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Short Review

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Secondary metabolites and pharmacological potential of *Thuja orientalis* and *T. occidentalis*: A short review

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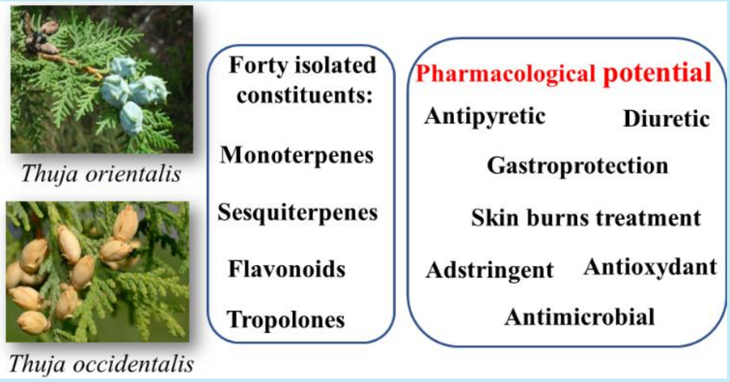
ABSTRACT: Species from *Thuja* genus (Cupressaceae) are found in Brazil, North America and Asia. In the traditional medicine, these plants are used in the treatment of cough, skin allergies, and asthma. In Brazil, *Thuja* species are also used in the ornamentation of urban areas. Different parts of these plants displayed insecticidal, antitumor, and antioxidant activities. The essential oil of the leaves from *Thuja* spp. are constituted by monoterpenes and sesquiterpenes. The main substances found in the extracts of these species are flavonoids, which display relevant biological activities. This brief review shows recent phytochemical studies involving *T. orientalis* and *T. occidentalis*, as well as 40 constituents isolated from these species. The existing pharmacological potential justifies the growing scientific interest in this genus.



CONTENTS

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1. Introduction

Scientific interest for plants is growing, mainly due to the accelerated loss of the biodiversity (Singh *et al.*, 2021). The world market of phytotherapeutics has attracted a growing number of people who seek cheaper medicines with fewer side effects, when compared to synthetic pharmaceuticals (Silva *et al.*, 2021). The diversified potential of natural products has been widely explored, and the resulting data are considered an important key for the development of new drugs (Atanasov *et al.*, 2021). Additionally, the development of green semisynthesis of metal nanoparticles (Gour and Jain, 2019) and biosensors (Kumar and Arora, 2020) highlighting the variety of application of plants. Within the plant biodiversity, species of the Cupressaceae family stand out.

Cupressaceae trees comprise important classes of organic compounds, especially terpenes and terpenoids, both of which have intense and often pleasant odors. These compounds are mainly present in heartwood, bark and leaves of Cupressaceae trees (Bhardwaj *et al.*, 2021). The most known terpenoids found in conifers are sesquiterpenoids, diterpenes, and tropolones. Some sesquiterpenoids, e.g., bisabolanes, cubenanes, guaianes, ylanganes, himachalanes, longifolanes, longibornanes, longipinanes, cedranes, thujopsanes, are also present in the Pinaceae, Podocarpaceae (Pereira *et al.*, 2020) and Taxodiaceae (Jiang *et al.*, 2018) families. However, tropolone derivatives, such as nootkatin, chanootin, and hinokitiol, are particularly characteristic in Cupressaceae (Park *et al.*, 2021; Yatoo *et al.*, 2018).

In this context, species from the *Thuja* genus (Cupressaceae family) represent a relevant object of study, considering its use in the traditional medicine for the treatment of scurvy and rheumatism. It is endemic in Asia and is cultivated in Northern Europe and Brazil as an ornamental shrub (Pradhan *et al.*, 2021; Viezzer *et al.*, 2018). Species of the genus *Thuja*, similar to various other conifers, are evergreen trees that grow from 3 to 60 meters tall, with stringy-textured reddish-brown bark. There are five species belonging to this genus of which *T. orientalis* and *T. occidentalis* L. are well characterized (Gupta and Sharma, 2021). These species are monoecious and large evergreen shrub or small to medium sized trees (Jain and Sharma, 2017). The main secondary metabolites associated to the therapeutic potential of *Thuja* spp. are flavonoids, terpenes, and coumarins (Bhardwaj *et al.*, 2021; Gupta and Sharma, 2021).

Thuja orientalis is a synonym of *Platycladus orientalis* (L.) Franco, an accepted name in the genus *Platycladus* (Cupressaceae family). All parts of *T. orientalis*, popularly known as *tuia*, are used for several objectives. Extracts from leaves have antipyretic, diuretic, and astringent properties, while the root bark extracts are used to treat skin burns. The leaves extract of *T. orientalis* also shows relevant antimicrobial activity (Burange *et al.*, 2021). Extracts from stems are used against parasites of the skin, dysentery, and constipation. *T. orientalis* extracts can be also used for dermatological treatments, renal, and gastrointestinal disorders (Gupta and Sharma, 2021). Also, the significant occurrence of phenolic compounds in the polar extracts from this species is related to its antioxidant activity (Moawad and Amin, 2019).

Thuja occidentalis L., commonly known as white cedar, is used in traditional medicine to treat bronchial catarrh, enuresis, psoriasis, uterine carcinomas, amenorrhea, and other diseases (Gupta and Sharma, 2021). The tincture from this species is used in the treatment of warts, papillomas, and condylomas related to human papilloma virus (Aguilar-Velázquez *et al.*, 2018). *T. occidentalis* also present pharmacological properties, such as antioxidant, gastroprotective, antimicrobial, antitumor, antidiabetic, and anti-atherosclerotic activities (Gupta and Sharma, 2021; Stan *et al.*, 2019).

Due to the scientific importance of this species, the aim of this work was to provide a short review related to chemical constitution and biotechnological potential of *T. orientalis* and *T. occidentalis* reported in the last five years.

