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Revisión / Review

Phytochemistry and biological properties of *Drimys winteri* JR et G. Forster var *chilensis* (DC) A.

[Fitoquímica y propiedades biológicas de *Drimys winteri* JR et G. Forster var *chilensis* (DC) A.]

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Section **Review**

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Abstract: *Drimys winteri* JR et G. Forster var *chilensis* (DC) A. is a tree native to central and southern Chile. Also it found in part of Argentina. It is abundant in wet swampy localities from sea level to an altitude of 1700 m. This tree is sacred for the Mapuche culture; it is used in folk medicine in such as inflammatory and painful processes. Phytochemical studies have demonstrated that this plant contains mainly sesquiterpenes of the drimane type, flavonoids, essential oils, phytosterols and some lignans. These drimanes have attracted interest because of their antifeedant, plant growth regulation, cytotoxic, antimicrobial and insecticidal properties. The objective of this review is to establish clearly the phytochemistry and biological activity of *Drimys winteri* JR et G. Forster var *chilensis* (DC) A. Articles based on other varieties are not considered.

Keywords: *Drimys winteri*; Sesquiterpenes; Essential oils; Lignans; Flavonoids; Biological properties.

Resumen: *Drimys winteri* JR et G. Forster var *chilensis* (DC) A. es un árbol nativo del centro y sur de Chile. Tambien se encuentra en parte de Argentina. Es abundante en localidades pantanosas y húmedas desde el nivel del mar hasta una altitud de 1700 m. Este árbol es sagrado para la cultura mapuche. Se utiliza en la medicina popular para tratar enfermedades como procesos inflamatorios y dolorosos. Los estudios fitoquímicos han demostrado que esta planta contiene principalmente sesquiterpenos del tipo drimano, flavonoides, aceites esenciales, fitoesteroles y algunos lignanos. Estos drimanos han despertado interés debido a sus propiedades antialimentarias, regulación del crecimiento de las plantas, propiedades citotóxicas, antimicrobianas e insecticidas. El objetivo de este examen es establecer claramente la fitoquímica y la actividad biológica de *Drimys winteri* JR et G. Forster var *chilensis* (DC) A. No se consideran los artículos basados en otras variedades *D. winteri* var *winteri*.

Palabras clave: *Drimys winteri*; Sesquiterpenos; Aceites esenciales; Lignanos; Flavonoides; Propiedades biologicas.

INTRODUCTION

Plants of the genus *Drimys*, (Winteraceae) are widely distribute all over the America (from Mexico until Chile and part of Argentina). The species, descrited for this continent are: *Drimys angustifolia* Miers (south of Brasil), *Drimys brasiliensis* Miers (Brasil until south of México), *Drimys confertifolia* Phil. (endemic plant of Juan Fernandez Island, Chile), *Drimys andina (*Reiche) R. A. Rodr. & Quez. (syn *D. winteri* var. *andina*) endemic of Chile, *Drimys granadensis* L.f. south México until south of Perú), *Drimys winteri* J. R. Forst. & G. Forster var *chilensis* (DC) A. (Chile, and south Argentina), and *Drimys winteri* var *winteri* occurring in Southwestern Patagonia (45º44'- 55º58'S) (Rodriguez & Quezada, 1991; Ruiz *et al*., 2008). Most of these species, are traditionally used as wild vegetables and as a therapeutic agent.

The genus *Drimys* includes approximately between six and eight Central and South American species that are distributed from Mexico to Navarin Island (Molina *et al*., 2016). One species (*Drimys confertifolia* Phil. is endemic to the Juan Fernandez Islands (Silva *et al*., 1992). Of these species, only *Drimys winteri* JR et G. Forster *var chilensis* (DC) A. (*Dwch*) (Figure No. 1) commonly called canelo is well known in cultivation (Hernandez *et al.*, 1996; Jordan, 2005). It is found up to 1200 m above sea level and between latitude 32° south and Cape Horn at latitude 56° south in Patagonia. *Drimys winteri* JR is an evergreen shrub growing to 7.5 m (24 ft) by 6 m (19ft) at a medium rate. It is hardy to zone. It is in leaf all year, in flower from January to June. The species is hermaphrodite. Suitable for: light (sandy) and medium (loamy) soils and prefers well-drained soil. Suitable pH: acid and neutral soils. It can grow in semi-shade (light woodland). It prefers moist soil. The plant can tolerate strong winds but not maritime exposure (Jordan, 2005). There are three species of *Drimys* in Chile: *D. winteri* (two varieties have been described) and *D. andina* Reiche (Rodriguez & Quezada, 1991). The most abundant is the tree *Dwch*, whereas *D. andina* is a shrub and less common (Marticorena & Quezada, 1985; Muñoz-Concha *et al.*, 2007). Currently two arbnorescent species are recognized in Chile: *D. winteri* JR Forst et G. Forst with two varieties, *D. winteri* var. *winteri* occurring in Southwestern Patagonia (45°44¨-55°58´S) and *D. winteri* var. *chilensis* (DC.) A. Gray being widespread in Chile and Argentina (30°20¨-46° 25¨S) (Ruiz *et al*., 2008). According to the literature, the variety *chilensis* it is not found in Brazil (Santos *et al*., 2017)

The objective of this review is to establish clearly the phytochemistry and biological activity of *Drimys winteri* JR et G. Forster var *chilensis* (DC) A. As in many studies the variety analyzed is not specified but in its totality corresponds to samples collected in Chile (except from Patagonia), we have assumed that the samples are from *Dwch*. Articles based on others varieties, are not considered.

Figure No. 1
***Drimys winteri* JR et G. Forster var *chilensis* (DC) A. (Vogel *et al*., 2008)**
(Photo S. Teillier)

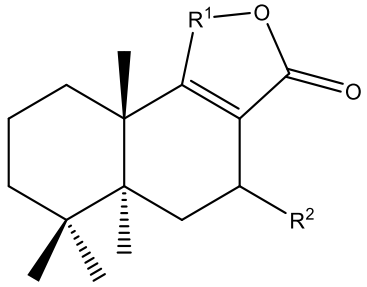
D. winteri JR et G. Forster var *chilensis* (DC) A. is a sacred plant to the indigenous Mapuche people, who use its aerial parts for the treatment of dermatitis, stomach pain, toothache, tumors, and other illnesses (Muñoz & Barrera, 1981; Muñoz *et al*., 2001; Estomba *et al*., 2006). Extracts of the stem bark have long been used to treat human (Muñoz & Barrera, 1981) and bovine diseases: gastrointestinal nematodes, (Rodriguez *et al*., 2005). In the past, the stem bark of *Dwch* was exported to Europe as an antiscorbutic medicine (Muñoz *et al*., 2001; Jordan, 2005). The tree is also used for commercial purposes, in wood production, crafts, manufacturing and the pulp industry, due to the high quality of its fibers. Its architectural characteristics and natural resistance to insects and microorganisms are advantageous for playgrounds in parks and gardens in a wide range of climatic conditions. The wood of this species is highly valued and used to manufacture furniture and musical instruments as well as to protect crops (Rodriguez, 1998; Franco *et al*., 2006; Monsálvez *et al*., 2010). Furthermore, extracts of aerial parts of *Dwch* have shown industrial applications in products such as cosmetics (Rodriguez, 1998; MINSAL, 2010), phytonutrients and pest repellent agents (Jansen & de Groot, 2004; Zapata *et al*., 2009; Monsálvez *et al*., 2010); the bark produces a pungent bitter herb tonic that relieves indigestion. It is antiscorbutic, aromatic, febrifuge, and also used as a parasiticide (Moya & Escudero, 2015). The bark is harvested in autumn and winter and is dried for later use. Another important use of bark infusion is in the treatment of rheumatic illnesses (Muñoz *et al*., 2015).

