International Journal of Secondary Metabolite
2022, Vol. 9, No. 1, 103–111
https://doi.org/10.21448/ijsm.1029080
Published at https://dergipark.org.tr/en/pub/ijsm
Review Article

A review on essential oil analyses and biological activities of the traditionally used medicinal plant *Thymus vulgaris* L

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Abstract: Since the old times, seeds producing plants have played a vital role in the progress of human culture to treat diseases. Medicinal plants are used traditionally by the local communities to treat diseases. Recently, a report has shown that more than 250,000 flowering plant species are available globally. Scientists are continuously working on higher plants to help and understand plant poisonousness and to defend humans and animals from natural toxins. A plant`s toxicity and its medical use are dependent on the plant's volatile phytochemicals. *Thymus vulgaris* L is a common aromatic plant used widely as a folk medicine to treat various diseases by different ethnic communities around the globe including the Sultanate of Oman. Previous studies in Oman showed that the selected plant species contains several groups of phytochemicals such as essential oils and secondary metabolic compounds they can enhance their biological and toxicological activities. Therefore, the aim of the present review is to explore the volatile phytochemicals, biological and toxicological features of *Thymus vulgaris* grown in Oman. The results can be helpful for discovering new drugs to treat asthma, cough, chronic bronchitis and other infectious diseases. In conclusion, this review provides information on the volatile phytochemicals, pharmacological and toxicological aspects of the selected plant species.

ARTICLE HISTORY
Received: Nov. 27, 2021
Revised: Jan. 19, 2022
Accepted: Feb. 27, 2022

KEYWORDS
Thymus vulgaris, Medicinal uses, Phytochemicals, Pharmacological, Toxicological activity, Sultanate Oman.

1. INTRODUCTION

Due to the increasing demands for daily foods that contain bioactive constituents such as volatile oils and secondary metabolic compounds, which may occur as health assistance, nutrition, as well as herbal. Nowadays, medicinal plants are used as sources in most countries of alternative medicines in many countries. Different traditional systems are revived to treat diseases instead of using synthetic drugs (Hossain, 2019). As drug resistance is becoming a global health issue, the main target of scientists is to discover herbal extracts or pure ingredients that may act as microbial, antifungal or anticancer agents. Numerous spices and their extracts are used for food preservation as antimicrobial agents and natural antioxidants. Some of the species are used in natural healing and as appetizers. Now, many local plant species are used by the local ethnic communities as safe medicine to treat aliments (Ait M'barek *et al*., 2007).

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ISSN-e: 2148-6905 / © IJSM 2022

The World Health Organization (WHO) reported that a large percentage of the population in most developing countries depend on plants and herbal medicine for their primary healthcare needs (Aziz & Rehman, 2008). In the process of drug discovery, medicinal plants played a significant part due to the presence of safe bioactive ingredients including essential oils (Hossain, 2019). The ingredients normally present in the plants and their crude extracts are essential oils, saponins and steroids derivatives, phenolics and flavonoids derivatives, lignans and glycosides complexes, terpenes, and alkaloids. Due to their powerful therapeutic and biological properties, all the ingredients have been used for a long time to discover modern pharmaceutical drugs (Wayne *et al.*, 2004; Cronquist, 1988; Cruz *et al*., 1989). Among the aromatic plants, some plants are economical and have played a crucial part in human illness (Cruz *et al.,* 1989). In addition, a good number of medicinal plants can be used as fuel for the survival of all of living things. All the higher plants contain ingredients with synergistic effects that can neutralize toxicity.

1.1. Synonyms

More than fifteen synonyms of the selected plant species are identified and available globally (Dob *et al.,* 2006). Some significant synonyms are as follows: *Origanum thymus, Origanum webbianum, Thymus baeticus* var. *prostrates, Thymus chinensis, Thymus collinus, Thymus ilerdensis, Thymus sublaxus, Thymus vulgaris* var. *Thymus vulgaris* var. *latifolius, Thymus vulgaris, Thymus vulgaris subsp. Thymus vulgaris* var. *palearensis, Thymus vulgaris* var. *verticillatus, Thymus vulgaris* subsp. *Thymus webbianus, Thymus webbianus* var. *prostrate, Thymuswelwitschii subsp. Ilerdensis Thyymus zygis subsp ilerdensis*.

1.2. Taxonomic Classification

Kingdom Plantae-plantes, Planta, Vegetal, plants; Subkingdom: Viridiplantae-green plants; Infrakingdom: Streptophyta-land plants; Superdivision; Embryophyta; Division: Tracheophyta–vascular plants, tracheophytes; Class: Magnoliopsida; Superorder: Asteranae; Family: Lamiaceae– mints, menthes; Genus: *Thymus* L; Species: *T. vulgaris* L.

