parts	China	β -selinene n-nonan; α -pinene; Camphene; verbenen; β -pinene; 6-metil-5-hepten-2-on; mirsen; n-dekan; α -terpinen; p-simen; limonen; 1,8-sineol; (Z)- β -osimen; (E)- β -osimen; γ -terpinen; terpinolen; n-undekan; n-nonanal; ekzo-fenkol; α -kamfolenal; trans-pinokarveol; borneol; naftalen; α -longipinen; siklosativen; α -ylangen; α -kopaen; β -patchulen;	Demirci et al. (2005)
<i>perfoliatum</i>	aerial parts	Greece	(E)-karyofillen; β -guryenen; aromadendren; α -humulen; alloaromadendren; γ -muurolen; germakren-D; (E)- β -ionon; viridifloren; bisiklogermakren; α -muurolen; γ - cadinene; δ -kadinen; kadina-1,4-dien; α -kalakoren; (Z)-3-hekzenilbenzoat; spatulenol; karyofillen oksit; 1-epi-kubenol; kubenol; α -muurolol; α -kadinol; kadalen	Couladis et al. (2001), Petrakis et al. (2005)
<i>perforatum</i>	aerial parts, flowers and leaves	India; France, Lithuania, Greece, Serbia, Türkiye, Uzbekistan	2-mehyl-oktan; n- nonane; α -pinene; 3-mehyl- nonane; β -pinene; myrcene; o-caymene; limonene; (E)- β -ocimene; γ -terpinene; 2- methyl-decane; linalol; trans-sabinene hydrate acetate; n-undecane; α -copaene; 1,7-di-epi-b- cedrene; (E)-caryophyllene; aromadendrene; (E)-b- farnesene; g-Muurolene; Germacrene-D; α -selinene; β -Selinene; Valencene; γ -cadinene; Cadina-1,4-diene; Caryophyllene oxide; spathulenol; myrcene; linalool; cis- linalool oxide; trans-linalool oxide; α -terpineol; 3-carene; geranyl acetate; α -cuprenene; β -funebrene; γ -muurolene; β -farnesene; caryophylladienol; tetradecanal; manool	Weyerstahl et al. (1995), Cakir et al. (1997), Baser et al. (2002), Schwob et al. (2004), Petrakis et al. (2005), Radusiene et al. (2005), Saroglou et al. (2007), Çırak et al. (2010)
<i>pseudohenryi</i>	aerial parts	China	β -selinene α -pinene β -pinene n-undecane	Demirci et al. (2005)
<i>reflexum</i>			(E)- caryophyllene δ -cadinene α -cadinol caryophyllene oxide	Zorzetto et al. (2015)
<i>roeperanum</i>	aerial parts	Africa	γ -curcumene (-)- α -pinene	Crockett et al. (2007)
<i>rumeliacum</i>	aerial parts	Serbia	(-)- β -pinene (-)-limonene	Saroglou et al. (2007)

TABLE. 2. Cont.

<i>Hypericum</i> species	Used parts	Regions	Phytochemical compound	References
<i>scabrum</i>	aerial parts	Uzbekistan	a-Pinene Spathulenol p-Cymene acetophenone carvacrol	Baser et al. (2002)
<i>tomentosum</i>	aerial parts	Tunusia	n-octane α -pinene β -caryophyllene menthone	Hosni et al. (2008)
<i>triquetrfolium</i>	aerial parts	Greece, Türkiye	2-Methyl-octane; n-Nonane; Camphene; 3-Methyl-nonane; Sabinene; β -pinene; Myrcene; n-Decane; α -Phellandrene; o-Cymene; p-Cymene; Limonene; 1,8-Cineole; a-Pinene; γ -terpinene; 2-Methyl-decane; n-Undecane; n-Nonanal; trans-Pinocarveol; a-Terpineol; Carvone; Geraniol; α -Cubebene; α -Ylangene; α -Copaene; β -Elemene; (E)- Caryophyllene; β -Gurjunene; Germacrene-D; (E)- β -Ionone; Aromadendrene; α -neo- Glovene; α -Humulene; (E)- β -Farnesene; Dehydro-aromadendrene; allo-Aromadendrene; γ -Muuroleone; β -Selinene; Valencene; α -Muuroleone; trans- β -Guaiene; (Z)- α - Bisabolene; β -Bisabolene; γ -cadinene; δ -cadinene; Cadina-1,4-diene α -cadinene; α -Calacorene; α -Agarofuran; (E)-Nerolidol; Spathulenol; ; α -Bisabolol; 1-hexanal; Caryophyllene oxide; Humulene epoxide II; β -Oplopenone; 1-epi-Cubenol; Cubenol; Cedr- 8(15)-en-9- α -ol; Vulgarone B; α -Cadinol; 14-Hydroxy-9-epi-(E)-caryophyllene; Bulnesol; Cadalene; Khusinol3-methylnonane	Petrakis et al. (2005), Yuce & Bagci (2012)
<i>X moserianum</i>	aerial parts	China	δ -cadinene	Demirci et al. (2005)

