PLANT SCIENCE TODAY
ISSN 2348-1900 (online)
Vol 9(2): 399–404
https://doi.org/10.14719/pst.1494

HORIZON
e-Publishing Group
HePG

REVIEW ARTICLE

Pharmacological, biological and phytochemical aspects of *Thymus munbyanus* Boiss. & Reut.: A review

Hamza Elbouny[1*], Brahim Ouahzizi[1], Eimad Dine Tariq Bouhlali[1,3], Khalid Sellam[1,2] & Chakib Alem[1]

[1] Biochemistry of Natural Ressources Team, Faculty of Sciences and Techniques, Errachidia, Moulay Ismail University, Zitoune 11201 Meknes, BP, Morocco
[2] Biology, Environment and Health Team, Faculty of Sciences and Techniques, Errachidia, Moulay Ismail University, Zitoune 11201Meknes, BP, Morocco
[3] National Institute for Agricultural Research, Regional Center of Errachidia, Morocco

*Email: h.elbouny@edu.umi.ac.ma

OPEN ACCESS

ARTICLE HISTORY

Received: 19 October 2021
Accepted: 07 November 2021

Available online
Version 1.0 (Early Access): 13 March 2022
Version 2.0: 01 April 2022

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, etc. See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

CITE THIS ARTICLE

Elbouny H, Ouahzizi B, Bouhlali E D T, Sellam K, Alem C. Pharmacological, biological and phytochemical aspects of *Thymus munbyanus* Boiss. & Reut.: A review . Plant Science Today 9(2): 399–404. https://doi.org/10.14719/pst.1494

Abstract

Thymus munbyanus Boiss. & Reut., is a small shrub endemic to Morocco and Algeria, and it is commonly used to treat several diseases, including digestive, circulatory, genital, skin, urinary, nervous and respiratory diseases. The extracts of this thyme are rich in a wide variety of phenolic compounds such as polyphenols and volatile phenols and exhibit numerous biological activities. The present review summarizes the literature investigations reported on *Thymus munbyanus* concerning various pharmacological and biological properties as well as phytochemical aspects. This species revealed a richness in phenolic compounds in its volatile oils, including thymol and carvacrol, as well as in its non-volatile extracts including phenolic acids phenolic acids (rosmarinic acid, caffeic acid, salvianolic acid, ferulic acid, etc.), flavonoids (luteolin, gallocatechin, quercetin, isorhamnetin, etc.). Moreover, powerful antioxidant and antimicrobial properties were reported for this *Thymus* species, which are attributed to its richness in bioactive antioxidants. Furthermore, this thyme was found to possess important nephroprotective, hepatoprotective, and tumor cytotoxic properties. In conclusion, *Thymus munbyanus* is an important natural source of bioactive phenolic compounds that can be used for developing alternative natural drugs for the treatment and prevention of several pathologies.

Keywords

Biological properties; pharmacological properties; phytochemical aspects; *Thymus munbyanus*

Introduction

Countless *Lamiaceae* species are used as medicinal and aromatic plants all over the world. This herbal family is one of the most important angiosperm families that consists of 236 genera and more than 7000 species. It also contains numerous species with medicinal and economic importance around the world. Among those 236 genera, the genus *Thymus* is one of the most important and diversified genera, comprising over 300 species distributed throughout the world (1). The plants of this genus have been used since ancient times for their beneficial health properties, which are attributed to their richness in phytochemical components, especially essential oils and polyphenols.

Thymus species are widely used medicinal plants in folk medicine, food, and pharmaceutical industries due to their pharmacological features. Moreover, these species have been used in the treatment of several diseas-

es, including digestive, circulatory, genital, skin, urinary, nervous and respiratory diseases (2,3).

Thymus munbyanus Boiss. & Reut. (*T. munbyanus*), is a small shrub endemic to Morocco and Algeria and it is commonly used in North Africa and several other countries to treat several diseases. This species englobes four subspecies namely *T. munbyanus* subsp. *munbyanus, T. munbyanus* subsp. *coloratus, T. munbyanus* subsp. *ciliates,* and *T. munbyanus* subsp. *abylaeus* (4). Moreover, this thyme was reported in several studies for its interesting biological and pharmacological properties.

In the present review, we will summarize and discuss the studies reported on *T. munbyanus*, including phytochemical, pharmacological, and biological investigations.

