A review on Moroccan thyme species: ethnopharmacological, phytochemical, and biological aspects

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Morocco is characterized by a great richness and biodiversity in *Thymus* plants. This genus is represented in this country by 22 thyme species and subspecies, 13 of which are endemic. The present review aims to study the ethnopharmacological, phytochemical, and biological aspects of these thyme species. To carry out this study, the research studies on Moroccan Thymus plants were reviewed in the scientific literature. We found that the species of this genus have widespread uses and applications in Moroccan folk medicine. These plants possess potent pharmacological and biological properties. Moreover, the extracts and volatile oils of thyme plants are rich in a wide variety of phenolic and terpene compounds. These bioactive compounds exert countless biological and pharmacological properties. The present review concludes that there is an important biodiversity in thyme species in Morocco. These species are endowed with several biological properties and ethnopharmacological uses. However, several species of this genus are still not exploited and need more botanical, phytochemical, and pharmacological investigations.

Keywords:
biology, ethnopharmacology, Morocco, phytochemistry, Thymus genus

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Introduction

Thyme plants are valuable species that belong to the Lamiaceae family. Thymus genus is represented with 214 species and 36 subspecies worldwide [1]. These species possess impressive organoleptic, medicinal, and nutritional properties and have been widely used in food, cosmetics, perfumery, and pharmaceutical industries [2]. Moreover, thyme plants contain valuable bioactive phytochemicals such as volatile compounds, flavonoids, organic acids, phenolic acids, tannins, lignans, and terpenoids [2]. These compounds have been reported to exhibit numerous pharmacological and biological properties, including anti-inflammatory, anticoagulant [3], hepatoprotective [4], anti-HIV-1, gastroprotective, antidyslipidemic, antimicrobial [5], and antidiabetic activities [6].

In Morocco, aromatic and medicinal flora is characterized by its richness, diversity, and socioeconomic value [7]. The biodiversity of aromatic and medicinal plants in this country is related to the ecological heterogeneity of its biotopes and climatic variations [8]. Moreover, Morocco is a traditional supplier of the world market in aromatic and medicinal plants including thyme plants. In this country, Lamiaceae family consists of more than 225 species. Thymus genus is represented with 21 thyme species, 12 of which are endemic [9]. In another botanical reference, Thymus is represented with 22 thyme species and subspecies, 13 of which are endemic (Table 1) [10].

This review is conducted to report the botanical, ethnopharmacological, phytochemical, and pharmacological studies on the various species of Thymus in Morocco. Our objective was to give a general view on Thymus genus and to valorize the Moroccan thyme species. The potential species of this genus needs to be more investigated so they can be exploited as a source of therapeutic agents.

General morphology

Thymus plants are small aromatic perennial herbaceous plants that grow in well-drained calcareous soil and need full sun to develop to their full potential [5]. The species of this genus appears as perennial and aromatic subshrubs or shrubs with quadrangular stem erect to prostrate. Usually, the plants have big clusters of flowers of diverse colors (white, cream, pink, or violet) [12].

The leaves can be flat and more or less wide, or with revolute margins and almost acicular. The

Table 1 Moroccan thyme species, geographic distribution, and endemism status according to Fennane *et al.* [10]

Thyme species	Geographic distribution	Endemism status
Thymus atlanticus	AA, HA, MA	*M*
Thymus riatarum	MA	*M*
Thymus broussonnetii subsp. *Broussonnetii*	HA, Mam, Man	*M*
Thymus broussonnetii subsp. *hannonis*	HA, Mam, Man	*M*
Thymus maroccanus subsp. *maroccanus*	AA, HA, Mam, Man	*M*
Thymus maroccanus subsp. *rhombicus*	AA, HA, Mam, Man	*M*
Thymus lythroides	AA, HA, MA	*M*
Thymus leptobotrys	AA, HA, Mam	*M*
Thymus zygis subsp. *Gracilis*	HA, MA, Mam, Man	*M, IP*
Thymus pallidus subsp. *Pallidus*	HA	*M*
Thymus pallidus subsp. *Eriodontus*	HA	*M*
Thymus hyemalis subsp. *Fumanifolius*	LM	*M, IP, A*
Thymus bleicherianus	Man, Om	*M, A*
Thymus munbyanus subsp. *Ciliates*	AA, HA, MA, Man, Op, Om, LM, R	*M, A*
Thymus munbyanus subsp. *munbyanus*	AA, HA, MA, Man, Op, Om, LM, R	*M, A*
Thymus munbyanus subsp. *coloratus*	AA, HA, MA, Man, Op, Om, LM, R	*M, A*
Thymus willdenowii	As, AA, HA, MA, Op, R	*M, IP, A*
Thymus satureioides subsp. *Pseudomastichina*	As, AA, HA, MA, Mam	*M*
Thymus satureioides subsp. *satureioides*	As, AA, HA, MA, Mam	*M*
Thymus satureioides subsp. *commutatus*	As, AA, HA, MA, Mam	*M, A*
Thymus algeriensis	AA, HA, MA, R	*M, A, T, L* [11]
Thymus hesperidum	Ms, AA, Mam	*M*