Phytochemical Analysis

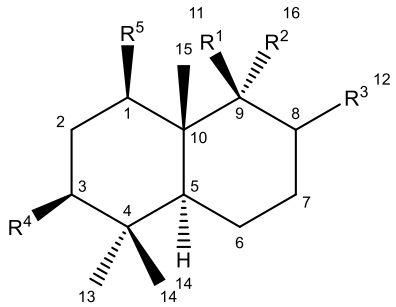
Phytochemical studies of the extracts of aerial parts of *Dwch* performed several decades ago in Chile (Appel *et al*., 1964; Appel *et al*., 1960; Brown, 1994) reported phytonutrients and pest repellent agents (Jansen & de Groot, 2004; Zapata *et al*., 2009; Monsálvez *et al*., 2010). Phytochemical reports on the chemical composition of continental *Dwch* indicated the presence of tannins, flavonoids, essential oils**,** drimane-type sesquiterpenes, sesquiterpene lactones (Muñoz *et al.*, 2001), lignans and phytosterols (Muñoz *et al.*, 2015).

Drimane-type sesquiterpenes

The name *drimane* was proposed for the saturated hydrocarbon with the structure and absolute configuration depicted in Figure No. 2 (Jansen & de Groot, 1991; Jansen & de Groot, 2004). This structure is related to the sesquiterpene drimenol, isolated from the bark of *Dwch* Forst. reported by Appel (Appel, 1948). The structures of the sesquiterpenes isolated up to now from *Dwch* (Figure No. 2), and the numbering of the carbon skeleton follows the system established by Djerassi (Djerassi *et al.*, 1954).



Compound	R^1	R^2	References
Confertifolin	CH_2	H	Appel *et al*., 1960
Valiviolide	CH_2OH	H	Appel *et al*., 1963
Fueguin	CH_2OH	OH	Appel *et al*., 1963
Winterin	C=O	H	Appel *et al*., 1963
Futronolide	C=O	OH	Appel *et al*., 1963



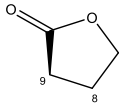
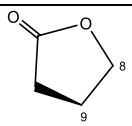
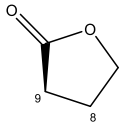
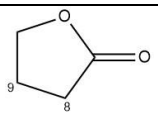
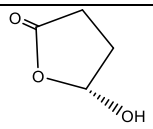
Compound	R^1	R^2	R^3	R^4	R^5		References
Drimenol	CH_2OH	H	CH_3	H	H	Δ^7	Sierra *et al*., 1986
Polygodial	CHO	H	CHO	H	H	Δ^7	Arias *et al*., 2018
Isotadeonal	H	CHO	CHO	H	H	Δ^7	Zapata *et al*., 2009
Drimendiol	CH_2OH	H	CH_2OH	H	H	Δ^7	Brown, 1994
Isodrimeniol		R^2=H	R^4=R^5=H			Δ^7	Rodriguez *et al*., 2005
Isodrimenin			R^2=R^4=R^5=H			Δ^8	Appel *et al*., 1960
Drimenin			R^2=R^4=R^5=H			Δ^7	Appel *et al*., 1960
3β-Acetoxydrimenin		R^2= R^5=H	R^4=AcO			Δ^7	Sierra *et al*., 1986
Cryptomeridiol	R1=R2=R4=H	R^3= ter-butOH	R^5=OH				Appel *et al*., 1963
Cinnamolide		R^2= R^4=R^5=H				Δ^7	Arias *et al*., 2018
Dendocarbin A		R^2= R^4=R^5=H				Δ^7	Arias *et al*., 2018

Figure No. 2
Structures of natural drimanes sesquiterpenes isolated from of *Drimys winteri* JR et G. Forster var *chilensis* (DC) A.

To the best of our knowledge, so far 18 drimane-type sesquiterpenoids of *Dwch* have been characterized and analyzed from continental Chile and Chiloé Island**;** studies made with leaves and bark

of different populations of *D. andina*, they also showed some similar sesquiterpenes (Muñoz-Concha *et al*., 2007). From *Dwch*, it has also been isolated one aromadendrane derivative and one drimane sesquiterpene double (Aasen *et al.*, 1977).

Drimane sesquiterpenes are not limited to the genus *Drimys*; they have also been isolated from the *Cannellaceae*, a small family of four genera and nine species (Jansen, 1993)

Dwch also is described in Brazil, although it has been widely analyzed it is not established which variety is the subject of the studies. The secondaries metabolites of samples from Brazil and Chile are similar since they have compounds with a drimane skeleton. However, they differ in their pattern of substitution and oxidation, in addition, there are different substituent groups in both plants (Cechinel Filho *et al*., 1998; Malheiros *et al*., 2001). The usual structures of the drimanes isolated from the genus *Drimys* have carbon atoms 11 and 12 very often oxidized; oxidation at other positions is also frequently observed, but in other genera. No sesquiterpenes that are re-ordered or form dimers or trimers have been reported in this genus

The drimane-type sesquiterpenoids possess a wide variety of biological activities, including antimicrobial, pungency, antibacterial, antifungal, antifeedant, cytotoxic**,** molluscicidal, piscicidal, growth regulation and phytotoxic properties (Jansen & de Groot, 2004). The pungency of several drimanes and their irritant properties on the skin (allergies) has also attracted attention (El Sayah *et al.*, 1997; Tratsk *et al.*, 1997). The reactivity of the unsaturated dialdehyde functionality towards biological nucleophiles is considered to be responsible for the antifeedant activity of those compounds (polygodial and epipolygodial) (Fujita & Kubo, 2003; Cerda-García-Rojas *et al.*, 2010).

Miscellaneous sesquiterpenes

Cyclocolorenone

This sesquiterpene was isolated by Brown in 1994 from the aerial parts of *Dwch* collected in Chile and was reported for the first time in this plant. Cyclocolorenone is an unusual aromadendrane sesquiterpene; aromadendranes (Figure No. 3) are dimethyl cyclopropa[e]azulen-6-one. These terpenes occur frequently in nature; higher plant essential oil and *Dwch* collected in Chile is not an exception; biological properties that have been reported for isolated aromadendranes include antifungal (Moreira *et al.*, 2003), antibacterial (Gaspar-Marques *et al.*, 2004), antiviral (De Tommasi *et al.*, 1990; Nishizawa *et al.*, 1992), plant growth regulatory (Matsuo *et al.*, 1981), antifeedant and repellent properties (Messer *et al.*, 1990).

