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Endemic *Achillea* Species in Türkiye: Phytochemical Contents and Pharmacological Activities

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bstract

Asteraceae is the world's largest family of flowering plants, consisting of 23000 species distributed worldwide in 13 subfamilies, 44 tribes and more than 1600 genera. *Achillea* L. is one of the youngest evolutionary genera of the family Asteraceae with a worldwide widespread distribution of more than 100 species. This genus is represented by 110-140 species worldwide, centered in South East Europe and South West Asia, and extending through Eurasia to North America. In Türkiye, the genus is represented by 48 species with 54 taxa, 24 (about 50 %) of which are endemic to Türkiye. *Achillea* species have used for treatment of fatigue, inflammatoion, spasms, cold, bleeding, pneumonia, skin disorders, rheumatic pains. Furthermore, the species has diuretic and emmenagogic using in traditional medicine. *Achillea* species have various phytoconstituents such as sesquiterpenes, essential oils, flavonoids and phenolic acids. Flavonoids and phenolic acid derivatives are the most significant effective metabolites of *Achillea* species. Phenolics and flavonoids have been noticed to apply in wide range of pharmacological properties, including anti-cancer, anti-inflammatory, and antioxidant effects. In this review, endemic *Achillea* species were reviewed in terms of phytochemical content and pharmacological activities.

Key Words: *Achillea*, yarrow, endemic species, yarrow phytochemicals, biological activities of yarow

1. Introduction

Asteraceae is the world's largest family of flowering plants, consisting of 23000 species distributed worldwide in 13 subfamilies, 44 tribes and more than 1600 genera. The family is naturally distributed on all continents except Antarctica and is thought to have its phylogenetic origin in South America. the Asteraceae family is represented by 1209 species, 447 of which are endemic species, with an endemism rate of 37 % in the flora of Türkiye. Asteraceae family has largest number of endemics in Türkiye. *Achillea* L. is one of the youngest evolutionary genera of the family Asteraceae with a worldwide widespread distribution of more than 100 species. Türkiye is one of the main diversity centers of the genus *Achillea*. This genus is represented by 110-140 species worldwide, centered in South East Europe and South West Asia, and extending through Eurasia to North America (Tekin and Akdere, 2021). In

Türkiye, the genus is represented by 48 species with 54 taxa, 24 (about 50 %) of which are endemic to Türkiye. *Achillea* genus is divided into four sections: *Achillea* (with 13 species and, 4 subspecies), *Babounya* (with 30 species and 2 subspecies), *Otanthus* (only one species), and *Ptarmica* (with 4 species). The basic chromosome number in *Achillea* is nine and polyploidy often occurs. The karyological studies revealed that the genus has chromosome numbers of 2n = 18, 36, 54 and (Kiran et al., 2012; Tekin and Akdere, 2021).

The list of *Achillea* species recorded in the flora of Türkiye is given alphabetically and, endemic species in the plant list are marked with an asterisk (*) (Fig. 1.) (Davis 1975; Arabacı, 2012; Aytaç et al., 2016; Semiz et al., 2022). The name of the genus comes from the ancient use of the Trojan hero Achilles as a wound healer. Different *Achillea* species have traditionally used in Türkiye Iranian traditional medicine for healing abdominal pain, wound healing, as diaphoretic, diuretic carminative, emmenagogue and tonic agent (Eruygur et al., 2019). *A. millefolium*, a popular species among *Achillea* members, are widely used in European traditional medicine for healing of skin problems (wound, inflammations etc.), gastrointestinal disorders, hepatobiliary complaints. There are numerous reports describing the anti-inflammatory, antinociceptive, human erythrocyte and leukocyte protective, antispasmodic, antimicrobial and antioxidant effects of the compounds of many *Achillea* species. *Achillea* species have used as tonic, anti-inflammatory, anti-spasmodic, diaphoretic, diuretic and emmenagog agents and have traditionally been used to treat bleeding, pneumonia, rheumatic pain and wound healing. Unbalanced antioxidant systems lead to various problems such as inflammation, neurodegenerative and tumoral disorders. Clinical studies have indicated that some *Achillea* species have potential against episiotomy wound, multiple sclerosis, ulcerative colitis, irritable bowel syndrome, primary dysmenorrhea, oral mucositis etc. (Salehi et al., 2020). Ethanolic extracts from *A. setacea* showed potent anti-inflammatory and antinociceptive activity against *in vivo* carrageenan-induced hind paw oedema model in mouse without causing any gastric disease. Studies have shown that they can reduce the risk of inflammation-related diseases (Küpeli et al., 2007).