2. Methodology

Data relating to *T. orientalis* and *T. occidentalis* were obtained through PubMed and Google Scholar published in the last five years. The following exclusion criteria were adopted: (i) article whose full text was not accessible in the database; (ii) publications that did not include the search phrases in the abstract or title; (iii) articles in other languages; and (iv) articles in which the phytochemicals used in the biological activity assays were not isolated from these species, but were acquired from industries. The chemical structures of compounds from these species were drawn using ChemDrawn 12.0 software.

3. Chemical composition

Essential oils from *T. orientalis* and *T. occidentalis* leaves are mainly constituted by terpenes **1** to **21** (Fig. 1). The major compounds found in the oil from *T. orientalis* collected in India are α-pinene (**1**, 29.2%), δ-3-carene

Eclética Química Journal, vol. 47, n. 4, 2022, 17-26
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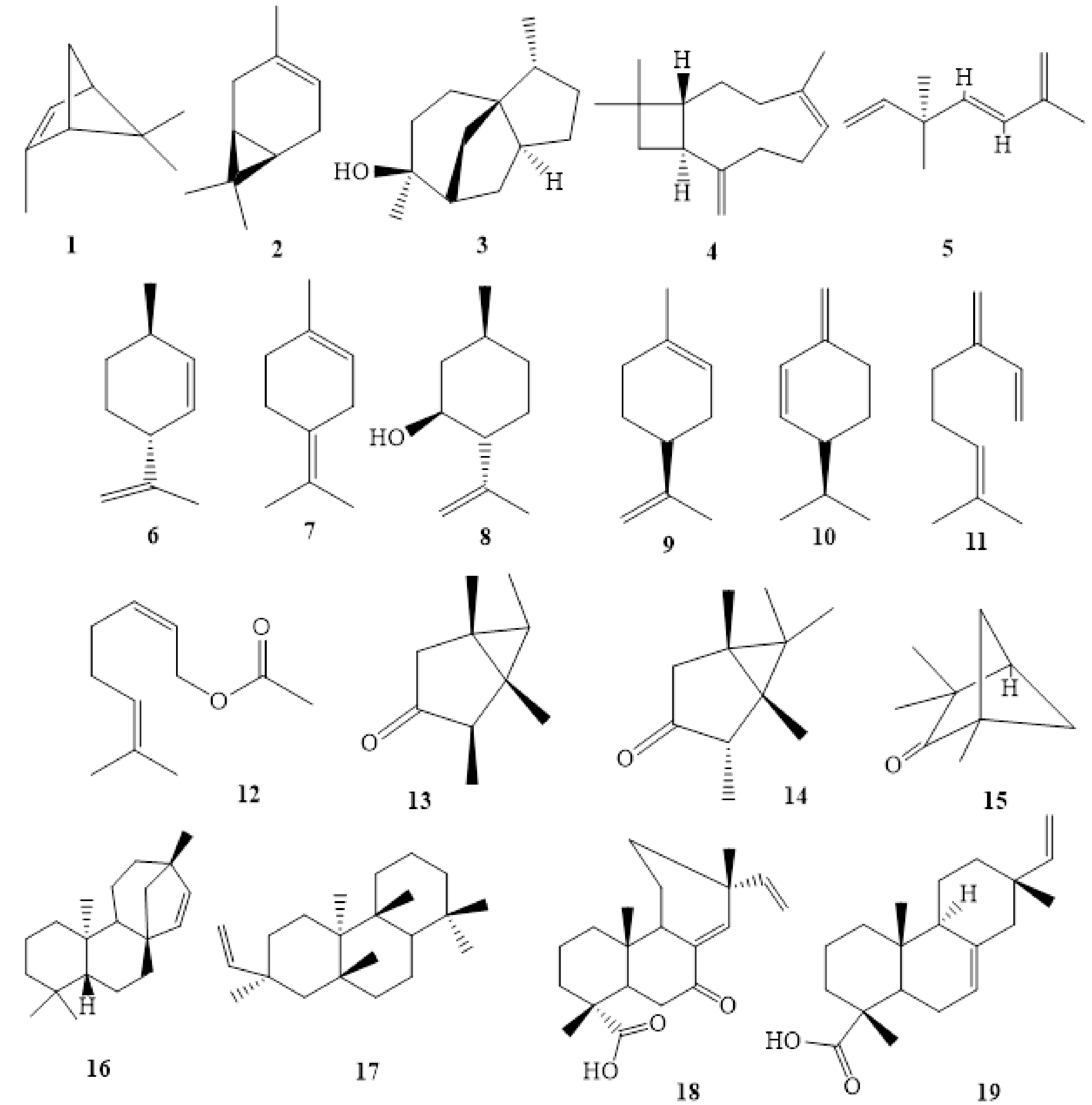
(**2**, 20.1%), and the sesquiterpene alcohol α-cedrol (**3**, 9.8%) (Bhardwaj *et al*., 2021). A similar profile was reported for an oil sample of *T. orientalis* collected in Iran (Sanei-Dehkordi *et al*., 2018). Terpenes **1** to **3**, and β-caryophyllene (**4**) are the major compounds found in essential oil from Chinese populations of *T. orientalis* (Bae *et al*., 2021). A comparison of the chemical composition of essential oils extracted from wild and planted *T. orientalis* leaves in Korea was carried out (Seo *et al*., 2019). The main compounds found in these essential oils were artemisiatriene (**5**, 17.7%), *trans*-isolimonene (**6**, 17.2%), terpinolene (**7**, 5.2%), and isopulegol (**8**, 4.8%). The main constituents of essential oil from *T. orientalis* cultivated in Tokat, Turkey, were d-limonene (**9**, 36.7%), β-phellandrene (**10**, 36.7%), and β-myrcene (**11**, 15.3%). The quantitative and qualitative characteristics of secondary metabolites variation observed in these essential oils occur due to the existence of different chemotypes of a same species (Seo *et al*., 2019) and mainly by the influence of environmental conditions (Li *et al*., 2022).