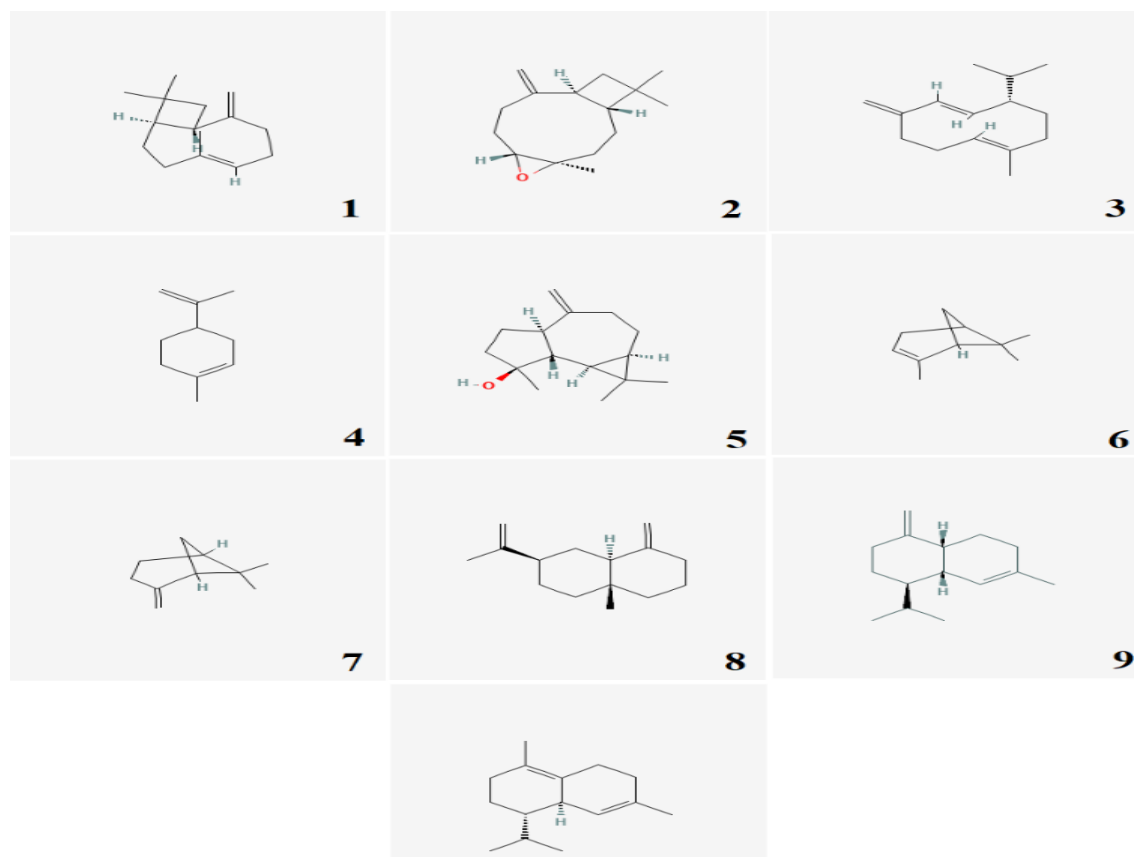


Fig. 1. The 10 most common compounds in *Hypericum* species

TABLE 3. Summarized studies on the biological activities of *Hypericum* species

<i>Hypericum</i> species	Biological activities	Extractions	References
<i>Hypericum calycinum</i> L.	Antioxidant, anticholinesterase, antiurease	Essential oil, methanol	Ersoy et al. (2020)
<i>Hypericum hircinum</i> L. subsp. <i>majus</i> (AITON) ROBSON	Antimicrobial, Antioxidant, antiproliferative, anti-collagenase	Essential oil, n-hexane, chloroform, methanol, ethyl acetate, n-butanol	Maggi et al. (2010), Quassinti et al. (2012), Tocci et al. (2018)
<i>Hypericum androsaemum</i> L.	Antioxidant, antimicrobial, cytotoxic effect	Essential oil, methanol, n-hexane, n-butanol, dichloromethane, ethyl acetate	Caprioli et al. (2016), Saddige et al. (2020)
<i>Hypericum helianthemoides</i> (SPECH) BOISS.	Antioxidant, antimicrobial	Essential oil	Pirbalouti et al. (2013), Moein et al. (2015)
<i>Hypericum pamphylicum</i> ROBSON ET DAVIS	Antioxidant, antimicrobial, cytotoxic effect	Essential oil, methanol	Eroglu-Ozkan et al. (2013)
<i>Hypericum thymbrifolium</i> BOISS. ET NOE	Antimicrobial, Antioxidant, anticholinesterase, cytotoxic effect	Essential oil, methanol	Eroglu-Ozkan et al. (2018a)
<i>Hypericum vacciniifolium</i> HAYEK ET SIEHE	Antimicrobial	Essential oil, ethanol	Dulger & Hacıoglu (2014)

TABLE 3. Cont.

<i>Hypericum</i> species	Biological activities	Extractions	References
<i>Hypericum linarioides</i> BOSSE	Antimicrobial, Antioxidant, cytotoxic effect, antiproliferative, apoptotic effect	Essential oil, methanol, water, hexane	Çakir et al. (2005), Radulović et al. (2007), Altay et al. (2022)
<i>Hypericum heterophyllum</i> VENT.	Antifungal, Antimicrobial, antioxidant,	Essential oil, acetone, ethanol, water	Çakir et al. (2004), Unal et al. (2008)
<i>Hypericum rumeliacum</i> BOISS.	Antimicrobial, Antioxidant	Essential oil, hidrodistilasyon, methanol	Saroğlu et al. (2007), Radulović et al. (2007)
<i>Hypericum spectabile</i> JAUB. ET SPACH	Antimicrobial, Antioxidant, anticholinesterase, cytotoxic effect	Essential oil, methanol, ethanol	Eroğlu-Ozkan et al. (2018a, 2019), Mohammed et al. (2020c)
<i>Hypericum amblysepalum</i> HOCHST.	Antioxidant, anticancer, anticholinesterase	Essential oil, methanol	Keskin (2015)
<i>Hypericum lysimachioides</i> BOISS. ET NOE var. <i>lysimachioides</i> BOISS. ET HAYIR	Antimicrobial, antioxidant	Essential oil, ethanol	Toker et al. (2006), Hakimoğlu et al. (2007), Barış et al. (2011)
<i>Hypericum lysimachioides</i> BOISS. ET NOE var. <i>spathulatum</i> RABSON	Antioxidant, anticholinesterase, cytotoxic effect	Essential oil, ethanol	Akdeniz et al. (2020)
<i>Hypericum elongatum</i> LEDEB. subsp. <i>elongatum</i> LEDEB.	Antifungal, Antimicrobial, antioxidant	Essential oil, acetone, ethanol, water	Çakir et al. (2004), Unal et al. (2008)
<i>Hypericum elongatum</i> LEDEB. subsp. <i>microcalycinum</i> (BOISS. ET HELDR.) ROBSON	Antioxidant, antimicrobial	Essential oil, methanol	Sarıkaya-Aydın et al. (2020)
<i>Hypericum lydium</i> BOISS.	Antioxidant	Essential oil, methanol	Şerbetçi et al. (2012)
<i>Hypericum retusum</i> AUCHER	Antioxidant, anticholinesterase, cytotoxic effect, antimicrobial	Essential oil, methanol, ethanol	Barış et al. (2011), Keskin et al. (2017)
<i>Hypericum pseudolaeve</i> ROBSON	Antimicrobial, Antioxidant, anticholinesterase, cytotoxic effect	Essential oil, methanol	Eroğlu-Ozkan et al. (2018a, 2019)
<i>Hypericum rupestre</i> JAUB. ET SPACH	Antimicrobial	Essential oil, ethanol	Dulger & Dulger (2014)
<i>Hypericum uniglandulosum</i> HAUSSKN. EX BORNM.	Antioxidant, antimicrobial	Essential oil, methanol, water, chloroform	Turkoglu et al. (2015)
<i>Hypericum capitatum</i> CHOISY var. <i>capitatum</i> CHOISY	Antioxidant, antimicrobial, anticholinesterase, DNA protective effect	Essential oil, methanol	Boga et al. (2016)

TABLE. 3. Cont.