Achillea species have several constituents; flavonoids and phenolic acids, sesquiterpenes and essential oils. The most important therapeutical metabolites of *Achillea* species are considered as phenolic acids and flavonoids (Uzun and Arslan, 2020). Non-endemic *A. cretica* has been shown to be highly potent against gram-positive microorganisms *Staphylococcus aureus* and *Bacillus cereus*. *A. cretica* has used for healing wounds contaminated with bacterial infections in traditional medicine by its antibacterial properties. Carvone, caryophylladienol-II, *β*-maaliene, neo-intermedeol, spathulenol, selina-3,11-diene-6-ol, palmitic acid have been characterized as the main compounds of the essential oil of this species (Küçükbay et al., 2012).

A. adenii Aytaç & M.Ekici
A. aleppica DC. subsp. *aleppica*
A. aleppica DC subsp. zederbaueri (Hayek) Hub-Mor.*
A. alimeana Semiz & Uysal sp. nov. of sect. Santolinoidea DC.
A. armenorum Boiss. & Hausskn.*
A. arabica Kotschy.
A. baltai H.Duman & Aytaç
A. biebersteinii AFAN.
A. biserrata M.Bieb.
A. boissieri Hausskn. ex Boiss.*
A. brachyphylla Boiss. & Hausskn.*
A. cappadocica Hausskn. & Bornm.*
A. clypeolata Sibth. & Sm.
A. coarctata Poir.
A. cretica L.
A. crithmifolia Waldst. & Kit.
A. cucullata Bornm.*
A. falcata L.
A. filipendulina Lam.
A. formosa (Boiss.) Sch. Bip. subsp. *formosa*
A. formosa (Boiss.) Sch. Bip. subsp. *amanica* (Rech.f.) Ehrend &Y. Guo
A. fraasii Sch. Bip.*
A. goniocephala Boiss. & Balansa*
A. grandifolia Friv.
A. gypsicola Hub.-Mor.*
A. hamzaoglui Arabacı & Budak
A. ketenoglui H.Duman*
A. kotschyi Boiss. subsp. *kotschyi*
A. kotschyi Boiss. subsp. *canescens* Bässler*
A. latiloba Ledeb. ex. Nordm.
A. lycaonica Boiss. & Heldr.*
A. magnifica Heimerl ex Hub.-Mor.*
A. maritima (L.) Ehrend. & Y.P.Guo subsp. maritima
A. membranacea (Labill.) DC.
A. millefolium L. subsp. *millefolium* L.
A. millefolium L. subsp. *pannonica* (Scheele) Hayek
A. milliana H. Duman*
A. monocephala Boiss. & Balansa*
A. multifida (DC.) Griseb.*
A. nobilis L. subsp. *densissima* (O. Schwarz ex Bässler) Hub-Mor.*
A. nobilis L. subsp. *kurdica* Hub-Mor.*
A. nobilis L. subsp. *neilreichii* (A. Kern.) Velen
A. nobilis L. subsp. *sipylea* (O. Schwarz) Bässler*
A. oligocephala DC.
A. pannonica Scheele
A. phrygia Boiss. & Balansa*
A. pseudoaleppica Hausskn. ex Hub-Mor.*
A. salicifolia Besser subsp. *salicifolia*
A. santolinoides Lag. subsp. *wilhelmsii* (K. Koch.) Greuter
A. schischkinii Sosn.*
A. setacea Waldst. & Kit.*
A. sieheana Stapf*
A. sintenisii Hub.-Mor*
A. sipikorensis Hausskn. & Bornm.*
A. sivasica Çelik & Akpulat
A. spinulifolia Fenzl ex Boiss.*
A. tenuifolia Lam.
A. teretifolia Willd.*
A. vermicularis Trin.
A. wilhelmsii C. Koch
*endemic species

Figure 1. *Achillea* species recorded in the flora of Türkiye.