Eclética Química Journal, vol. 47, n. 4, 2022, 17-26
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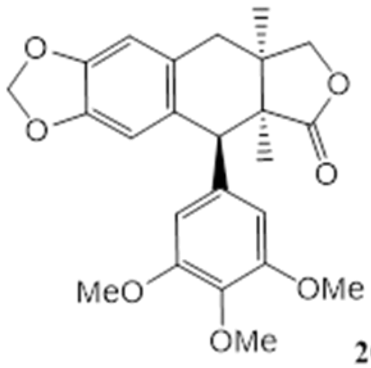

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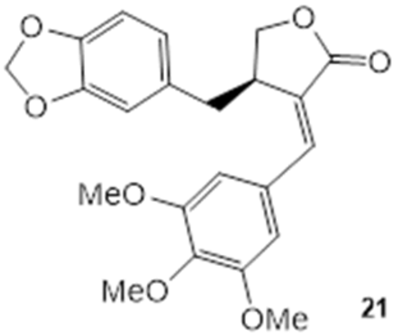

21

Figure 1. Chemical structure of compounds **1** to **21** found in *T. orientalis* and *T. occidentalis* essential oils.

Gas chromatography coupled to mass spectrometry (GC-MS) analysis of the essential oil from leaves of *T. orientalis* cultivated in Egypt and Saudi Arabian showed a similar profile considering the major compounds (α-cedrol and β-caryophyllene). In contrast, limonene was present in the Saudi Arabian *T. orientalis* essential oil, while caryophyllene oxide and vellerdiol were found in the Egyptian sample (Elsharkawy *et al*., 2017). In general, the chemical constitution of essential oils is determined by GC-MS. However, the use of high-performance counter current chromatography, allowed to the isolation of α-cedrol (**3**) from essential oil of *T. orientalis* leaves (Rehman *et al*., 2022).

The analysis of fruit oil from *T. orientalis* grown in Egypt revealed the occurrence of sesquiterpenes α-pinene (**1**, 11.3%), α-cedrol (**3**, 11.2%), β-myrcene (**11**, 9.6%), geranyl acetate (**12**, 9.0%) and β-caryophyllene (**4**, 8.9%) (Moawad and Amin, 2019). A comparison between the essential oil from Egyptian *T. orientalis* leaves with the one cultivated in Saudi Arabia was performed, being **3** and **4** the main terpenes found in the two oil samples. However, the third major compound, d-limonene (**9**), found in the Saudi sample, was absent in the Egyptian oil, probably due to influence from the severe environmental conditions of this country (Moawad and Amin, 2019).

The main compounds found in the essential oil from *T. occidentalis* L. leaves, known as cedar oil, are α-thujone (**13**, 65%), isothujone (**14**, 8%), and fenchone (**15**, 8%) (Caruntu *et al*., 2020). Besides compound (**13**, 57%), the diterpenes hibaene (**16,** 7.3%) and rimuene (**17**, 5%) were detected in expressive amount in the essential oil from Chinese cultivar for this species (Bai *et al*., 2020). The constituents of the essential oil from leaves and cones of *T. occidentalis* collected in Tunisia was described (Bellili *et al*., 2018). Interestingly, the chemical profile of the essential oil of *T. occidentalis* leaves was similar to that of *T. orientalis* essential oil collected in India.

A bioassay-guided fractionation of *T. occidentalis* extract carried out by Nakano *et al*. (2021) led to the isolation of the compounds (+)-7-oxo-13-*epi*-pimara-14,15-dien-18-oic acid (**18**), (+)-isopimaric acid (**19**), isopicrodeoxypodophyllotoxin (**20**), and (−)-deoxypodorhizone (**21**) (Fig. 1).

Phytochemical methods applied to study extracts of *T. orientalis* showed that it is a source of flavonoids and diterpenes, which are considered the majority compounds found in this species. From methanolic extract of *T. orientalis* fruits, the metabolites cupressuflavone (**22**), amentoflavone (**23**), robustaflavone (**24**), (+)-catechin (**25**), kaempferol-3-rhamnoside (afzelin) (**26**), quercitrin (**27**), 3-glucosylquercetin (isoquercitrin) (**28**), and myricitrin (**29**), quercetin (**30**), rutin (**31**), luteolin (**32**), and naringenin (**33**), (Fig. 2) were isolated (Bai *et al*., 2019; Chakraborty *et al*., 2018; Darwish *et al*., 2021).

Quercitrin (**27**), isocupressic acid (**34**), *trans*-communic acid (**35**), isopimara-7,15-dien-3β-ol (**36**), abietatriene-3β-ol (**36**), and 15-isopimaren-3β,8β-diol (**37**) (Fig. 2) were isolated from methanolic extract of leaves and stems of *T. orientalis* (Bae *et al*., 2021). In this context, extracts from *T. occidentalis* also were considered a source of the flavonoids afzelin (**26**), quercitrin (**27**), isoquercitrin (**28**), and coumarins (Caruntu *et al*., 2020).

The above data demonstrate the significant variety of secondary metabolites in *T. orientalis* and *T. occidentalis* species, and their potential to be applied mainly in pharmacological areas.

Eclética Química Journal, vol. 47, n. 4, 2022, 17-26
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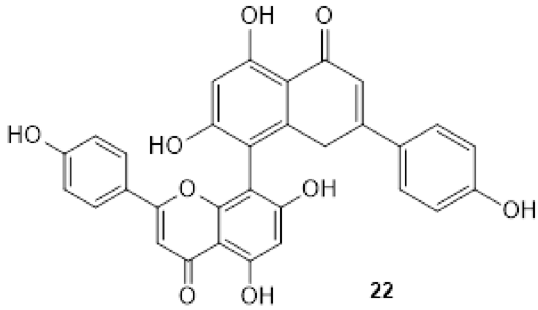