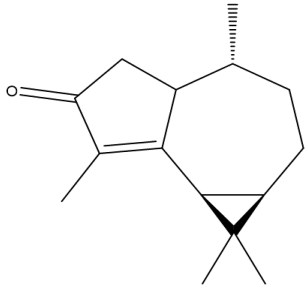


Figure No. 3
Structure of cyclocolorenone

Double sesquiterpene

An unusual sesquiterpene with a new structure (11ξ,12ξ)-Di(7-drimen-11-oxy)-11,12-epoxy-7-drimene ($C_{45}H_{72}O_3$) (Aasen *et al.*, 1977) was isolated from aerial parts of *Dwch*. The structure (Figure No. 4) was determined by chemical and spectroscopic data; hydrolysis produced drimenol and polygodial, thus establishing that it is a compound sesquiterpene, up to now not described in other members of the family.

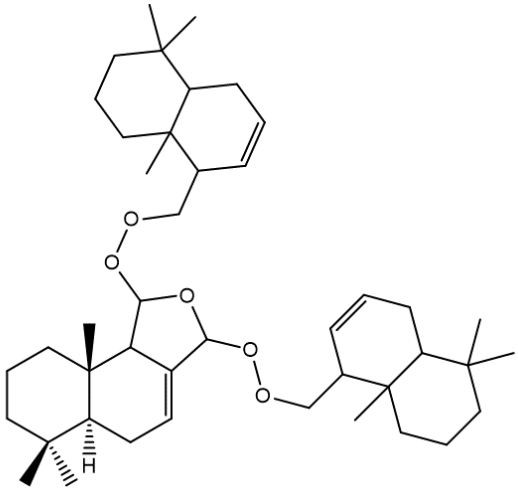
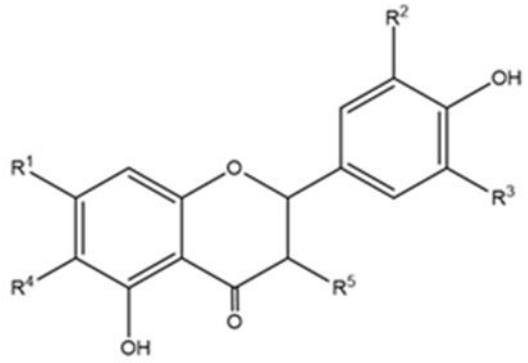


Figure No. 4
Structure of (11ξ,12ξ)-11,12-Di (7-drimen-11-oxy)-11,12-epoxy-7-drimene

Flavonoids

Phenolic compounds are one of the main classes of secondary metabolites. There has been considerable research on flavonoids from plant sources because of their versatile health benefits reported in various epidemiological studies. These compounds have served as markers for chemical systematics, including the Winteraceae (Williams & Harvey, 1982; Ruiz *et al.*, 2002). Studies on flavonoids as chemosystematic markers in chilean species of *Drimys* J. R. Forst et G. Forst made with three chilean species (*D. confertifolia Dwch* and *D. andina*), they showed that endemic species *D. confertifolia* is closely related with *Dwch*; the three species are very different in flavonoids contents (Ruiz *et al.*, 2002). Flavonoids are directly associated with human dietary ingredients and health; thus, there is a need to evaluate relationships between their structures and functions. The bioavailability, metabolism and biological activity of flavonoids depend upon the configuration, total number of hydroxyl groups and substitution of functional groups around their nuclear structure. Most recent studies have focused on the health aspects of flavonoids for human illnesses (Tripoli *et al.*, 2007; Romano *et al.*, 2013). Many flavonoids are shown to have antioxidative activity, free radical scavenging capacity, coronary heart disease prevention, hepatoprotection, anti-inflammatory and anticancer activities, and some flavonoids exhibit potential antiviral activities (Kaul *et al.*, 1985; Orallo & Alvares, 2003; Ozcelik *et al.*, 2011).

Dwch has a wide biological spectrum, which may be attributed to its varied secondary metabolites, in which flavonoids are implicated. However, up to now few of its flavonoids and their structural variants have been reported. A study of populations of *Dwch* and *D. andina* found significant quantitative variation in flavonoids of leaves in a number of localities of south-central Chile, especially in the southern area, probably associated with environmental effects (photochemical, climatic, hydric, etc) (Muñoz-Concha *et al.*, 2004). It has also been suggested that this genus has a very uniform flavonoid profile compared to other genera of the Winteraceae (Figure No. 5). A systematic study of the flavonoid pattern performed with 59 representatives of nine genera of the Winteraceae and related families found that luteolin 7,3'-dimethyl ether (77%) and flavonols (81%) were major constituents. The study reported simple flavones (16%) in some *Drimy*s. Similarly, the distribution of flavone C-glycosides was restricted to both varieties of *Dwch* and two other genera (Williams & Harvey, 1982).



Apigenine	R^1=OH	Δ^3	Williams *et al*., 1982
Luteoline	R^1=R^2=OH	Δ^2	Williams *et al*., 1982
Kaempferol	R^1=R^5=OH	Δ^2	Williams *et al*., 1982
Quercitrine	R^1=R^3=R^5=OH	Δ^2	Cruz & Silva, 1973
Taxifoline	R^1=OH; R^5=αOH	2-1'β	Cruz & Silvas, 1973
Quercetin	R^1=R^2=R^4=OH	Δ^2	Williams *et al*., 1982
Cirsimaritin	R^1=R^2=CH3O	Δ^2	Cruz & Silva, 1973
Fisetin	R^3=R^5=OH	Δ^2	Ruiz *et al*., 2002
Astilbin	R^3=OH; R^5=αOH	2-1'β	Ruiz *et al*., 2002

Figure No. 5
Flavonoids isolated from of *Drimys winteri* JR et G. Forster var *chilensis* (DC) A.

