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Revisión / Review

Past, present and future of *Psoralea glandulosa* Linn, Chilean medicinal plant, an inexhaustible resource: A literature review

[Pasado, presente y futuro de *Psoralea glandulosa* Linn, planta medicinal chilena fuente inagotable de recursos: Una revisión de la literatura]

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Abstract: Culén is the popular term used in Chile for the only endemic species of the Fabaceae family, *Psoralea glandulosa* Linn. It is one of the most widely used medicinal plants in Chile and in some regions of South America, not only as a home remedy, but also recommended by medicine and widely used in the gastronomic industry. Many properties are known, supported by biological tests both *in vitro* and *in vivo*. Because it is so highly appreciated, it is included in the book "Medicamentos Herbarios Tradicionales" (Traditional Herbal Medicines) of the Chilean Ministry of Health. Given the great interest in this plant since time immemorial, this review contains information on its history, popular uses and scientific studies, for a better knowledge, management and sustainable care of this Chilean natural resource.

Keywords: *Psoralea glandulosa*; Medicinal; Mystela; Bakuchiol; Antimicrobial.

Resumen: Culén es el término popular utilizado en Chile para la única especie endémica de la familia Fabaceae, *Psoralea glandulosa* Linn. Se trata de una de las plantas medicinales más utilizadas en Chile y en algunas regiones de Sudamérica, no solamente como remedio curativo casero, sino también recomendada por la medicina y con amplia utilización en la industria gastronómica. De ella se conocen un gran número propiedades avaladas por ensayos biológicos tanto *in vitro* como *in vivo*. Por ser tan apreciada, se encuentra incluida en el libro "Medicamentos Herbarios Tradicionales" del Ministerio de Salud de Chile. Dado el gran interés que despierta esta planta desde tiempos inmemoriales, se recoge en este capítulo la información sobre su historia, usos populares y estudios científicos, para un mejor conocimiento, manejo y cuidado de manera sustentable de este recurso natural chileno.

Palabras clave: *Psoralea glandulosa*; Medicinal; Mistela; Bakuchiol; Antimicrobiano.

INTRODUCTION

Since ancient times, Chilean indigenous peoples have utilized plants as a medicinal source for treating a variety of illnesses. The World Health Organization (WHO, 2003) reported that 71% of the Chilean population relies on traditional medicine to attend to their primary healthcare needs. In 2010, the Chilean Ministry of Health officially recognized 103 plant species, including *Psoralea glandulosa* Linn, commonly referred to as culén, as traditional herbal medicines. This plant is widely used in traditional medicine in Chile, as well as in neighboring countries of Argentina and Peru. The entire plant, particularly its leaves, possesses medicinal properties for treating several ailments. The infusion of leaves was used both internally and externally, as a disinfectant, laxative, anthelmintic, and diuretic, and was suggested for the treatment of diabetes and inflammatory skin disorders.

At present, several compounds have been isolated and identified from *P. glandulosa*, including furanocoumarins, meroterpenes, phenols, fats, resins, and oils. From a biological point of view, the main active components are furanocoumarins and meroterpenes, most of which are found in the leaves of the plant. The bioactivities established for these active metabolites include antioxidant, antibacterial, antifungal, anti-inflammatory, antipyretic and antitumor properties. Positioning culén as an inexhaustible source of resources. The genus *Psoralea* belongs to the *Fabaceae* family, which was first established by Linnaeus in 1742 (Murray, 1894). *Psoralea* is a cosmopolitan genus comprising 105 species, distributed mainly in South Africa, Australia, North and South America (The Plant List, 2013). According to Grimes (1990), there are 8 species distributed throughout South America, among which *Psoralea glandulosa* stands out and is considered endemic to Chile (Riedemann *et al*., 2014). *Psoralea glandulosa* L. is commonly known as "culén", "cule" and "hualhua". It is also known by its Aymara name of "*Wallikaya*" (Girault, 1984). The generic name "Psoralea" derives from the Greek term "Psoraleos", meaning "affected with itching or leprosy" (Koul *et al*., 2019), and the specific "glandulosa" means "with glands or glandular" (Riedemann & Aldunate, 2001).

