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Review

Bioactive Properties and Pharmaceutical Potential of New World Mistletoes of the Genus *Tristerix*: A Review

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Abstract

Mistletoes of the genus *Tristerix*, native to South America, represent a unique group of mostly hemiparasitic plants with potential medicinal applications. This review synthesizes existing knowledge on their biological and phytochemical properties, focusing on three main species endemic to Chile: *Tristerix aphyllus*, *T. corymbosus*, and *T. verticillatus*. These species exhibit diverse interactions with host plants, animal pollinators, and seed dispersers, where host identity can influence their chemical profile. Around 17 metabolites have been found in flowers, fruits, and leaves from *Tristerix* spp., including flavonoids (e.g., quercetin, apigenin, luteolin), phenolic acids (e.g., caffeic acid; gallic acid), and alkaloids (e.g., pronuciferine and glaucine). Those have demonstrated antioxidant, anti-inflammatory, antimicrobial, and anti-tumoral properties. Despite their traditional uses in Chilean medicine for ailments such as gastric ulcers and throat infections, experimental research on *Tristerix* spp. remains scarce. This review highlights their bioactive potential, emphasizing the need for further investigation into their pharmacological applications, including in vivo and clinical studies.

Keywords: bioactive compounds; Chilean native plants; phytochemicals; medicinal plants

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1. Introduction

The use of medicinal plants in ancestral cultures has been the basis of present-day pharmaceutical prescriptions, and the country of Chile is no stranger to the use of native botanical species in various applications [1,2]. Chilean endemic plants have garnered

significant research attention due to their unique properties and conservation importance. With a diverse climate that incorporates temperate rain forests, deserts, and mountainous and marine regions, the Chilean territory is the source of over 80 genera of endemic plants, with the southern regions harboring more phylogenetic diversity than expected [3,4]. Several indigenous groups from Chile, such as the Mapuches people, have used this traditional knowledge for centuries, which include the use of various plant species for medicine, food, crafting, cosmetics, and rituals, among other uses. To this day, this kind of documented data are still being researched to fully understand the biological properties of these natural sources and the impact that they caused in their culture [5].

A particular group of plant species that have received attention belongs to the family Loranthaceae, commonly known as New World mistletoes, which comprises approximately 1000 species distributed across 77 genera [6]. This family is composed of mostly hemiparasitic plant species [7], presenting photosynthetically active organs (usually green leaves), while receiving nutrients and water from the host with their specialized roots called haustoria, which are connected to the xylem of the host plant [8,9].

In Chile, this family is represented by the genera *Notanthera*, *Desmaria*, *Ligaria*, and *Tristerix*; with the latter being the most diverse, including three species: *T. aphyllus*, *T. corymbosus*, and *T. verticillatus* [10]. Species of *Tristerix* occur primarily in the Andean regions of South America, reflecting their adaptation to high-altitude environments [7]. Members of this genus are characterized by their distinctive red flowers [9]. They are pollinated mainly by hummingbirds, whereas seed dispersal is mediated by native and endemic birds and marsupials [11,12]. As noted above, *Tristerix* species have long been used in traditional medicine by indigenous and local communities for the treatment of various ailments [5,9,13].

Leaves, flowers, and fruits of *T. corymbosus* are used as pigments, astringents, for treating gastric ulcers and sore throats, and lowering blood cholesterol [12]. Fruits of *Tristerix* are edible, with a sweet taste, but are consumed mostly in rural areas [9,13–15]. Fruits and other organs of *T. corymbosus* and *T. verticillatus* can be used as a natural black pigment for staining [9,16]. However, studies regarding its biological properties are few, and most of them are focused on determining their phytochemicals to give support to their medicinal properties [17,18]. Furthermore, there are no studies performed on in vivo models, not even clinical studies in order to demonstrate safety of these extracts.

This lack of proper research is relevant since the genus *Tristerix*, and its family Loranthaceae, are part of the Santalales order, which incorporates a broad number of different species, including the genus *Viscus*, commonly known as mistletoes. These species of hemiparasitic plants have been used in traditional medicine around the globe for centuries, with well-documented studies on their anti-inflammatory, antibiotic, antioxidative, antihypertensive, hepatoprotective, neuroprotective, anti-tumoral, and immunomodulatory properties; even to the point that standardized preparations of compounds found on *Viscus album* L., mainly lectins and viscotoxins, are available commercially for the treatment of cancer [18,19].

In this narrative review, we examine the botanical characteristics and analyze the bioactive properties of the genus *Tristerix*, along with its chemical composition. A narrative approach was considered appropriate due to the limited and highly heterogeneous literature available regarding *Tristerix* spp., particularly concerning their ethnobotanical uses, phytochemistry, and biological activities, which precludes a systematic quantitative synthesis. Here, we compile the reliable information available to assess its potential for pharmaceutical use, including ethnobotanical records and experimental studies that highlight its medicinal applications.

2. Material and Methods

This study was conducted as a narrative review to synthesize the fragmented and heterogeneous data surrounding the genus *Tristerix*. To ensure methodological transparency and reproducibility, the literature search and study selection were guided by the following parameters:

Rationale for Database Selection: The scientific literature search was performed using NCBI-PubMed, Google Scholar, and Mendeley databases. These platforms were selected due to their comprehensive coverage of biomedical, chemical, and multidisciplinary Latin American scientific literature, which is essential for capturing studies on regional endemic flora.