<i>Hypericum</i> species	Biological activities	Extractions	References
<i>Hypericum scabroides</i> ROBSON ET POULTER	Antioxidant, DNA protective effect , Antiinflammatory, Antimicrobial	Essential oil, ethanol	Kızıllı et al. (2004, 2008), Kızıllı & Ceken (2009), Mansour et al. (2014) Duman & Sevimli (2008), Unal et al. (2008), Barış et al. (2011), Pirbalouti et al. (2013), Uysal & Gunes (2015), Seyrekoglu et al. (2022)
<i>Hypericum scabrum</i> L.	Antioxidant, antimicrobial	Essential oil	Douichene et al. (2016), Koç & Arabaci (2021)
<i>Hypericum thymopsis</i> BOISS.	Antioxidant, neuroprotective	Essential oil	Saroğlu et al. (2007), Radulović et al. (2007)
<i>Hypericum hirsutum</i> L.	Antimicrobial, Antioxidant	Essential oil, hidrodistilasyon, methanol	Çırak et al. (2005), Uysal & Gunes (2015), Radušienė et al. (2019)
<i>Hypericum pruinautum</i> BOISS. ET BAL.	Antifungal , Antioxidant, Antimicrobial	Essential oil, methanol, nitrogen, acetone, chloroform	Duman & Sevimli (2008), Duman (2012)
<i>Hypericum kotschyianum</i> BOISS.	Antimicrobial, antiherpetic	Essential oil, ethanol, acetone, chloroform, ethyl acetate	Duman (2012), Eroglu-Ozkan et al. (2018b, 2019)
<i>Hypericum neurocalycinum</i> BOISS. ET HELDR	Antimicrobial, antioxidant, anti-acetylcholinesterase	Essential oil	Ersoy et al. (2020)
<i>Hypericum confertum</i> CHOISY subsp. <i>confertum</i> CHOISY.	Antioxidant, anticholinesterase, antiurease	Essential oil, methanol	Spiteller et al. (2008)
<i>Hypericum venustum</i> FENZL	Antioxidant	Essential oil, ethanol, water	Aydemir et al. (2020)
<i>Hypericum crenulatum</i> BOISS.	Anticancer	Essential oil	Dulger e al. (2008), Dulger & Dulger (2014)
<i>Hypericum havvae</i> GÜNER	Antifungal , Antimicrobial	Essential oil, ethanol, n-hexane, ethyl acetate	Eroglu- Ozkan et al. (2018b, 2019)
<i>Hypericum malatyanum</i> PEŞMEN	Antimicrobial, antioxidant, anti-acetylcholinesterase	Essential oil	Boga et al. (2021)
<i>Hypericum empetrifolium</i> WILLD.	Antioxidant, antimicrobial, cytotoxic effect	Essential oil, hidrodistilasyon	Jaradat (2022)
<i>Hypericum lanuginosum</i> LAM. var. <i>lanuginosum</i> LAM.	Antioxidant, antimicrobial, cytotoxic effect	Essential oil, methanol, acetone, hexane	Ceylan et al. (2020)
<i>Hypericum montbretii</i> SPACH	Antioxidant, antimicrobial	Essential oil, methanol	Dimitrov et al. (2014)
<i>Hypericum aucheri</i> JAUB. ET SPACH	Antidepressant	Essential oil	

TABLE 3. Cont.

<i>Hypericum</i> species	Biological activities	Extractions	References
<i>Hypericum kazdaghensis</i> GEMICI ET LEBLEBICI	Antimicrobial	Essential oil, acetone, methanol	Dulger & Gonuz (2005)
<i>Hypericum adenotrichum</i> SPACH	Antigenotoxic, apoptotic	Essential oil, methanol	Sarimahmut et al. (2016)
<i>Hypericum orientale</i> L.	Antioxidant, anticholinesterase, Antiaflatoxicogenic	Essential oil, hexane, ethanol, water	Zengin-Kurt et al. (2018)
<i>Hypericum olympicum</i> L.	Antioxidant, antimicrobial	Essential oil, methanol, n-hexane, dichloromethane, ethyl acetate, n-butanol	Radulović et al. (2007), Uysal & Gunes (2015), Saddige et al. (2020)
<i>Hypericum organifolium</i> WILLD.	Antioxidant, Anti-aging	Essential oil, ethanol	Boran (2018), Seyrekoglu et al. (2022)
<i>Hypericum salsugineum</i> RABSON & HUB.- MOR.	Anticancer, antikolinesteraz	Essential oil	Duman (2012), Bender et al. (2018)
<i>Hypericum imbricatum</i> POULTER	Antimicrobial	Essential oil, ethanol	Dulger & Hacıoglu (2014)
<i>Hypericum tetrapterum</i> FRIES	Antioxidant, antimicrobial	Essential oil, methanol	Radulović et al. (2007)
<i>Hypericum perforatum</i> L.	Antioxidant, anticholinesterase, antiurease, antimicrobial	Essential oil, methanol	Çırak et al. (2005), Conforti et al. (2005), Duman & Sevimli (2008), Radulović et al. (2007), Pirbalouti et al. (2013), Ersoy et al. (2020), Seyrekoglu et al. (2022)
<i>Hypericum triquetrifolium</i> TURRA	Antioxidant, DNA protective effect, Antimicrobial	Essential oil, ethanol	Kızıl et al. (2004, 2008), Kızıl & Ceken, 2009)
<i>Hypericum × moserianum</i> André	Antioxidant, antimicrobial	metanol, etanol, n-hexane, ethyl acetate, dichloromethane, n-butanol	Saddige et al. (2020)
<i>Hypericum barbatum</i> Jacq.	Antioxidant, antimicrobial	metanol	Radulović et al. (2007)
<i>Hypericum richeri</i>	Antioxidant, antimicrobial	metanol	Radulović et al. (2007)
<i>Hypericum bupleuroides</i>	Antioxidant, antimicrobial	metanol	Ceylan et al. (2020)

Antioxidant activity

Reactive oxygen species are oxidising compounds that are routinely generated as a result of metabolic activities. Although minimal concentrations of oxidant compounds do not pose a threat, elevated levels can result in significant harm (Hafez & Fouad, 2020; Krupodorova & Sevindik, 2020). The antioxidant defensive system aids in the suppression of oxidant chemicals. However, in situations such as stress, nutrient deficiency, negative effects of environmental factors, the antioxidant defense system may be insufficient to suppress oxidant compounds (Bal et al., 2017). Oxidative stress occurs as a result of the imbalance between oxidant compounds and the antioxidant defense system. Multiple sclerosis, Parkinson's illness, Alzheimer's disease, cardiac ailments, and other illnesses, neurodegenerative diseases, and cancer may arise as a result of oxidative stress (Selamoglu et al., 2020; Saridogan et al., 2021; Sevindik, 2021). Supplementary antioxidants are utilised in reducing the oxidative stress's consequences (Abdel-Farid et al., 2021; Eraslan et al., 2021; Abdel-alim et al., 2023). Plants are significant sources in terms of being a supplement for antioxidants. In this study, a compilation of literature on the anti-oxidant activity studies of *Hypericum* species is presented.