Some *Achillea* species are also consumed as diet such as additives, beverages, vegetables, and spices, and horticulture and cosmetic industry. Previous phytochemical works have revealed that the *Achillea* species are rich in terpenic compounds and phenolics, such as flavonoids, phenolic acids, and lignans as potential bioactive compounds. Flavonoid derivatives (like quercetin, luteolin apigenin) are mainly found as flavones and flavonols in the genus *Achillea*. In addition to flavonoid derivatives, hydroxycinnamic acids (caffeic acid, chlorogenic acid, dicaffeoylquinic acid) and hydroxybenzoic acids (syringic acid, vanillic acid) have also been characterized and quantified in some *Achillea* species (Agar et al., 2015). The essential oils by using hydro-distillation have been usually obtained from dried aerial parts of 31 *Achillea* species. n-hexane was used to recover the essential oil of some oil-poor species in during distillation. Oil yields modified between 0.01 %-1.2 % (Başer, 2016).

2. Phytochemicals and biological activities of Endemic *Achillea* species

Both phytochemical investigations and biological activity studies on endemic species "*A. armenorum* Boiss. & Hausskn.", "*A. brachyphylla* Boiss. & Hausskn.", "*A. kotschyi* Boiss. subsp. *canescens* Bässler", "*A. milliana* H. Duman", "*A. nobilis* L. subsp. *densissima* (O. Schwarz ex Bässler) Hub-Mor.", and "*A. nobilis* L. subsp. *kurdica* Hub-Mor." could not be found in the articles. The endemic species that were studied are described in the rest of the article.

2.1. *A. aleppica* DC subsp. *zederbaueri* (Hayek) Hub-Mor.

In a study examining the antimicrobial and antifungal activities of *A. aleppica* DC subsp. *zederbaueri* (Hayek) Hub-Mor. extracts (ethanolic, methanolic and aqueous extracts)

by disc diffusion, assay against several microorganisms, it was seen that all extracts reduced the zone diameter on Pseudomonas aeruginosa. The 2,2-diphenyl-1-picrilhydrazile (DPPH) free radical scavenging ability of aqueous and ethanolic extracts of *A. aleppica* subsp. *zederbaueri* were found to be in the range of 37.80-47.60 % and 86.30-90.60 %, respectively, at the concentration range between 50-500 µg/mL (Barış, 2016).

2.2. *A. boissieri* Hausskn. ex Boiss.

As a result of a study examining the antioxidant effect, the methanolic *A. boissieri* extract showed remarkable DPPH free radical scavenging activity (68.51 % at 37.5 mg/L) comparable with references (butylated hydroxyanisole (BHA), α-tocopherol and butylated hydroxytoluene (BHT)). Whereas the ferric reducing capacity of the extract was found to be moderate, the chelating capacity of the extract was found to be lower. Total phenol content of the plant extract was determined as 23.63 ± 0.17 mg gallic acid equivalents/gram extract; total flavonoid content of the extract was found as 29.70 ± 0.03 (mg quercetin equivalent/gram extract) (Tekin et al., 2021).

2.3. *A. cappadocica* Hausskn. & Bornm.

The main compounds in the fatty acid of *A. cappadocica* were determined as oleic (34.7 percent), palmitic (23.1 percent), and linoleic acids (20.6 percent). The methanolic and aqueous extracts exhibited higher 2, 2′-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) diammonium salt (ABTS) cation radical scavenging effect compared to α-tocopherol and BHT at 100 mg/L. The acetone extract inhibited butyrylcholinesterase enzyme about 70.62 % at 200 mg/L concentration. The acetone and methanolic extracts demonstrated moderate antimicrobial activity (Ertaş et al., 2014).

2.4. *A. cucullata* Bornm.

The results of the studies noted that *A. cucullata* can be used in the pharmaceutical and food industry as an important source of natural antioxidants. The ethanolic extract from the aerial parts of *A. cucullata* demonstrated potent anticholinesterase inhibitor, antioxidant, antidiabetic and mild antimicrobial effects. As reported in previous studies, *A. cucullata* contains 1,8-cineole isoborneol and camphor (Eruygur et al., 2019).

2.5. *A. fraasii* Sch. Bip.