Search Strategy and Time Frame: The search covered articles published over a 38-year period from 1986 to 2024. Search strings utilized combinations of Boolean operators and the following keywords: ("*T. aphyllus*" OR "*T. corymbosus*" OR "*T. verticillatus*") AND ("antioxidant property" OR "antioxidant activity" OR "antimicrobial property" OR "antimicrobial activity" OR "anti-inflammatory property" OR "anti-inflammatory activity").

Language Restrictions: The search was limited to articles published in English and Spanish, considering that a significant portion of ethnobotanical and historical data on Chilean native plants are documented in local Spanish-language journals.

Inclusion and Exclusion Criteria:

Inclusion criteria: Peer-reviewed original research articles, short communications, academic theses, and botanical field guides that provided direct experimental data (in vitro, in vivo, or phytochemical profiling) or documented ethnobotanical uses of the specified *Tristerix* species.

Exclusion criteria: Studies focused exclusively on other Loranthaceae genera without comparative data for *Tristerix*, non-peer-reviewed blog posts, conference abstracts lacking full data, and duplicates.

In order to enhance this narrative review, a patent search was performed through Google Patents, Espacenet, and WIPO PATENTSCOPE. Scientific names *Tristerix*, *T. aphyllus*, *T. corymbosus*, and *T. verticillatus*, as well as relevant taxonomical synonyms, were used as keywords in the search process. In addition, other keywords relating to bioactive compounds and their applications, like extract, phytochemical, pharmaceutical, nutraceutical, and antioxidant, were searched.

Chemical structures were redrawn using MarvinSketch (ChemAxon, version 17.14) based on structural information available in the PubChem and ChemSpider databases.

3. Results and Discussion

3.1. Botanical Characteristics, Ecology, and Host Association of Tristerix Species

Tristerix species, commonly known as South American mistletoes, are found in South America, particularly in countries like Argentina, Chile, Colombia, Ecuador, and Peru. The Chilean species are characterized by racemose inflorescences bearing bright red flowers, which may also exhibit a golden-yellow coloration in some species. Flowers are tubular, commonly associated with bracts, and with yellow stamens. Leaves are green, usually glabrous, and ovate to narrowly lanceolate in *T. corymbosus* and *T. verticillatus*, but absent in *T. aphyllus* [9]. Pollination is aided mainly by birds, primarily hummingbirds, while its edible fruits are eaten by birds and mammal species [7,18]. Fruits are ovoid berries, usually yellow (in *T. corymbosus* and *T. verticillatus*) to light pink (in *T. aphyllus*). Fruit dispersers can be found perched atop trees or shrubs; these animals then release seeds in their droppings. Seeds are covered in a sticky substance that allows them to hold on to branches and/or leaves of the host plant. Then, it germinates and a petiolar tube emerges, ending in a

haustorial holdfast that attaches to branches and initiates parasitism. If the seed cannot find any living branches within a certain time (or a compatible host in some cases), the parasite dies. In most species, the haustoria penetrates the cambial layer and connects itself to the xylem of the host [8].

Tristerix species, unlike some other genera such as *Desmaria*, usually infect a wide range of host species [20], and the host identity can influence the biochemistry of the parasite; for example, modifying the composition of emitted volatiles [21]. Some of these species have developed a parasitic association to certain host plants, most of them of native origin, which include *Aristotelia chilensis* (Elaeocarpaceae), *Peumus boldus* (Monimiaceae), *Rhaphithamnus spinosus* (Verbenaceae), *Luma apiculata* (Myrtaceae), and even cacti plants such as *Echinopsis chiloensis* (Cactaceae). *Tristerix* spp., particularly *T. corymbosus*, can also parasite a wide range of introduced woody species such as *Populus nigra* (Salicaceae) and *Acacia* spp. (Fabaceae) [7,9].

T. aphyllus is one of the few species that is holoparasitic, lacking photosynthetic tissues and relying on its host for sugars and water [9]. Its main hosts are native cacti, the most common being *Leucostele chiloensis* (Cactaceae) (Table 1). It is pollinated, as mentioned above, by the hummingbird *Sephanoides sephanoides*, and its seeds are mainly dispersed by *Mimus thenca*, another native bird [22–24]. Being holoparasitic, the reproductive structures (inflorescence and fruits) are the only portion of the plant that is visible outside their host. This parasitic interaction negatively impacts the health of their hosts, directly affecting their fitness [25,26].

Table 1. Hosts found to be infected by *Tristerix* spp. in Chile.

Species	Native Hosts	Introduced Host	References
T. aphyllus	*Leucostele* spp. (Cactaceae), *Eulychnia* spp. (Cactaceae), rarely species of *Copiapoa* and *Opuntia* (Cactaceae)	Not known	[7,22,23,25–27]
T. corymbosus	*Gevuina avellana* (Proteaceae), *Kageneckia oblonga* (Rosaceae), *Aristotelia chilensis* (Elaeocarpaceae), *Retanilla trinervia* (Rhamnaceae), *Azara integrifolia* (Salicaceae), *Peumus boldus* (Monimiaceae), *Rhaphithamnus spinosus* (Verbenaceae), *Berberis darwinii* (Berberidaceae), *Colletia hystrix* (Rhamnaceae), *Maytenus boaria* (Celastraceae), *Colliguaja odorifera* (Euphorbiaceae) and *Luma apiculata* (Myrtaceae)	*Salix* spp. (Salicaceae), *Populus* spp. (Salicaceae), *Acacia dealbata* and *A. melanoxylon* (Fabaceae)	[7,11,28–30]
T. verticillatus	*Ephedra andina* (Ephedraceae), *Schinus polygama* (Anacardiaceae), *Colletia hystrix* (Rhamnaceae), *Quillaja saponaria* (Quillajaceae), *Vachellia caven* (Fabaceae), *Escallonia illinita* (Escalloniaceae) *Luma apiculata* (Myrtaceae) *Discaria chacaye* (Rhamnaceae), *Schinus montanus* (Anacardiaceae), *Fabiana imbricata* (Solanaceae) and *Berberis montana* (Berberidaceae)	Not known	[7,17,21,28]

