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Genus *Thymbra*: A Review on Their usage areas, Phytochemical contents and Biological Activities

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ABSTRACT

The use of Herbs in nutrition and in medicine has been recognized over the years. Herbal treatment is one of the traditional methods used in the treatment of diseases since early ages. Different plant species in different cultures have been used by trial and error and have been very effective. In this study, information is given about the phytochemical contents, biological activities, usage areas and general characteristics of Genus *Thymbra*. As a result of the literature research, it has been reported that it has remarkable activities such as antioxidant, antimicrobial and anticancer as well as common usage areas. In this study, the use of *Thymbra* species in pharmacological designs was emphasized. Therefore, members of the genus *Thymbra* are one of the important plant genera used in complementary medicine and thought to be important natural resources in pharmacological designs.

Keywords: Mediterranean thyme, antimicrobial, traditional medicine, anticancer, anti-oxidant

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INTRODUCTION

Over the years, herbs and medicinal plants were widely used in nutrition and in complementary medicine. The link between health and nutrition has always been proven ***(Mohammed et al., 2018; Unal et al., 2022).*** Plants are widely used in the treatment of many diseases in developed and developing countries according to the World Health Organization (WHO) data ***(Sevindik et al., 2017; Mohammed et al., 2019).*** Beside their nutritional value, plants also produce secondary metabolites known as phytochemicals which exert different bioactivities with high medicinal effects ***(Mohammed et al., 2020a; Mohammed et al., 2021a).*** Many plant species have been reported to have antioxidant, antimicrobial, anticancer, antiproliferative, anti- inflammatory, DNA protective, antiaging, hepatoprotective effects ***(Bouarab Chibane et al., 2019; Mohammed et al., 2020b; Kapoor et al., 2021; Mohammed et al., 2021b; Yarley et al., 2021; Kamli et al., 2022; Sevindik et al., 2023; Uysal et al., 2023).*** In this review, thebiological activities, phytochemical contents and general properties of Genus *Thymbra* have been reported by using literature data.

GENUS THYMBRA

Thymbra, known as Mediterranean thyme, is a genus of plants in the Lamiaceae family. It is commonly native to the Mediterranean region of Southern Europe, North Africa, and the Middle East. It generally spreads on calcareous rocks and steppes. It is known that the flower color of Thymbra consists of purple, pink or blue color. In addition, glandular hairs are abundant ***(BräuChler, 2018).*** *Thymbra calostachya* (Rech.f.) Rech.f., *Thymbra capitata* (L.) Cav., *Thymbra sintenisii* Bornm. &Azn., *Thymbra spicata* L. and *Thymbra spicata* subsp. *intricata* (P.H. Davis) R. Morales are species belonging to the genus *Thymbra*.

Benefits and usage

Members of the Genus Thymbra are used in many different areas. In nutrition, the leaves and flower parts of *T. spicata* and *T. spicata* subsp. *intricata* species are dried and preferred for spice consumption ***(Akkol et al., 2009).*** In addition, these species are consumed for breakfast and canned. It has been reported that the fresh parts of the plant are used in salads. It is known that members of the genus *Thymbra* are used as herbal tea ***(Dirican et al., 2012).*** For therapeutic uses, it has also been reported to be used in diseases such as cough, asthma, diarrhea, bronchitis, cholesterol, stomach pains. It has been observed that *T. capitata* species is used in tea, spice, breakfast, salad, soup, pastries and ice cream. It has been reported that it is preferred in conditions such as antiseptic, ulcer, hypertension, colic, diarrhea, circulatory system, digestive system, diuretic and wart removal ***(Hazzit et al., 2009; Kaya et al., 2013; Prasanth et al., 2014).***

Nutritional and Mineral Composition

Plants contain many nutrients. Their nutritional properties have put herbs at the top of their diet lists. In this study, the mineral and nutrition contents of *Thymbra* species reported in the literature were compiled. It is shown in Table 1.