The species is distributed in Chile from Elqui, in the Coquimbo Region, to Valdivia in the Los Ríos Region, between 25 and 1,500 m.a.s.l. This shrub grows in humid places in valleys and ravines of the foothills, with plenty of sunshine (Montes *et al.*, 1992; Riedemann & Aldunate, 2001). Due to human intervention since the end of the last century, either for direct utilization of leaves, flowers, trunks, and roots (Montes & Wilkomirsky, 1985) or for the clearing of soils for agriculture, its distribution in the valleys has been relegated to growing in isolation or in small groups mainly in meadows and on the banks of watercourses such as estuaries and rivers (San Martín & Muñoz, 2013). However, in Chile in recent years, field cultivation protocols have been successfully developed for this species using seeds, seedlings, and cuttings (Hirzel *et al*., 2004). In other countries such as Argentina and Peru, culén has been cultivated since ancient times for medicinal, ritualistic, and gastronomic purposes (Arenas, 2012).

MATERIAL Y METHODS

Selection

The articles studied correspond to the bibliographic search of titles and/or abstracts that met one or more of the following criteria: literature reporting the chemical characterization or bioactive properties of extracts, resins, oils or other natural products of *Psoralea glandulosa*, including full texts available in English, Spanish or French. Exclusion criteria for the review include articles that do not adjust to the methodological guidelines for the conduct of biological assays (e.g., absence of positive control) or did not provide a correct identification of the species. The search was performed in the following databases: Google Scholar, Scielo, Science Direct and Pubmed. In addition, books were used as resources to gather information.

Keywords searched

"Psolarea", "glandulosa", "culén" "essential oil", "extracts", "resinous exudate", "chemical composition", "bioactivity", "activity", "medicinal", "prehispanic", combined in pairs using the Boolean operator "and".

Time period

Literature available in the databases used updated as of September 2023.

RESULTS

Description

Culén (syn. *Otholobium glandulosum* (L.) J.W. Grimes) occurs as a deciduous shrub or sapling in winter, which has a subway evergreen and semi-woody root, as shown in Figure No. 1. It reaches up to 6 m in height, with a trunk up to 3 m in diameter, presenting a dark brown and scratched trunk and its branches are thin and erect.

While its leaves are pleasant-smelling, petiolate, composed of lanceolate leaflets, and pointed-glandular in shape (Hoffmann *et al.*, 1992), see Figure No. 2. This last characteristic is since this shrub has glandular trichomes that cover the surface of the leaves and shoots, producing a protective resin (Riedemann & Aldunate, 2001). This biosynthesized resin in the trichomes plays an important role for plants such as culén (Modak *et al*., 2011), as it acts as a barrier against various external factors, such as herbivores and pathogens, UV-B radiation, extreme temperatures, and excessive water loss (Valkama *et al*., 2004). Culén blooms in late spring and its flowers are gathered in elongated racemes 10 to 15 cm long, axillary and terminal; with a pale blue corolla with a whitish base, typically papilionate formed by a banner, two wings and a keel, androceous with 9 stamens united and one free; gynoecium with monocarpellar ovary, see Figure No. 3. The fruit is a dry, monocarpellar (bearing a single seed), dicotyledonous legume or pod, measuring 6 to 7 mm (Hoffmann *et al*., 1992).

Figure No. 1
Leaves of *P. glandulosa*

Traditional and modern uses

It has long been used in folklore and in the indigenous medicine system. Several culén by-products are successfully marketed and are in the popular markets of Argentina, Bolivia, Peru, and Chile. The use of this shrub is dated from time

immemorial, proof of that is that culén takes its name from the Mapuche ethnic group, which was widely used by this native people of South America before the arrival of the European conquerors in Chile (Farga *et al*., 1988). Once the Spaniards settled in the indigenous territory, this shrub attracted their attention because the Mapuches consumed it as a refreshing drink at any time of the day, which is why they baptized culén as the "indigenous tea of Chile" due to the recurrence and popularity of its consumption, the way culén leaves were prepared as an infusion, and its fresh, aromatic, slightly fruity and with astringent flavor.