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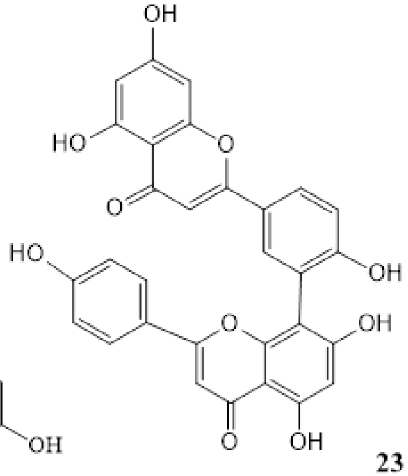
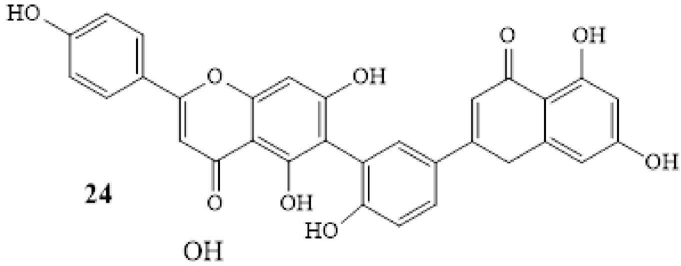


23



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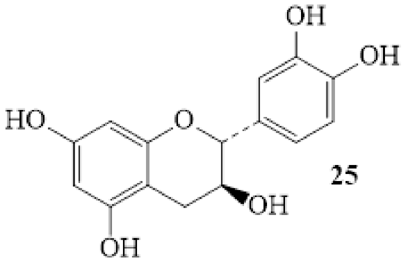
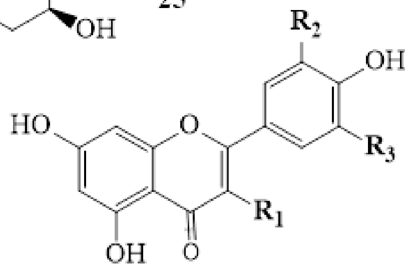
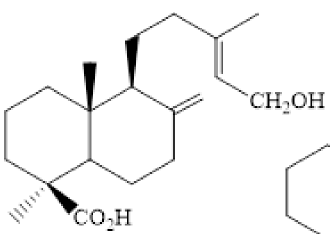


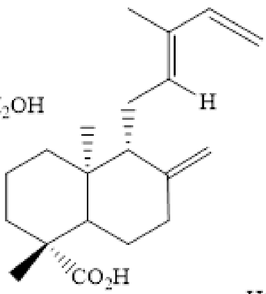
25



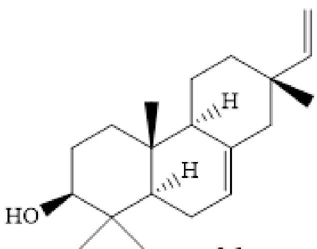
Compound	R_1	R_2	R_3
26	L-Rham	H	H
27	L-Rham	H	OH
28	D-Glu	OH	H
29	L-Rham	OH	OH
30	OH	OH	H
31	Glu-Rham	OH	H
32	H	OH	H
33	H	H	H



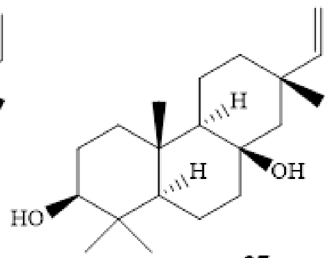
34



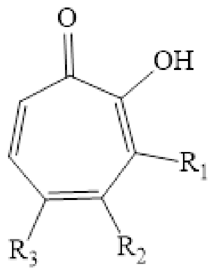
35



36



37



Compound	R_1	R_2	R_3
38	iPropyl	H	H
39	H	iPropyl	H
40	H	H	H

Figure 2. Chemical structure of compounds **22** to **40** found in *T. orientalis* and *T. occidentalis* essential oils or extracts. Glu = D-glucosyl, Rham = L-rhamnosyl.

Eclética Química Journal, vol. 47, n. 4, 2022, 17-26
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4. Pharmacological potential of *T. orientalis and T. occidentalis*

T. orientalis and *T. occidentalis* are used for the treatment of different diseases and symptoms, such as cough, asthma, cutaneous affections, bacterial dysentery, and premature blindness. Its leaves also show astringent, diuretic, antipyretic, and emmenagogue properties (Gupta and Sharma, 2021). The seeds of these two species have sedative effects and their barks are used to treat skin burns (Caruntu *et al.*, 2020; Srivastava *et al.*, 2022). There are a large number of research papers that support the traditional use of these plants, as is described in the sequence.

The essential oil from *T. orientalis* exhibits antimicrobial activity. For instance, the inhibition of the growth of *Salmonella mutans* and *S. typhimurium* was attributed to three naturally occurring monocyclic tropolones: α-thujaplicin (**38**), β–thujaplicin (**39**) and γ–thujaplicin (**40**) (Fig. 2), which act as chelating agents in the bacterial wall cell (Jain and Sharma, 2017).

The antimicrobial potential of *T. orientalis* and *T. occidentalis* has been reported. The antimicrobial property of *T. occidentalis* leaves extract obtained with methanol inhibited the growth of *Bacillus cereus* and *Candida albicans* (Caruntu *et al.*, 2020). A synergism between *Psidium guajava* and *T. orientalis* leaves extracts was observed when they were evaluated against methicillin-resistant *Staphylococcus aureus.* This synergism was probably due to the combined inhibitory effect of phenolics present in the leaf extracts, *i.e.*, quercetin and gallic acid and catechin (Chakraborty *et al.*, 2018).

Extracts from leaves and cones from *T. orientalis* grown in Tunisia were assayed against foodborne microorganisms, such as *Listeria monocytogenes* ATCC 7644, *S. aureus* ATCC 29213, *Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa* ATCC 27853, *S. typhimurium* NCTC 6017, *Aspergillus flavus* (foodborne isolate), and *Aspergillus niger* CTM 10099. The highest antimicrobial activities by disk diffusion assay were observed for *T. orientalis* essential oil from leaves. The most potent antimicrobial activity was recorded against *E. coli* and *S. typhimurium*, highlighting the potential of this essential oil as a natural preservative against foodborne pathogens (Bellili *et al.*, 2018).