Table 1. Nutritional and Mineral composition of *Thymbra* species

Nutritional Composition	Values (%)
Protein	12.70-19.51
Ash	3.85-7.82
Mouisture	4.50-6.80
Crude fiber	8.89-30.63
Crude fat	6.23-19.97
Carbohydrate	54.61
Mineral Composition	**Values (mg/kg)**
Mg	1923-3598
K	15610-68250
Na	14080-75900
Fe	102.52-684.0
Ca	11416-29965
Zn	9.97-557
Cu	6.77-136.3
Mn	27.20-231

In *Thymbra* species, protein (12.70-19.51%), ash (3.85-7.82%), mouisture (4.50-6.80%), crude fiber (8.89-30.63%), crude fat (6.23-19.97%) and carbohydrate (54.61%) (***Uçan et al., 2014; Hayoglu et al., 2016; Tercan et al., 2016; Baytok et al., 2017; Köten and Satouf, 2019***). It has also been reported that *Thymbra* species have mineral contents such as Mg (1923-3598 mg/kg), K (15610-68250 mg/kg), Na (14080-75900 mg/kg), Fe (102.52-684.0 mg/kg), Ca (11416-29965 mg/kg), Zn (9.97-557 mg/kg), Cu (6.77-136.3 mg/kg) and Mn (27.20-231 mg/kg) (***Özcan, 2004; Kizil et al., 2014; Hayoglu et al., 2016; Tercan et al., 2016; Gedik et al., 2022***).

THYMBRA SPECIES BIOACTIVITIES

Plants are natural resources responsible for many biological activities. Many studies have shown that plants have different biological activities ***(Mohammed et al., 2022; Mohammed et al., 2023).*** By reviewing the different studies published on the members of genus *Thymbra* and their bioactivities in the literature, it has been concluded that the pharmacological effects are usually obtained for *Thymbra* essential oils after extraction using solvents such as methanol, ethanol, water, hydrodistillation and butanol. Some of the bioactivities reported for genus *Thymbra* in previously published studies are summarized in Table 2.

Table 2. Biological activities studies on *Thymbra* species

Thymbra plants	Biological activity	Usage	References
T. spicata (Syn: T. spicata L. subsp. *spicata* L.)	Antimicrobial, Antioxidant, antibiofilm, cytotoxic, anticholinesterase, antidiabetic, antihypercolesterolemic, antisteatotic, antitumor, antiviral	Essential oil, ethanol extract, methanol extract, hydrodistillation extract	***(Al and Yıldırım, 2020; Almeida et al., 2022; Bayan et al., 2017; Demiralay et al., 2011; Duran et al., 2012; Eruygur et al., 2021; Gumus,2010; Khalil et al., 2019; Khalil et al., 2021; Kirkan et al., 2019; Kılıç, 2006; Mohammed et al., 2020c; Yılar and Bayar, 2018)***
T. spicata subsp. *intricata* (P.H.Davis) R.Morales	Antimicrobial	Essential oil, hydrodistillation extract	***(Sarac et al., 2009)***
T. sintenisii Bornm. &Azn. *(Syn: T. sintenisii* subsp. *sintenisii)*	Antimicrobial, antioxidant, cytotoxic	Essential oil, butanol extract and water extract, ethanol extract	***(Gür et al., 2020;Tutar et al., 2018)***
T. sintenisii subsp. *isaurica* P.H.Davis	Antioxidant, anticancer, cytotoxic	Essential oil, ethanol extract	***(Hepokur et al., 2020a)***
Thymbra capitata (L.) Cav.	Antioxidant, Antimicrobial, Antigiardia, cytotoxic, herbicidial	Essential Oil, ethanol extract, methanol extract	***(Charfi et al., 2019; de-Oliveira et al., 2012; Hepokur et al., 2020b; Karampoula et al., 2016; Machado et al., 2010; Merino et al., 2019; Miguel et al., 2005; Moukhles et al., 2020; Faleiro et al., 2005; Verdeguer et al.,2020)***

T. spicata (Syn: *T. spicata* L. subsp. *spicata* L.)

In the literature researches, it has been reported that *T. spicata* has many activities using different extracts (ethanol and hydrodistillation) and essential oil. In antimicrobial activity studies of the plant species, it has been reported to be effective against *Listeria monocytogenes, Salmonella typhimurium, Staphylococcus aureus, Monilinia fructigena, Staphylococcus epidermidis, Bacillus subtilis, Pseudomonas aeruginosa, Enterococcus faecalis, Candida*