Figure No. 2
Leaves of *P. glandulosa*

Another name given at that time was "albaquilla" because of its similarity to the basil of Europe with respect to the shape and form of the leaves, although different in aroma and flavor (Hoffmann *et al*., 1992). On the other hand, in times of the Spanish conquest, culén enjoyed popularity not only for its character of refreshing drink, but also as a capillary refreshing, since its green leaves were placed inside the hats or helmets used at the time, Moreover, we can assume that the leaves were used as a kind of insipient sunblock, since the chronicles mention that it prevented the worst sunburns (Farga *et al*., 1988). In this period of Chilean history, culén was also used in the midst of the Indigenous-Spanish war, chroniclers as Ovalle and Rosales reported that was used as a vulnerary, that is, to wash wounds and sores resulting from the fighting between the two sides, for this objective, they washed the wound with the infusion of leaves and then on the wound made a compress with the warm leaves used in the infusion,

which were renewed the next day, this process allowed them to avoid infections. This process was complemented by using ground dry leaves of culén, which were sprinkled on the wound in question to dry and cover the wound (Ovalle, 1969; Rosales, 1989). As mentioned above, culén has been one of the medicinal herb par excellences since pre-colonial times, perpetuating its use generation after generation. As stated by de Möesbach at the beginning of the 20th century, culén is "a whole apothecary supplied by the Creator" (de Möesbach, 1992).

Figure No. 3
Flowers of *P. glandulosa*

In this context, one of the longest documented medicinal properties of culén is its use in the treatment of hemorrhoids or piles (Plath, 2009). The treatment consisted of constant washing with the cooked water of its leaves, in the case of internal hemorrhoids, otherwise, if these were exposed (external hemorrhoids) the solution was to perform sitz baths with powdered culén leaves (Vicuña Mackenna, 1974). The protocol consisted of mixing the leaves with 2 liters of water and letting it boil for more than 12 minutes. When the mixture was lukewarm, it was to be strained and placed in a bucket or a large container. Then, the patient should sit on the container, without underwear, for 20 minutes. This home treatment should be repeated for at least 5 days to achieve the desired effect (Mayo Clinic, 2021). It should be noted that this procedure is still used at home in Latin America, both with corns

and other medicinal plants with analgesic and anti-inflammatory properties that help relieve pain in a few minutes, such as: chamomile (*Matricaria recutita* L.), lavender (*Lavandula angustifolia* Mill.), horse chestnut (*Aesculus hippocastanum* L.), arnica (*Arnica montana* L.) and witch hazel (*Hamamelis virginiana* L.).

Another property attributed to the infusion of culén leaves (1 tablespoon of leaves per 1 liter of freshly boiled water) is to eliminate intestinal parasites, especially worms, in doses of one cup three times a day (Minsal, 2010). If the preparation is increased to a proportion of 2 tablespoons per liter of water, the infusion acts as a sudorific and emollient (i.e., it softens and softens tumors and hardnesses) (Rozzi, 1984). On the other hand, the teiform infusion mixed with orocoipo leaves (*Myoschilos oblongum* Ruiz & Pav) is prescribed for cases of chills and general malaise (Rozzi, 1984). The infusion made with the ashes of the shoots of ~~the~~ culén, is used as a purgative, stomach problems and serves for gastric ulcers, in the same proportions given for the leaves (Farga *et al.,* 1988). It should be noted that both the bark and root have the same properties as the leaves in cases of indigestion, diarrhea, dysentery and general stomach pains (Minsal, 2010), however, popular culture gives the protective resin or resinous exudate, which protects the bark of the branches the ability to heal and heal wounds, through the preparation of ointments based on it (Farga *et al*., 1988); for the root on the other hand, when preparing an infusion of 2 tablespoons per liter of boiled water, it was attributed an exclusive property of causing vomiting (Rozzi, 1984). A controversial property named and emphasized by Chilean arbolaria texts is the ability to lower blood sugar or antidiabetic plant (Farga *et al.*, 1988; de Möesbach, 1992). The protocol described for the treatment of diabetes consists of preparing 5 tablespoons of culén buds or shoots in a liter and a half of water, boiling the mixture and reducing the liquid by half and filter the solution, consuming several cups a day for a period of 2 weeks. Alternatively, boil a spoonful of peeled branches in a liter of water for 10 minutes, and drink this amount of decoction during the day, repeating the process for 2 weeks (Rozzi, 1984).