A, Algeria; AA, Anti-Atlas; As, Saharian Atlas (Fig. 1); HA, High Atlas; *IP*, Iberian Peninsula; *L*, Libya; LM, Mediterranean Coastline; *M*, Morocco; MA, Middle Atlas; Mam, Middle Atlantic Morocco; Man, North Atlantic Morocco; Ms, Saharian Morocco; Om, mountains of eastern morocco; Op, Plateaus of Eastern Morocco; R, Rif; *T*, Tunisia.

indumentum is very variable. Some species have leaves without hairs. The tector hairs in Thymus are always simple, but rarely single celled. Leaves are very frequently ciliate at the margins, either at the whole margin or only at the base or on the petiole. There exist two types of glandular trichomes (contains volatile oils): pedicellate glands with the upper cells full of essential oils, or big globose glands with some basal cells. The flowers grow more or less in clusters in the nodes. Few species have only two flowers per node, but usually, there are bigger clusters of flowers. Species with shorter internodes have globose and capituliform inflorescences. In these cases, both leaves of the inflorescence node have different form and size from the rest of the plant's leaves [10,13].

Moroccan thyme species

The following table regroups the species of Thymus of Morocco with their geographical distribution and their status of endemism as well as the botanical classification of this genus (Table 1 and Fig. 1).