A. fraasii, native to Southeastern Europe and Türkiye, is a plant that has demonstrated to antimicrobial activity. According to the literature, *A. fraasii* has several phytochemicals, such as flavonoids, sesquiterpene lactones, tannins, and that antibacterial, antioxidant, anti-inflammatory and antifungal activities (Tunca-Pinarli et al., 2023).

2.6. *A. goniocephala* Boiss. & Balansa

The chitosan-tripolyphosphate nanoparticles from *A. goniocephala* chloroform extract showed higher anti-cancer (on MCF-7 and HT-29 cells lines) and antioxidant (DPPH, ferric reducing antioxidant power (FRAP), cupric reducing antioxidant capacity (CUPRAC) tests) activities compared to unencapsulated extracts (Taşkın et al., 2021).

2.7. *A. gypsicola* Hub.- Mor.

1,8-cineole, α-terpineol, borneol, camphor piperitone and sabinaketone were identified as major phytochemicals in the essential oil of *A. gypsicola* obtained in 0.65 % yield (Başer, 2016; Açikgöz and Kara, 2019).

2.8. *A. ketenoglui* H.Duman

The methanolic *A. ketenoglui* plant extract was detected to have high phenolic and flavonoid content. In these study, it's IC_{50} values of antioxidant and cytotoxic activities were found as 40.03±0.38, 263-350 µM respectively. According to phytochemical analysis results, apigenin, baicalin, casticin, chlorogenic acid, eupatorin, genistin, and luteolin were found in the methanolic extract. When scientists observed gen expressions (HCT 116 and HT-29 cells lines for colorectal cancer treatment, an increase in p53 expression and caspase-3 was found in both cell lines treated with the extract (Ayan et al., 2022). In the hydrodistilled essential oils of *A. ketenoglui* analyzed by GC/MS (Gas Chromatography-Mass Spectrometry), the main components in the oil were determined as borneol (14.1 %) and terpinen-4-ol (14.5 %) (Baser et al., 2001).

2.9. *A. kotschyi* Boiss. subsp. *kotschyi* subsp. *canescens* Bässler

The results of these studies provide important data on the phenolic compounds, antioxidant, cytotoxic and wound healing potential of methanolic extracts from non-endemic *A. kotschyi* Boiss. subspecies "*A. kotschyi* subsp. *kotschyi*". According to phytochemical investigations, it was considered as an important source of flavonoids like apigenin, hesperidin, hyperoside, kaempferol, rutin, and luteolin. In terms of total phenolics, this species extract contains significantly higher amounts. It exhibited a very pronounced wound healing potential and moderate cytotoxic activity at very small concentrations. To summarise the results of the present investigation, *A. kotschyi* subsp. *kotschyi* is a precious source of phenolic asit such as chlorogenic acid, and flavonoids had significant antioxidant, cytotoxic and wound healing activities. Therefore, it can be used in the development of additives, food, new drugs and cosmetics products (Agar et al., 2015). The oil of this species was rich in *p*-cymene~hexadecanoic acid, caryophyllene oxide and 1,8-cineole, respectively increasing, (Başer, 2016). However, no literature studies have been found regarding endemic "*A. kotschyi* Boiss. subspecies *A. kotschyi* Boiss. subsp. *kotschyi* subsp. *canescens* Bässler".

2.10. *A. lycaonica* Boiss. & Heldr.

In the hydrodistilled essential oils of *A. lycaonica* analyzed by GC/MS, the main component in the oil was determined as trans-sabinene hydrate (9.3 %) (Baser et al., 2001). In another study conducted in 2008 using the GC and GC-MS methods, L-camphor (43.19 %) was determined as a main component in the hydrodistilled essential oils of *A. lycaonica* (Azaz et al., 2008). In a study comparing three plant extracts, soxhlet extraction with ethyl acetate and maceration with chloroform were found to show the maximum total phenolic and total flavonoid contents with antioxidant capacity and antiurease activity. The phenolic compounds were determined to be caffeic, chlorogenic, dicaffeoylquinic, salicylic acids, and flavonoids such as apigenin, 8-hydroxy-salvigenin, quercetin, luteolin, rutin and naringenin. Among the solvent extraction processes, Soxhlet method was determined to have more recoveries compared to other approaches, and to show high effective antiurease activity in maceration with chloroform (Taşkın et al., 2017).