In this context, the IC₅₀ values of DPPH test results of methanolic extracts of *H. calycinum*, *H. confertum* and *H. perforatum* collected from Turkey were reported to be 10.05, 23.32 and 29.35 µg/mL, respectively. The IC₅₀ values of ABTS test results were reported as 6.00, 9.42 and 9.01 µg/mL, respectively. Also, the IC₅₀ values of the metal chelation test results were reported as 286.58, >1000 and >1000, respectively. The results of CUPRAC test IC₅₀ values were reported as 1.621, 1.204 and 1.133 µg/mL, respectively (Ersoy et al., 2020).

According to reports, the methanol extract of *H. perforatum* collected from Italy has antioxidant activity by β-carotene bleaching and DPPH tests (Conforti et al., 2005). In another study also reported from Italy, the EC₅₀ value of the essential oil of *H. hircinum* subsp. *majus* was reported as 680 µg/mL as a result of the DPPH test, and the EC₅₀ value as 270 µg/mL as a result of the ABTS test (Quassinti et al., 2012).

Antioxidant activity of methanolic, ethanolic, dichloromethane, n-butanol, n-hexane, ethyl

acetate and aqueous extracts of *H. androsaemum*, *H. olympicum*, *H. ericoides*, and *H. x moserianum* collected from the United Kingdom were reported using the DPPH test. The highest DPPH inhibition values were reported as 96.197% (methanol) in *H. androsaemum*, 73.732 % (ethanol) in *H. ericoides*, 92.528 % (ethanol) in *H. x moserianum* and 87.098% (ethanol) in *H. olympicum* (ethanol) (Saddige et al., 2020).

In another study conducted by Mohammed et al., (2020c), the total antioxidant value of *H. spectabile* was reported as 4.215 mmol/L. The DPPH activity values of the methanol extract of *H. androsaemum* collected from Italy were reported to be in the range of 27.7-36.5 µg/mL, and the β-Carotene/Linoleic acid activity values were reported as 9.6-23.7 µg/mL. It has also been reported that the scavenging activity value of hypochlorous acid is in the range of 9.50-45.5 µg/mL (Caprioli et al., 2016).

Iranian essential oils of *H. perforatum*, *H. helianthemoides*, and *H. scabrum* were reported to have DPPH activity of 311.7, 253.4, and 93.9 g/mL, respectively (Pirbalouti et al., 2013). The IC₅₀ value of the DPPH radical scavenging activity of the ethanol extract of *H. helianthemoides* collected from Iran has been reported as 309.35 µg/mL, and the nitric oxide scavenging activity value of 85.2% at 200 µg/mL. In addition, it has been reported that the IC₅₀ value of the FRAP activity is 109.7 µg/mL, the IC₅₀ value of the ferric thiocyanate (FTC) activity is 109.7 µg/mL, and the OH scavenging activity is 70.3 at 125 µg/mL (Moein et al., 2015).

The EC₅₀ value of the DPPH radical scavenging test of methanol extract of *H. pamphylicum* collected from Turkey has been reported as 0.50 mg/mL, and the EC₅₀ value of the liposome peroxidation test has been reported as 6.76 mg/mL. In addition, the EC₅₀ value of the superoxide radical scavenging activity test has been reported as 0.77 mg/mL and the EC₅₀ value of the ferric reducing antioxidant power test has been reported as 0.65 mg/mL (Eroglu-Ozkan et al., 2013). Inhibition of lipid peroxidation EC₅₀ values of methanol extracts of *H. thymbrifolium*, *H. spectabile* and *H. pseudolaeva* collected from Turkey were reported as 4.39, 2.80 and 5.41 mg/mL, respectively. In the same study, it was reported that DPPH radical scavenging activity EC₅₀ value was 0.622, 0.567 and 0.916 mg/mL, respectively, and superoxide radical scavenging

activity EC₅₀ value was 0.641, 0.430 and 1.730 mg/mL, respectively. In addition, the value of ferric reducing antioxidant power was reported to be 2.58, 2.66 and 2.21 at 5 mg/mL concentration, respectively (Eroglu-Ozkan et al., 2018a). Inhibition of lipid peroxidation EC₅₀ values of *H. neurocalycinum* and *H. malatyanum* obtained from Turkey were reported to be 2.49 and 4.82mg/mL, respectively, and DPPH radical scavenging activity EC₅₀ values as 0.251 and 1.54mg/mL, respectively. It has also been reported that the EC₅₀ value of superoxide radical scavenging activity is 0.613 and 0.802mg/mL, respectively (Eroglu-Ozkan et al., 2018b). It has been reported that methanol extract of *H. linarioides* collected from Turkey has higher DPPH activity and ferric ion reduction capacity than water and hexane extracts (Altay et al., 2022). It has been reported that acetone, chloroform, ethanol and water extracts of *H. heterophyllum*, *H. hyssopifolium* and *H. scabrum* collected from Turkey have strong DPPH activities (Unal et al., 2008). In a study reported from Serbia and Montenegro, the antioxidant activities of methanol extracts of *H. barbatum*, *H. richeri*, *H. maculatum*, *H. perforatum*, *H. tetrapterum*, *H. olympicum*, *H. hirsutum* and *H. linarioides* were between 540 and 73.100µmol/g (Radulović et al., 2007). Keskin (2015) reported that the DPPH inhibition value of the methanol extract of *H. amblysepalum* in the concentration ranges of 10-500 µg/mL was between 20.20-89.07% of the flower parts, 24.46-83.17 of the fruit parts and 25.24-84.13 of the seed parts. In addition, it has been reported that reducing power activity is between 0.28-0.62 in flower parts, 0.27-0.66 in fruit parts and 0.25-0.63 in seed parts in concentration ranges of 10-500µg/mL. Whereas according to Hakimoğlu et al. (2007), the IC₅₀ value for the *in vitro* DPPH activity of the ethanol extract of *H. lysimachioides* var. *lysimachioides* was reported to be 28µg/mL. In another study conducted by Akdeniz et al. (2020), the CUPRAC test results of the ethanol extract of the aerial parts and root parts of *H. lysimachioides* var. *spathulatum* and the essential oil of the plant were determined to be 57.02, 56.61 and 177.84µg/mL, respectively. It has also been reported that the IC₅₀ value of the DPPH test result is 73.86, 80.21 and ≥ 200µg/mL, and the IC₅₀ value of the ABTS test result is 30.78, 31.63 and 60.79µg/mL. In a different study Sarıkaya-Aydin et al. (2020) reported that the IC₅₀ value of the aqueous extract of *H. microcalycinum* was 51.8µg/mL for the DPPH test result, >1000µg/

mL for the NO radical scavenging test result and 134.5µg/mL for the SO radical scavenging test. In another study, it was reported that the lipid inhibiting activities of methanol extracts of the fruits and flowers parts of *H. lydiu*m were 86.40% of the fruits parts and 88.86% of the flowers parts at a concentration of 5mg/mL. In addition, it was reported that DPPH test results were 90.75% of fruit parts and 90.77% of flowers parts at 2.5mg/mL concentration, superoxide radical scavenging activity results were 98.83% of fruit parts and 99.04% of flowers parts at 10mg/mL concentration (Şerbetçi et al., 2012).