Lignans

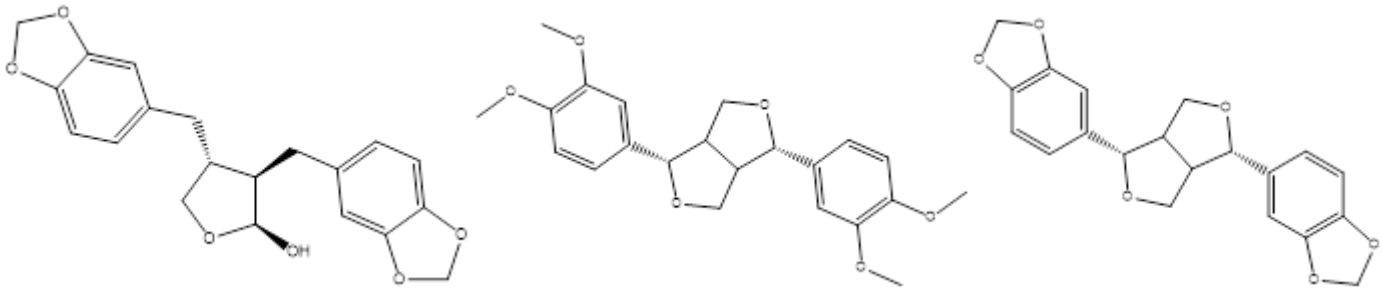
The lignans are a group of natural chemical compounds widely distributed in plants, whose structural units are synthesized by the shikimic acid pathway (Landete, 2012). Interest in lignans and their synthetic derivatives has grown due to their applications in cancer chemotherapy and their various other pharmacological effects (Saleem *et al.*, 2005).

The lignans sesamin, two epimeric cubebins, and eudesmin have been isolated from leaves and bark of *Dwch* (Muñoz *et al.*, 2015) (Figure No. 6). Sesamine is one of the main tetrahydrofuran lignans in the cortical parenchyma of *D. winteri*; its formula is 5,5'-(tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl) bis(1,3-benzodioxole). The same research group reported earlier that the sesamin content of canelo from Chiloé Island (Chile) was 40% greater than in other populations of continental Chile (Muñoz *et al.*, 2015).

Sesamin is particularly appreciated as an insect repellant to protect building materials against undesired insect infestation. Because some lignans have potent antimicrobial, antifungal, antiviral, antioxidant, insecticidal and antifeedant properties, they probably play an important role in plant defense against various biological pathogens and pests (Saleem *et al.*, 2005). The lignans play an important role in the interaction of plants with other organisms, mainly because of their defense function and in protection of plants against physical damage (Saleem *et al.*, 2005). Substituents such as methoxy or methylendioxy groups enhance the activity not only in lignans but also in simple phenylpropanoids (Harmatha & Nawrot, 2002). This fact could explain the anti-insect activity of *Dwch* from Chiloé. The high quantities of this lignan found in leaves of the insular *Dwch* compared to the continental species could also explain the insecticidal properties of the insular trees. Sesamin has a strong allemone-like biological activity, making it useful as a natural industrial insecticide and pest repellent (Phitak *et al*., 2012) showed conclusively that sesamin is the main active principle in the seeds of *Sesamum iindicum* L, a medicinal plant used in Asia for treatment of arthritis, probably by inhibiting the enzyme delta-5-desaturasa in the synthesis of polyunsaturated fatty acids (Phitak *et al.*, 2012).

Among the minor lignans of canelo is the (-) cubenin, a dibenzylbutyrolactone lignin chemically described as 2,3-bis(3,4-methylendioxybenzyl)-

butyrolactone, isolated from the bark. This lignan is known to possess anti-inflammatory (Bastos *et al.*, 2001; Da Silva *et al.*, 2005), analgesic and antimicrobial activities (Da Silva *et al*., 2005; Da Silva Filho *et al.*, 2008). (-) Cubebin was found as an epimer mix, which made it difficult to separate them and obtain their structure. These compounds were described for the first time in this genus. Their structures were elucidated with a simple 1D HNMR method, which allowed their resolution in spite of a complex pattern of overlapping signals (Jeannerat *et al.*, 2009).



Cubebin **Eudesmin** **Sesamin**

Figure No. 6
Structure of lignanes isolated from *Dwch*

Eudesmin is another of the minor lignans isolated from the aerial parts of canelo (Muñoz *et al*., 2015). Its chemical structure is 1,4-bis(3,4-dimethoxyphenyl)-hexahydrofuro[3,4-c]furan.

Eudesmin (Figure No. 6) has important biological functions already described that could help to explain in part the medicinal properties of canelo; in immunological studies, eudesmin inhibits tumor necrosis factor (TNF)-α production and T cell proliferation (Yang *et al.*, 2018). A previous study reported that eudesmin-induced vascular relaxation of rat aorta could be facilitated by the endothelial histamine receptor-mediated release of nitric oxide and prostanoids (Cho *et al.*, 1999). (+)-Eudesmin can also induce neurite outgrowth from PC12 cell neurons by stimulating signaling upstream of the mitogen-activated protein kinase, protein kinase C and protein kinase A pathways (Jiang *et al.*, 2017). Biological studies of this lignin are still underway.

Essential oils

The chemical composition of the essential oils obtained by hydrodistillation of stems, bark and leaves of *Dwch* from continental Chile (Santiago) has been studied for a long time (Barrero *et al.*, 2000); this study used GC/MS and found that most of the compounds were the monoterpenes alpha-pinene (11.9%) and alpha-cubebene (10.1%). A later analysis (Muñoz-Concha *et al.*, 2004) described the variations in the essential oil content of five populations of *Dwch* and one *D. andina* of south-central Chile, including Chiloé Island; this study found significant differences in essential oil content, with means ranging from 0.5 mL 100 g^{-1} for essential oils (Muñoz-Concha *et al.*, 2004) and were considerably greater in the southern populations (0.68 mL 100 g^{-1}). A more recent study with extracts of populations of continental Chile and Chiloé, also using hydrodistillation of bark and leaves, found some quantitative and qualitative differences in the composition of the essential oils (Muñoz *et al.*, 2011); the differences may be due to regional climatic differences such as differences in precipitation, soil types, geographic surroundings, solar radiation, etc. Other reasons have been the resistance of *Dwch* to the attack of insects, fungi and pathogenic agents, given that some essential oils are recognized insecticides and thus varied extracts of bark and leaves of this tree have been tested as a biological insecticide; most of these volatile monoterpene compounds attract or repel insects (Asakawa *et al.*, 1988), show antimicrobial activity and on processes of pain perception (Lunde & Kubo, 2000; Malheiros *et al.*, 2001). This study showed that the essential oils obtained from leaf and stem bark oils of *Dwch* from Chiloé Island (lD) had yields of 0.26% (w/w) and 0.23% (w/w), respectively, whereas yields of 0.05% (w/w) and 0.15% (w/w) were

obtained for the leaves and stem bark oils from continental Chile (Santiago). Sesquiterpene hydrocarbons constituted the main chemical groups in the stem bark oils, with alpha-santalene, trans-beta-bergamotene and curcumenes as the major components. Monoterpenes were the main chemical groups in the leaves of Island plants, with alpha-pinene (23.1 %), beta-pinene (43.6%) and linalool (10.5%) as the main components, whereas sesquiterpenes (germacrene17.6%) and phenylpropanoids (safrole 20.8%) were the most abundant in the leaves of continental plants.