As mentioned before, *T. corymbosus* and *T. verticillatus* are both hemiparasitic, featuring green leaves capable of performing photosynthesis (Figure 1). Both species are pollinated by the same hummingbird species as *T. aphyllus*. Their fruits are dispersed not only by *Mimus thenca* and other bird species but also by *Dromiciops gliroides*, an endemic marsupial of Chile and Argentina [31–33]. These species are capable of infesting different hosts, mainly native shrubs and trees (Table 1). *T. corymbosus*, additionally, parasites non-native trees such as *Populus* and *Acacia* species, as previously mentioned [7,9,11]. Moreover, it has been suggested that this keystone species could negatively impact invasive tree species and

indirectly benefit native species, providing a resistance to invasion in natural ecosystems in Chile [34].

Figure 1. *Tristerix corymbosus*. (**A**) Leaves and flowers. (**B**) Leaves and fruits. Original photograph provided by the authors.

3.2. Phylogenetic Relationships of Chilean Tristerix Species

Beside the taxonomic treatment of the Loranthaceae, Chilean species seem to be well-defined and form clear, separate systematic groups. This may have an impact on their phytochemical profiles, not considering the effect of their hosts [35]. When an ITS-based dendrogram is performed using sequences present in databases, two clusters are visualized (namely A and B) which present a 31.3% distance with the outgroup. Cluster A (in blue color) is integrated by a subgroup composed of accession numbers DQ442964 and DQ442969 (with a distance of 24.2%), with a difference of 27.2% regarding accession DQ442974 (Figure 2). On the other hand, Cluster B (yellow) comprises a subgroup of accessions with a mean genetic distance of 26.8%. These results suggest that the division in two clusters could suggest the presence of a separation due to species evolution according to geographic location. Cluster A corresponds to species with a more meridional (Mediterranean–oceanic climates) geographic location, while cluster B groups species with a location around the tropic of Capricorn (tropical climates). Chilean species (*T. aphyllus*, *T. corymbosus*, and *T. verticillatus*) form a separate clade from other South American species. Within this clade, *T. aphyllus* and *T. corymbosus* are more closely related, and this may indicate that these species share evolutionary similarities that could be reflected in aspects of their secondary metabolism, although this hypothesis requires phytochemical confirmation.

3.3. Chemical Constituents of Tristerix spp. Extracts

One study used samples of *T. tetrandus* leaves and flowers to identify metabolites using UHPLC-PDA-HESI-Orbitrap mass spectrometry. They identified a total of 36 metabolites (28 found in leaves and 6 in flowers), with some having well documented antioxidant properties such as chlorogenic acid, catechin, rutin, quercetin-3-O-glucose, quercetin-3-O-pentose, 5-O-caffeoylquinic acid, cyanidin-3-glucoside, malvidin, quercetin, luteolin, naringenin, and apigenin, among others tentatively identified. From these, only malvidin was identified in flowers [36]. Torres et al., determined the qualitative presence of several metabolites from leaves and flowers in different extracts (hexane, dichloromethane, ethyl acetate, and methanol) of *T. corymbosus* parasitizing *Populus nigra* (Salicaceae), *Aristotelia chilensis* (Elaeocarpaceae), and *Rhaphitamnus spinosus* (Verbenaceae). Tannins, flavonoids, steroids, quinones, saponins, triterpenes, and cardiac glycosides were found. Leaves and flowers of *T. corymbosus* presented different contents of these metabolites, which could be due to its presence in different hosts [37].