The antioxidant activity of the methanol extract of the flowers, fruits and seeds of *H. retusum* collected from Turkey was studied and from the results, it was reported that the result of reducing power activity test at concentrations between 10-500µg/mL was 0.27-0.60 for flower parts, 0.27-0.68 for fruits parts and 0.22-0.82 for seed parts. In addition, it has been reported that the DPPH test results at concentrations between 10-500µg/mL are 22.2-83.7 on the flower parts, 28.97-77.71 on the fruits parts and 22.98-83.13 on the seeds (Keskin et al., 2017). In an earlier study, the ethanol extract of the stems, leaves and flowers of *H. scabrum*, *H. lysimachioides* var. *lysimachioides*, and *H. retusum* has antioxidant potential using reducing power, free radical scavenging, deoxyribose assay, metal chelating tests (Barış et al., 2011). The antioxidant activity of methanol, water and chloroform extracts of *H. uniglandulosum* was evaluated and it was concluded that the IC₅₀ values of the DPPH test result varied between 40-27mg/mL for methanol extract, 50-61mg/mL for water extract, and 108-124mg/mL for chloroform extract (Turkoglu et al., 2015). It has been also found that the lipid peroxidation test results of petroleum ether, acetone, methanol and water extracts of *H. capitatum* var. *capitatum* were >200, >200, 41.69 and 92.85, respectively. In addition, it was reported that the DPPH test result was >200, >200, 16.82 and >200, >200µg/mL, respectively, and the ABTS test results were >200, 88.84, 9.24 and 9.76, respectively (Boga et al., 2016).

It has been also proved that the ethanol extracts of aerial parts of *H. triquetrifolium* and *H. scabroides* have potent antioxidant potential using DPPH, metal chelation, hydroxyl radical and lipid peroxidation tests. (Kızıl et al., 2008). The IC₅₀ values of the essential oils of *H.*

thymopsis and *H. perforatum* were revealed to be in the range of 67.53-148.20g/mL and 50.41-142.84 g/mL, respectively, in a different study from Turkey (Koç & Arabaci, 2021). It has been reported that the ethanol and water extract of *H. venustum* collected from Turkey exhibited strong antioxidant activities at different concentrations by reducing power, superoxide anion scavenging, free radical scavenging, hydrogen peroxide scavenging and metal chelating activity tests (Spiteller et al., 2008).

The IC₅₀ results of the ethanol extracts of the root and aerial parts of *H. empetrifolium* collected from Turkey have been reported as 42.14 and 11.98µg/mL for the DPPH test, 6.77 and 5.32µg/mL for the ABTS test, and 12.91 and 4.01µg/mL for the CUPRAC test (Boga et al., 2021). In a study conducted in Palestine, it was reported that the IC₅₀ value of the DPPH test result of aqueous, methanol, acetone and hexane extracts of *H. lanuginosum* was between 6.16-1258µg/mL (Jaradat, 2022). Methanol extracts of *Hypericum montbretii* and *H. bupleuroides* collected from Turkey have been reported to have antioxidant potentials using DPPH, FRAP and CUPRAC tests (Ceylan et al., 2020). It has been reported that the IC₅₀ values of hexane, ethanol and water extracts of *H. orientale* collected from Turkey are in the range of 42.39-114.49µg/mL for the ABTS test and 58.06-124.80µg/mL for the CUPRAC test (Zengin-Kurt et al., 2018).

The IC₅₀ value of the ethanol extracts of *H. perforatum*, *H. scabrum* and *H. origanifolium* collected from Turkey was reported as 3.17-3.79µg/mL in the DPPH test, and 9.54-11.28 mM/g DW in the TEAC test. It has also been reported that the ferric reducing power test result is in the range of 10-45%, and the FTC test result is in the range of 81.97-90.83% (Seyrekoglu et al., 2022). It has been reported that the IC₅₀ value of the DPPH activity of the ethanol extract of *H. origanifolium* collected from Turkey is 270µg/mL and the IC₅₀ value of the β-carotene bleaching test is 230µg/mL (Boran, 2018).

Also, according to El-Hawary (2022) the methanolic extract of blooming aerial parts of *Hypericum sinaicum* Boiss. obtained from Saint Catherine Protectorate in Egypt showed an IC₅₀ value for DPPH scavenging activity of 50 22.9µg/mL and with 13.10µg/mL for IC₅₀ of ABTS.

In this context, when the literature data was examined, it was seen that *Hypericum* species had important antioxidant activities. As a result, it is thought that *Hypericum* species can be used as a natural antioxidant source.

Antimicrobial activity

The incidence of diseases caused by microorganisms has increased recently. Today, antimicrobial drugs are used in the treatment of microbial diseases (Mohammed et al., 2023b). The increase in the prevalence of resistant bacteria due to unconscious drug use renders the antimicrobial drugs used insufficient (Sevindik et al., 2023). In this context, researchers focused on the discovery of new antimicrobial drugs (Sevindik et al., 2016). Many people have turned to new and natural antimicrobial products in order not to deal with the problems that may arise from the possible side effects of the synthetic drugs used (Sevindik, 2020). This review compiles the identification of natural antimicrobial uses of *Hypericum* species as an agent.

According to studies reported in the literature, it has been reported that *Hypericum hircinum* subsp. *majus* collected from Italy is effective in antimicrobial activity against *Staphylococcus aureus*, *Streptococcus mutans*, *Enterococcus faecalis*, *Bacillus subtilis*, *Escherichia coli* and *Candida albicans* strains at concentrations of 155-5000µg/mL (Maggi et al., 2010). Methanol extracts of *H. hirsutum* subsp. *hirsutum*, *H. hircinum* subsp. *majus*, *H. maculatum*, *H. montanum*, and *H. perforatum* collected from Italy have been reported to be effective against *Candida albicans*, *C. parapsilosis*, *C. tropicalis*, *C. lusitaniae* and *C. glabrata* in MIC (minimum inhibitory concentration) values between 0.13 and >500µg/L (Tocci et al., 2018).

The methanol, ethanol, n-hexane, dichloromethane, ethyl acetate, n-butanol and aqueous extracts of *H. androsaemum*, *H. ericoides*, *H. x moserianum* and *H. olympicum* collected from the United Kingdom have been reported to be effective at different concentrations against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* (Saddige et al., 2020). The activities of essential oils of *H. helianthemoides*, *H. perforatum*, and *H. scabrum* collected from Iran against *Listeria monocytogenes*, *Bacillus cereus*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*

were reported. According to the findings of the study, *H. perforatum* was effective between 250-500mg/mL, *H. scabrum* 62-250mg/mL and *H. helianthemoides* 125-500mg/mL (Pirbalouti et al., 2013).