Phytosterols

Plant sterols (phytosterols) and their reduced forms (phytostanols) are bioactive compounds of plant origin widely distributed in nature and thus in plants consumed, whose structure is similar to vertebrate cholesterol in terms of their function (stabilization of the bi-layers of phospholipids in cell walls) and chemical structure (a steroid nucleus with a hydroxyl in C-3, a double bond in C-5,6) and a methyl or ethyl group or extra double bonds, that is alocyclic structures with 28-30 carbon atoms. A chemical analysis of the phytosterols of *Dwch* was published recently (Muñoz *et al*., 2015). It was performed with the unsaponifiables using GC/MS, which found that the main unsaponifiable is β-sitosterol, along with sesamin, phytol and several 18-24 carbons saturated alcohols. β-sitosterol is a common sterol in plants which has acquired special relevance due to its inhibitory effect in benign prostate hyperplasia.

Biological activity

The secondary metabolites of *Dwch* have wide and varied biological activity. The sesquiterpenes are among the most notable for their biological effects, especially those derived from drimane. There are some reviews of the biological activities of these sesquiterpenes which has been isolated from different sources (Jansen & de Groot, 2004; Muñoz *et al.*, 2015). Drimanes have been identified in organisms ranging from fungi to marine sponges. They have also been found in species of the genus *Warburgia*. (Leonard & Viljoen, 2015). The drimane-type sesquiterpenoids have a wide variety of biological activities, including antimicrobial, pungency, antibacterial, antifungal, antifeedant, cytotoxic, molluscicidal, piscicidal, growth regulation and phytotoxic properties (Jansen & de Groot, 2004). The pungency of several drimanes and their irritant properties on the skin (allergies) has also attracted attention (Leonard & Viljoen, 2015). The reactivity of the unsaturated dialdehyde functionality towards biological nucleophiles is considered to be responsible for the antifeedant activity of these compounds (polygodial and epipolygodial) (Jansen & de Groot, 2004).

It will be briefly treat the biological activities of secondary metabolites isolated from canelo.

Cytotoxic activities

Sesquiterpenes with drimane skeletons obtained from stem bark of adult *Dwch* trees collected in the Malleco Province (Chile) were evaluated for cytotoxic activity *in vitro* against cell lines. Also semi-synthetic derivatives were included in this study. The cell lines employed were HT-29, MDA-MB231, DHF, MCF-7, PC-3, DU-145 and CoN. Natural compounds and semisynthetic derivatives were tested. It was determined that polygodial and two semisynthetic derivatives induced changes in mitochondrial membrane permeability in CoN, MCF-7, and PC-3 cells. Polygodial also showed a good apoptotic response against prostate cancer cell cultures. The chemical modifications did not improve significantly the biological activities measured, suggesting that the presence of a dialdehyde was relevant for the apoptotic activity in the cell lines studied (Montenegro *et al*., 2014).

The effects of *Dwch* bark extract (ethyl acetate) and four sesquiterpenes on human melanoma cells were studied. With all treatment of melanoma cells gave significant reduction in cell viability. However, polygodial showed the highest inhibitory growth activity. In addition, an apoptotic response after treatment with drimenol, isordrimenone and polygodial was found. This effect probably involves the reduction of Hsp70 expression and reactive oxygen species production. Alternatively, the inhibition of caspase cascade at bigger concentrations, correlated with additional reactive oxygen species increase, probably switches natural product-induced cell death from apoptosis to necrosis. (Russo *et al*., 2019).

Antimicrobial activities

Fungicidal activity

Saprolegniasis is a pathological condition that affects different stages of freshwater fish farming and involves different species of fungi belonging to the genus *Saprolegnia*. Cells of head kidney of the Atlantic salmon (*Salmo salar*) kidney (ASK-1) were used in a study of this disease. They were incubated

with D. winteri extract (ethyl acetate) and polygodial before exposure to *S. parasitica*. The expression of the immune-related genes interleukin 1β (IL-1β), interferon α (IFNα), and major histocompatibility complex II (MHCII) was evaluated. The extract and pure compound shown immunomodulatory capacities by increasing gene expressions. This immunomodulation related to a mitigatory action counteracting the immunosuppressing effects of fungus. This effect related to a mitigatory action counteracting the immunosuppressing action of *S. parasitica*. These experiments shown, despite that most immune-related genes were up-regulated, the down- regulation of MHCII, characteristic of *S. parasitica* infection, was lessened (Pereira-Torres *et al*., 2016)

The effect of poligodial, a secondary metabolite isolated from canelo, on mycelial growth of different strains of *Botrytis cinerea* was evaluated. The results show that polygodial affects growth of normal and resistant isolates of *B. cinerea* (Carrasco *et al.*, 2017). Furthermore, polygodial markedly decreases the germination of *B. cinerea* (Montenegro *et al.*, 2014). This compound affects the growth of normal and resistant isolates of this fungus. This sesquiterpene also reduces the germination speed of the fungus. This was measured 6 hours after incubation, showing that germination decreased by 92% in the control and by 25% in the presence of 20 ppm polygodial. A study of gene expression confirmed that the effect of polygodial in the fungus may be attributed to inhibition of germination and that appears in the primary stages of fungal development. This same study showed that dimenol, whose structure is similar to that of polygonal, also inhibited the growth of mycelia.

The antifungal activity of drimenol and the derivatives drimenyl acetate, nordrimenone and drimenyl-epoxy-acetate was evaluated on *B. cinerea* growth. All compounds are able to affect *B. cinerea* growth with EC_{50} values of between 80 to 314 ppm. The values obtained suggest that the activity of these compounds would be determined by the double bond between carbons 7 and 8 of the drimane ring. The germination of *B. cinerea* in presence of 40 and 80 ppm of drimenol is reduced almost to 50% of the control value. According with this proposal, a preliminary assessment of the action mechanism for drimenol indicates that drimenol causes membrane damage on *B. cinerea*. (Robles-Kelly *et al*., 2017).

Canelo bark was extracted sequentially with n-hexane, acetone and methanol. The extracts were tested against *Gaeumannomyces graminis* var tritici (Ggt) Ground bark of *D. winteri* was mixed with potato dextrose agar growth medium at different concentrations in Petri dishes. Plates were inoculated in the center with a 5 mm disk of mycelium and incubated at 24 ± 1°C. Radial growth of the mycelium was measured daily to estimate the growth rate and percentage of growth inhibition. A concentration of 978 mg L^{-1} ground bark was necessary to produce 50% inhibition of Ggt growth, while the n-hexane and acetone extracts only required 198 and 234 mg L^{-1}, respectively. The methanol extract only inhibited growth by 33% at the highest concentration. The ground bark and crude extracts inhibited Ggt growth when applied *in vitro*. The n-hexane extract was the most effective in inhibitory growth activity (Zapata *et al*., 2011a).