Phytochemistry

T. munbyanus is a natural source of bioactive phytochemicals. This thyme is reported to have important amounts of total polyphenols and volatile oils. Several studies investigated the chemical composition of the essential oils of the four subspecies of *T. munbyanus.* Benomari *et al.* (2020) determined the chemical composition of three subspecies of *T. munbyanus (T. munbyanus subsp. abylaeus, T. munbyanus subsp. ciliates,* and *T. munbyanus subsp. coloratus).* This study showed that the main components of the three subspecies were α-terpinyl acetate (51.7%), α-terpineol (9.7%), and borneol (6.8%) for *T. munbyanus* subsp. *abylaeus*, carvacrol (65.7%), g-terpinene (13.6%), and p-cymene (7.9%) for *T. munbyanus* subsp. *ciliates,* and camphor (25.9%), myrcene (16.9%), and 1,8-cineole (6.5%) for *T. munbyanus* subsp. *coloratus* (5). Moreover, tthe chemical composition of *T. munbyanus* subsp. *munbyanus* essential oil was evaluated by Bendif et al. (2018). The results showed that (E)- nerolidol (13.7%), terpinenol (10.6%), and camphor (7.6%) are the major compounds of this subspecies (6). In another study, Ouknin *et al.* (2018) analyzed the chemical composition of the essential oil of this species and revealed that it contains carvacrol (31.7%), β-terpinene (21.9%), p-cymene (14.7%), and thymol (7.6%) as the major volatile compounds (7). These studies indicated that the composition of the volatile oils differs from one subspecies to another. Thus, some subspecies contain in their composition volatile phenolic compounds, namely thymol and carvacrol. Regarding the chemical composition of the non-volatile extracts of *T. munbyanus,* there are only a few reports. The study of Bendif *et al.* (2020) revealed that the extract of *T. munbyanus* contains phenolic constituents including phenolic acids (rosmarinic acid, caffeic acid, salvianolic acid, ferulic acid, etc.), flavonoids ((luteolin, gallocatechin, quercetin, isorhamnetin, etc.), and glycosides (luteolin 7-O-glucuronide, quercetin 3-O-glucuronide, eriodictyol-7-O-hexoside, etc.) (8). These polyphenolic constituents are present in great amounts in this species and have important bioactivity. However, they are less studied when compared to volatile oils. Therefore, more phytochemical investigations on the polyphenolic phytochemicals of this thyme are needed. After all, these studies showed that this species is rich in a wide variety of bioactive compounds in both volatile and non-volatile extracts (Fig. 1).

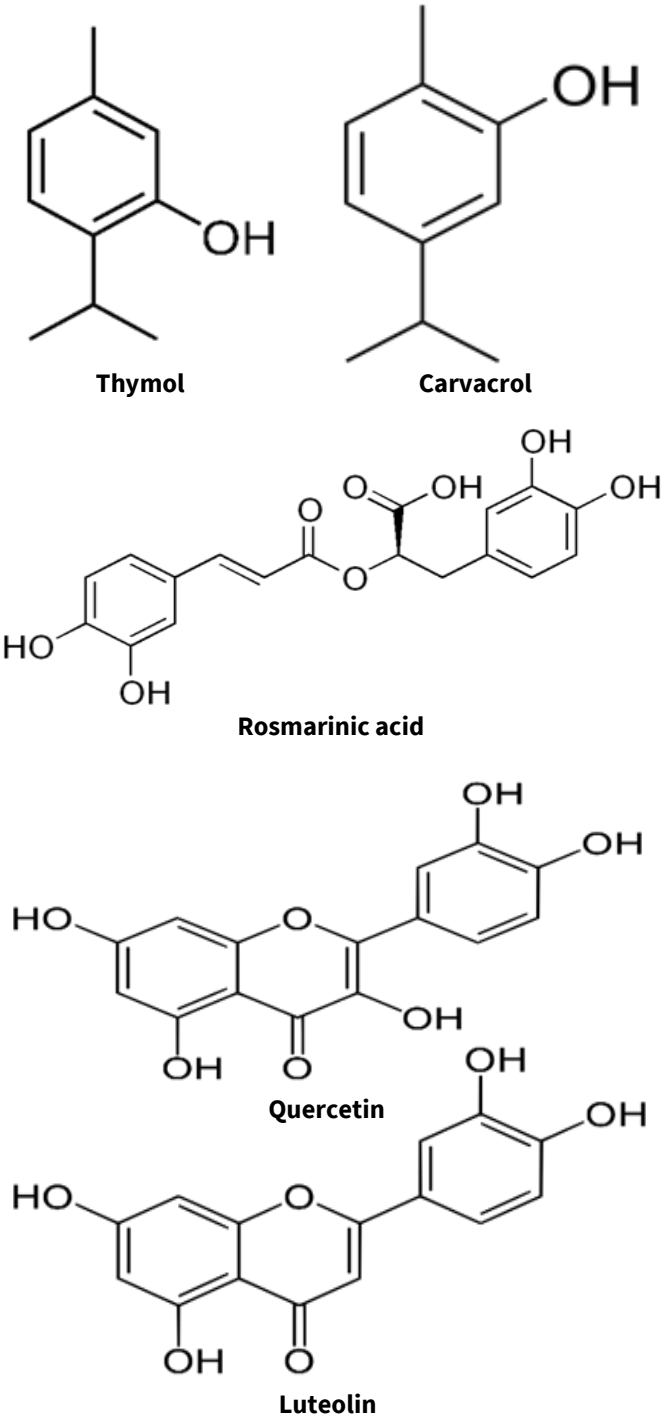

Fig. 1. Chemical structure of some abundant phenolic compounds in *Thymus munbyanus*