2.11. *A. magnifica* Heimerl ex Hub.-Mor.

The triterpenic compound magnificol was isolated from methanolic *A. magnifica* extract

(Ulubelen et al., 2007). A study, which was compared the antioxidant, anti-urease, anticholinesterase, and antiproliferative properties of various extracts of *A. magnifica*, demonstrated that chloroform extract has the highest antiproliferative and antioxidant activities. Elenolic acid, luteolin, eupatilin were obtained from this extract. When the cytotoxic capacities of the chitosan nanoparticles with chloroform extract were investigated, potent antiproliferative activity similar to that of the raw extract. The apigenin hexosides, ferulic acid derivative and diosmetin derivatives and vitexin were obtained from ethanolic plant extract (Taşkın et al., 2020). In another work, 22 different components such as 1,8-cineole, borneol, sabinyl acetate, camphor, germacrene and linalool, have been identified in the essential oil of *A. magnafica*. In it's fixed oil, components, linoleic, palmitic, ɣ-linolenic, oleic, behenic and caproic acids were determined as major components (Gedik et al., 2022).

2.12. *A. monocephala* Boiss. & Balansa

When the essential oils of *A. monocephala* flower and leaf were analysed, camphor and borneol in the leaf oil and 1,8-cineole borneol, camphor, and *α*-campholenal in the flower oil were determined as major compounds by comprehensive GC–time of flight mass spectrometry (TOF–MS) (Gogus et al., 2006). According to phytochemical analysis results by LC–MS/MS (Liquid Chromatography-Mass Spectrometry/Mass Spectrometry) method, it was found that ethanolic and methanolic-chloroform extracts of stems and aerial parts of *A. monocephala* have to flavonoids (apigenin, apigetrin, hesperidin, luteolin, isoquercitrin, rutin) and organic acids (chlorogenic, fumaric, malic, quinic, and vanillic acids) and. Additionally, total phenolic and flavonoid amounts, antioxidant, anti-tyrosinase, anticholinesterase, anti-urease and cytotoxic activities of *A. monocephala* exhibited significant results that could be a potential agent (Yılmaz et al., 2018).

2.13. *A. multifida* (DC.) Griseb.

In the water-distilled essential oils of *A. multifida* analyzed by GC and GC/MS, *α*-, *β*-thujone, camphor and sabinene were characterised as the main compounds. The antimicrobial activity of the essential oil was conducted by using a micro-dilution assay, minimum inhibitory concentration (MIC) was calculated as 62.5-250 µg/mL (Başer et al., 2002). Further in another study, MIC value of *A. multifida* flower extract was found to range from 50 to 75 µg/mL against three *Staphylococcus* bacteria (Karaalp et al., 2009). According to the study performed to evaluate the total phenolic amount, cytotoxic effects and antioxidant and antimicrobial capacities of heptane, chloroform and methanolic extracts from aerial parts of *A. multifida*, the phenolic compounds were isolated chlorogenic acid, dicaffeoyl quinic acid, quercetin hexoside, luteolin-7-O-glucoside, luteolin from methanolic plant extract. The chloroform extract showed strong cytotoxic activity (Taşkın et al., 2016).

2.14. *A. nobilis* L. subsp. *sipylea* (O. Schwarz) Bässler

There are a few study about *A. nobilis* L. subspecies. Studies on non-endemic *A. nobilis* subsp. *neilreichii* have antioxidant, antinociceptive and anti-inflammatory activities (Demirci et al., 2009). Fragranol, *β*-eudesmol and fragranyl acetate were isolated as the main compounds of *A. nobilis* subsp. *neilreichii* essential oil and Antioxidant and non-high antimicrobial activities were found

(Başer, 2016). As a result of a study examining the antioxidant effect, the methanolic *A. nobilis* subsp. *sipylea* extract showed low antioxidant capacity by DPPH radical scavenging activity, the ferric reducing and the chelating capacity. Total phenol amount of the extract was calculated as 17.33 ± 0.09 mg gallic acid equivalents/gram herbal extract; total flavonoid amount of the extract was determined as 18.20 ± 0.03 (mg quercetin equivalent/gram herbal extract) (Tekin et al., 2021). No studies on endemic "*A. nobilis* L. subsp. *densissima* (O. Schwarz ex Bässler) Hub-Mor." and "*A. nobilis* L. subsp. *kurdica* Hub-Mor. " species could be found.