albicans, *Mycobacteria smegtigenasis*, and *Fusarium oxysporum* f. *splycopersici* and *Escherichia coli* ***(Kılıç, 2006; Gumus, 2010; Bayan et al., 2017; Yılar and Bayar, 2018; Al and Yıldırım, 2020).*** In addition, it has been reported that the plant has antiviral effects ***(Duran et al., 2012).*** The antioxidant activity of *T. spicata* was investigated using DPPH, FRAP, CUPRAC, ABTS, ORAC and TAS kits and it was found to have high antioxidant activity ***(Bayan et al., 2017; Khalil et al., 2019; Kirkan et al., 2019; Mohammed et al., 2020c; Eruygur et al., 2021).*** In addition, it has been reported that *T. spicata* has antihypercolesterolemic, antidiabetic, antisteatotic, antitimor activities in different studies ***(Demiralay et al., 2011; Khalil et al., 2019; Kirkan et al., 2019; Khalil et al., 2021).*** In a different study, it was reported that the hydrodistillation extract of *T. spicata* has an inhibitory effect on breast cancer cells (MCF-7) and prostate cancer cells (PC3), and its anticholinesteraseactivity is high ***(Eruygur et al., 2021).***

T. spicata subsp. *intricate* (P.H.Davis) R.Morales

Previously, antimicrobial activity of hydrodistillation extract of *T. spicata* subsp. *intricata* against *B. subtilis, E. coli, P. aeruginosa, P. fluorescens, P. stutzer, Stenotrophomonas maltophilia, S. aureus, S. epidermidis, Streptococcus mutans, Micrococcus luteus, Cryseomonas luteola* and *C. albicans* was investigated using disc diffusion method. According to the results of the study, it was reported that the highest activity was against *B. subtilis* and the lowest activity was against *S. aureus* ***(Sarac et al., 2009).***

T. sintenisii Bornm. &Azn. (Syn: *T. sintenisii* subsp. *sintenisii)*

It has been reported in the literature that the ethanol extract of *T. sintenisii* (Syn: *T. sintenisii* subsp. *sintenisii*) has antimicrobial activity against *K. pneumoniae, Shigella boydii, P. aeruginosa, Proteus vulgaris, S. aureus, B. cereus* and *C. tropicalis*. In addition, in the same study, it was reported that the DPPH activity of the plant was high and it was highly effective on breast cancer cell (MCF-7), human osteosarcoma cell (MG63) and mouse fibroblast cell (L929) ***(Tutar et al., 2018).*** In a different study, it was reported that the butanol and water extract of the plant had an inhibitory effect on angiotensin converting enzyme (ACE), which plays a role in cardiovascular disorders and plays a role in hypertension ***(Gür et al., 2020).***

T. sintenisii subsp. *isaurica* P.H.Davis

Antioxidant activity of the ethanol extract of *T. sintenisii* subsp. *isaurica* has been reported in the literature using the DPPH method. According to the results of the study, DPPH radical scavenger was used in its antioxidant activity. The result obtained was 27.15 μg/mL, and breast cancer cell (MCF-7) and mouse fibroblast cell (L929) were used for the anticancer activity of the same extract. It has been reported that it acts between 7.55 -10.48 μg/mL for breast cancer cells and between 9.26-12.63 μg/mL for mouse fibroblast cells between 24 and 48 hours ***(Hepokur et al., 2020a).***

Thymbra capitata (L.) Cav.

In the literature researches, it has been reported that *T. capitata* has many activities using different extracts (methanol and ethanol) and essential oil. The antimicrobial activities of the

plant species have been reported to be effective against *P. vulgaris, E. coli, P. mirabilis, B.subtilis, S. aureus, Salmonella enterica* subsp. *enterica* serovar *Typhimurium, L. monocytogenes, Candida* spp., *K. pneumoniae, S. boydii, P. aeruginosa* and *B. cereus* ***(Almeida et al., 2022; Charfi et al., 2019; de-Oliveira et al., 2012; Faleiro et al., 2005; Hepokur et al., 2020b; Karampoula et al., 2016; Merino et al., 2019; Moukhles et al., 2020).*** In a different study, it was reported that it has an antigiardia effect against *Giardia trophozoites* ***(Machado et al., 2010).*** In another study, *T. capitata* was reported to have antioxidant properties using the DPPH test ***(Faleiro et al., 2005; Hepokur et al., 2020b; Miguel et al., 2005).*** In a different study, it was reported that it showed cytotoxic effects against human breast cancer cell line (MCF-7), bone cancer cell line (MG63) and fibroblast cell line (L929) ***(Hepokur et al., 2020b).***In addition, it has been reported that *T. capitata* has herbicidial activity in a different study ***(Verdeguer et al., 2020).***

ESSENTIAL OIL CONTENTS

Usually, the aerial parts of the members of the Genus *Thymbra* were used for the essential oil preparation. Essential oil content studies on Genus *Thymbra* are shown in Table 3.