Biological and pharmacological properties

Antioxidant activity

Thyme plants are an important source of natural antioxidants. Numerous *Thymus* species from different countries around the world are reported to exhibit powerful antioxidant effects (9–11). Likewise, *T. munbyanus* antioxidant potential was studied using different methods. The antioxidant activity of chloroform, ethyl acetate, and n-butanol extracts, as well as isolated compounds from *T. munbyanus* using total antioxidant capacity and free

radical scavenging activity assays were analyzed. The results of these studies showed that the different solvent extracts have an antioxidant effect comparable to that of the antioxidant standards butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), whereas some of the isolated compounds, including methyl caffeate, tetrahydroxyflavanone, and pluchoic acid exerted a higher antioxidant effect than those of antioxidant standards which are known to be potent antioxidants (12, 13). Moreover, the antioxidant potential of the essential oils of *T. munbyanus* has been evaluated in several studies. Benchabane *et al.* (2014) evaluated the antioxidant activity of *T. munbyanus* essential oil using DPPH free radical and thiobarbituric acid reactive substances assays and reported that *T. munbyanus* essential oil exerted a powerful antioxidant activity, which was similar to that of BHT (14). Moreover, Bendif *et al.* (2016) studied the antioxidant activity of essential oils from different parts (Leaves/stems and flower) of *T. munbyanus* using DPPH, ABTS, and FRAP in-vitro antioxidant tests. The results of this study showed that all the oils showed moderate antioxidant activity. Leaves with stems essential oils exhibited a considerably higher activity compared to flowers essential oils, but significantly lower than that exerted by the standard antioxidant Trolox (15). Furthermore, the powerful antioxidant potential reported for this thyme is generally attributed to the presence of powerful phenolic antioxidants in its volatile and non-volatile extracts in important amounts.

Antimicrobial activity

Thymus species essential oils exhibit a broad range of biological properties, including antibacterial and antifungal activities. Heni *et al.* studied the antibacterial activity of *T. munbyanus* essential oil against *Listeria monocytogenes* and *Bacillus cereus,* which are implicated in the contamination and poisoning of food. The results of this study demonstrated that the essential oil of this thyme exhibited a very good antibacterial activity against the two pathogenic strains. These pathogens displayed high sensitivity against the essential oil with inhibition diameters of 28.6 mm (*L. monocytogenes*) and 40 mm (*B. cereus*) and with a relatively low minimum inhibitory concentration (0.18 mg/ml) (16). Moreover, Bendifa *et al*. screened the antimicrobial activity of the essential oils of *T. munbyanus* using the disc diffusion method against four bacterial strains (*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa,* and *Enterococcus faecalis*) and one yeast strain (*Candida albicans*). The results revealed that the essential oil of this thyme had a moderate antimicrobial effect on *S. aureus, E. coli, and C. albicans* with inhibition zone diameters in the range of 9 to 10 mm (15). Other studies investigated the antimicrobial properties of *T. munbyanus* essential oils against different microbial strains (17, 18) and showed that the essential oil of this thyme displays good antimicrobial effects.

Hepatoprotective activity

The liver is a vital organ with important metabolic functions, including body detoxification. However, hepatic dysfunction can cause serious complications. Liver disorders are associated with multiple factors such as biological, chemical, and drug overdose (19). Several plants were investigated for their hepatoprotective effects, including *Thymus* species (20). Furthermore, investigation was carried out to analyze the hepatoprotective effect of *T. munbyanus* against 2,4-dichlorophenoxyacetic acid (2,4-D) induced hepatic oxidative stress in albino Wistar rats by evaluating the biomarkers of hepatic function (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, lactate dehydrogenase, and gamma-glutamyl transferase), glutathione (GSH) levels, protein, and albumin contents, lipid peroxidation marker (malondialdehyde MDA), enzymatic antioxidants (superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione s-transferase (GST) enzymes), and histopathological evaluation. This study revealed that the alterations induced by 2,4 -D at a dose of 5 mg/kg bw in the histological and biochemical parameters of the liver were significantly attenuated. It was reported that 2,4-D increased the biomarkers of hepatic function and MDA level significantly, decreased protein and albumin contents and hepatic GSH level, and the major enzymatic antioxidants, as well as the development of histological alterations of liver tissue with severe damages on liver cells. However, *T. munbyanus* extract attenuated all the alterations significantly in the histological and biochemical parameters of the liver (21). This study reported promising findings on the hepatoprotective potential of this *Thymus* species. However, testing the extracts of this thyme using other methods and different models is recommended to confirm its hepatoprotective effects.