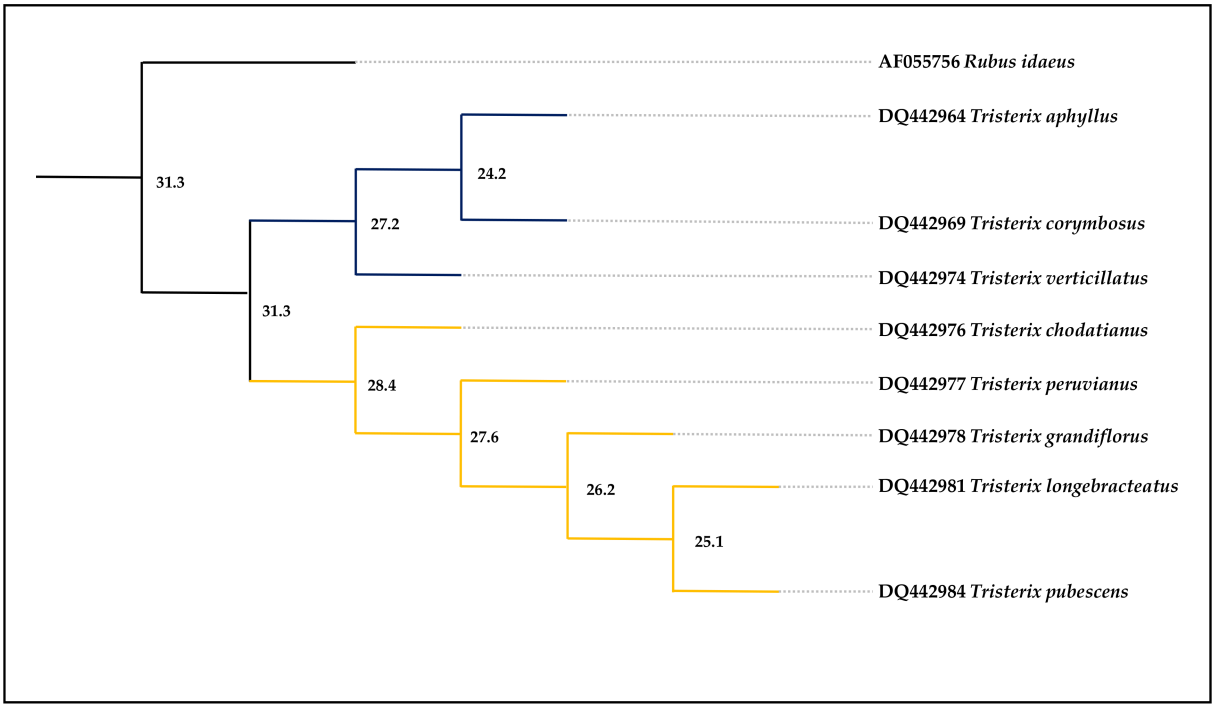

Figure 2. Dendogram using Neighbor-joining of ITS1 section of several *Tristerix* spp. Phylogenetic analysis was performed using ITS sequences from the genus *Tristerix*, such as *T. aphyllus* (DQ442964), *T. corymbosus* (DQ442969), *T. verticillatus* (DQ442974), *T. chodatianus* (DQ442976), *T. peruvianus* (DQ442977), *T. grandiflorus* (DQ442978), *T. longebracteatus* (DQ442981), and *T. pubescens* (DQ442984). As outgroup, a sequence of *Rubus idaeus* (AF055756) was used.

Cifuentes-Araya et al., investigated the application of nanofiltration as a green separation strategy for the recovery of bioactive compounds from *T. tetrandus* fruits. Using three nanofiltration membranes with different molecular weight cut-offs, followed by UHPLC-ESI-MS/MS analysis, the authors successfully separated and identified several phenolic compounds, including chlorogenic acid, cryptochlorogenic acid, caffeic acid, p-coumaric acid, gallic acid, rutin, and quercetin [38]. Other studies have demonstrated the composition of phenolic compounds across three fractions isolated from the flowers (esterified, free, and insoluble fractions). The esterified fraction contained a significant number of phenolic compounds, including chlorogenic acid, coumaric acid, and sinapic acid [39].

The work of Alarcón-Acuña, studied the phytochemical composition of ethanolic extracts of *T. chodatianus* leaves (a species infecting *Polylepis* spp. in Peru). Through various biochemical reaction tests on different fractions of the ethanolic extracts, phytochemical compounds such as phenolic acids, flavonoids, triterpenes, steroids, leucoanthocyanidins, and saponins were found [40].

In 2009, the translocation of alkaloids to *T. verticillatus* from its hosts was evaluated by comparing the alkaloid content of *T. verticillatus* hosted by an alkaloid-containing species, *Berberis montana* (Berberidaceae), a genus known for the presence of isoquinoline alkaloids, and an alkaloid-lacking *Schinus montanus* (Anacardiaceae) species. The alkaloids pronuciferine and glaucine, which were also found in the host *B. montana*, were found in *T. verticillatus* leaves [41].

To facilitate comparison among the available phytochemical studies on *Tristerix* species, the main characteristics of each investigation are summarized in Table 2. The table compiles information on the species studied, plant material, extraction procedures, analytical techniques, major identified metabolites, collection site (when reported), and corresponding

references, providing an integrated overview of the current phytochemical knowledge on this genus. Figure 3 summarizes the metabolites reported in the aforementioned studies.

Table 2. Summary of phytochemical studies on *Tristerix* species.

Specie	Plant Organ	Extraction Solvent/Method	Analytical Technique	Major Identified Compounds	Collection Site/Host	Reference
Tristerix tetrandus	Leaves and flowers	Methanolic extracts for antioxidant assays	UHPLC-PDA-HESI-Orbitrap MS	Chlorogenic acid, catechin, rutin, quercetin-3-O-glucoside, quercetin-3-O-pentose, 5-O-caffeoylquinic acid, cyanidin-3-glucoside, malvidin, quercetin, luteolin, naringenin, apigenin	Not reported	[36]
Tristerix corymbosus	Leaves and flowers	Sequential extraction with hexane, dichloromethane, ethyl acetate and methanol	Qualitative phytochemical screening	Tannins, flavonoids, steroids, quinones, saponins, triterpenes, cardiac glycosides	Hosts: *Populus nigra*, *Aristotelia chilensis*, *Rhaphithamnus spinosus* (Chile)	[37]
Tristerix tetrandus	Fruits	Nanofiltration (polyamide-TFC NF membranes)	UHPLC-ESI-MS/MS	Gallic acid, cryptochlorogenic acid, chlorogenic acid, caffeic acid, p-coumaric acid, rutin, quercetin	Not reported	[38]
Tristerix corymbosus	Flowers	Fractionation into free, esterified and insoluble phenolic fractions	Phenolic profiling	Chlorogenic acid, p-coumaric acid, sinapic acid	Not reported	[39]
Tristerix chodatianus	Leaves	Ethanolic extraction	Phytochemical screening	Phenolic compounds, flavonoids, triterpenes, steroids, leucoanthocyanidins, saponins	*Polylepis* spp., Peru	[40]
Tristerix verticillatus	Leaves	Alkaloid extraction	Alkaloid analysis/comparative phytochemical analysis	Pronuciferine, glaucine	Host comparison: *Berberis montana* vs. *Schinus montanus*	[41]