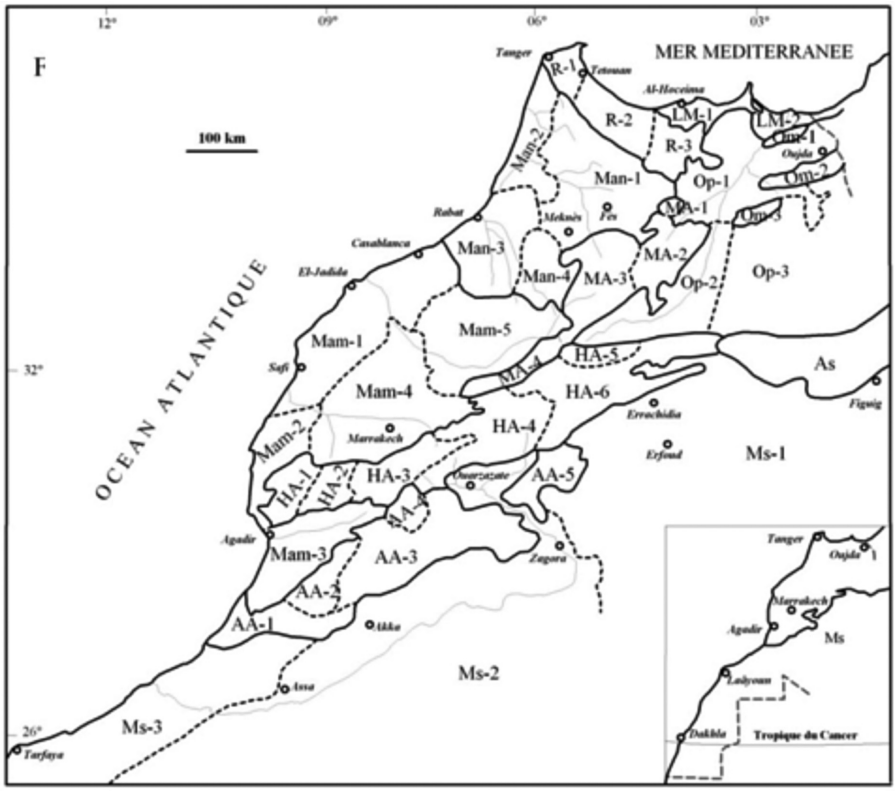
Traditional uses and ethnopharmacology

Thyme has various uses in Moroccan folk medicine; it can be used as powder, decoction, or infusion, alone or as a mixture with other plants. It has tonic and antiseptic properties. It is used to treat diarrhea, fever, cough, and infected areas and wounds. Moreover, it is also used for its anti-inflammatory properties [14]. Furthermore, thymes are used to treat gastric troubles, lung ailments, cold, gastrointestinal infections, liver diseases, colitis, coughs, bronchitis, throat and mouth infections, and influenza. In southwest Morocco, thyme is used to treat respiratory, digestive, skin, circulatory, genital, nervous, and urinary diseases [15]. It is also chewed to treat canker sores and gingivitis. Thyme is used in the Moroccan kitchen as a flavoring agent (condiment and spice) [16]. Some thymes are used as an important ingredient to make a popular soup of snails. In winter, this soup is reputed to prevent and cure all ailments caused by cold. Moreover, thyme honey is very valuable to Moroccans owing to its multiple properties and health benefits. Thyme is also used to conserve traditional fermented butter [17].

Socioeconomic value

MAPs (Medicinal and aromatic plants) have traditionally provided a source of income for families in rural areas [18]. Men and women who live in these rural areas have considerable knowledge and practical expertise gained from many years of living with medicinal plants and herbs in the wild. Moreover, Morocco is a traditional supplier of the world market in MAPs. Actually, it is the 12th largest exporter of MAPs in the world with 52 000 tons of

Figure 1



Map representing geographical divisions of Morocco (Fennane and Ibn Tattou, 2018). AA, Anti-Atlas; MA: Middle Atlas; Mam: Middle Atlantic Morocco; Man: North Atlantic Morocco; LM: Mediterranean Coastline; Om: mountains of eastern morocco; HA: High Atlas; Op: Plateaus of Eastern Morocco; Ms: Saharian Morocco; R: Rif; As: Saharian Atlas.

plants and 5000 tons of essential oils (1.2 billion MAD). According to the National Agency of Medicinal and Aromatic Plants, annual production has reached 140 000 tons, providing alternative income to local communities, by generating an average of 500 000 working days per year. More than 90% of this production is ensured by spontaneous MAPs, including rosemary, pennyroyal, artemisia, oregano, myrtle, carob along with thyme [19]. According to the Department of Water and Forests, rosemary (63%) and thyme (24%) were the most exported PAMs in 2018. The thyme is collected in the regions of Agadir, Azilal, and Marrakech. This makes thyme a plant with important socioeconomic value.

Phytochemistry

Thymus species possess an important diversity of phytochemicals, including a wide variety of volatile compounds, flavonoids, and other phenolic compounds [20]. These phytochemicals can be divided into volatile compounds (essential oils) and nonvolatile compounds. Table 2 summarizes the main phytoconstituents of various species of Moroccan Thymus species, and Fig. 2 represents the chemical structures of the most commonly occurring major volatile and nonvolatile compounds.