1.3. Plant Description

Thymus vulgaris (*T. vulgaris*) is one of the tiny plant species with flowers. Several species including *T. vulgaris* are available in Oman. Locally, the plant species is called “kekik” (Al Hashmi *et al.,* 2013). The species grow up to 40 cm. It has a branch of stems and the stems are woody when the plant is matured (Hossain *et al.,* 2013). Figure 1 shows different parts of *T. vulgaris* L. (Hazzit *et al.,* 2009). The leaves of this species is approximately not more than 5 mm and it is covered by white hair. The shape of the leaves is oval or rectangular. The whole aerial parts including leaves are fleshy and they contain maximum essential oils. The species have a strong smell, but the smell may differ due to the chemical ingredients of different types (Houmania *et al.,* 2002).

Figure 1. Pictures of *T. vulgaris*

1.4. Traditional Use

Traditionally, the selected thyme species have been used widely to treat heart failure, chest infections, and encourage saliva production (Al Hashmi *et al.,* 2013; Hudaib *et al*., 2002). All parts of this plant are medicinally important and used widely to treat human diseases because of their medicinal values. In addition, several prescription drugs contain ingredients from this plant species. In Oman, local ethnic communities used it as a juice to kill worms (Hossain *et al.,* 2013; Hwang *et al.,* 2004). Leaves paste is taken to release sore throats (Hossain *et al.,* 2013; Hwang *et al.,* 2004). The flowers are edible with an acceptable taste. It also has a powerful capability to kill bacteria, fungi and viruses (Karaman *et al.,* 2001). The dried aerial part of this species is used by the local communities as a tea to treat sore throats. Thyme species have a very rich flora in all over the world including the Sultanate of Oman. Based on the traditional uses of the plant species, scientists and researchers are highly interested in working on the selected plant species for the isolation of active ingredients and to use them to treat diseases.

1.5. Pharmaceutical Importance of T. vulgaris

Since ancient times, people have been using thyme in alternative traditional systems to treat numerous respiratory diseases, especially chronic cough, bronchitis, and asthma (Hossain et al., 2013). Based on the active ingredient, the plant species are also used to treat vascular problems, diseases of the urinary tract, teeth pain and indigestion (Hudaib *et al.,* 2002; Karaman *et al*., 2001). The plant contains the highest percentage of thymol (approximately 60%); thymol has a good ability to increase appetite as well as to kill bacterial infections. Recently, the plant has been used for treating asthma. In the last decades, the authors carried out several studies and concluded that the essential oil and plant crude extracts showed significant biological activities. The plant is also a good source of Fe, Ca, Mg and vitamin K that can increase blood flow (Hudaib *et al.,* 2002; Karaman *et al.,* 2001; Hwang *et al.,* 2004).

1.6. Sample Process and Extraction

Several methods such as steam distillation, solvent extraction, supercritical fluid extraction, and pressurized liquid extraction procedure are extensively used for the extraction of essential oils, and other secondary metabolic constituents (Hossain *et al.,* 2019; Marino *et al.,* 1999; Maryam *et al.,* 2022). All these methods are efficient and can provide a great percentage of bioactive constituents. Mainly two methods, such as simple steam distillation and extraction with the solvent method, are used for the extraction of essential oils (Markovic, 2011). Nowadays, supercritical carbon dioxide and pressurized liquid extraction are relatively recent solvent-solvent extraction techniques to minimize the degradation of the active compounds because both processes can function in the absence of light and air (Miura *et al.,* 2002).

1.7. Distribution of The Plant

T. vulgaris is a perennial plant species that belongs to the Lamiaceae family. Globally, its common name is thyme (Al Hashmi *et al.,* 2013). The selected plant species is indigenous to some parts of EU countries, and indigenous in several South Asian and Gulf countries (Farooqi *et al.,* 2005). In addition, this plant is also native to Northern Africa, parts of Africa. Some of the countries such as Egypt, Cameroon, Algeria, Tunisia, Nigeria, South Africa, and Libya have cultivated the plant species due to its and economic medicinal values (Ghasemi, 2009; Giordiani *et al.,* 2008; Giweli *et al.,* 2013; Guillen & Manzanos, 1998).

2. BIOCHEMICAL STUDIES

Several secondary bioactive compounds were isolated and identified from the selected plant species described by several authors (Pina-Vaz *et al.,* 2004; Naghdi-Badi, 2004). The types of compounds such as polar and non-polar compounds isolated and identified by chromatographic

and spectroscopic methods from this plant species are presented in Table 1. Some of the compounds are used as herbal medicine as well as modern medicine; another group of them are used as food nutrients, natural antioxidants and food preservatives (Naghdi-Badi, 2004). Normally, it is a continuous process to isolate the bioactive compounds from the traditionally used plants that are used by the local communities to treat diseases. Scientists and researchers are working on pure isolated compounds to explore their *in-vitro* and *in-vivo* biological and pharmacological activities to enhance formulation of drug for treatments of human diseases (Nickavar *et al.,* 2005; Nikolić *et al.,* 2012).