3.4. Biological Properties of Tristerix spp. Extracts

3.4.1. Antioxidant Properties

The study of Simirgiotis et al., evaluated the antioxidant properties of flower and leaf extracts of *T. tetrandus* with 2,2-diphenyl-1-picrylhydrazyl radical scavenging assay (DPPH), showing that the leaves possess a higher antioxidant activity in comparison with the flowers, which coincides with their higher phenolic and flavonoid content. Ferric reducing antioxidant power (FRAP) assays were also performed on each extract, with flower extracts showing a higher reducing power in comparison. This result also correlates with the flowers' total anthocyanin content. It is also worth mentioning that the results of the leaves in this assay were comparable with the results obtained from an anthocyanin standard sample of cyanidin-3-glucoside [36].

The study of Torres et al., determined the reductive powers of extracts of *T. corymbosus* samples from the three different hosts. The extracts were made using different solvents of different polarities, and the solvent that produced the highest yield of extract was methanol. *Tristerix* leaf extracts from *R. spinosus* host showed higher reducing power, predominantly the methanol extracts; as well as ethyl acetate extracts of *Tristerix* flowers parasitizing *A. chilensis* and *R. spinosus*. Interestingly, each host resulted in extracts with different contents of secondary metabolites, varying with the presence of flavonoids, phenols, quinones, triterpenes, and glycosides, among others [37]. Besides, in the study of Velásquez et al., the different fractions obtained (esterified, free, and insoluble fractions) exhibited antioxidant capacity against FRAP, DPPH, and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical cation decolorization assay [39].