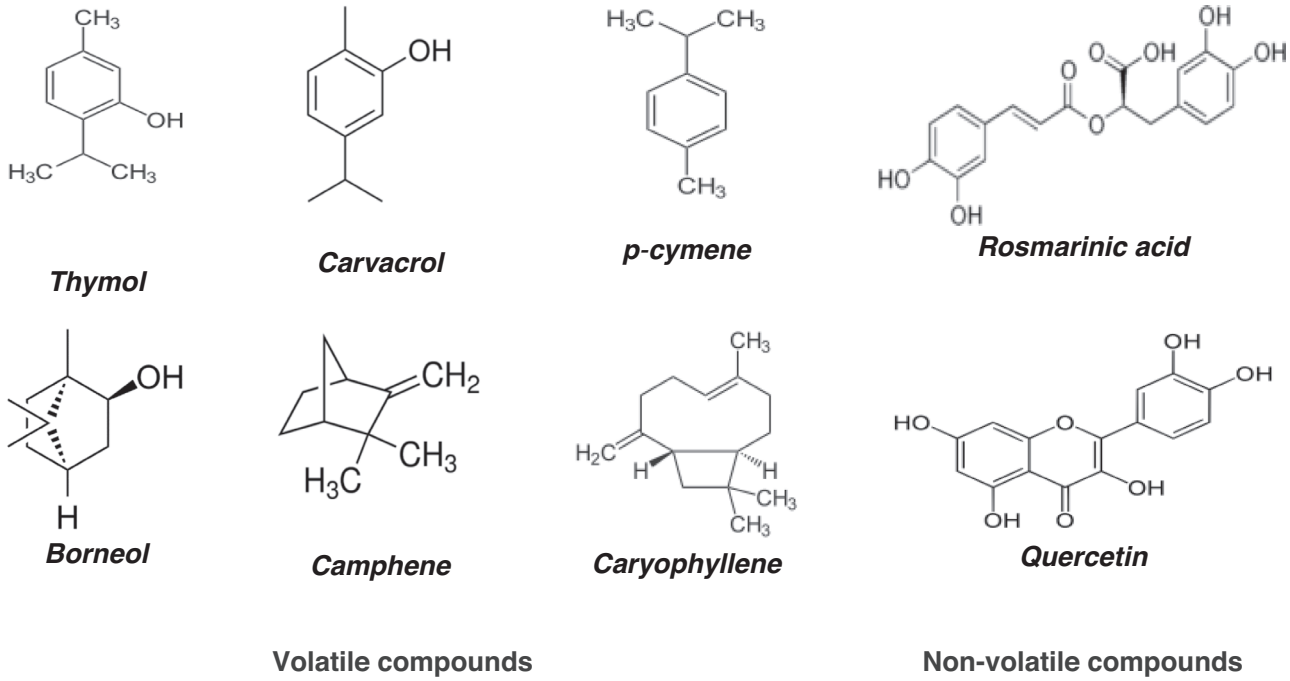
The composition and content of flavonoids in Thymus species have an important role as taxonomic marker providing distinction parameter of species [35]. Several studies have shown that Thymus plants are rich in phenolic compounds such as flavonoids and phenolic acids [36–40]. Many biological activities such as antioxidant and anti-inflammatory properties of thyme plants are associated with their phenolic composition [12]. However, the composition of the nonvolatile composition of Moroccan thyme species is still poorly investigated and needs to be studied. In the chemical composition of the reported thymes, rosmarinic acid, rutin, quercetin, and luteolin are the major occurring nonvolatile compounds. On the contrary, essential oils are more investigated compared with nonvolatile compounds. Borneol, carvacrol, thymol, camphene, α-pinene, p-cymene, and caryophyllene are the major occurring volatile compounds in the volatile fraction of Moroccan thymes (Table 2).

Within each species of thyme, there can be distinct chemotypes. A chemotype is a group of plants differing