Table 1. List of phytochemicals of different leaves extracts of T. vulgaris.

Hexane Extract	Ethyl acetate extract	Butanol extract
Linalyl anthranilate	o-Cymol	4-Heptanone
Bicyclo[3.1.0]hexan-2-ol	Linalyl anthranilate	n-Butyl ether
α-Terpineol	1,5-Octadiene-3,7-diol	Hexanal
Thymol	α-Terpineol	4-Heptanone
O-Thymol	Thymol	Butanoic acid, butyl ester
2.Thymol acetate	o-Thymol	5-Methyl-3-heptanone
Bicyclo[7.2.0]undec-4-ene, 4,11,11-trime	4-Methoxy-2,3,6-trimethylphenol	o-Cymol
O-methoxy-α,α-dimethylbenzyl	Spathulenol	Linalool
Spathulenol	Phytol	4-Terpineol
α.-farnesene	Naringenin	Terpineol
1-octadecyne	1-Iodo-2-methylundecane	Thymol
n-Hexadecanoic acid	3,7-Octadiene-2,6-diol	o-Thymol
Naringenin	2,4-Dimethylbenzaldehyde	Thymol acetate
	Thymol	Bicyclo[7.2.0]undec-4-ene, 4,11,11-trime
	o-Thymol	Aromadendrene
		Spathulenol
		Alpha.-farnesene
		3,7,11,15-Tetramethyl-2-hexadecen-1-ol
		n-Hexadecanoic acid

2.1. Essential Oil

Based on the essential oil, *T. vulgaris* plant is used by different ethnic communities to treat asthma, bronchitis and cough. The essential oil was isolated from various parts of the selected plant species by using different methods such as steam distillation method, cohobating method and many others (Nickavar *et al.,* 2005; Nikolić *et al.,* 2012; Markovic, 2011; Ozguven & Tansi, 1998; Akhtar *et al.,* 2012). The percentage of essential oils varies due to the extraction methods, the parts of the plants used and the different environmental conditions. Our previous study showed that the selected species contains more than 80 compounds. However, most of the authors identified more than 70 compounds. The major compounds are presented in Table 2. They are mainly oxygenated monoterpenes and sesquiterpenes. Some of them show significant antimicrobial, cytotoxic and antioxidant activities. Most of the researchers reported that the highest percentage ingredient was thymol approximately (56-60%).

Table 2. List of phytochemicals in the essential oil of *T. vulgaris.*

Sl. No	Name of Phytochemicals	Percentage
1	Tetra hydro-3-methylfuran	12.76
2	Cyclohexane	0.15
3	Camphene	0.13
4	α-Pinene	0.71
5	β-Myrcene	0.32
6	Octanol-3	0.18
7	Carene	0.28
8	*p*-Cymene	2.27
9	o-Cymene	0.39
10	γ-Terpinene	1.21
11	Terpinen-4-ol	0.35
12	α-Terpineol	0.33
13	Thymol	9.91
14	o-Thymol	41.90
15	2-Methyl-5-(1-methylethyl) phenolacetate	0.58
16	Caryophyllene	1.01
17	Humulene	0.11
18	Caryophyllene oxide	0.61

2.2. Nutritional Value

The selected thyme species showed remarkable health benefits that can be endorsed due to its nutritional value. The main nutrients in this species are namely vitamins, minerals, volatile oils and antioxidants. Most of them have strong disease-preventing activities as well as health - promoting properties (Naghdi-Badi *et al.,* 2004; Ozguven & Tansi, 1998; Penalver *et al.,* 2005). The selected plant species contain different phytonutrients, natural minerals and vitamins that are energetic for maintaining good health (Ozguven & Tansi, 1998). Thyme is a natural source of vitamins C and A and carbohydrates. In addition, the plant also contains vitamin B-complex and vitamin B_6. All these vitamins are essential for maintaining healthy skin and protecting the infectious diseases. The selected plant also contains several minerals such as K, Ca, Mg, Fe, and Se. These minerals are essential to maintain the electrolyte balance in the human body (Penalver *et al.,* 2005).

3. PHARMACOLOGICAL ACTIVITIES

The oil and extracts of the selected species showed significant antiseptic, antibacterial, anticancer, and anti-cough properties that can enhance the healing of different diseases (Kizil & Uyart, 2006).