As the drimane sesquiterpenoid moiety is similar to the first two cycles of lanosterol, then the drimane could also interact with the enzyme 14-alpha demethylase. With this hypothesis, isodrimeninol isolated from barks of *Dwch* was used it as starting material for the hemi-synthesis of four derivatives by oxidation with pyridinium chlorochromate. Antifungal activity assays against *C. albicans, C. glabrata,* and *C. krusei* was studied. Results reveal that the terpenoid show MIC values lower than 200 µg/mL. The antifungal activity of isodrimeninol was rationalized in terms of their capability to inhibit lanosterol 14-alpha demethylase using molecular docking, molecular dynamics simulations, and MM/GBSA binding free energy calculations. In silico analysis revealed that one compound bind to the outermost region of the catalytic site of 14-alpha demethylase and block the entrance of lanosterol to the catalytic pocket. The suggestion that one of them displays a more stable complex with the enzyme is in accord with the inhibitory activity in vitro, where this compound has an IC_{50} value of 75 µg/mL, compared to 125 µg/mL for starting material (Marin *et al*., 2020).

The essential oil of leaves of canelo was obtained and tested against the fungi *Botritys cinerea.* A good activity was observed (Becerra *et al*., 2010).

Hexane extract of *D. winterii (sic*), which was collected in Santa Fe, Argentina, was tested against *Penicillium digitatum*, *Botrytis cinerea*, *Monilinia fructicola* and *Rhizopus stolonifer*. The extract showed significant activity against *M. fructícola* and *R. stolonifer* and displayed moderate growth inhibition of *P. digitatum* and *B. cinerea*. Just polygodial was reported as constituent (Di Liberto *et*

al., 2019).

Quorum-sensing inhibition

In populations of one-celled organisms the individuals do not act independently; they maintain communication known as quorum-sensing. This conduct may explain why some pathogenic bacteria acquire resistance to antibiotics. This mechanism is based on the liberation of signaling molecules called autoinductors that may act on the cell that liberated them and can trigger a genetic response in the entire population. These molecules include acyl-homoserine lactones, oligopeptides, quinotones, cyclic dipeptides and the diffusible signal factor (Monsálvez *et al.*, 2010). Polygodial, drimenol, isodrimeninol and drimenin were inactive against the reporter strain, but cinnamolide and valdiviolide have shown inhibitory activity of QS. Cinnamolide and valdiviolide are αβ unsaturated lactones with the carbonyl in position 12 of the drimane skeleton, whereas drimenin, isodrimenin and isodrimeninol have the carbonyl group at position 11 and are not active. This relationship between structure and activity shows the high specificity of the QS system (Cárcamo *et al.*, 2014).

Polygodial, drimenol and drimendiol are drimane were isolated from *Dwch* and tested on *Chromobacterium violaceum* ATCC 12472, showed that drimendiol is an inhibitor of QS, decreasing violaceine production in *C. violaceum* and decreasing biofilm formation of *Pseudomonas syringae* strains. Consequently, it increased the biocide effects of CuSO4 on biofilms of *P. syringae*. Drimendiol is the first drimane sesquiterpene reported to have QS inhibition activity against *C. violaceum* (Paz *et al*., 2013).

Antiprotozoan activity. Chagas disease

The acetyl acetate extract of canelo bark allowed isolation of four secondary metabolites. All of them together with extract were tested against three evolutive forms (epimastigote, trypomastigote and amastigote) of *Trypanosoma cruzi*. Sesquiterpenoid poligodial was the most active in all (bloodstream trypomastigotes, epimastigotes and intracellular amastigotes) and presented low host toxicity. Also led to important effects on the parasite mitochondrion, including organelle swelling and loss of its membrane potential, together with ROS generation and subsequent lysis of the protozoan (Souza *et al*., 2018).

Cardiovascular effects

Alterations in the normal functioning of the heart and blood vessels are called cardiovascular illnesses. These include coronary cardiopathy (heart attack), cerebrovascular illness (cerebrovascular accident), hypertension, peripheral arteriopathy, rheumatic cardiopathy, congenital cardiopathy and cardiac insufficiency. Hypertension is one of the cardiovascular illness with greatest incidence in the chilean population. Other pathologies such as atherosclerosis, thrombosis and vascular inflammation affect the irrigation of organs and may produce ischemia, hypoxia and necrosis of tissues and organs. Two antagonistic substances called endothelium relaxation factor and concentration factor are produced that maintain vascular tension and the endothelial function. An alteration of the balance of these two substances is produced in hypertension and alterations of hemodynamics.

The vaso-relaxation activity of polygodial isolated from the bark of *D. winteri* was studied *in vitro* on the portal vein of rats previously contracted with various agonists. The sesquiterpene produced antagonism of the contraction caused by bradykinin, endothelin-1, noradrenaline, the stable analogue of thromboxane A2 U46619, substance P, neurokinin B, and senktide (an NK3-selective agonist). Polygodial also produced graded inhibition of the contractile response induced by potassium chloride and by phorbol ester. At the median inhibitory concentration (IC_{50}) level, polygodial was approximately 114- to 177-fold more active in inhibiting mediated contractions than senktide and phorbol ester. Polygodial (01-100 μM) produced concentration-dependent relaxation of the tonic contraction induced by endothelin-1 (5 μM) and by phorbol (3 μM), with maximal inhibition ($E_{(max)}$) of 62 ± 2% and 100%, respectively. Also, polygodial (01-100 μM) inhibited the rhythmic spontaneous contractions of the rat portal vein (E_{max} by 75 ± 2%.) These results strongly suggest that the vasorelaxant actions produced by polygodial in rat portal vein are associated with inhibition of calcium influx through voltage-sensitive channels and interaction with protein kinase C-dependent mechanisms (Cárcamo *et al.*, 2014).

Bronco-relaxation

Inflammation of the lungs produces a common illness called asthma. Persons with asthma develop a chronic inflammatory process in the smallest respiratory pathways, which causes the person to have very sensitive lungs. Environmental factors that are well-

tolerated by a normal person such as pollen, smoke, dust, cold, *etc* cause an intense allergic reaction of these people. This reaction produces the formation of edema in the branchia, increasing the mucous and producing spasms in the lung muscles called bronchospasms. As a consequence, the people who have asthma have difficulty breathing, especially exhaling, which produces an inflammation of the lungs. It has been suggested that there is a relation between asthma and allergies, however not all people who have allergies develop asthma, and not all asthma cases are related to allergies.

Antinociceptive activity

Pain mechanisms have been classified as 'nociceptive', 'peripheral neuropathy' and 'central', and there are both subjective and objective clinical indicators for each. The pain caused by burn, contusion, infection or muscle damage are detected by the nociceptors. These receptors are found in somatic and visceral tissues (El Sayah *et al*., 1998). This property has been extensively studied in Brazilian *D. winteri*.

Just as an example of this kind of studies it can be mentioned that a compound with antinociceptive properties was isolated from a sample of *D. winteri* collected in the state of Santa Catarina, Brazil. An *in vivo* pharmacological study with male Swiss mice showed that drimanial produces complete inhibition of the abdominal contractions produced by acetic acid, with a dose-response relation (Smart *et al.*, 2010).