T. orientalis is appointed as a relevant alternative to improve the immunity, considering the infections caused by viruses, with emphasis on SARS-CoV-2 (Srivastava *et al.*, 2022). Considering the cytotoxic activity of these two species of the Cupressaceae family, *T. occidentalis* extracts also showed antiproliferative and proapoptotic activity against the A549 lung cancer cell line, and *T. orientalis* was active against breast cancer and leukemia cells (Srivastava *et al.*, 2022). Based on teratogenic assays, the *T. orientalis* extract revealed low therapeutic index (TI = 0.808) with and median lethal concentration (LC_{50} = 0.703 mg mL^{-1}) after a period of 24 h that is within the desirable value (below 1) for drug administration (Breeta *et al.*, 2018).

The presence of phenolic compounds in *Thuja* spp. evidence their antioxidant potential. The mother tincture of *T. orientalis* showed higher inhibitory activity against the generation of the 1,1-diphenyl-2 picryl-hydrazyl (DPPH) radical, and effective oxygen radical absorbance capacity (Stan *et al.*, 2019). The antioxidant activity of *T. orientalis* extracts obtained using solvents of different polarities was tested in erythrocytes from a healthy donor. The ethyl acetate extract showed the higher reduction of reactive oxidant species (Alamdari *et al.*, 2018).

The antidiabetic activity of hydroalcoholic extract from *T. orientalis* aerial parts, collected from three different regions of India, showed an expressive activity when compared to glibenclamide, used as positive control (Pradhan and Sarangdevot, 2020). This antidiabetic effect was attributed to the presence of flavonoids such as quercetin (**27**), rutin (**31**), luteolin (**32**), and naringenin (**33**), previously reported as potential antidiabetic drugs (Bai *et al.*, 2019).

The administration of methanolic extracts of *T. occidentalis* twigs in alloxan-induced rats significantly increased glucose homeostasis and alleviate kidney and liver functions. The twigs of this species could be a potential source of the new oral antidiabetic drug (Tyagi *et al.*, 2019). To flavonoids **27**, **31–33** was also attributed the potential phytotherapeutic of a mother tincture from a mixture of branches and leaves of *T. occidentalis*. This sample inhibited the inflammation of colitis induced by 2,4,6-trinitrobenzenesulfonic acid (Stan *et al.*, 2019). The efficacy of the gastroprotective effect induced by the methanolic extract of *T. occidentalis* was similar to that produced by omeprazole, a proton pump inhibitor that decreases the amount of acid produced in the stomach (Caruntu *et al.*, 2020).

The anti-inflammatory activity of the aqueous extract and of a polysaccharide rich fraction of *T. occidentalis*, both at 300 mg kg^{-1}, did not induce gastric toxicity in experimental models of acute inflammation. The effect of these samples was attributed to mechanisms involving mediators such as histamine, serotonin, prostaglandin E_2, and bradykinin, as well as reduction of the vascular permeability and neutrophil migration to the damaged site. In addition, both of the samples reduced

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the production of proinflammatory cytokines (TNF- and IL-6), decreased immunostaining of COX-2 and iNOS, and inhibited oxidative stress (Silva *et al.*, 2017). The successful anti-inflammatory property of *T. occidentalis* was also proved considering the decreasing of the gene expression of the inflammation markers (interleukin-6 and tumor necrosis factor-α) induced by the administration of f 2,4,6-trinitrobenzenesulfonic acid after the application of the mother tincture from this plant (Stan *et al.*, 2019).

The antioxidant potential of the essential oil from cones and leaves of *T. occidentalis* grown in Tunisia was assayed by DPPH free-radical scavenging activity method. All essential oils tested showed better antioxidant activity than trolox against DPPH radical scavenging. However, the essential oil from leaves exhibited the highest total antioxidant activity (Bellili *et al.*, 2018). The cytotoxic effect of α-thujone, the major compound of *T. occidentalis* essential oil, was evaluated against glioblastoma multiforme (GBM) cells, with special emphasis on the mechanisms of its effect on cell viability and invasiveness (Nakano *et al.*, 2021; Pudełek *et al.*, 2019). An attenuating effect on the viability and proliferation of GBM cells was observed when α-thujone was administered at doses varying from 660 to 3.2 mmol L^{-1}. This effect was correlated with the induction of apoptosis in GBM cells and with considerable inhibition of GBM cells motility. Mechanistic analyses demonstrated the induction of oxidative stress and autophagy in α-thujone-treated tumor cells. It was demonstrated that α-thujone exerts pro-apoptotic and anti-invasive effects on GBM cells, confirming the potential of this monoterpene for the treatment of glioblastoma multiforme. Other reports demonstrate the potential of *T. occidentalis* for the treatment of polycystic ovary syndrome (Ahmad and Safuan, 2019; Nakano *et al.*, 2021; Parveen and Das, 2021) and inform that there is no contraindication in the administration of *T. occidentalis* mother tincture in the sycosis secondary to cancer treatments (Bagot, 2020).

Besides the relevant biological potential of species from *Thuja* genus, *T. orientalis* extract is a very important bioresource for synthesis of metal nanoparticles with silver (Bandyopadhyay *et al.*, 2017; Burange *et al.*, 2021), gold (Dong *et al.*, 2020) and copper (García-Hernández *et al.*, 2021). The aqueous leaves extract of *T. orientalis* was also efficient in the green synthesis of silica nanoparticles (SiO_2NPs) through magnetic stirrer method and using cold plasma. The biofilm inhibition of SiO_2NPs were evaluated against *S. aureus* and *E. coli*. The SiO_2NPs synthesized by cold plasma method showed the highest antimicrobial effect (Al-Azawi *et al.*, 2019).

The dried leaves of *T. orientalis* was evaluated as an adsorbent and showed an effective result in the remotion of Remazol Brilliant Blue R dye from aqueous solution (Arya *et al.*, 2020). Other important application reported for *T. orientalis* seeds extract is related to its use as a green reductant of graphene oxide. The analysis through GC-MS confirmed that α-tocopherol present in *T. orientalis* seeds extract was most likely responsible for the reduction of graphene oxide to reduced graphene oxide (Kumar *et al.*, 2021). Besides, the leaves extract of *T. orientalis* was capable of retard the oxidation of soybean biodiesel (Devi *et al.*, 2019).