Table 2 Volatile and nonvolatile compounds of various Moroccan species of Thymus

Thyme species	Major volatile compounds	Major nonvolatile compounds
Thymus broussonetti	Borneol; Camphene; p-cymene; g-terpinene; Camphor; Carvacrol; Bornyl acetate; (E)-β-caryophyllene; caryophyllene oxide [21]	–
Thymus algeriensis	α-Pinene; Camphene; p-Cymene; 1,8-Cineole; Linalool; Camphor; Borneol; α-Terpineol; Carvacrol; Thymol; β-Caryophyllene [22]	–
Thymus riatarum	Carvacrol; α-Pinene; Camphene; Octan-3-ol; α-Phellandrene; *p*-cymene; γ-Terpinene; Borneol; Thymol; β-Caryophyllene; β-Bisabolene [23]	–
Thymus leptobotrys	Carvacrol; α-Pinene; *p*-cymene; γ-Terpinene; Terpinen-4-ol; Borneol [23]	–
Thymus capitatus	Camphene; α-Pinene; p-Cymene; γ-Terpinene; Borneol; Carvacrol; Thymol; Geranyl acetate; (E)-β-caryophyllene [24]	Gallic acid; Ferulic acid; Quercetin; Luteolin; Apigenin; Rosmarinic acid; trans-2-Hydroxycinnamic acid; p-Coumaric acid [25]
Thymus willdenowii	α-Pinene; Camphene; 1,8-cineole; Camphre; Bornéol; α-Grujunene; Sabinene; Germacrene D; γ-murolene [26]	–
Thymus atlanticus	carvacrol (47.1%), p-cymene (7.5%), α-pinene (3.7%) [27]	Rosmarinic acid; Rutin; Hyperoside; Quercetin; Apigenin-7-O-glucoside; Caffeic acid [28]
Thymus satureioides	Borneol (34.26%); carvacrol (31.21%); E-caryophyllene (6.32%); thymol (3.71%) [29]	Luteolin –7-glycoside; Rosmarinic acid; Hesperetin [30]
Thymus munbyanus	Carvacrol; g-terpinene, p-cymene; thymol; linalool; borneol [31]	–
Thymus pallidus	Thymol; p-cymene; γ-terpinene; linalool; carvacrol [32]	–
Thymus zygis	Carvacrol; ocymene; and thymol [33]	Caffeic acid; Rosmarinic acid [3]
Thymus bleicherianus	Thymol; β-ocymene; Camphor; *p*-cymene [34]	–

Figure 2



Chemical structures of the commonly occurring major volatile and nonvolatile components of Moroccan Thymus species.

significantly from other plants of the same species in the concentration of one or several compounds [41]. In thyme, there are thymol types, carvacrol types, thymol with carvacrol types, and those where other compounds dominate, including 1,8-cineole, borneol, borneol with carvacrol, geraniol, linalool, citral, and d-limonene [42]. Thymus essential oils possess high chemical variability owing to different intrinsic (genetic variation) and extrinsic (ecological and environmental aspects) factors [43]. However,

chemical polymorphism can be considered as an important property of thyme plants [44]. Thymol and carvacrol are the main compounds in most thyme essential oils [45]. These two phenolic compounds have many activities such as antileishmanial [46], antimicrobial [47], anti-inflammatory [48], and antioxidant properties [49].

Pharmacological and biological properties

Thymus atlanticus from the southeastern Morocco has been studied for its biological and pharmacological properties. The aqueous extract and the polyphenolic rich extract of this thyme have shown important hypolipidemic, anti-inflammatory, anticoagulant, and antioxidant activities in several in vivo and in vitro studies [28,50–52]. Moreover, this species was reported to possess beneficial effects on paraoxonase activity and to attenuate insulin resistance in high-fat diet-fed hamsters [53]. These studies encourage the use of *T. atlanticus* as an alternative treatment for the control of various diseases.

Thymus satureioides was investigated in several studies mainly for its antimicrobial effects. The antimicrobial activity of the essential oil of this thyme was reported in several studies [29,54,55]. The results showed that this thyme has important antibacterial and antifungic activities. Moreover, the aqueous extract of this thyme exhibited remarkable anti-inflammatory, antioxidant, and antihemolytic activities [30]. Other studies have shown that *T. satureioides* possesses antiproliferative, procoagulant [56], and acaricidal activities [57].

Thymes pallidus essential oil was investigated for its antibacterial activity against bacteria isolated from hospital infections [58]. The essential oil of this thyme has shown strong antibacterial activity. In vitro antioxidant assays have shown that essential oil and extract of this thyme have good antioxidant properties [55,59,60]. *Thymes zygis* polyphenol-rich extract was evaluated for its antioxidant, hypolipidemic, and antihemolytic activities [61]. The results showed that this thyme has important in vitro antioxidant and antihemolytic activities. Another study showed that the essential oil of this thyme possesses antibacterial effects [62].

The anti-inflammatory effect of *Thymus leptobotrys* methanolic extract was evaluated in vivo in adult wistar female rats [63]. This thyme showed a significant decrease in inflammation compared with the standard medicament (indomethacin). In another study, aqueous, butanolic, and ethyl acetate extracts of this thyme were tested on the nociceptive response in mice [64]. The results of this study showed that this thyme possesses active principles that exhibit marked analgesic effects. Moreover, this thyme showed great antimicrobial and antioxidant properties [65–67].