3.1. Antioxidant Properties

Generally, *in-vivo* and *in vitro* methods were used to determine antioxidant properties of various extracts and essential oils from the plant species as described by several authors (Penalver *et al.,* 2005; Pirbalouti *et al.,* 2013; Raal *et al.,* 2004). Our previous experimental results showed that various polarities extracts and essential oils at different concentrations showed significant activity against DPPH (2,2-diphenyl-1-picrylhydrazyl), superoxide and hydroxyl radical scavenging activity and bestows protection (Pirbalouti *et al.,* 2013; Raal *et al.,* 2004; Al-Matani et al., 2015). Among the existing phytochemicals in this plant, thymol is the main ingredient about 60% and it shows powerful antioxidant activity against superoxide, DPPH radical scavenging and reducing capacity at various concentrations (Penalver *et al.,* 2005; Pirbalouti *et*

al., 2013; Raal *et al.,* 2004). The thymol ingredient also showed modest activity against V79 Chinese hamster lung fibroblast cells (Rasooli & Mirmostafa, 2002). It also showed strong antioxidant activity against lipid system in gamma-ray induced V79 Chinese hamster cells (Raal *et al.,* 2004). The carvacrol is the isomer of thymol that also showed better antioxidant capacity in lipid systems due to its synergetic effect.

3.2. Antimicrobial Activity

A good number of scientists evaluated the antimicrobial activities at various concentrations of essential oils and different polarities crude extracts of thyme plant species against various bacterial and fungi strains (Reis *et al.,* 2004; Rota *et al*., 2004; Soliman & Badeaa, 2002). They revealed that both the essential oils and crude extracts showed significant activity against the applied bacterial and fungi strains. These significant biological activities of the plant extracts and essential oil are due to the main chemical ingredients. Among the phytochemicals present in the selected plant, two phytochemicals, carvacrol and p-cymene, are significant components that have very weak antibacterial properties due to their synergy effect with carvacrol (Stahl-Biskup, 1991). Some scientists reported previously that polar extracts such as ethanol and aqueous extracts demonstrated high antimicrobial activity against gram-positive bacterial strains (Thompson *et al.,* 2003; Al-Matani et al., 2015). Tsukatani *et al.* (2012) conducted a comparative study of the antibacterial activity of the essential oils of cultivated *T. vulgaris* L. and wild thyme species against gram (+ and -) bacterial strains and the results revealed that wild thyme essential oil showed less activity compared the essential oil of the cultivated plant (Tsukatani *et al.,* 2012). Other work by Verma et al. reported that the microbial activity of the essential oil, either it is from the wild or the cultivated thyme species, depends on the phenolic compounds and their derivatives (Verma *et al.,* 2009 & 2011). Furthermore, the antimicrobial activity of essential oils also depends on incubation, synergistic ingredient effects, and the other ingredients.

3.3. Cytotoxic Activity

The preliminary screening of cytotoxic activity of various polarity plant extracts and essential oil of the thyme herb is assessed against the Brine Shrimp Lethally (BSL) and 96-cell wall described by several authors ((Vichai *et al.,* 2006; Vukovic-Gacic & Simic, 1993; Zaidi & Crow, 2005). The majority of reports showed that both plant extracts and essential oil at different concentrations attribute potential cytotoxic activity against (BSL) and 96-cell walls. However, some of the researchers mentioned that the cytotoxic activity only showed when the concentration of chemical ingredients is high of the extracts and essential oil. They mentioned that low concentration extracts and essential oil of the selected species did not show any activity. In addition, the non-polar extracts showed high activity compared to polar extracts which mean that the toxic compounds are present only in the non-polar extract. Similar results were also obtained by the 96-cell wall method.

4. CONCLUSION

T. vulgaris L. is a small plant that has been used as a spice, remedy, drug, and cosmetics. The essential oil of this plant is used in medicine, food, and cosmetics industries as preservative and antioxidant. This current review focuses on the latest status of phytochemicals, pharmacological and toxicological activities reported on *T. vulgaris.* The selected plant species contains a high amount of phytochemicals named phenolic derivatives and flavonoids; therefore, the plant exhibits antioxidant and antibacterial activity, anticancer and larvicidal effects. Thyme native to Oman can be used as a natural antioxidant in food products, supplements and drugs so that more clinical and pathological studies must be conducted to investigate the unexploited potentials of the *T. vulgaris* plant grown in Oman before using the plant for treating different diseases.

Acknowledgments

The authors are grateful to the University of Nizwa for providing all kinds of facilities. Special thanks to Mr. Erno Muzamel, Coordinator, Student Support System (SSS), Writing Center (TWC) for his professional assistance to edit the manuscript.

Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

Authorship contribution statement

Mohammad Amzad Hossain: Data curation; Design study; Data analysis; Wrote a first draft of the review. **Yahya Bin Abdullah Alrashdi**: Literature survey; Data collection; Edit data. **Salem Said Jaroof Al-Touby**: Contributed to the design and results interpretation; Review manuscript.

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