The above data showed the versatile application of *Thuja* genus species and demonstrated the scientific potential of these plants.

5. Concluding remarks

Forty constituents have been identified from *T. orientalis* or *T. occidentalis*. Due to its diversified chemical structures, important pharmacological properties are attributed to these species, a part of their application in different areas within an industry context. The effective biotechnological potential of these species stimulates the research of new applications for these plants, which can improve the economic value of this natural resource and its sustainable management.

Authors' contribution

Conceptualization: Tech, M. E.; Magalhães, C. G.
Data curation: Tech, M. E.
Formal Analysis: Magalhães, C. G.; Vieira Filho, S. A.
Funding acquisition: Not applicable.
Investigation: Tech, M. E.
Methodology: Tech, M. E.
Project administration: Magalhães, C. G.
Resources: Not applicable.
Software: Not applicable.
Supervision: Magalhães, C. G.; Vieira Filho, S. A.
Validation: Not applicable.
Visualization: Not applicable.
Writing – original draft: Tech, M. E.
Writing – review & editing: Magalhães, C. G.; Vieira Filho, S. A.

Data availability statement

Data sharing is not applicable.

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References

Aguilar-Velázquez, G.; Espinosa, D.; Ordaz-Pichardo, C. Effects of Homeopathic Dilutions of *Echinacea angustifolia* and *Thuja occidentalis* on Cervical Cancer Cells. *Homeopathy*. **2018**, *107* (S1), 55–78. https://doi.org/10.1055/s-0037-1608960

Ahmad, F.; Safuan, S. Assessing the Effectiveness of Plant Extracts in Polycystic Ovarian Syndrome: A Systematic Review. *Mal. J. Med. Health Sci.* **2019**, *15* (2), 120–129.

Alamdari, D. H.; Aghasizadeh-Sharbaf, M.; Mohadjerani, M.; Ferns, G. A.; Avan, A. Prooxidant-Antioxidant Balance and Antioxidant Properties of *Thuja orientalis* L: A Potential Therapeutic Approach for Diabetes Mellitus. *Curr. Mol. Pharmacol*. **2018**, *11* (2), 109–112. https://doi.org/10.2174/1874467210666170404112211

Al-Azawi, M. T.; Hadi, S. M.; Mohammed, C. H. Synthesis of silica nanoparticles via green approach by using hot aqueous extract of *Thuja orientalis* leaf and their effect on biofilm formation. *Iraqi J. Agric. Sci*. **2019**, *50* (Special Issue), 245–255. https://doi.org/10.36103/ijas.v50iSpecial.196

Arya, M. C.; Bafila, P. S.; Mishra, D.; Negi, K.; Kumar, R.; Bughani, A. Adsorptive removal of Remazol Brilliant Blue R dye from its aqueous solution by activated charcoal of *Thuja orientalis* leaves: an eco-friendly approach. *SN Appl. Sci.* **2020**, *2* (2), 265. https://doi.org/10.1007/s42452-020-2063-2

Atanasov, A. G.; Zotchev, S. B.; Dirsch, V. M.; Supuran, C. T. Natural products in drug discovery: advances and opportunities. *Nat. Rev. Drug Discov.* **2021**, *20* (3), 200–216. https://doi.org/10.1038/s41573-020-00114-z

Bae, S.; Han, J. W.; Dang, Q. L.; Kim, H.; Choi, G. J. Plant Disease Control Efficacy of *Platycladus orientalis* and Its Antifungal Compounds. *Plants.* **2021**, *10* (8), 1496. https://doi.org/10.3390/plants10081496

Bagot, J.-L. How to prescribe *Thuja occidentalis* in oncology? Analysis of the literature, study of practices and personal experience. *Rev. Homeopath.* **2020**, *11* (3), e26–e32. https://doi.org/10.1016/j.revhom.2020.07.001

Bai, L.; Li, X.; He, L.; Zheng, Y.; Lu, H.; Li, J.; Zhong, L.; Tong, R. Antidiabetic Potential of Flavonoids from Traditional Chinese medicine: A Review. *Am. J. Chinese Med.* **2019**, *47* (5), 933–957. https://doi.org/10.1142/S0192415X19500496

Bai, L.; Wang, W.; Hua, J.; Guo, Z.; Luo, S. Defensive functions of volatile organic compounds and essential oils from northern white-cedar in China. *BMC Plant Biol.* **2020**, *20* (1), 500. https://doi.org/10.1186/s12870-020-02716-6

Bandyopadhyay, A.; Banerjee, P. P.; Shaw, P.; Mondal, M. K.; Das, V. K.; Chowdhury, P.; Karak, N.; Bhattacharya, S.; Chattopadhyay, A. Cytotoxic and Mutagenic Effects of *Thuja occidentalis* Mediated Silver Nanoparticles on Human Peripheral Blood Lymphocytes. *Mater. Focus.* **2017**, *6* (3), 290–296. https://doi.org/10.1166/mat.2017.1405

Bellili, S.; Aouadhi, C.; Dhifi, W.; Ghazghazi, H.; Jlassi, C.; Sadaka, C.; El Beyrouthy, M.; Maaroufi, A.; Cherif, A.; Mnif, W. The Influence of Organs on Biochemical Properties of Tunisian *Thuja occidentalis* Essential Oils. *Symmetry*. **2018**, *10* (11), 649. https://doi.org/10.3390/sym10110649

Bhardwaj, K.; Silva, A. S.; Atanassova, M.; Sharma, R.; Nepovimova, E.; Musilek, K.; Sharma, R.; Alghuthaymi, M. A.; Dhanjal, D. S.; Nicoletti, M.; Sharma, B.; Upadhyay, N. K.; Cruz-Martins, N.; Bhardwaj, P.; Kuča, K. Conifers Phytochemicals: A Valuable Forest with Therapeutic Potential. *Molecules*. **2021**, *26* (10), 3005. https://doi.org/10.3390/molecules26103005