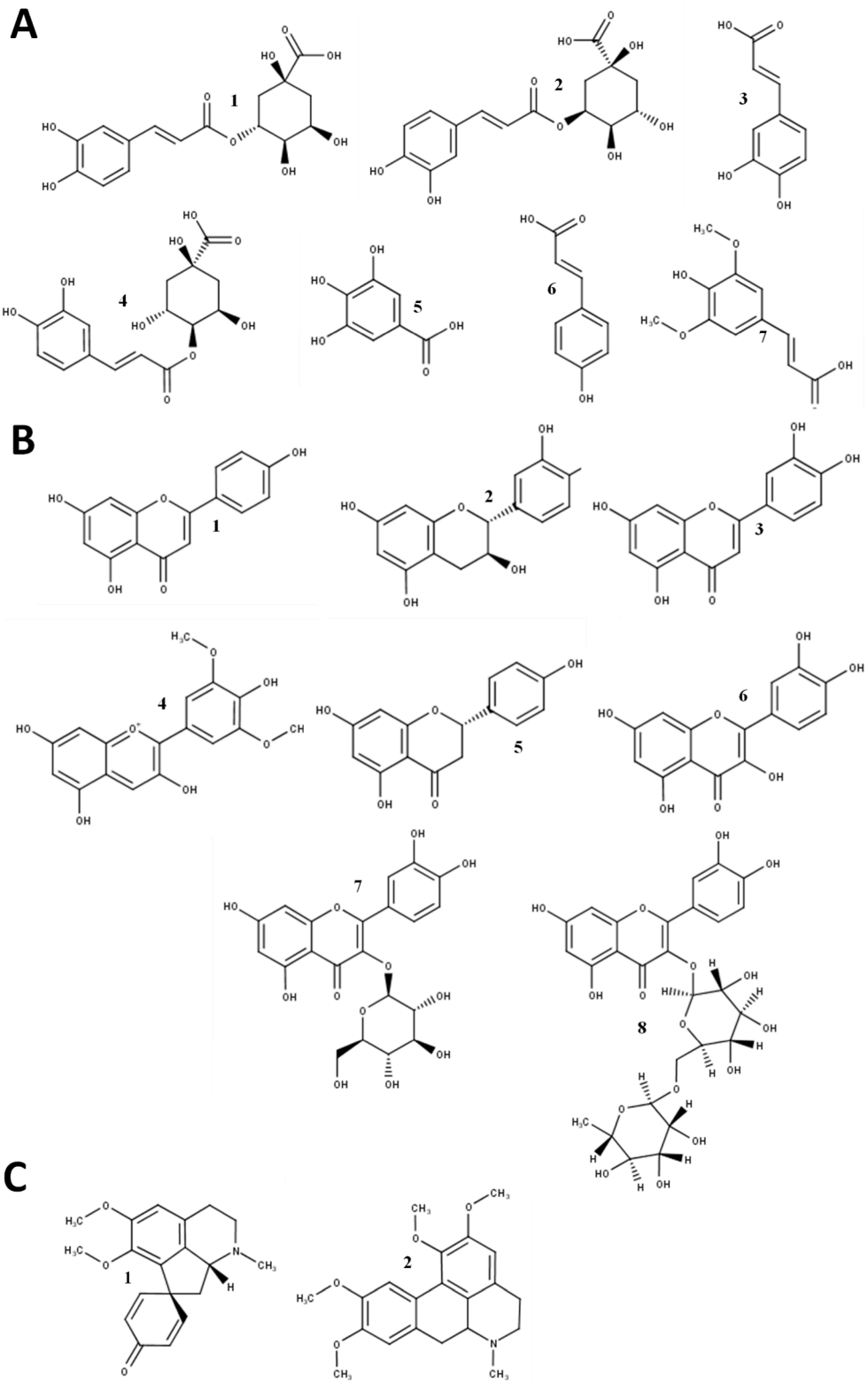

Figure 3. Chemical structures of the main phytochemicals identified in *Tristerix* spp. (**A**) Phenolic acids. (**1**) 3-O-caffeoylquinic acid, (**2**) 5-O-caffeoylquinic acid, (**3**) caffeic acid, (**4**) cryptochlorogenic acid, (**5**) gallic acid, (**6**) p-coumaric acid, and (**7**) sinapic acid (**B**) Flavonoids. (**1**) apigenin, (**2**) catechin, (**3**) luteolin, (**4**) malvidin, (**5**) naringenin, (**6**) quercetin, (**7**) quercetin-3-O-glucoside, and (**8**) rutin (**C**). Alkaloids. (**1**) pronuciferine and (**2**) glaucine.

In the work performed by Alarcón-Acuña, the antioxidant activity of ethanolic extracts of *T. chodatianus* leaves was assayed. Antioxidant assays such as DPPH and FRAP resulted in a dose-dependent activity in both tests, with a IC_{50} value of 0.242 mg/mL for the DPPH

assay and a Trolox equivalent antioxidant capacity (TEAC) value of 0.642 + 0.008 mg/mL for the FRAP assay [40].

3.4.2. Antimicrobial Properties

In the work of Velásquez et al., the free and esterified fractions presented antibacterial capacity against *Escherichia coli*, *Salmonella enterica* serovar Typhy, and *Staphylococcus aureus*. Chlorogenic and sinapic acids were correlated with the antibacterial capacity against *E. coli* and *S. typhi*, while coumaric acid were correlated with the antibacterial capacity against *S. aureus*. These findings enable the exploration of potential applications for the different fractions [39]. Mølgaard et al., determined the antimicrobial properties of 40 plant species used traditionally by the Huilliche people of Chile, among these *T. corymbosus*. Using a thin-layer chromatographic (TLC) agar overlay protocol, they determined a minimal inhibitory amount (MIA) against *S. aureus* (ATCC 6538) for a methanolic extract of *T. corymbosus* stem leaves, resulting in a value of ~1 mg [42].

3.4.3. Cytotoxic Properties

The study performed by Vidal-Pérez, evaluated the cytotoxic properties of several extracts of *T. corymbosus* using leaves and flowers from three different hosts: *P. nigra*, *A. chilensis*, and *R. spinosus*. They used extracts made with different solvents of increasing gradients of polarity. Results of the sulforhodamine B assay showed that the cell viability of AGS gastric cancer cell lines was significantly reduced by the highest concentration (50 μg/mL) of the ethyl acetate (~90% cell viability) and methanol (~70% cell viability) extracts of *Tristerix* flowers with *P. nigra* as a host. Similar concentrations of flower extracts with *R. spinosus* host prominently reduced cell viability at ~40% with ethyl acetate, and ~50% with methanol. Regarding the extracts of *Tristerix* with *A. chilensis* as host, the flower extracts at 50 μg/mL significantly reduced cell viability at ~50% with ethyl acetate as solvent and ~70% with methanol as solvent. Leaf extracts, in comparison, reduced cell viability of AGS to a lesser degree, with the best results (~50%) obtained from 50 μg/mL methanol extracts with *A. chilensis* as a host. The cytotoxic activity against PC-3 prostatic cancer cell lines was also evaluated, and the most significant results were observed on flower extracts. Extracts with *R. spinosus* as host in concentrations of 50 μg/mL resulted in a cell viability of ~50% with ethyl acetate, and ~60% with methanol, while flower extracts with *A. chilensis* as host resulted in a cell viability of ~70% with ethyl acetate as solvent. Concentrations of 100 μg/mL of the aforementioned extract resulted in a cell viability of ~40%. A final cytotoxicity assay was performed using MCF-7 breast cancer cells. Similar to the results obtained with PC-3 cells, the flower extract exhibited the highest cytotoxic activity. Ethyl acetate extracts with *R. spinosus* as host gave a cell viability of ~70% at concentrations of 50 μg/mL and ~40% at 100 μg/mL. Interestingly, dichloromethane extracts of leaves with the same host managed a significant reduction in cell viability, with a value of ~70% at its highest concentration, 50 μg/mL. A similar result was observed on these cell lines with extracts of flowers and leaves with *A. chilensis* as host, with the highest activity obtained from 100 μg/mL of ethyl acetate flower extracts (~50%) and 50 μg/mL of dichloromethane leaf extracts (~70%) [43].

Another work performed by Anicama-Lizarzaburo also studied the biological properties of *T. chodatianus*, focusing on its cytotoxic activities. An in vivo toxicity assay using *Artemia salina* revealed that the ethanolic extracts of leaves did not cause death in the animal models at any concentration tested, including the highest concentration of 1000 ppm, which had a survival rate of 96.7%. The same results were obtained in another toxicity assay using *Lactuca sativa* (Asteraceae) seeds, with no significant germinative reduction observed [44].