Table 3. Essential oil contents studies on *Thymbra* species

***Thymbra* species**	**Geographic regions**	**Essential oil contents**	**References**
T. spicata (Syn: T. spicata subsp. *spicata*)	Türkiye, Lebanon	Carvacrol (34.9-78.53%), γ-terpinene (6.87-25.6%), *p*-cymene (0.85-22.11%), *trans* caryophyllene (5.1-10.41%), β –myrcene (4.8%), α-terpinene (6.9%), thujene (5.2%), thymol (11.98%)	***(Akgül and Özcan, 1999; Khalil et al., 2019; Kirkan et al., 2019; Kılıç, 2006; Koçer, 2021; Bayan et al., 2017; Yücel-Sengun et al., 2021)***
T. spicata subsp. *intricata*	Türkiye	Carvacrol (9.21%-70.98%), Thymol (50.71%), *p*-Cymene (12.80%), γ-Terpinene (14.97%)	***(Tümen et al., 1994)***
T. sintenisii (Syn: T. sintenisii subsp. *sintenisii)*	Türkiye	Carvacrol (43.31%), Thymol (32.51%), γ-Terpinene (9.40%), *p*-Cymene (4.57%), β-Caryophyllene (4.67%)	***(Tümen et al., 1997)***
T. sintenisii subsp. *isaurica*	Türkiye	Carvacrol (39.01%), *p*-Cymene (26.38%), γ-Terpinene (12.68%),	***(Başer et al., 1996)***
T. capitata	Portekiz, Morocco, Spain, Portugal	Carvacrol (%24.35-83), γ-terpinene (2-26%), p-cymene (4.90-17%) thymol (9-49.33%), β-caryophyllene (1-6.45%)	***(Bounatirou et al., 2007; Charfi et al., 2019; de-Oliveira et al., 2012; Faleiro et al., 2005; Figueiredo et al., 2008; Gagliano et al., 2019; Machado et al., 2010; Merino et al., 2019; Miceli et al., 2006; Miguel et al., 2005; Moukhles et al., 2020)***

It has been reported that the main components in the essential oil content of *T. spicata* species are carvacrol (34.9-78.53%), γ-terpinene (6.87-25.6%), p-cymene (0.85-22.11%), trans caryophyllene (5.1-10.41%), β-myrcene (4.8%), α-terpinene (6.9%), thujene (5.2%) and thymol (11.98%) ***(Akgül and Özcan, 1999; Khalil et al., 2019; Kirkan et al., 2019; Kılıç, 2006; Koçer, 2021; Bayan et al., 2017; Yücel-Sengun et al., 2021).***It has been reported that the main

components in the essential oil content of *T. spicata* subsp. *intricata* species are carvacrol (9.21%-70.98%), thymol (50.71%), p-cymene (12.80%) and γ-terpinene (14.97%) ***(Tümen et al., 1994).***It has been reported that the main components in the essential oil content of *T. sintenisii* species are carvacrol (43.31%), thymol (32.51%), γ-terpinene (9.40%), p-cymene (4.57%) and β-caryophyllene (4.67%) ***(Tümen et al., 1997).***It has been reported that the main components in the essential oil content of *T. sintenisii* subsp. *isaurica* species are carvacrol (39.01%), p-cymene (26.38%) and γ-terpinene (12.68%) ***(Baser et al., 1996).***It has been reported that the main components in the essential oil content of *T. capitata* species arecarvacrol (24.35-83%), γ-terpinene (2-26%), p-cymene (4.90-17%), thymol (9-49.33%) and β- caryophyllene (1-6.45%) ***(Bounatirou et al., 2007; Charfi et al., 2019; de-Oliveira et al. , 2012; Faleiro et al., 2005; Figueiredo et al., 2008; Gagliano et al., 2019; Machado et al., 2010; Merino et al., 2019; Miceli et al., 2006; Miguel et al., 2005; Moukhles et al., 2020).***

CONCLUSION

In this study, the usage areas, phytochemical compounds contents and biological activities of genus *Thymbra* were compiled. In addition, it stands out with its different biological activities such as antioxidant, anticancer, antimicrobial, cytotoxic. In this context, members of genus *Thymbra* can be used as natural materials in pharmacological designs.

Conflicts of Interest

The authors declares that there is no conflict of interest regarding the publication of this paper.

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