Breeta, R. E.; Jesubatham, P. D.; Grace, V. M. B.; Viswanathan, S.; Srividya, S. Non-toxic and non-teratogenic extract of *Thuja orientalis* L. inhibited angiogenesis in zebra fish and suppressed the growth of human lung cancer cell line. *Biomed. Pharmacother.* **2018**, *106*, 699–706. https://doi.org/10.1016/j.biopha.2018.07.010

Burange, P. J.; Tawar, M. G.; Bairagi, R. A.; Malviya, V. R.; Sahu, V. K.; Shewatkar, S. N.; Sawarkar, R. A.; Mamurkar, R. R. Synthesis of silver nanoparticles by using *Aloe vera* and *Thuja orientalis* leaves extract and their biological activity: a comprehensive review. *Bull. Nat. Res. Centre*. **2021**, *45* (1), 181. https://doi.org/10.1186/s42269-021-00639-2

Caruntu, S.; Ciceu, A.; Olah, N. K.; Don, I.; Hermenean, A.; Cotoraci, C. *Thuja occidentalis* L. (Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules.* **2020**, *25* (22), 5416. https://doi.org/10.3390/molecules25225416

Chakraborty, S.; Afaq, N.; Singh, N.; Majumdar, S. Antimicrobial activity of Cannabis sativa, Thuja orientalis and Psidium guajava leaf extracts against methicillin-resistant Staphylococcus aureus. J. Integr. Med. 2018, 16 (5), 350–357. https://doi.org/10.1016/j.joim.2018.07.005

Darwish, R. S.; Hammoda, H. M.; Ghareeb, D. A.; Abdelhamid, A. S. A.; Harraz, F. M.; Shawky, E. Seasonal dynamics of the phenolic constituents of the cones and leaves of oriental Thuja (Platycladus orientalis L.) reveal their anti-inflammatory biomarkers. RSC Adv. 2021, 11 (40), 24624–24635. https://doi.org/10.1039/D1RA01681D

Devi, A.; Das, V. K.; Deka, D. A green approach for enhancing oxidation stability including long storage periods of biodiesel via Thuja oreantalis L. as an antioxidant additive. Fuel. 2019, 253, 1264–1273. https://doi.org/10.1016/j.fuel.2019.05.127

Dong, Y.; Hu, X.-M.; Cao, Y.-F.; Wang, Y.-C.; Li, L.-Z.; Lu, J.-Y.; Li, X.-X. Thuja occidentalis mediated AuNPs as wound dressing agents for abdominal wound healing in nursing care after surgery. Appl. Nanosci. 2020, 10 (9), 3577–3584. https://doi.org/10.1007/s13204-020-01459-y

Elsharkawy, E. R.; Aljohar, H.; Donia, A. E. R. M. Comparative study of antioxidant and Saudi Arabia. J. Pharm. Res. Int. 2017, 15 (5), 1–9. https://doi.org/10.9734/BJPR/2017/32387

García-Hernández, L.; Flores-Saldivar, J. A.; Ortega, P. R.; Guerrero, M. U. F. Synthesis of colloidal CuNPs using the extract of Thuja orientalis. ECS Trans. 2021, 101 (1), 131. https://doi.org/10.1149/10101.0131ecst

Gour, A.; Jain, N. K. Advances in green synthesis of nanoparticles. Artif. Cells Nanomed. Biotechnol. 2019, 47 (1), 844–851. https://doi.org/10.1080/21691401.2019.1577878

Gupta, M.; Sharma, K. A Review of Phyto-Chemical Constituent and Pharmacological Activity of Thuja Species. Int. J. Pharm. Res. Appl. 2021, 6 (1), 85–95.

Jain, N.; Sharma, M. Ethanobotany, Phytochemical and Pharmacological Aspects of Thuja orientalis: A Review. Int. J. Pure App. Biosci. 2017, 5 (4), 73–83. https://doi.org/10.18782/2320-7051.2976

Jiang, L.; George, S. C. Biomarker signatures of Upper Cretaceous Latrobe Group hydrocarbon source rocks, Gippsland Basin, Australia: distribution and palaeoenvironment significance of aliphatic hydrocarbons. Int. J. Coal Geol. 2018, 196, 29–42. https://doi.org/10.1016/j.coal.2018.06.025

Kumar, V.; Arora, K. Trends in nano-inspired biosensors for plants. Mat. Sci. Energy Technol. 2020, 3, 255–273. https://doi.org/10.1016/j.mset.2019.10.004

Kumar, P.; Andersson, G.; Subhedar, K. M.; Dhami, H. S.; Gupta, G.; Mukhopadhyay, A. K.; Joshi, R. P. Utilization of green reductant Thuja orientalis for reduction of GO to RGO. Ceramics Int. 2021, 47 (10 – Part B), 14862–14878. https://doi.org/10.1016/j.ceramint.2020.08.063

Li, R. W.; Smith, P. N.; Lin, G. D. Variation of biomolecules in plant species. In Herbal Biomolecules in Healthcare Applications. Academic Press, 2022; pp 81–99. https://doi.org/10.1016/B978-0-323-85852-6.00028-7

Moawad, A.; Amin, E. Comparative antioxidant activity and volatile oil composition of leaves and fruits of Thuja orientalis Growing in Egypt. Wal. J. Sci. Technol. (WJST) 2019, 16 (11), 823–830. https://doi.org/10.48048/wjst.2019.3269

Nakano, D.; Ishitsuka, K.; Ishihara, M.; Tsuchihashi, R.; Okawa, M.; Tamura, K.; Kinjo, J. Screening of promising chemotherapeutic candidates from plants against Human adult T-Cell Leukemia/Lymphoma (VII): active principles from Thuja occidentalis L. Molecules. 2021, 26 (24), 7619. https://doi.org/10.3390/molecules26247619

Park, J. S.; Ko, K.; Kim, S.-H.; Lee, J. K.; Park, J.-S.; Park, K.; Kim, M. R.; Kang, K.; Oh, D.-C.; Kim, S. Y.; Yumnam, S.; Kwon, H. C.; Shin, J. Tropolone-Bearing Sesquiterpenes from Juniperus chinensis: structures, photochemistry and bioactivity. J. Nat. Prod. 2021, 84 (7), 2020–2027. https://doi.org/10.1021/acs.jnatprod.1c00321