There is another medicinal property attributed to culén, which refers to the treatment of indigestion ("empacho"). This pathology is part of the history of Latin American folk medicine where its first reports date back to the sixteenth century and remains to this day (Campos-Navarro & Coronado, 2009), empacho in simple terms is defined as a disorder of the digestive tract caused by excessive eating and the ingestion of indigestible products that cause alterations of the gastrointestinal transit (Campos-Navarro, 2016). Treatments related to empacho are usually performed by mothers of families, and in more complicated or serious cases by healers, existing throughout Spanish America specialists known as "medidores o quebradores de empacho" (empacho measurers or empacho breakers). The treatment is based on dislodging and cleaning the digestive tract in any of its sections. Culén is used in Chile to combat empacho because this shrub acts at the digestive level as a soothing and evacuating (Cuadernos de Historia de la Salud Pública, 2007). The procedure in Chile to break the empacho, according to Baeza (1930), consisted approximately in scraping the bark of culén branches, which were boiled with water and salt, making the patient take a good amount of the decoction, they rubbed his belly, then they put him face down, they took him with both hands of the skin in the lumbar region, they loaded him with a knee and, when by the efforts that the healer made, that region sounded, the operation was finished, with which the "empacho" was "broken".

On the other hand, from a culinary point of view, it is appreciated for two popular beverages such as the refreshing "culén aloja" and "mistela" or better known as "culén punch". Culén aloja (the most named preparation in ancient texts) (Pardo & Pizarro, 2013) at the beginning of the Chilean tradition was prepared by boiling water with branches of culén; to which little sugar was added and could finally be with or without brandy. Later recipes indicate that it was made with culén and "Guindo" (*Nothofagus betuloides* (Mirb.) Oerst.) stick scrapings, plus a little of quinine. This was left to macerate and was simmered with corn and sugar. Once ready, the liquid was strained and cinnamon sticks and cloves were added, leaving it to rest together with a few grains of toasted corn. This is a glimpse of the history of the punch (Cocinarte Chile. 2011). Culén punch, which is served cold, is prepared by soaking the branches of the bush in hot water. After about 20 minutes, the branches are peeled and boiled in 3 liters of water with cloves, cinnamon and sugar. The mixture is then boiled for 30 minutes, cooled, strained and mixed with schnapps. Finally, the mixture is bottled in glass bottles and stored in the dark (Memoria Campesina, 2016). Other uses described for this plant, but less known are its application in the arts, since the superficial resin of its branches was used to wax the

thread by cordoneros (Murillo, 1861). And from a ritualistic point of view of the indigenous tradition of the Mocovíes, native people of Argentina, used the decoction of culén leaves "for the purification of the blood and chest" (Arenas, 2012).

Phytochemistry

Culén has been investigated since the beginning of the 20th century. In the 1930s, a preliminary study was carried out in which the bark and leaves of culén were investigated by means of a decoction in distilled water, to which a basic phytochemical screening was applied in which mucilaginous substances, tannins and saponins were characterized. Subsequently, with a distillation of the leaves of culén and the extraction with ether and chloroform (in equal parts), it was estimated that the extracts could contain essential oils, volatile alkaloids, bitter substances, fats, waxes and resins. The resin and essential oil obtained were studied without any conclusive data (Alcoholado, 1932).

Erazo *et al*. (1990), carried out a study on culén leaves obtained in the vicinity of the city of Santiago, Chile. For this purpose, dried and ground leaves were used, which were extracted with petroleum ether. The ethereal extract was subjected to a chromatographic process and four major compounds plus two groups of compounds identified as triglycerides and fatty acids were identified by means of spectroscopic techniques. The major compounds, ordered from the highest to the lowest presence in the culén leaves, were: bakuchiol (**1**), angelicin (**2**), drupanin methylester (**3**) and psoralen (**4**), which are illustrated in Figure No. 4.