It has been reported that petroleum ether, diethyl ether, chloroform, acetone, methanol and total methanol extracts of *H. pamphylicum* collected from Turkey are effective against *Staphylococcus aureus*, *S. epidermidis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella flexneri*, *Proteus mirabilis* and *Candida albicans* at 19.52-2500mg/mL extract concentrations by microdilution method (Eroglu-Ozkan et al., 2013).

It has been also reported that petroleum ether, diethyl ether, chloroform, acetone, methanol and total methanol extracts of *H. spectabile*, *H. psedolaeve*, *H. thymbriifolium*, *H. neurocalycinum*, *H. malatyanum* and *H. perforatum* collected from Turkey are effective against *Staphylococcus aureus*, *Staphylococcus aureus* MRSA and *Staphylococcus epidermidis* at MIC values between 4.8-625µg/mL (Eroglu-Ozkan et al. al., 2019). The ethanol and aqueous extracts of *H. vacciniifolium*, *H. rupestre* and *H. imbricatum* collected from Turkey were found to be effective between 0.2-12.5mg/mL against *Staphylococcus aureus* (Dulger & Hacıoglu, 2014). Also, the essential oils of *H. linarioides* collected from Turkey were reported as effective against *Fusarium acuminatum* *F. culmorum*, *F. equiseti*, *F. oxysporum*, *F. sambucinum*, *F. solani* and *Verticillium albo-atrum* with inhibition zones between 8.1-41.8mm at 2.5mg/mL concentration and between 5.7-49.4mm at 5mg/mL concentration (Çakır et al., 2005).

The essential oils of *H. hyssopifolium* subsp. *elongatum* var. *elongatum* and *H. heterophyllum* collected from Turkey were found to be effective against *Fusarium oxysporum*, *F. culmorum*, *F. sambucinum*, *F. solani* and *F. acuminatum* and *Rhizoctonia solani* (Çakır et al., 2004). The acetone, chloroform, ethanol and water extracts of *H. heterophyllum*, *H. hyssopifolium* and *H. scabrum* collected from Turkey have been reported to be effective against *Bacillus megaterium*, *B. subtilis*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Streptococcus pyogenes* and *Staphylococcus aureus* (Unal et al., 2008). In another study, *H.*

rumeliacum and *H. hirsutum* collected from Turkey showed strong effects against *Escherichia coli*, *Bacillus cereus* *Proteus mirabilis*, *Agrobacterium tumefaciens*, *Pseudomonas aeruginosa*, *P. tolaasii*, *Salmonella enteritidis*, *Staphylococcus aureus*, *Micrococcus luteus*, *Sarcina lutea* and *C. albicans* by microdilution method (Saroğlu et al., 2007).

In a study reported from Serbia and Montenegro, it was proved that methanol extracts of *H. barbatum*, *H. richeri*, *H. maculatum*, *H. perforatum*, *H. tetrapterum*, *H. olympicum*, *H. hirsutum* and *H. linarioides* were effective against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Salmonella enteritidis*, *Candida albicans* and *Aspergillus niger* at different concentrations (Radulović et al., 2007). It has been reported that *H. lysimachioides* var. *lysimachioides* collected from Turkey has antimicrobial activity against *Staphylococcus aureus*, *Brevibacillus brevis*, *Bacillus cereus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa* and *Candida albicans*. It has also been reported to exhibit the best effect against *C. albicans* (Toker et al., 2006).

It was reported that water extract of *H. uniglandulosum* was effective between 23-24 mm against *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhimurium*, *Escherichia coli*, *Candida glabrata* and *C. tropicalis* at 25µg extract concentration (Turkoglu et al., 2015). The MIC values of petroleum ether, acetone, methanol and water extracts of *H. capitatum* var. *capitatum* were reported to be 250-300µg/mL against *Staphylococcus aureus* and 250-2000µg/mL against *Streptococcus pyogenes*. It has also been reported to be 10-15µg/mL against *Escherichia coli*, 260-2200µg/mL against *Pseudomonas aeruginosa*, and 25-2200µg/mL against *Candida albicans* (Boga et al., 2016). It was also reported that the essential oils of *H. scabrum*, *H. scabroides* and *H. triquetrifolium* were effective at different concentrations against *Bacillus brevis*, *Escherichia coli*, *Streptococcus pyogenes*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans* (Kızıl et al., 2004) and in another study, it was found that *H. perforatum* and *H. pruinaum* have antifungal effects on *Phytophthora capsici* and *Diploceras hypericinum* (Çırak et al., 2005). In another study conducted in Turkey, acetone, methanol and chloroform extracts of *H.*

pruinatum, *H. olympicum* and *H. scabrum* were reported to be effective at different concentrations against *Streptococcus mutans*, *Staphylococcus aureus* and *Candida albicans* (Uysal & Gunes, 2015).

Antimicrobial activities of chloroform, ethyl acetate, acetone and ethanol extracts of *H. perforatum*, *H. scabrum* and *H. kotschyianum* collected from Turkey have been reported against *Sarcina lutea*, *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus faecalis*, *S. mutans*, *S. pneumoniae*, *S. salivarius*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* strains and were effective on all but *S. faecalis* and *S. pneumoniae* species (Duman & Sevimli, 2008). It has been recorded that hydroethanol extracts of the leaf and root parts of *H. havvae* collected from Turkey are effective between 3.12-25mg/mL against *Candida albicans*, *C. tropicalis*, *C. guilliermondii*, *C. krusei*, *C. glabrata*, *C. parapsilosis*, *Cryptococcus neoformans* and *C. laurentii* (Dulger & Dulger, 2014). It has been reported that n-Hexane, ethyl acetate, ethanol and aqueous extracts of *H. havvae* collected from Turkey are effective against *Escherichia coli*, *Enterobacter aerogenes*, *Alcaligenes faecalis*, *Salmonella typhimurium*, *Citrobacter freundii*, *Staphylococcus aureus*, *Bacillus cereus*, *B. subtilis*, *B. brevis*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Micrococcus luteus*, *M. flavus*, *Candida albicans*, *Rhodotorula rubra* and *Kluyveromyces fragilis* (Dulger et al., 2008).

It has been reported that ethanol extracts of root and aerial parts of *H. empetrifolium* collected from Turkey are effective against *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus aureus*, *S. epidermidis*, *Enterococcus faecalis*, *Candida albicans*, *C. parapsilosis* and *C. tropicalis* with MIC values in the range of 78.12-625µg/mL and 4.88-625µg/mL, respectively (Boga et al., 2021). In a study conducted in Palestine, the effects of aqueous, methanol, acetone and hexane extracts of *H. lanuginosum* against *Candida albicans*, *Enterococcus faecium*, *Epidermophyton floccosum*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella sonnei* MRSA and *Staphylococcus aureus* were reported to be between 0.78-12.5µg/mL (Jaradat, 2022).