Elhabazi *et al.* [68] reported the immunotropic and behavioral effects of *Thymus broussonnetii* aqueous and ethyl acetate extracts on mice. The results of this study showed that this thyme was capable of stimulating the immunizing system and for protection against stress owing to neurotropic activity. Another study showed that the essential oil of *T. broussonnetii* possesses antimicrobial and insecticidal activities [69]. Moreover, this thyme was reported to possess various biological properties including antioxidant, anticancer, anti-inflammatory, antipyretic, and antinociceptive [70].

Thymus maroccanus and other 74 moroccan plants were evaluated for their antiviral activity against three mammalian viruses: herpes simplex virus, sindbis virus, and poliovirus [71]. *T. maroccanus* was among the nine remarkable plants with the most important antiviral activity. Another study demonstrated that *T. maroccanus* essential oil can restore antibiotic effects by targeting bacterial membranes [72]. This can make this thyme a great candidate for developing new adjuvants for combating resistant bacteria. Moreover, El Bouzidi *et al.* [54] reported that essential oils of this thyme species exert a potent antioxidant potential.

Thymus riatarum ethanol extract has been reported to exert important antioxidant activities evaluated by two in vitro assays: DPPH free radical scavenging activity and total antioxidant capacity [73]. This study showed that *T. riatarum* has great antioxidant capacity and suggested the use of this thyme as an excellent natural source of antioxidant components. Boubaker *et al.* [23] evaluated the antifungal activity of *T. riatarum* volatile oil against the germination of spores of citrus fungal pathogens. The essential oil of this thyme displayed remarkable inhibition of spore germination. Thus, this thyme is a source of volatile compounds that can be useful and effective against citrus fungal pathogens. Moreover, the antibacterial activity of the essential oil of this thyme was reported in the study of Fadli *et al.* [74]. This study showed that the essential oil of this species revealed a noticeable antibacterial activity, by disrupting bacterial cell wall and cytoplasmic membrane, which provoke the leakage of cytoplasmic constituents.

Thymus willdenowii extract was investigated for its anti-inflammatory activity [75]. The chloroform

extract of this thyme showed an important anti-inflammatory potency similar to that of the standard medicament (indomethacin). Moreover, the essential oil of this thyme showed important antioxidant and antimicrobial effects [76]. Radi *et al.* [33] reported the antioxidant and antimicrobial effects of *T. willdenowii* and *T. zygis*. This study showed that these two species exhibited high ferric reducing antioxidant power (EC50=2.46±0.01 for *T. zygis* and 5.17±0.2 µg/ml for *T. willdenowii*) and important DPPH radical scavenging activity (IC50=6.13±0.11 for *T. zygis* and 6.78±0.3 µg/ml for *T. willdenowii*). Furthermore, their volatile oils exerted antimicrobial effects against six bacterial strains and five fungal strains.

Thymus bleicherianus, *Thymus algeriensis*, *Thymus munbyanus*, and *Thymus hyemalis* essential oils were reported for their antifungal and antibacterial activities [77–80]. The volatile oils of these thymes displayed important antimicrobial properties. *T. algeriensis* also demonstrated a potent antioxidant capacity [21,81]. Labiad *et al.* [82] investigated the antioxidant, antibacterial, antifungal, and insecticidal activities of three thyme species from morocco (*T. algeriensis*, *Thymus broussonetii*, and *Thymus vulgaris*). The results of this study revealed that the essential oils of these thymes exert important radical scavenging activity, high insecticidal effects at low concentrations, and important antimicrobial activity.

Discussion

The medicinal properties of thyme have been extensively used in traditional medicine for many years in many countries. In Morocco, the thyme is represented by many species of which certain are endemic. The ecological, ethnopharmacological, and socioeconomic values of thyme in Morocco make it one of the most important aromatic and medicinal plants in this country.

The phytochemical investigations of Moroccan thyme were mainly interested in the composition of their essential oils. Only a few number of studies investigated the composition of the nonvolatile fraction, which is rich in polyphenols. However, the nonvolatile extracts of these thymes need to be more investigated. These compounds are represented in a wide variety of polyphenols such as phenolic acids and flavonoids. Rosmarinic acid, rutin, quercetin, and luteolin are the most occurring polyphenols in Moroccan thyme plants. Furthermore, many other thymes were investigated for their phenolic composition. Rosmarinic acid is found to be the major phenolic compound in many thymes around the world [83–87], which makes thyme an important natural source of this bioactive compound.