Parveen, S.; Das, S. Homeopathic treatment in patients with polycystic ovarian syndrome: a case series. Homeopathy. 2021, 110 (3), 186–193. https://doi.org/10.1055/s-0041-1725039

Pereira, R.; Lima, F. J.; Simbras, F. M.; Bittar, S. M. B.; Kellner, A. W. A.; Saraiva, A. Á. F.; Bantim, R. A. M.; Sayão, J. M.; Oliveira, G. R. Biomarker signatures of Cretaceous Gondwana amber from Ipubi Formation (Araripe Basin, Brazil) and their palaeobotanical significance. J. S. Am. Earth Sci. 2020, 98, 102413. https://doi.org/10.1016/j.jsames.2019.102413

Pradhan, P.; Sarangdevot, Y. S. Evaluation of antidiabetic activity of aerial parts of Thuja occidentalis. Plant Arch. 2020, 20 (Suppl. 1), 957–962.

Pradhan, P.; Sarangdevot, Y. S; Vyas, B. Quantitative estimation of total phenols and flavonoids content in Thuja orientalis. J. Pharmacogn. Phytochem. 2021, 10 (1), 687–689.

Pudełek, M.; Catapano, J.; Kochanowski, P.; Mrowiec, K.; Janik-Olchawa, N.; Czyż, J.; Ryszawy, D. Therapeutic potential of monoterpene α-thujone, the main compound of Thuja occidentalis L. essential oil, against malignant glioblastoma multiforme cells in vitro. Fitoterapia. 2019, 134, 172–181. https://doi.org/10.1016/j.fitote.2019.02.020

Rehman, R.; Zubair, M.; Bano, A.; Hewitson, P.; Ignatova, S. Isolation of industrially valuable α-Cedrol from essential oil of Platycladus orientalis (Thuja orientalis) leaves using linear gradient counter current chromatography. Ind. Crops Prod. 2022, 176, 114297. https://doi.org/10.1016/j.indcrop.2021.114297

Sanei-Dehkordi, A.; Gholami, S.; Abai, M. R.; Sedaghat, M. M. Essential oil composition and larvicidal evaluation of

ISSN: 1678-4618
DOI: 10.26850/1678-4618eqj.v47.4.2022.p17-26

Platycladus orientalis against two mosquito vectors, Anopheles stephensi and Culex pipiens. J. Arthropod Borne Dis. 2018, 12 (2), 101–107. https://doi.org/10.18502/jad.v12i2.35

Seo, K.-S.; Lee, B.; Yun, K. W. Chemical composition and antibacterial activity of essential oils extracted from wild and planted Thuja orientalis leaves in Korea. J. Essent. Oil-Bear. Plants. 2019, 22 (5), 1407–1415. https://doi.org/10.1080/0972060X.2019.1689177

Silva, I. S.; Nicolau, L. A. D.; Sousa, F. B. M.; Araújo, S.; Oliveira, A. P.; Araújo, T. S. L.; Souza, L. K. M.; Martins, C. S.; Aquino, P. E. A.; Carvalho, L. L.; Silva, R. O.; Rolim-Neto, P. J.; Medeiros, J. V. R. Evaluation of anti-inflammatory potential of aqueous extract and polysaccharide fraction of Thuja occidentalis Linn. in mice. Int. J. Biol. Macromol. 2017, 105 (Part 1), 1105–1116. https://doi.org/10.1016/j.ijbiomac.2017.07.142

Silva, P. E. S.; Furtado, C. O.; Damasceno, C. A. Utilização de plantas medicinais e medicamentos fitoterápicos no Sistema Público de Saúde Brasileiro nos últimos 15 anos: uma revisão integrativa. Braz. J. Dev. 2021, 7 (12), 116235-116255. https://doi.org/10.34117/bjdv7n12-402

Singh, V.; Shukla, S.; Singh, A. The principal factors responsible for biodiversity loss. Open J. Plant Sci. 2021, 6 (1), 11–14. https://doi.org/10.17352/ojps.000026

Srivastava, A.; Jit, B. P.; Dash, R.; Srivastava, R.; Srivastava S. Thuja Occidentalis: an unexplored phytomedicine with therapeutic applications. Comb. Chem. High Throughput Screen. 2022, 25, 1537–1548. https://doi.org/10.2174/1386207325666220308153732

Stan, M. S.; Voicu, S. N.; Caruntu, S.; Nica, I. C.; Olah, N.-K.; Burtescu, R.; Balta, C.; Rosu, M.; Herman, H.; Hermenean, A.; Dinischiotu, A. Antioxidant and anti-inflammatory properties of a Thuja occidentalis Mother tincture for the treatment of ulcerative colitis. Antioxidants. 2019, 8 (9), 416–435. https://doi.org/10.3390/antiox8090416

Tyagi, C. K.; Porwal, P.; Mishra, N.; Sharma, A.; Chandekar, A.; Punekar, R.; Punniyakoyi, V. T.; Kumar, A.; Anghore, D. Antidiabetic activity of the methanolic extracts of Thuja occidentalis Twings in Alloxan-induced Rats. Curr. Tradit. Med. 2019, 5 (2), 138–143. https://doi.org/10.2174/2215083805666190312153743

Viezzer, J.; Biondi, D.; Martini, A.; Grise, M. M. A vegetação no paisagismo das praças de Curitiba-PR. Cienc. Florest. 2018, 28 (1), 369–383. https://doi.org/10.5902/1980509831608

Yatoo, M. I.; Gopalakrishnan, A.; Saxena, A.; Parray, O. R.; Tufani, N. A.; Chakraborty, S.; Tiwari R.; Dhama, K.; Iqbal, H. M. N. Anti-inflammatory drugs and herbs with special emphasis on herbal medicines for countering inflammatory diseases and disorders - a review. Recent Pat. Inflamm. Allergy Drug Discov. 2018, 12 (1), 39–58. https://doi.org/10.2174/1872213X12666180115153635

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