The methanol extracts of *H. montbretii* and

H. bupleuroides collected from Turkey have been reported to be between 0.26-100 µg/mL against *Bacillus subtilis*, *Staphylococcus aureus*, *S. epidermidis*, *Escherichia coli*, *Proteus vulgaris* and *Candida albicans* (Ceylan et al., 2020). It has been reported that *H. perforatum* collected from Italy is effective against *Staphylococcus aureus* subsp. *aureus*, *Enterococcus faecalis*, *Micrococcus luteus*, *Proteus mirabilis*, *Proteus vulgaris*, *Escherichia coli*, *Pythium ultimum*, *Trichophyton mentagrophytes* var. *mentagrophytes* at different concentrations (Conforti et al., 2005). It has been reported that chloroform, acetone and methanol extracts of endemic *H. kazdaghensis* collected from Turkey are effective between 9-17.6µg/mL against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium* and *Staphylococcus aureus* (Dulger & Gonuz, 2005).

In this context, it has been observed that *Hypericum* species reported in the literature have important antimicrobial properties. As a result, it is thought that *Hypericum* species can be used as a natural antimicrobial agent.

Anticholinesterase activity

Anticholinesterases are chemicals that prevent the breakdown of the neurotransmitter butyrylcholine or acetylcholine. These substances are potential therapeutics for myasthenia gravis and Alzheimer's disease. It can also be used as insecticides (Taylor, 2006; Smaili et al., 2022). In this context, in a study conducted in Turkey, the cholinesterase inhibitory activity of methanol extracts of *H. calycinum*, *H. confertum* and *H. perforatum* was reported against acetylcholinesterase and butyrylcholinesterase at 200mg/mL concentration. As a result of the study, percent inhibition values against acetylcholinesterase were reported as 45.33, 32.61 and 38.89, respectively, and percent inhibition values against butyrylcholinesterase as 64.75, 76.08 and 82.50, respectively (Ersoy et al., 2020).

The acetylcholinesterase (AChE) inhibitory activity of methanol extracts of *H. thymbrifolium*, *H. spectabile* and *H. pseudolaeve* collected from Turkey was reported to be 63.41%, 59.49 and 49.37%, respectively (Eroglu-Ozkan et al., 2018a). Also, the acetylcholinesterase and butyrylcholinesterase inhibitory activities of methanol extract of *H. amblysepalum* were reported to be 20.39 and 76.89µg/mL (Keskin,

2015). Whereas, the ethanolic extract of aerial parts and root parts of *H. lysimachoides* var. *spathulatum* and the essential oil of the plant have high acetylcholinesterase and butyrylcholinesterase inhibitory activities (Akdeniz et al., 2020). In a study conducted in Turkey, it was reported that the methanol extract of *H. retusum* has acetylcholinesterase and butyrylcholinesterase activity. (Keskin et al., 2017) and in another research, the acetylcholinesterase and butyrylcholinesterase activities of petroleum ether, acetone, methanol and water extracts of *H. capitatum* var. *capitatum* were 14-14.63% and 45.60-0.74%, respectively (Boga et al., 2016).

It has been reported that the IC₅₀ values of hexane, ethanol and water extracts of *H. orientale* collected from Turkey have anticholinesterase activity in the range of 165.20->200 and butyrylcholinesterase activity in the range of 50.57->200 (Zengin-Kurt et al., 2018). The EC50 value of the anticholinesterase inhibitory activity of the methanol extract of *H. neurocalycinum* and *H. malatyanum* collected from Turkey has been reported to be 2.16 and 6.83mg/mL (Eroglu-Ozkan et al., 2018b). Acetylcholinesterase and butyrylcholinesterase activities of ethanol extracts of root and aerial parts of *H. empetrifolium* collected from Turkey were reported. As a result of the study, it has been reported that the aerial parts have no activity and the root parts were 38.89 and 88.69%, respectively (Boga et al., 2021). It has been reported that the acetylcholinesterase inhibitory activity of *H. salsugineum* collected from Turkey is 1.689mg/g and the butyrylcholinesterase inhibitory activity is 0.244mg/g (Bender et al., 2018).

In this context, it has been seen that *Hypericum* species reported in the literature are important natural materials in terms of their cholinesterase inhibition potential. As a result, it can be a natural source in the treatment of diseases such as Alzheimer's.

Other biological activities

It has been seen in the literature that *Hypericum* species have different kinds of biological activities. The IC₅₀ values of the methanol extract of *H. androsaemum* collected from Italy against A375 (Human malignant melanoma cell line), MDA-MB 231 (Human breast adenocarcinoma cell line) and HCT116 (Human colon carcinoma cell line) were reported to be 19.31-32.29µg/

mL, 12.88-30.05µg/mL and 8.40-19.40µg/mL, respectively (Caprioli et al., 2016).

The counter effects of methanol extracts of *H. thymbrifolium*, *H. spectabile* and *H. pseudolaeva* collected from Turkey were investigated against HeLa, NRK-52E cell lines and it was found that *H. thymbrifolium* and *H. spectabile* did not show activity, and *H. pseudolaeva* was 1.218mg/mL against HeLa cell lines and 0.964mg/mL against NRK-52E cell lines (Eroglu-Ozkan et al., 2018a).

In other studies conducted in Turkey, it was reported that ethanol extract of aerial parts and root parts of *H. lysimachoides* var. *spathulatum* and essential oil of the plant have antiproliferative effects on breast cancer cell line (MCF-7) and colon cancer cell line (HT-29) (Akdeniz et al., 2020). Also, methanol extract of *H. retusum* was reported to be between 0.781-50µg/mL at concentrations of 25.45-78.40% against HeLa cell line and 4.61-90.80% against NRK-52E cell line (Keskin et al., 2017).

It has been reported that the root and aerial parts of *H. empetrifolium* collected from Turkey are 60.6%-86.74% against A498 cell line, 90.76-79.74% against UO31 cell line, 99.28-92.13% against COLO205 cell line, 86.56-92.5% against KM12 cell line, 99.71-99.93% against MG633 cell line and 97.33-97.25% against MG63 cell line, respectively. (Boga et al., 2021).

In a study conducted in Palestine, it was reported that the IC₅₀ value of aqueous, methanol, acetone and hexane extracts of *H. lanuginosum* against breast cancer (MCF-7), hepatocellular carcinoma (Hep 3B and Hep G2), Hek293t and HeLa cell lines varied in the range of 46.9-331.87µg/mL (Jaradat, 2022).

Antiurease effects of methanol extracts of *H. calycinum*, *H. confertum* and *H. perforatum* collected from Turkey have been reported. As a result of the study, the percent inhibition value of *H. calycinum* was reported as 19.44. It has also been reported that *H. confertum* and *H. perforatum* have no antiurease effect (Ersoy et al., 2020).

In a study reported from Italy, the IC₅₀ values of the essential oil of *H. hircinum* subsp. *majus* against PC3 human prostatic adenocarcinoma, T98G human glioblastoma, A431 human squamous carcinoma and B16-F1 mouse

melanoma cell lines were reported to be 80.7, 117.2, 63.7 and 78.3 µg/mL, respectively (Quassinti et al., 2012).