2.15. *A. phrygia* Boiss. & Balansa

A. phrygia is a perennial herb, grows up to 0.45 meters in height and has golden yellow flowers. Studies have shown that *A. phrygia* has antioxidant by free radical scavenging activity. According to the experimentals results the plant is a potential natural antioxidants in medicinal preparations (Akcin et al., 2014).

2.16. *A. pseudoalepica* Hub.-Mor.

A. pseudoaleppica Hub.-Mor. is traditionally used in female disorders, menstrual problems and intestinal inflammations (with leaves and flowers), preventing hair-lossing and skin beauty (above-ground parts), frequent urination at night (flowers). It is thought that the capacity of preventing the inflammation, of the plant is related to its antioxidant capacity. *A. pseudoaleppica* contains high amounts of camphor. When the antioxidant, memory enhancing, antidepressant and anxiolytic activities of its essential oils have been examined *in vivo* animal model, significant activity results have been revealed such as healing neurological diseases including dementia and Alzheimer's disease, by confirming the potent ethnopharmacological use of many *Achillea* species. The extracts obtained from leaves of *A. pseudoaleppica*, especially the ethanolic extract, showed high amounts of flavonoids and phenolic constituents. Studies depict the medicinal values of *A. pseudoaleppica* as a promising source of phenolic compounds and antidiabetic, anti-cholinesterases and antioxidant properties (Yılmaz et al., 2023).

2.17. *A. sieheana* Stapf

Two different study showed that the essential oil obtained from aerial parts of *A. sieheana* was isolated by using hydro-distillation, main components of it were identified as Artemisia ketone, camphene, camphor and 1,8-cineole (Albayrak, 2013; Tabanca et al., 2004). Feruloylquinic acid, isorhamnetin, isovitexin, luteolin, luteolin glucoside, chrysoeriol were detected in ethylacetate extract, which was found to have a higher phenolic content compared to methanol, dichloromethane and n-hexane (Dikpınar et al., 2022).

Methanolic extract obtained from aerial parts of *A. sieheana* showed an effective DPPH radical scavenging activity with IC_{50} = 87.04 µg/mL, and a high reducing activity (71.08 %) on the oxidation of *β*-carotene (Albayrak, 2013). While a high anti-inflammatory effect was observed in dichloromethane and ethylacetate extracts, the highest antioxidant capacity was determined in ethylacetate extract (IC_{50} =96 µg/mL for DPPH, and IC_{50} =156 µg/mL for ABTS). Also, ethylacetate extract exhibited moderate *α*-glucosidase inhibitory activity (IC_{50} = 774 µg/mL) in the same study (Dikpınar et al., 2022). When the antimicrobial effects of the methanolic extract and the oil were also compared, the

results showed that both had high antimicrobial activity against 13 bacteria and two yeasts (Albayrak, 2013).

2.18. *A. sintenisii* Hub.-Mor.

In a study examining the antimicrobial effects of the *A. sintenisii* essential oil and methanol extract against 12 bacteria and two yeasts, *Candida albicans* and *C. krusei*, essential oil exhibited stronger activity than the other extracts tested. In this study, 32 different compounds such as borneol, camphor, eucalyptol and piperitone were determined in the essential oil using GC-MS analysis (Sökmen et al., 2003). The results of another phytochemical analysis study revealed the presence of quinic acid and chlorogenic acid in the extract obtained from aerial part of *A. sintenisii* by the LC/MS/MS. In the same study, it was revealed through experimental studies that the enzyme (elastase, hyaluronidase, and collagenase) inhibition capacity and antioxidant effect of the plant support wound healing activity (Eruygur et al., 2023).