Receptors interaction

The pharmacological activity of drimenin, cinnamolide, dendocarbin A, and polygodial obteined from the Canelo were determined on hα4β2, hα3β4, and hα7 nicotinic acetylcholine receptors (AChRs) by Ca^{2+} influx measurements. The results established that drimane sesquiterpenoids inhibit AChRs with the following selectivity: hα4β2 > hα3β4>hα7. In the case of hα4β2 AChRs, the following potency rank order was determined (IC_{50}'s in μM): drimenin (0.97 ± 0.35) > cinnamolide (1.57 ± 0.36) > polygodial (62.5 ± 19.9). Dendocarbin A was inactive. Also structure−activity relationship and molecular docking experiments were performed. The Ca^{2+} influx and structural results supported a noncompetitive mechanism of inhibition, where drimenin interacted with luminal and nonluminal (TMD-β2 intrasubunit) sites. The results suggest that the lower the ligand polarity, the higher the inhibitory potency, supported the nonluminal interaction. Ligand binding to both sites might inhibit the hα4β2 AChR by a cooperative mechanism, as shown experimentally (nH > 1). Drimenin could be a start point for the development of more potent inhibitors with higher selectivity for the hα4β2 AChR (Arias *et al*., 2018).

Plaguicidal activity: Insecticidal activity

As *Dwch* seems to be a well-defended plant since it contains a substantial amount of essential oils as well as drimane-type sesquiterpenes (eg drimendiol, isotadeonal, isodrimeninol and polygodial) which possess antibacterial, antifungal, antifeedant and plant growth regulatory properties (Martini *et al.*, 2006; Martini *et al.*, 2007), several studies have been made to test for possible activities against insects.

Polygodial isolated from canelo was used to prepare some derivatives. Thus, polygonone, acetals with propylene and ethylene were synthetized and their antifeedant activity and toxic effects evaluated on several insect species with different feeding ecologies (*Spodoptera littoralis*, *Leptinotarsa decemlineata*, *Myzus persicae* and *Rhopalosiphum padi*). Also it was tested their selective cytotoxic effects on insect-derived (*Spodoptera frugiperda* ovarian Sf9 cells) and mammalian Chinese hamster ovary (CHO) cells. It was suggested that antifeedant activity of these compounds is related to an adduct formation with amino groups on the insect molecular targets for *M. persicae* and *R. padi* but is neither consistent for *L. decemlineata* nor for the cytotoxic effects on insect-derived Sf9 and mammalian CHO cells. (Moreno-Osorio *et al*., 2008)

Using Polygodial, drimenol and confertifolin that were isolated from dichloromethane extract of *Dwch* bark, 15 derivatives were synthetized. All compounds were assessed the potential as antifeedants against insects *Spodoptera frugiperda* and *Epilachna paenulata*. Also, the EC50 of these compounds were used to develop quantitative structure-activity relationships (QSAR). Each compound was tested at 50 μg/cm2 and the results obtained indicated that nine drimanes exhibit moderate to excellent activities against *S. frugiperda*. Among the 18 tested compounds, polygodial, two epoxy derivatives, an α,β unsaturated ketone derivative, were the most active ones. In other lepidopteran larvae, polygodial can block stimulant effects of glucose, sucrose, and inositol on cellular chemoreceptors in insect mouth parts. The antifeedant activity found for the drimanes derivatives suggested that they could act in the same

chemoreceptor of *S. frugiperda*. In other lepidopteran larvae, polygodial can block stimulant effects of glucose, sucrose, and inositol on cellular chemoreceptors in insect mouth parts. The Qsar analysis of the antifeedant activity against *S. frugiperda* and *E. paenulata* determined that the presence of carbonyl groups and epoxide at C-8 and C-9 group within the drimanic skeleton provides selectivity for the bioactivity against each of the tested species. (Montenegro *et al*., 2018)

Drimenol, polygodial, confertifolin and isodrimenin were isolated from the dichloromethane extract of *Dwch* (Winteraceae). In this work polygodial did not show effective antifeedant activity against *Drosophila melanogaster til-til.* The most active compound was isodrimenin which presented a higher larvicidal activity of 4.5 ± 0.8 mg/L. At very low concentrations drimenol, confertifolin, and drimanol displayed antifeedant and larvae growth regulatory activity. The antifeedant results of nordrimanic and drimanic compounds were better in first instar larvae. Thus, EC_{50} value of polygodial was 60.0 ± 4.2 mg/L (Montenegro *et al*., 2013).

Antifeedant and toxic activity of extracts (n-hexane, acetone, methanol:water (80:20) and the drimanes (drimendiol, isodrimeninol, isotadeonal and polygodial) isolated from stem bark of *Dwch* were studied in the Egyptian cotton leafworm *Spodoptera littoralis* (Boisduval) (Lep, Noctuidae) using different bioassays. An n-hexane extract at 5000 ppm and a polygodial at 1000 ppm showed the strongest antifeedant activity against sixth instar larvae when applied to leaf disks in choice and no choice tests (feeding dissuasion index: 75.5% and 94.7% for n-hexane and polygodial, respectively, in the choice test). The nutrition indices were calculated after exposure of LG to the drimanes for 12 h, which resulted in reduced rates of feeding and growth; they were significantly greater with polygodial. To distinguish between the antifeedant and toxic effects, the growth efficiency calculated from the relative consumption values and relative growth rates after 12 additional hours of exposition to non-treated leaf disks of the same larvae exposed in the previous bioassay. The results showed that only polygodial and isodrimeninol had physiological toxic effects. Polygodial was the most potent inhibitor of feeding and growth for *S. littoralis.* (DC_{50} 708 ppm and EC_{50} 198 ppm, respectively) (Zapata *et al*., 2009).

The pea aphid *Acyrthosiphon pisum* (Harris) is a cosmopolitan pest that attacks a wide variety of legume crops and important virus diseases of plants. The essential oils of leaves and bark of *Dwch* were extracted and their dissuasive and insecticidal activities were tested. Both oils were active in choice tests with *A. pisum.* The respective dissuasion indices were 0.87 and 0.46 after 24 h of exposure to 4 µL mL^{-1}. Although spraying fava bean leaves before aphid infestation did not produce mortality, spraying settled aphids with both essential oils produced less than 18% mortality. Application of a dose of 64 µL L^{-1} of air by fumigation to fava plants infested with *A. pisum*; both oils caused 68 and 63% mortality, respectively. Both essential oils showed limited effectiveness, and at high concentrations they are phytotoxic, which does not recommend their use in practice (Zapata *et al*., 2009). Furthermore, the oils evaluated had very strong repellent activity against *T. castaneum* in a field test with filter paper. After 4 h exposition there was 90% repellence activity with *Dwch* at high oil concentrations. It was also shown that the oils are toxic to *T. castaneum* when applied topically or by fumigation. The LD_{50} values for topical application of the oils were from 75 to 85 µg/mg of insect. By fumigation, the LC_{50} values µL/L of air were 90-105 µL/L air for the oils. Also, with oils of 100 µL/L air the LT_{50} values were 61-74 h. In the essential oils extracted from the leaves and bark of *D. winteri* 32 and 16 compounds were identified, respectively. The main constituents in the leaf oil were more diverse, with γ-curcumene (11.12%) as a major compound and then a group of 5 compounds consisting of 6–9%, ie limonene + myrcene, limonene, trans-caryophyllene, α-pinene, sabinene and 4-terpineol. The main constituents in the oil from bark were α-pinene (57.82%) and γ-curcumene (11.22%) and β-pinene + myrcene (7.37%). The essential oils tested were active repellents of *Tribolium castaneum* and also were effective insecticides. Topical application of the extracted oils on *T. castaneum* adults showed median lethal concentrations comparable to those reported previously for the oils of *Elletaria cardamomum* L applied by contact against *S. zeamais* and *T. castaneum*. (Zapata & Smagghe, 2010).