This can be explained by the importance of the volatile fraction of this plant. The essential oils of Moroccan thyme have a remarkable variability and diversity in their composition. Borneol, carvacrol, thymol, camphene, α-Pinene, p-cymene, and caryophyllene are the major occurring volatile compounds. However, there are not many differences between the essential oil chemical profile of Moroccan thyme species and the volatile profile of some Algerian and Spanish [88–90] thyme species. The chemical profile of thyme essential oils is dominated by oxygenated monoterpenes (e.g. borneol and 1,8-Cineole), monoterpene hydrocarbons (e.g. α-Pinene and camphene), and monoterpene phenols (thymol and carvacrol) [54,91].

The antibacterial and antifungal activities of Moroccan thyme essential oils were the most investigated biological activities. However, these studies showed that thyme species have powerful antimicrobial effects. The antimicrobial activity of different thyme species from various countries was evaluated and demonstrated that Thymus genus is a source of potent antimicrobial volatile compounds [92–98].

Thyme has one of the highest antioxidant capacities among herbs [99]. Moreover, the reported thyme species have shown exceptional antioxidant properties. There is a big difference between the antioxidant effects of nonvolatile extracts and volatile oils of thyme plants. Khouya *et al.* [3] reported that the antioxidant capacities of *T. zygis*, *T. atlanticus*, and *T. satureioides* (DPPH IC50: 0.12–0.44 mg/ml) extracts were bigger than the antioxidant activity of the antioxidant standard Trolox (0.51 mg/ml). Concerning essential oils, the antioxidant effect of *T. satureioides*, *T. broussonetii*, *T. maroccanus*, *Thymus ciliatus, T. pallidus*, *T. leptobotrys,* and *Thymus serpyllum* essential oils was reported by Jamali *et al.* [91]. Their antioxidant effects (DPPH IC50: 25–122 µg/ml) were very lower than the antioxidant effect of the antioxidant standards quercetin and BHT (1.07–4.21 µg/ml). The difference can be explained by the richness of thyme extracts in a wide variety of antioxidant phenolic compounds such as phenolic acids and flavonoids. However, the essential oil has only thymol and carvacrol as the main phenolic compounds.

Polyphenols and flavonoids exhibit potent anti-inflammatory properties [100,101]. The richness of

Thymus species in phenolic compounds and flavonoids gives them excellent anti-inflammatory capacities. *T. zygis* and *T. atlanticus* extracts demonstrated this pharmacological effect by reducing the inflammation (carrageenan-induced paw edema) in mice and rats with a similar activity of the standard anti-inflammatory medicament (indomethacin) [3].

Thyme is one of the important Moroccan MAPs that has an important socioeconomic value. *T. satureioides* is the species that has gained a lot of attention, and it is the most exploited thyme for exportation [102]. However, there are many other species that can be exploited and valorized. Some of these thymes possess remarkable pharmacological and biological properties. For example, *T. atlanticus* has been proven in many studies to have interesting biological properties such as hypolipidemic, anti-inflammatory, and anticoagulant activities [28,103,104]. However, thyme regions are ecologically very fragile and vulnerable to climate change and successive years of drought. Cultivation interventions can be suggested to save and preserve these species and their biodiversity.

Conclusion

Thyme is considered as an important aromatic and medicinal plant in Morocco. It has a wide range of traditional and ethnopharmacological uses. It also has an important ecological role owing to its biodiversity and its endemic value. The extracts of thyme are rich in phenolic compounds and possess important antioxidant properties. The essential oils of thyme species have a variety of terpene compounds that exhibit potent antimicrobial effects. The Moroccan species of this genus showed that they have important biological and pharmacological properties. Furthermore, the nonvolatile extracts of Moroccan thyme need more studies and more researches. In addition, some thyme species are still poorly studied, and they need to be more investigated botanically, phytochemically, and pharmacologically.

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Conflicts of interest

There are no conflicts of interest.

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