It has been reported that methanol extract of *H. linarioides* collected from Turkey has potent activities against MCF-7 and HT-29 cancer cell lines (Altay et al., 2022). In a study conducted in Turkey, it was reported that *H. capitatum* var. *capitatum* had a DNA protective effect at 250, 350, and 500 µg/mL concentrations at 18.67, 22.07, and 73.75% (Boga et al., 2016). It has been reported that ethanol extracts of *H. scabroides* and *H. triquetrifolium* collected from Turkey have a DNA protective effect (Kızıl & Ceken, 2009).

It has been reported that the methanol extract of *H. scabroides* collected from Turkey has a strong anti-inflammatory effect at a dose of 200mg/kg (Mansour et al., 2014). The LC₅₀ values of methanol extract of *H. amblysepalum* against HeLa and NRK52E cell lines were reported to be 11.67 and 4.39mg/mL, respectively (Keskin, 2015). It has been reported that *H. crenulatum* collected from Turkey has strong antiproliferative activity against MCF-7 and MDA-MB-231 breast cancer cell lines (Aydemir et al., 2020). It has been reported that methanol extract of *H. salsugineum* collected from Turkey has strong antiproliferative activity against MCF-7 and (B) MDA-MB-231 cell lines (Bender et al., 2018). It has been reported that the antidepressant properties of *H. aucheri* collected from Bulgaria are dose-dependent (Dimitrov et al., 2014). It has been reported that *H. adenotrichum* collected from Turkey has strong effects against human breast cancer cell lines (MCF-7 and MDA-MB-231) (Sarimahmut et al., 2016). It has been reported that the anti-aflatoxigenic effect of hexane, ethanol and water extracts of *H. orientale* collected from Turkey is in the range of 5.26-18.42% (Zengin-Kurt et al., 2018). It has been reported that the % inhibition values of the anti-collagenase, anti-elastase and anti-hyaluronidase activities of the ethanol extract of *H. origanifolium* collected from Turkey ranged from 7.5 to 79.28% (Boran, 2018). It has been reported that *H. thymopsis* collected from Algeria has neuroprotection effect (Douichene et al., 2016). It has been reported that methanol extract of *H. neurocalycinum*, *H. salsugineum* and *H. kotschyianum* collected from Turkey has antiproliferative effects against Vero cells and antiherpetic effects against HSV-1 (Duman, 2012). Based on the studies reported in the literature within the scope of this review, it

is seen that *Hypericum* species have significant anticancer potential. In this instance, *Hypericum* species is thought to be an important natural agent for several therapeutic uses.

Conclusion

As a result of our thorough review, we can say that plants from the genus *Hypericum* are good sources of natural compounds with potential therapeutic biological activity in terms of antioxidant, antimicrobial and anticancer. Studies on phytochemistry and pharmacology have shown that *Hypericum* species are valuable medicinal plants with noteworthy bioactivities. Further studies are required to expand the natural compounds' therapeutic applications. Also, in order to fulfil the increasing needs of the pharmaceutical business and to fully use their preventative and therapeutic potential, careful investigations on pharmaceutical standardisation, the mechanism of action of the active ingredients, and toxicity of *Hypericum* species are required.

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نباتات جنس العرن: الخصائص العامة والأنشطة البيولوجية والمحتويات الكيميائية ومجالات الاستخدام

غدير الشغبي⁽¹⁾، فلاح محمد⁽²⁾، سيد رشاد⁽¹⁾، عمران أويسال⁽³⁾، أوغوزهان كوجر⁽⁴⁾، عمر ليكسيز⁽⁵⁾، محمد دوغان⁽³⁾، علي سابيك⁽⁶⁾، مصطفى سيفينديك⁽⁵⁾

(1) معمل التحاليل الحيوية- المركز الإقليمي للأغذية والأعلاف- مركز البحوث الزراعية- الجيزة- مصر،
 (2) قسم الأحياء- كلية العلوم- جامعة زاخو- دهوك- 42001 العراق، (3) قسم تجهيز الأغذية- مدرسة بهجة المهنية- جامعة عثمانية كوركوت آتا- عثمانية 80000 - تركيا، (4) قسم خدمات الصيدلة- المدرسة المهنية للخدمات الصحية- جامعة عثمانية كوركوت آتا- عثمانية 80000 - تركيا، (5) قسم الأحياء- كلية العلوم والآداب- جامعة عثمانية كوركوت آتا - العثمانية 80000 - تركيا، (6) قسم الكيمياء وتقنيات المعالجة الكيميائية- مدرسة بهجة المهنية- جامعة عثمانية كوركوت آتا- عثمانية 80000 - تركيا.

تنتشر نباتات جنس العرن (*Hypericum L. Genus*) بالعديد من الأنواع على نطاق واسع في جميع أنحاء العالم.

وبالإضافة إلى خواصها الغذائية، فإن نباتات جنس العرن *Hypericum L.* تتميز أيضا بخصائصها الدوائية. ولطالما كانت هذه النباتات جزءاً من الطب التقليدي في العديد من الدول. ويُقدم العمل الحالي استعراضاً موجزاً عن أنواع نباتات جنس العرن؛ ويشمل ذلك الخصائص العامة، ومجالات الاستخدام، والنشاط الحيوي، والتركيب الكيميائي كما ورد في الأبحاث المنشورة سابقاً. ومن خلال الأبحاث التي تمت مراجعتها خلال العمل الحالي، تم التأكيد على أن أنواع نباتات جنس العرن تحتوي على مستويات عالية من مضادات الأكسدة ومضادات الميكروبات وأنشطة مضادة للسرطان من حيث النشاط البيولوجي والتي يمكن الأنواع من الاستخدام الشائع في مكافحة الأمراض.

كما تم إثبات احتواء الأنواع النباتية لنباتات جنس العرن على تركيزات عالية من المعادن الهامة بما في ذلك الحديد والزنك والكالسيوم والصوديوم. وتمتلك النباتات من جنس العرن أيضاً أنشطة مثبطة لأستيل كولين أستيراز وأوكسيداز أحادي الأمين بالإضافة إلى الخصائص القابضة، والمضادة لفرط سكر الدم، والمضادة للبكتيريا، والمضادة للالتهابات، والمضادة للأكسدة، والمضادة للإلتهابات الكبد. بالإضافة إلى ذلك، تم استنتاج أن المركبات الكيميائية النشطة بيولوجياً الأكثر شيوعاً التي تم تسجيلها والموجودة في أنواع نباتات جنس العرن هي (1) caryophyllene، (2) caryophyllene oxide، (3) germacrene-D، (4) limonene، (5) spathulenol، (6) β -pinene، (7) α -pinene، (8) γ -muurolene، (9) β -selinene، (10) δ -cadinene. مع أخذ كل هذه المعلومات في الاعتبار، من الواضح أن أنواع نباتات جنس العرن تقدم فوائد طبية محتملة بالإضافة إلى قيمتها الغذائية.