Nephroprotective activity

The kidney is a vital organ that displays crucial functions, including the elimination of metabolic nitrogen waste, regulation of the pH, the fluid and electrolyte balance, production of hormones, and activation of vitamin D (22). However, renal dysfunction can lead to serious complications, including cardiovascular disease, hypertension, anaemia, etc. (23). Numerous medicinal plants were investigated for their nephroprotective effects (24). they can attenuate the biochemical, functional, and structural renal toxicities and represent effective nephroprotective alternatives (25). Likewise, Trea *et al.* tested the protective effects of *T. munbyanus* aqueous extract against 2,4-D induced nephrotoxicity at a dose of 5 mg/kg of body weight in male albino rats. This chemical compound causes oxidative stress and renal injury in the kidney, which increases the potential markers of renal filtration (urea and creatinine), malondialdehyde, and carbonyl protein levels, a decrease in uric acid, GSH, and antioxidant enzymes levels (SOD, GPx, and GST). The results showed that *T. munbyanus* extract supplementation for one month restored some blood parameters and alleviated the adverse cytotoxic effects of 2,4-D by increasing the levels of certain antioxidants, consequently attenuating the intensity of oxidative stress induced by 2,4-D, and attenuated the histological alterations observed in the kidneys (26).

Tumor Cytotoxicity and anti-proliferative activity

Bendif *et al.* investigated the tumor cytotoxicity of *T. munbyanus* flowers, leaves, and stems essential oils against three human tumor cell lines, namely human glioblastoma

multiforme, human breast adenocarcinoma, and human malignant melanoma. The results of this study revealed that the essential oils exhibited a slight cytotoxic effect against all cell lines. Flowers essential oils showed the highest cytotoxic effect against malignant melanoma cell line (IC_{50} value = 46.95 µg/ml), whereas the lowest effects were shown by stems and leaves essential oil against the same tumor cell line (15). Moreover, Tefiani *et al.* (2015) compared the anti-proliferative activity of the essential oils of *T. munbyanus* and an Apiaceae species (*Ammoides pusilla)* against human acute monocytic leukaemia cell line (THP-1). The results showed that *T. munbyanus* essential oil showed a significant ($p<0.05$) anti-proliferative activity, in which after seven days of incubation at a concentration of 100 µg/mL of essential oils, the proliferation percentage of THP-1 cells was 13% for *T. munbyanus* comparing to 64% for *A. pusilla* (27).

Discussion

Thyme plants are known to have important amounts of phenolic compounds and exhibit strong antioxidant effects. Several studies showed that the species of this genus are rich in flavonoids, phenolic acids, and their derivatives (28,29). For example, Sarfaraz *et al.* (2021) carried out a chemical analysis of the methanolic extract polyphenolic composition of 11 Iranian *Thymus* species. The results of the analysis showed that these species possess high amounts of polyphenols in which rosmarinic acid, salvianolic acid, and cinnamic acid are the major phenolic acids, and apigenin, epicatechin, and naringenin as the major flavonoids. Moreover, Boros *et al.* (2010) evaluated the chemical composition of five Hungarian *Thymus* species. The results of the analysis of this study showed that the hydro-methanolic extracts of these species are rich in phenolic acids and flavonoids. Phenolic acids (rosmarinic acid, ferulic acid, caffeic acid, chlorogenic acid), flavanones (naringenin, eriodictyol and dihydroquercetin), flavones (apigenin), as well as flavonols (quercetin and rutin) were present in every examined *Thymus* species in which rosmarinic acid was the dominant compound (1.436 - 83.49 mg/g) (30). Likewise, *T. munbyanus* possess significant amounts of these polyphenols, including phenolic acids such as rosmarinic acid and different types of flavonoids. This suggests that the polyphenolic extracts of *Thymus* species, including *T. munbyanus* are an important source of these important metabolites. Furthermore, the chemical composition of the essential oils of *T. munbyanus* contains bioactive volatile phenols, namely thymol and carvacrol (7). *Thymus* species are a source of these volatile phenolic phytochemicals. Several studies investigated the chemical composition of several *Thymus* species essential oils and showed that thymol and carvacrol are abundant volatile compounds, including *T. serpyllum* and *T. algeriensis* (31), *T. daenensis* and *T. kotschyanus* (32)*, T. kotschyanus and T. vulgaris,* etc. (33).

The extracts and essential oils of *Thymus* species, including *T. munbyanus* are a potent source of a wide variety of antioxidant phenolic compounds. Several thyme species demonstrated important antioxidant properties using diverse in-vitro (34,35) and in-vivo (36,37) methods. Thus, the potent antioxidant effects of the extracts of these thymes, including *T. munbyanus* can help in the protection against free radicals and their harmful effects and reduce the risk of occurrence of numerous pathologies.