3.4.4. Analgesic Properties

In the work of Anicama-Lizarzaburo, analgesic properties of *T. chodatianus* extracts were also evaluated using a hot-plate test in a murine animal model. Testing of the analgesic effect was performed by orally administering to different animal groups various dilutions of leaf extract, saline solution as negative control, and tramadol as positive control, leaving them after 30 min of the treatment on the hot plate at 53.5 °C for a maximum of 30 s. It was observed that the negative control only lasted for a maximum of 8 s before showing an analgesic effect (paw licking or jumping out of the hot plate). Meanwhile, tests with dilutions of 400 mg/kg of leaf extracts showed an analgesic percentage of 95.19%, reflected by the longer duration of time of the animal models on the hot plate (longest time recorded of 18.10 s). Interestingly, concentrations of 200 and 600 mg/kg showed lower percentages of analgesia; 49.48% and 42.60%, respectively. In comparison with the positive control, tramadol resulted in an analgesia percentage of 165% (longest time recorded of 25.88 s). This confirms that, despite not being superior to the positive control, extracts of *T. chodatianus* possess significant analgesic properties [44].

Overall, the available evidence indicates that *Tristerix* spp. possess a broad spectrum of biological properties, including antioxidant, antimicrobial, cytotoxic, and analgesic activities, primarily attributed to their diverse phytochemical compositions. However, the magnitude of these effects varies according to the species, host plant, plant organ, extraction method, and experimental model employed. Despite these promising findings, the current evidence is largely limited to in vitro and preclinical studies. A summary of these results is shown in Table 3.

Table 3. Summary of the biological properties reported for *Tristerix* spp. extracts.

Specie	Plant Organ	Extract/Fraction	Experimental Model	Biological Activity	Main Findings	Reference
T. tetrandus	Leaves and flowers	Methanolic extracts	DPPH, FRAP	Antioxidant	Leaves showed higher DPPH radical scavenging activity, whereas flowers exhibited greater FRAP reducing power associated with higher anthocyanin content.	[36]
T. corymbosus	Leaves and flowers from different hosts	Methanol, ethyl acetate and other solvents	Reducing power assay	Antioxidant	Antioxidant capacity varied according to host species, plant organ, and extraction solvent, reflecting differences in secondary metabolite composition	[37]
T. corymbosus	Different fractions	Free, esterified and insoluble fractions	DPPH, ABTS, FRAP	Antioxidant	All fractions exhibited antioxidant activity, with variations depending on phenolic composition.	[39]
T. chodatianus	Leaves	Ethanolic extract	DPPH, FRAP	Antioxidant	Dose-dependent antioxidant activity (DPPH IC_{50} = 0.242 mg/mL; FRAP TEAC = 0.642 ± 0.008 mg/mL).	[40]
T. corymbosus	Different fractions	Free and esterified fractions	*E. coli*, *S. enterica* serovar Typhi, *S. aureus*	Antimicrobial	Antibacterial activity correlated with chlorogenic, sinapic and p-coumaric acids.	[39]
T. corymbosus	Stem leaves	Methanolic extract	*S. aureus* (TLC agar overlay)	Antimicrobial	Minimal inhibitory amount of approximately 1 mg.	[42]
T. corymbosus	Leaves and flowers from different hosts	Dichloromethane, ethyl acetate, methanol	AGS, PC-3, MCF-7 cell lines	Cytotoxic	Flower extracts showed stronger cytotoxicity than leaf extracts. Activity depended on host species, extraction solvent, and cancer cell line.	[43]
T. chodatianus	Leaves	Ethanolic extract	*Artemia salina* and *Lactuca sativa*	Cytotoxic	No significant toxicity under evaluated conditions.	[44]
T. chodatianus	Leaves	Ethanolic extract	Hot-plate test (mice)	Analgesic	Significant analgesic effect, greatest response at 400 mg/kg.	[44]

In this review, we explored the bioactive properties of *Tristerix* and their phytochemicals. Most of the studies found for this review discuss the presence of phenolic compounds and alkaloids. However, no study has directly tackled the presence of other secondary metabolites, such as volatile compounds or essential oils. There is speculation regarding the acquisition of volatile compounds from their hosts, but there is no study that has yet corroborated that theory [45]. The aforementioned compounds that had been found on *Tristerix* species have well-documented bioactive properties. Quercetin, one of its flavonoids, is found in several botanical sources, including some common fruits, vegetables, and medicinal plants. This compound has proven to exert anti-inflammatory and immunomodulatory activities based on different in vitro assays performed on animal and human cells, as well as in vivo assays on murine models. Most of the mechanisms involved are the inhibition of inflammatory intermediaries like interleukins (IL) IL-1β, IL-6, IL-8, tumor necrosis factor α (TNF-α), and enzymes such as cyclooxygenase (COX), among others [46]. Malvidin is another flavonoid, a member of the anthocyanin group, that possesses antioxidant and anti-inflammatory properties. As an antioxidant, it is capable of neutralizing free radicals by donating either an electron or a hydrogen atom and is capable of increasing the activity of antioxidant enzymes like catalase and superoxide dismutase. Meanwhile, the anti-inflammatory activities are associated with the modulation of pro-inflammatory cytokines and the inhibition of the NF-κB signaling pathway, which is related to the inflammatory response [47].