In a study examining the effects of aqueous and ethanolic *A. sintenisii* extracts, such as cell culture analysis, collagen synthesis, fibroblast proliferation, hydrogen peroxide-induced problems, hyaluronidase enzyme inhibitory activities antibacterial, antioxidant, , results showed that the both plant extracts increased fibroblast proliferation without toxicity. While hyaluronidase inhibitory effects were observed in both extracts, it was stated that the aqueous extract supported collagen synthesis. It was found that the ethanolic and the aqueous extract demonstrated antibacterial activity against *Klebsiella pneumoniae* and *Bacillus subtilis* (Anlas et al., 2023). According to phytochemical analysis, phenolic compounds such as apigenin, isorhamnetin, luteolin, quercetin, rutin were isolated from plant by using HPLC and, high performance liquid chromatography-electrospray ionization quadrupole time-of-flight mass spectrometry- mass spectrometry (HPLC–ESI-Q-TOF-MS-MS) methods (Anlas et al., 2023; Şabanoğlu et al., 2017).

2.19. *A. sipikorensis* Hausskn. & Bornm.

It has been revealed that *A. sipikorensis* seeds containing a total of 3.83 % fixed oil contain palmitic acid and (lin)oleic acid as major fatty acids. These study showed that *A. sipikorensis* seeds could be used as a source of unsaturated fatty acids (Zonuz et al., 2017). Another study showed that borneol, camphor, caryophyllene oxide, cis-chrysanthenol, 1,8-cineol, were determined in the essential oil obtained from aerial parts of *A. sipikorensis*. The same study revealed that essential oil has significant antioxidant, antimicrobial and cytotoxic activities effects (Eruygur et al., 2018).

2.20. *A. spinulifolia* Fenzl ex Boiss.

In a study, 6-hydroxyflavonols and methyl ethers of 6-hydroxyflavones were isolated from *A. spinulifolia* (Wollenweber et al., 1986).

2.21. *A. schischkinii* Sosn. & *A. teretifolia* Willd.

Methanolic, aqueous and chloroform extracts of *A. schischkinii* and *A. teretifolia* showed strong antioxidant activity as shown by DPPH ABTS, hydrogen peroxide and superoxide anion scavenging, and metal chelating activities compared to reference. The results of the studies indicated that methanolic and aqueous extracts of *A. teretifolia* could be used as a source of natural antioxidant in pharmaceutical and food industry due to their high antioxidant and antimicrobial

properties. Furthermore, the data of the studies show that *A. schischkinii* extracts contain antioxidants but not antimicrobial compounds (Turkoglu et al., 2010).

1,8-cineole, artemisia ketone, camphor, caryophyllene oxide, *β*-eudesmol, *β*-pinene, piperitone, spathulenol, *p*-cymene, (E)-nerolidol were obtained as the main components on the essential oils of *A. schischkinii* species. Many authors have reported on the essential oil of the endemic species *A. teretifolia*. It has been reported that the main constituents of the essential oil showing antimicrobial, antioxidant and antiangiogenic activity are *α*-tujone (5 percent), terpinen-4-ol (8 percent) 1,8-cineole (34 percent), camphor (11 percent), and (Başer, 2016). It was revealed that the essential oils of *A. schischkinii* have antimicrobial, antiinflammatory and antinociceptive activities. However, the oil had shown lowactivity against (*Enterobacter aerogenes*, *Escherichia coli*, *Bacillus cereus*, *Salmonella typhimurium*, *Staphylococcus aureus*, and *Candida albicans*, while no remarkable *in vivo* antiinflammatory and antinociceptive activity was found (Tabanca et al., 2016).

3. Results and Conclusion

Biological activity studies have mostly focused on the antimicrobial, antioxidant and anticancer (cytotoxic) activities of *Achillea* species. Enzyme inhibition tests have been carried out in some *A. pseudoaleppica* and *A. sintenisii* endemic species through experimental studies and significant results have been revealed. Accordingly, essential oils and phenolic compounds were considered as potentially responsible compounds and studies were mostly conducted on the quantification of these compounds and their derivatives.

Phytochemical and biological activity studies on endemic *Achillea* species carried out to date have been quite limited and insufficient compared to the rich plant diversity of Türkiye. Designing and implementing subsequent studies on species that have not been studied will ensure the most efficient use of the existing rich plant diversity. So, the plant extracts from endemic *Achillea* species different parts may be a natural sources in both medicine/dermocosmetics and the food industry.

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Author Contribution

All authors declare equal contribution to the collect the literatures interpretation of the results and editing the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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