T. munbyanus essential oils display great antimicrobial effects. This biological activity is commonly observed in thyme species. Several studies investigated the antimicrobial effects of *Thymus* plants and other Lamiaceae species. These studies showed that *Thymus* species display the most significant antimicrobial effects (38–40). In addition, these effects can be attributed to the richness of their essential oils in thymol and carvacrol. These two phenolic compounds exhibit powerful antimicrobial properties. Moreover, the most frequently reported mechanism of antibacterial effect of these compounds involves the disruption of the bacterial membrane causing bacterial lysis and leakage of intracellular contents (41).

The kidney and the liver are vital organs with indispensable functions in the body. Protecting these organs against harmful agents can prevent several diseases. The hepatoprotective and nephroprotective actions displayed by *T. munbyanus* show that this species can be efficient in the prevention of kidney and liver pathologies. Moreover, several thyme plants were also investigated for their hepatoprotective and nephroprotective effects (*T. vulgaris* (42)*, T. daenensis* (43)*,* etc.). These investigations showed that the species of this genus display important liver and kidney protective effects. Thus, thyme plants including *T. munbyanus* can be promising sources for developing more natural and safer hepatoprotective and nephroprotective alternative drugs.

Uncontrolled cell proliferation or cancer is a major health issue and it is the second leading cause of death worldwide. Moreover, cancer chemotherapy or radiation therapy are associated with a high mortality rate and toxicity (44). Therefore, developing newer and safer treatment methods, such as plant-based therapy can be a promising alternative method. The use of medicinal plants for the prevention and treatment of cancer is gaining more attention due to their richness in bioactive tumor cytotoxic constituents and fewer adverse effects (45). Several thyme plants were investigated for their anticancer properties particularly in in-vitro cellular models and revealed that they have a great potency as sources of anticancer agents (46). Hence, *T. munbyanus* extracts should be more investigated in in-vitro and in-vivo methods to confirm the beneficial effects of this species against cell proliferation.

Due to the beneficial effects of the different extracts of *T. munbyanus* on several pathologies and the richness of these extracts in a wide variety of bioactive compounds, this species can be considered as an important source of potent drugs in the future. However, more studies should be carried out, especially on the polyphenolic extracts of this species, to evaluate their bioactivity against several diseases such as diabetes, hyperlipidemia, atherosclerosis, etc.

Conclusion

This present study aims to review the phytochemical, pharmacological, and biological activities reported on *T. munbyanus*. This thyme showed that it is rich in a wide variety of volatile and non-volatile bioactive phenolic compounds, including rosmarinic acid, thymol, and carvacrol. The extracts of this thyme display significant antioxidant, antimicrobial, antitumoral, hepatoprotective, and nephroprotective properties. *T. munbyanus* can be used for developing alternative natural drugs for the treatment and prevention of several pathologies.

Acknowledgements

The authors express their gratitude to their respective institutions for the support. This work was funded by CNRST.

Authors contributions

HE and CA conceived of the presented idea and wrote the paper. KS, EDTB, along with BO revised and edited the paper. All authors have read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: The authors declare no conflict of interest.

Ethical issues: None.

