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
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, anti-aging, 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, the biological 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 Thymbr 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

<table>
<thead>
<tr>
<th>Nutritional Composition</th>
<th>Values (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>12.70-19.51</td>
</tr>
<tr>
<td>Ash</td>
<td>3.85-7.82</td>
</tr>
<tr>
<td>Moisture</td>
<td>4.50-6.80</td>
</tr>
<tr>
<td>Crude fiber</td>
<td>8.89-30.63</td>
</tr>
<tr>
<td>Crude fat</td>
<td>6.23-19.97</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>54.61</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mineral Composition</th>
<th>Values (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg</td>
<td>1923-3598</td>
</tr>
<tr>
<td>K</td>
<td>15610-68250</td>
</tr>
<tr>
<td>Na</td>
<td>14080-75900</td>
</tr>
<tr>
<td>Fe</td>
<td>102.52-684.0</td>
</tr>
<tr>
<td>Ca</td>
<td>11416-29965</td>
</tr>
<tr>
<td>Zn</td>
<td>9.97-557</td>
</tr>
<tr>
<td>Cu</td>
<td>6.77-136.3</td>
</tr>
<tr>
<td>Mn</td>
<td>27.20-231</td>
</tr>
</tbody>
</table>

In *Thymbra* species, protein (12.70-19.51%), ash (3.85-7.82%), moisture (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; Kızıl 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

<table>
<thead>
<tr>
<th>Thymbra plants</th>
<th>Biological activity</th>
<th>Usage</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T. spicata</em> (Syn: <em>T. spicata</em> L. subsp. <em>spicata</em> L.)</td>
<td>Antimicrobial, Antioxidant, antibiofilm, cytotoxic, antioestrogenic, anticancer, antidiabetic, antihypercholesterolemic, antisteatotic, antitumor, antiviral</td>
<td>Essential oil, ethanol extract, methanol extract, hydrodistillation extract</td>
<td>(Al and Yıldırım, 2020; Almeida et al., 2022; Bayan et al., 2017; Demiralay et al., 2011; Duran et al., 2012; Eruygur et al., 2021; Gümus, 2010; Khalil et al., 2019; Khalil et al., 2021; Kirkan et al., 2019; Kılıç, 2006; Mohammed et al., 2020c; Yılar and Bayar, 2018)</td>
</tr>
<tr>
<td><em>T. spicata</em> subsp. <em>intricata</em> (P.H.Davis) R.Morales</td>
<td>Antimicrobial</td>
<td>Essential oil, hydrodistillation extract</td>
<td>(Sarac et al., 2009)</td>
</tr>
<tr>
<td><em>T. sintenisii</em> Bornm. &amp;Azn. (Syn: <em>T. sintenisii</em> subsp. <em>sintenisii</em>)</td>
<td>Antimicrobial, cytotoxic, antioxidant</td>
<td>Essential oil, butanol extract and water extract, ethanol extract</td>
<td>(Gür et al., 2020; Tutar et al., 2018)</td>
</tr>
<tr>
<td><em>T. sintenisii</em> subsp. <em>isaurica</em> P.H.Davis</td>
<td>Antioxidant, anticancer, cytotoxic</td>
<td>Essential oil, ethanol extract</td>
<td>(Hepokur et al., 2020a)</td>
</tr>
<tr>
<td><em>Thymbra capitata</em> (L.) Cav.</td>
<td>Antioxidant, Antimicrobial, Antigiardia, cytotoxic, herbicidal</td>
<td>Essential Oil, ethanol extract, methanol extract</td>
<td>(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)</td>
</tr>
</tbody>
</table>

*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 smegtigenas, 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 anticholinesterase activity is high (Eruygur et al., 2021).

T. spicata subsp. intricata (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 antiangiardia 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 herbicidal 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>
<thead>
<tr>
<th><em>Thymbra</em> species</th>
<th>Geographic regions</th>
<th>Essential oil contents</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T. spicata</em> (Syn: <em>T. spicata</em> subsp. <em>spicata</em>)</td>
<td>Türkiye, Lebanon</td>
<td>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%)</td>
<td>(Akgül and Özcan, 1999; Khalîl et al., 2019; Kirkan et al., 2019; Kılıç, 2006; Koçer, 2021; Bayan et al., 2017; Yücel-Sengun et al., 2021)</td>
</tr>
<tr>
<td><em>T. spicata</em> subsp. <em>intricata</em></td>
<td>Türkiye</td>
<td>Carvacrol (9.21%-70.98%), Thymol (50.71%), p-Cymene (12.80%), γ-Terpinene (14.97%)</td>
<td>(Tümen et al., 1994)</td>
</tr>
<tr>
<td><em>T. sintenisii</em> (Syn: <em>T. sintenisii</em> subsp. <em>sintenisii</em>)</td>
<td>Türkiye</td>
<td>Carvacrol (43.31%), Thymol (32.51%), γ-Terpinene (9.40%), p-Cymene (4.57%), β-Caryophyllene (4.67%)</td>
<td>(Tümen et al., 1997)</td>
</tr>
<tr>
<td><em>T. sintenisii</em> subsp. <em>isaurica</em></td>
<td>Türkiye</td>
<td>Carvacrol (39.01%), p-Cymene (26.38%), γ-Terpinene (12.68%),</td>
<td>(Başer et al., 1996)</td>
</tr>
<tr>
<td><em>T. capitata</em></td>
<td>Portekiz, Morocco, Spain, Portugal</td>
<td>Carvacrol (%24.35-83), γ-terpinene (2-26%), p-cymene (4.90-17%), thymol (9-49.33%), β-caryophyllene (1-6.45%)</td>
<td>(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)</td>
</tr>
</tbody>
</table>

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; Khalîl 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 are carvacrol (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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REFERENCES