Apigenin is another flavonoid with a wide distribution on plant species and with well-studied bioactive properties. Various in vitro and in vivo studies have established its medicinal potential based on its antioxidant, anti-inflammatory, anti-tumoral, antidiabetic, and neuroprotective properties. Most of its activities are related to its inhibitory involvement with biological pathways related to inflammation and cell proliferation, as well as the neutralization of reactive oxidative species and stimulation of antioxidative enzymes such as glutathione and superoxide dismutase. The inhibition of certain enzymes, such as iNOS, COX-2, and MAO, is also related to the aforementioned biological activities. Neuroprotective activities are mainly associated with a reduction in fibrillar amyloid deposits and regulation of secretion of neurotransmitters such as GABA, serotonin, and dopamine, among others [1]. Catechin, another secondary metabolite found in *Tristerix*, shares some similar bioactive properties with apigenin, alongside cardioprotective, hepatoprotective, and nephroprotective activity, mainly related to its antioxidant nature [48].

Gallic acid is a phenolic acid that possesses a remarkable free radical scavenging capacity, widely used in the food industry as a flavoring agent and preservative. It is also known for its antimicrobial, anti-inflammatory, gastroprotective, cardioprotective, neuroprotective, and anti-tumoral properties. It was found that gallic acid can disrupt the integrity of the cell membrane on both Gram-positive and Gram-negative bacteria and can interfere with bacterial growth via inhibition of the dihydrofolate reductase. Gallic acid exerts most of its bioactive properties thanks to its antioxidant power, which in the case of its anti-tumoral properties can reduce carcinogenesis induced by reactive oxidative species through the increased activity of antioxidative enzymes. This phenolic acid also inhibits hyperglycemia and hypertriglyceridemia by increasing the cellular glucose uptake through stimulation of the PI3K/p-Akt signaling pathway, translocation of insulin-stimulated glucose transporters, and by reduction of the size of adipocytes [49].

Caffeic acid is a phenolic compound widely distributed in plant species, as well as one of the main components on propolis, and it also possesses antioxidant, anti-tumoral, and antibacterial properties [50]. Regarding the latter, its antibacterial effects are associated with its interaction with the cell membrane, leading to altered permeability and the inactivation of essential enzymes involved in energy production and structural synthesis. These

antibacterial activities were assessed against bacteria such as *S. aureus*, *E. coli*, *B. cereus*, and *L. monocytogenes*, among others [51].

Luteolin, a flavonoid extracted from various species of the genus, has been studied due to its notable anti-inflammatory, anti-tumoral, and antioxidant properties. Research has demonstrated its capacity to inhibit cytokine production and signal transduction pathways, along with its ability to neutralize reactive oxygen species (ROS), indicating a promising therapeutic application in cancer prevention and treatment [52]. Rutin, another bioactive flavonoid extracted from *T. tetrandus*, has shown significant protection against oxidative stress as well as neuroprotective effects. These findings suggest its potential in the prevention of neurodegenerative diseases and in the modulation of the inflammatory response [53].

There is a key gap in the *Tristerix* phytochemical research. Currently, there are no studies on the seasonal variation of the phytochemical profile in *Tristerix* species. Additionally, there are no studies addressing the impact of environmental factors such as light and water and nutrient availability on the secondary metabolites of these mistletoe species. These factors (time of the year and environment) can greatly influence metabolic profile, both quantitatively and qualitatively [54–56]. However, since *Tristerix* species are parasitic, the impact of season and environmental factors is indirect, mainly via their effect on their hosts. Thus, the impact on their phytochemical profile may not be simply predicted as in non-parasitic species. This opens a relevant area for further phytochemical studies on Chilean *Tristerix* species, which could disentangle the possible direct and indirect effects of season and key environmental factors.

4. Patent Data

The patent search identified very little intellectual property activity regarding *T. aphyllus*, *T. corymbosus*, and *T. verticillatus*. The search effort undertaken in this review yielded no patent applications or patents granted for any phytochemicals, standardized extracts, extraction techniques, pharmaceutical preparations, nutraceutical products, or cosmetics based on these three species. The results only pertain to the species dealt with in this review and do not preclude patents for any other species of *Tristerix* or other mistletoe genus.

5. Conclusions

In summary, species from the *Tristerix* genus possess several bioactive compounds, such as phenolic acids, flavonoids, and anthocyanins, which are associated with antioxidant, anti-inflammatory, antimicrobial, and anti-tumoral properties. This information correlates with what is traditionally known about this hemiparasitic plant species and its use in ancestral cultures. Based on the presence of these phytochemicals, as well as the few studies performed on plant samples, it is clear that *Tristerix* species possess medicinal properties. Despite the results obtained in this review, there is a clear lack of quantitative correlation between the phytochemical content and pharmacological properties, meaning that further study is required to fully validate its pharmaceutical potential. Future research needs to focus on experimental assays, either in vitro or in vivo studios, before going into clinical trials in order to determine the mechanisms involved in their biological activity and the beneficial effects of this overlooked mistletoe. Future research should prioritize the quantitative characterization of bioactive metabolites, the establishment of composition–activity relationships, the elucidation of molecular mechanisms of action, comprehensive toxicological assessments, and well-designed preclinical and clinical studies. Such efforts will be essential to validate the therapeutic potential of *Tristerix* spp. and facilitate their translation into innovative pharmaceutical, nutraceutical, and biotechnological applications.

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