References

1. Mustafa S, Hina S, Mahmood S *et al*. Exploring phytochemical potential of nature's bliss *Thymus vulgaris* L. Mini review. 2020;5:493–96.
2. Li X, He T, Wang X *et al*. Traditional uses, chemical constituents and biological activities of plants from the genus *Thymus*. Chem Biodivers. [Internet]. 2019 [cited 2021 Sep 7];16(9). Available from: https://onlinelibrary.wiley.com/doi/10.1002/cbdv.201900254
3. El Yaagoubi M, Mechqoq H, El Hamdaoui A *et al*. A review on Moroccan *Thymus* species: Traditional uses, essential oils chemical composition and biological effects. J Ethnopharmacol. [Internet]. 2021 [cited 2021 Sep 7];278:114205. Available from: https://www.sciencedirect.com/science/article/pii/S0378874121004323
4. Dobignard A, Chatelain C, Fischer M, Orso J, Jeanmonod D. Index synonymique de la flore d'Afrique du Nord. Genève, Suisse: Conservatoire et Jardin Botaniques, 2012.
5. Benomari F, Nassim D, Moumani M, Hassani F, Muselli A, Costa J. Chemical variability of essential oils of three subsp. of *Thymus munbyanus* Boiss. & Reut. from Western Algeria. J Essent Oil Res. 2020;32:1–11. https://doi.org/10.1080/10412905.2020.1772134
6. Bendif H, Adouni K, Miara MD *et al*. Essential oils (EOs), pressurized liquid extracts (PLE) and carbon dioxide supercritical fluid extracts (SFE-CO2) from Algerian Thymus munbyanus as valuable sources of antioxidants to be used on an industrial level. Food Chem 2018;260:289–98. https://doi.org/10.1016/j.foodchem.2018.03.108
7. Ouknin M, Abderrahmane R, Costa J, Majidi L, Ponthiaux P. Anticorrosion properties of *Thymus munbyanus* Boiss & Reut essential oil for mild steel in 1M HCl. Moroc J Chem. 2018;6:548–59.
8. Bendif H, Peron G, Miara MD *et al*. Total phytochemical analysis of *Thymus munbyanus* subsp. *coloratus* from Algeria by HS-SPME-GC-MS, NMR and HPLC-MSn studies. J Pharm Biomed Anal. [Internet]. 2020; [cited 2021 Sep 8];186:113330. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0731708520309298
9. Silva AM, Martins-Gomes C, Souto EB *et al*. *Thymus zygis* subsp. *zygis* an endemic Portuguese plant: Phytochemical profiling, antioxidant, anti-proliferative and anti-inflammatory activities. Antioxidants. [homepage on the Internet] 2020; [cited 2021 Sep 8];9 (6):482. Available from: https://www.mdpi.com/2076-3921/9/6/482
10. Habashy NH, Abu Serie MM, Attia WE, Abdelgaleil SAM. Chemical characterization, antioxidant and anti-inflammatory properties of Greek *Thymus vulgaris* extracts and their possible synergism with Egyptian *Chlorella vulgaris*. J Funct Foods. [Internet]. 2018 [cited 2021 Sep 8];40:317–28. Available from: https://www.sciencedirect.com/science/article/pii/S1756464617306941
11. Labiad MH, Hicham H, Ghanimi A, Tabyaoui M. Phytochemical screening and antioxidant activity of Moroccan *Thymus saturejoïdes* extracts. 2017;8:2132–39.
12. Ozen T, Koldas S, Tüfekçi AR *et al*. Phytochemical study and antioxidant activities of the water soluble aerial parts and isolated compounds of *Thymus munbyanus* subsp. *ciliatus* (Desf.) Greuter & Burdet *Thymus munbyanus* subsp. *ciliatus* (Desf.) [Internet]. 2021 [cited 2021 Sep 9]; Available from: https://semanticscholar.org
13. Chaouche M, Demİrtaş İ, Koldaş S, Tüfekçİ AR, Gül F, Özen T *et al*. Phytochemical study and antioxidant activities of the water-soluble aerial parts and isolated compounds of *Thymus munbyanus* subsp. *ciliatus* (Desf.) Greuter & Burdet. Turk J Pharm Sci. 2021;18. https://doi.org/10.4274/tjps.galenos.2020.44538
14. Benchabane O, Hazzit M, Baaliouamer A, Mouhouche F. Analysis and antioxidant activity of the essential oils of *Ferula vesceritensis* Coss. et Dur. and *Thymus munbyanus* Desf. J Essent Oil Bear Plants. [the Internet] 2012 [cited 2021 Sep 9];15(5):774–81. Available from: http://www.tandfonline.com/doi/abs/10.1080/0972060X.2012.10644119
15. Bendif H, Boudjeniba M, Miara MD, *et al*. Essential Oil of *Thymus munbyanus* subsp. *coloratus* from Algeria: Chemotypification and *in vitro* Biological Activities. Chem Biodivers [Internet]. 2017 [cited 2021 Sep 7];14(3):e1600299. Available from: https://onlinelibrary.wiley.com/doi/10.1002/cbdv.201600299
16. Heni S, Bennadja S, Djahoudi A. Chemical composition and antibacterial activity of the essential oil of *Thymus ciliatus* growing wild in North Eastern Algeria. 2015; https://doi.org/10.7324/JAPS.2015.501209
17. Hazzit M, Baaliouamer A, Faleiro ML, Miguel MG. Composition of the essential oils of *Thymus* and *Origanum* sp. from Algeria and their antioxidant and antimicrobial activities. J Agric Food Chem [Internet]. 2006 [cited 2021 Sep 10];54(17):6314–21. Available from: https://pubs.acs.org/doi/10.1021/jf0606104
18. Ghorab H, Kabouche A, Z S *et al*. Biological activities and compositions of the essential oil of *Thymus ciliatus* from Algeria. Pharm Lett. 2013;5:28–32.
19. Qadir MI, Ahmad Z. Advances in hepatoprotective medicinal plants research. Bangladesh J Pharmacol. [homepage on the Internet] 2017 [cited 2021 Sep 10];12(3):229–42. Available from: http://www.bdpsjournal.org/index.php/bjp/article/view/753
20. Sobhy HM, Hassanen NHM, Ahmed MAI. Hepatoprotective activities of thyme (*Thymus vulgaris* L.) in rats suffering from obesity. Egypt J Chem. [Internet] 2020 [cited 2021 Sep 10];63(12):5087–101. Available from: https://ejchem.journals.ekb.eg/article_112669.html
21. Tichati L, Trea F, Ouali K. The antioxidant study proprieties of *Thymus munbyanus* aqueous extract and its beneficial effect on 2, 4-Dichlorophenoxyacetic acid -induced hepatic oxidative stress in albino Wistar rats. Toxicol Mech Methods. [Internet]. 2021 [cited 2021 Sep 14];31(3):212–23. Available from: https://doi.org/10.1080/15376516.2020.1870183
22. Åkesson A, Chaney RL. Cadmium exposure in the environment:

Dietary exposure, bioavailability and renal effects [Internet]. In: Nriagu J. editor. Encyclopedia of Environmental Health (2nd edition). Oxford: Elsevier. 2019; [cited 2021 Sep 15]; p. 475–84.Available from: https://www.sciencedirect.com/science/article/pii/B9780124095489117464

23. Bello AK, Alrukhaimi M, Ashuntantang GE *et al*. Complications of chronic kidney disease: current state, knowledge gaps, and strategy for action. Kidney Int Suppl. [Internet]. 2017 [cited 2021 Sep 15];7(2):122–29. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6341007/

24. Negi K, Mirza A. Nephroprotective and therapeutic potential of traditional medicinal plants in renal diseases. J Drug Res Ayurvedic Sci. 2020;5:177–85. https://doi.org/10.5005/jdras-10059-0079

25. Al-Snafi A, Talab T. A review of medicinal plants with nephroprotective effects. GSC Biol Pharm Sci. 2019;8:114–22. https://doi.org/10.30574/gscbps.2019.8.1.0108

26. Trea F, Tichati L, Ouali K. Protective effect of *Thymus munbyanus* aqueous extract against 2,4-dichlorophenoxyacetic acid-induced nephrotoxicity in Wistar rats. Drug Chem Toxicol. [homepage on the Internet] 2020 [cited 2021 Sep 15];1–10. Available from: https://tandfonline.com/doi/full/10.1080/01480545.2020.1809669

27. Tefiani C, Riazi A, Fatma Y *et al*. *Ammoides pusilla* (Apiaceae) and *Thymus munbyanus* (Lamiaceae) from Algeria essential oils: Chemical composition, antimicrobial, antioxidant and anti-proliferative activities. J Essent Oil Res. 2015;27:1–9. https://doi.org/10.1080/10412905.2015.1006739

28. Ziani BEC, Heleno SA, Bachari K *et al*. Phenolic compounds characterization by LC-DAD- ESI/MSn and bioactive properties of *Thymus algeriensis* Boiss. & Reut. and *Ephedra alata* Decne. Food Res Int [Internet]. 2019 [cited 2021 Sep 15];116:312–19. Available from: https://www.sciencedirect.com/science/article/pii/S0963996918306616

29. Taghouti M, Martins-Gomes C, Schäfer J *et al*. *Thymus pulegioides* L. as a rich source of antioxidant, anti-proliferative and neuroprotective phenolic compounds. Food Funct. [Internet]. 2018 [cited 2021 Sep 15];9(7):3617–29. Available from: https://pubs.rsc.org/en/content/articlelanding/2018/fo/c8fo00456k

30. Boros B, Jakabová S, Dörnyei Á *et al*. Determination of polyphenolic compounds by liquid chromatography–mass spectrometry in *Thymus* sp. J Chromatogr A. [Internet]. 2010 [cited 2021 Sep 15];1217(51):7972–80. Available from: https://www.sciencedirect.com/science/article/pii/S0021967310009623

31. Nikolić M, Glamočlija J, Ferreira ICFR *et al*. Chemical composition, antimicrobial, antioxidant and antitumor activity of *Thymus serpyllum* L., *Thymus algeriensis* Boiss. and Reut and *Thymus vulgaris* L. essential oils. Ind Crops Prod. [Internet]. 2014 [cited 2021 Sep 16];52:183–90. Available from: https://www.sciencedirect.com/science/article/pii/S092666901300558X

32. Golkar P, Mosavat N, Jalali SAH. Essential oils, chemical constituents, antioxidant, antibacterial and *in vitro* cytotoxic activity of different *Thymus* sp. and *Zataria multiflora* collected from Iran. South Afr J Bot. [Internet]. 2020 [cited 2021 Sep 16];130:250–58. Available from: https://www.sciencedirect.com/science/article/pii/S0254629919318691

33. Mohammadi H, Amirikia F, Ghorbanpour M, Fatehi F, Hashempour H. Salicylic acid induced changes in physiological traits and essential oil constituents in different ecotypes of *Thymus kotschyanus* and *Thymus vulgaris* under well-watered and water stress conditions. Ind Crops Prod. [Internet]. 2019 [cited 2021 Sep 16];129:561–74. Available from: https://www.sciencedirect.com/science/article/pii/S0926669018310987