The essential oil isolated from leaves and shoots of *Dwch* was studied for its insecticidal action against *Acanthoscelides obtectus* and *Aegorhinus superciliosus.* The results demonstrated toxicological effects against *A. obtectus.* A concentration of 158.3 µL L^{-1} had a mortality rate of 94% after 24 h exposure. The LC_{50} and LC_{90} values at 24 h were 60.1 and 163.0 µL L^{-1}. Moreover, behavioral bioassays showed a repellent effect

against *A. superciliosus* with a dose of one microliter of CEO. Both sexes of the raspberry weevil stayed for very short times in the treated area with the oil (<0.8 min), showing a homogeneous repellency in the species. The data suggest that canelo leaves and shoots essentials oils have an insecticide effect (Tampe *et al*., 2020).

An n-hexane extract and polygodial isolated from the bark of *Dwch* was evaluated for its capacity to inhibit the settling of the aphid *Nasonovia ribisnigri* Mosley on lettuce leaves; the evaluations used leaf disks with and without choice. The n-hexane extract and polygodial significantly inhibited settling both with and without choice, but its application on lettuce leaves did not produce aphid mortality. The probing behavior of *N ribisnigri* in plants treated with polygodial was evaluated using the electrical penetration graph technique. Polygodial interfered with probing behavior of the aphids, reducing the total exploration time, number of probes and cell punctures. The aphids did not reach the sieve elements of the plants treated with polygodial during the 2-hour access period. The authors suggested in base to tested compounds that they have the potential to be used in the development of lettuce aphid control agents to reduce the risk of virus transmission (Zapata *et al*., 2010).

The grain damage, after 6 days, shows that the grains treated at 0.5%w/w with polygodial or drimenol were attacked less often than grains treated with drimenin, in the following order: polygodial and drimenol 13% and drimenin 80%. This result is in agreement with emergence of new insects compared to the number of insects born respect to the control after 21 days. At same concentration, grains treated with polygodial did not show evidence of insect reproduction such as eggs or offspring of new insects (under microscope). This result was not the same for drimenol, which had the same mortality as polygodial (80%) and the grains have the same feeding damage (13%). Grains treated with drimenol had 7% emergence of new insects. Emergence of insects from grains treated with drimenin is higher, 47% (Paz *et al*., 2018)

The anti-phytopathogenic activity of four drimane compounds (polygodial, drimenol, isonordrimenone, and nordrimenone) was evaluated against bacteria and fungus: *Clavibacter michiganensis* subsp. *michiganensis, Pseudomonas syringae*, *Fusarium oxysporum*, and *Phytophthora spp*. The results show that polygodial affects mycelial growth and powerfully inhibits germination of and *Phytophthora spp* and *Fusarium oxysporum*. Its mechanism of action involves membrane damage. Comparatively, this terpenoid is more effective against bacterial and fungal phytopathogens than nordrimenone. The results show that research on drimane compounds can generate new applications (Montenegro *et al*., 2018).

Herbacidal activity

The n-hexane extract obtained from *D. winteri* bark was tested on the germination and growth of *Convolvulus arvensis, Setaria pumila, Daucus carota* and *Cichorium intybus.* The phytotoxic effects of the extract on the germination of weeds were determined by bioassays in Petri dishes, adding the extract in the middle of germination at concentrations of 100 to 1000 mg L^{-1}. The phytotoxic effects of the extract on emergence and grown of weed seedlings were studied in pots; the extract was applied mixed with the growth medium at concentrations of 500 to 4000 mg kg^{-1}. The phytotoxic effects of the extract were also measured using spraying on weeds at concentrations of 800 to 6400 mg L^{-1}. In the germination tests, the extract retarded germination and decreased the growth of sprouts and radicles of all the weeds; germination decreased in all weeds except for *C. arvensis.* Application of the extract in the growth medium decreased and retarded the appearance of the noxious weeds; plants treated with the extract had lower height and reduced accumulation of biomass. The extract sprayed on the plants retarded the growth of the four species of weeds and decreased their accumulated biomass; plant mortality was observed at the highest concentration for *S. pumila, D. carota* and *C. intybus* (Zapata *et al*., 2011b).

Antioxidant activity

By UHPLC-MS/MS method twelve known aromatics compounds were identified in the extract (70% ethanol at room temperature) of aerial parts of *Dwch*. This study demonstrated the ability to inhibit lipid and protein oxidation in meat of the canelo. The extract significantly decreased lipid oxidation caused by AAPH and it showed a significant decrease in relation to the control group in spontaneous oxidation, even more efficient than BHT. Furthermore, a protective effect on protein structure (SDS−PAGE) can be observed during the incubation when compared to samples incubated with AAPH. Overall, canelo extract showed the best results in terms of protection against lipid and protein oxidation in bovine meat. All results suggested that

phytochemicals from this plant could be promising as active ingredients for antioxidant purposes (Bridi *et al*., 2019)

CONCLUSIONS

In this review, we summarized the phytochemistry and biological activities reported from specie, *Drimys winteri* JR Forst & G Forster var *chilensis* (DC) A Gray. From this review, it can be concluded that main compounds are sesquiterpenes, essential oils and lignanes. Chemical and biological studies are based on essential oils, aerial part, and bark extracts. In most cases the active phytochemicals have not been established although in some research's pure compound have been used.

The use in popular medicine can be explained by the chemical composition supported by measured biological activities. This is the case of anti-inflammatory activity and in the treatment of pain that can be based on the large amount of sesamine isolated in canelo collected in Chiloe. In addition, the wood of this plant has restricted use, for example in the elaboration of tables of dining room this not recommended due its effect piquant o purjent. This effect would be produced by the presence of polygodial and epipoligodial. Other uses of popular medicine could be supported by the presence of drimans whose effects have been studied in plants from other latitudes. Further studies to exploit phytochemical constituents and biological activities from this plant are necessary to develop more potentially value-added products useful in food and pharmaceutical.

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