34. Lamia SA, Moussa B, Marie-Laure F, Georges L. Chemical composition and antioxidant activity of *Thymus fontanesii* essential oil from Algeria. Nat Prod J. 2020;10(3):193–99. https://doi.org/10.2174/2210315508666180427162542

35. Silva AM, Martins-Gomes C, Souto EB, *et al*. *Thymus zygis* subsp. *zygis* an endemic Portuguese plant: Phytochemical profiling, antioxidant, anti-proliferative and anti-inflammatory activities. Antioxidants. [Internet]. 2020 [cited 2021 Sep 16];9(6):482. Available from: https://www.mdpi.com/2076-3921/9/6/482

36. Righi N, Boumerfeg S, Fernandes PAR *et al*. *Thymus algeriensis* Bioss & Reut: Relationship of phenolic compounds composition with *in vitro*/*in vivo* antioxidant and antibacterial activity. Food Res Int. [Internet]. 2020 [cited 2021 Sep 16];136:109500. Available from: https://www.sciencedirect.com/science/article/pii/S0963996920305251

37. Ramchoun M, Khouya T, Harnafi H *et al*. Effect of aqueous extract and polyphenol fraction derived from *Thymus atlanticus* leaves on acute hyperlipidemia in the Syrian Golden Hamsters. Evid Based Complement Alternat Med. [Internet]. 2020 [cited 2021 Sep 16];2020:e3282596. Available from: https://www.hindawi.com/journals/ecam/2020/3282596/

38. Saleh I, Abd-ElGawad A, El Gendy AE-N *et al*. Phytotoxic and antimicrobial activities of *Teucrium polium* and *Thymus decussatus* essential oils extracted using hydrodistillation and microwave-assisted techniques. Plants. [Internet]. 2020 [cited 2021 Sep 16];9(6):716. Available from: https://www.mdpi.com/2223-7747/9/6/716

39. Soulaimani B, Hidar NE, Ben El Fakir S, Mezrioui N, Hassani L, Abbad A. Combined antibacterial activity of essential oils extracted from *Lavandula maroccana* (Murb.), *Thymus pallidus* Batt. and *Rosmarinus officinalis* L. against antibiotic-resistant Gram-negative bacteria. Eur J Integr Med. [Internet]. 2021 [cited 2021 Sep 16];43:101312. Available from: https://www.sciencedirect.com/science/article/pii/S1876382021000305

40. Kačániová M, Vukovič N, Hleba L *et al*. Antimicrobial and antiradicals activity of *Origanum vulgare* l. and *Thymus vulgaris* essential oils. J Microbiol Biotechnol Food Sci. [Internet]. 2021 [cited 2021 Sep 16];2021(vol. 10):263–71. Available from: http://www.jmbfs.org/jmbfs-kacaniova-a/?issue_id=1307&article_id=19

41. Kachur K, Suntres Z. The antibacterial properties of phenolic isomers, carvacrol and thymol. Crit Rev Food Sci Nutr. [Internet]. 2020 [cited 2021 Sep 16];60(18):3042–53. Available from: https://doi.org/10.1080/10408398.2019.1675585

42. Soliman MM, Aldhahrani A, Metwally MMM. Hepatoprotective effect of *Thymus vulgaris* extract on sodium nitrite-induced changes in oxidative stress, antioxidant and inflammatory marker expression. Sci Rep. [Internet]. 2021 [cited 2021 Sep 16];11(1):5747. Available from: https://www.nature.com/articles/s41598-021-85264-9

43. Ansari Nejad R, Nazem H, Omidifar N, Sadeghi H. Evaluation of the hepatoprotective effect of hydroalcoholic extract of *Thymus daenensis* on carbon tetrachloride-induced hepatotoxicity in rats. Armaghane Danesh [Internet]. 2019 [cited 2021 Sep 10];24(3):413–26. Available from: http://armaghanj.yums.ac.ir/article-1-2296-en.html

44. Mazumder K, Biswas B, Raja IM, Fukase K. A review of cytotoxic plants of the Indian subcontinent and a broad-spectrum analysis of their bioactive compounds. Molecules. [Internet]. 2020 [cited 2021 Sep 16];25(8):1904. https://doi.org/10.3390/molecules25081904

45. Uğur D, Güneş H, Güneş F, Mammadov R. Cytotoxic activities of certain medicinal plants on different cancer cell lines. Turk J Pharm Sci. [Internet]. 2017 [cited 2021 Sep 15];14(3):222–30. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7227927/

46. Afonso AF, Pereira OR, Cardoso SM. Health-promoting effects of *Thymus* phenolic-rich extracts: Antioxidant, anti-inflammatory and antitumoral properties. Antioxidants. [Internet]. 2020 [cited 2021 Sep 16];9(9):814. Available from: https://www.mdpi.com/2076-3921/9/9/814

§§§