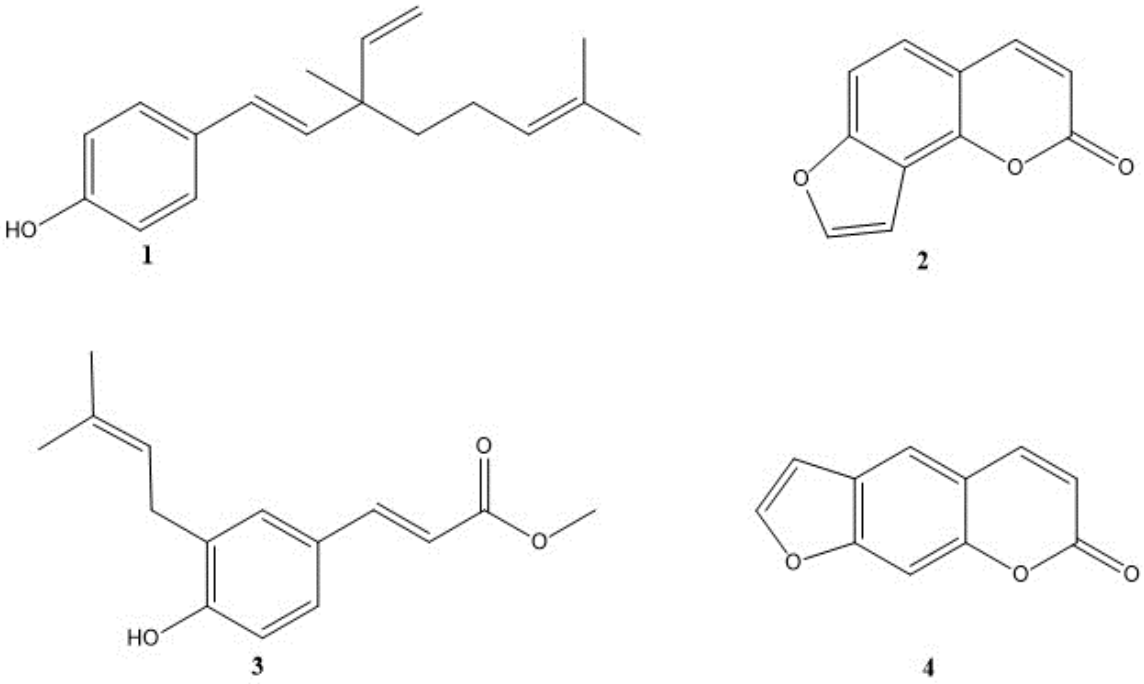

Figure No. 4
First secondary metabolites isolated from *P. glandulosa*

Subsequently, thanks to the detailed and extensive chemical research of the species in Chile, new secondary metabolites were identified and characterized. In a study developed by Backhouse *et al*. (1995), two new meroterpenes with cyclic characteristics were obtained from the dichloromethane extract of culén leaves, cyclobakuchiol A (**5**) and cyclobakuchiol B (**6**), which are illustrated in Figure No. 5.

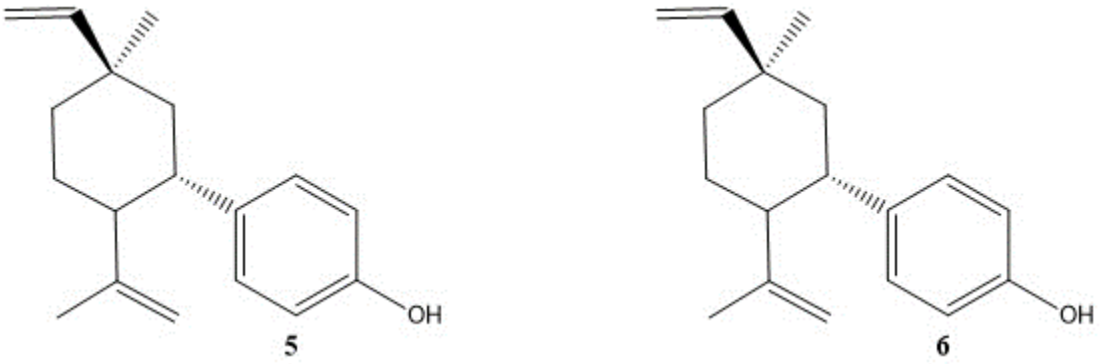

Figure No. 5
Cyclic meroterpenes isolated from *P. glandulosa*

The is following year Labbé *et al*. (1996), determined 4 new structures of terpenic nature from the methanol extract of culén leaves. These compounds were 3-hydroxybakuchiol (**7**), 12,13-dihydro-12,13-epoxybakuchiol (**8**), 12-hydroxyisobakuchiol (**9**) and Δ3-2-hydroxybakuchiol (**10**), which are illustrated in Figure No. 6.

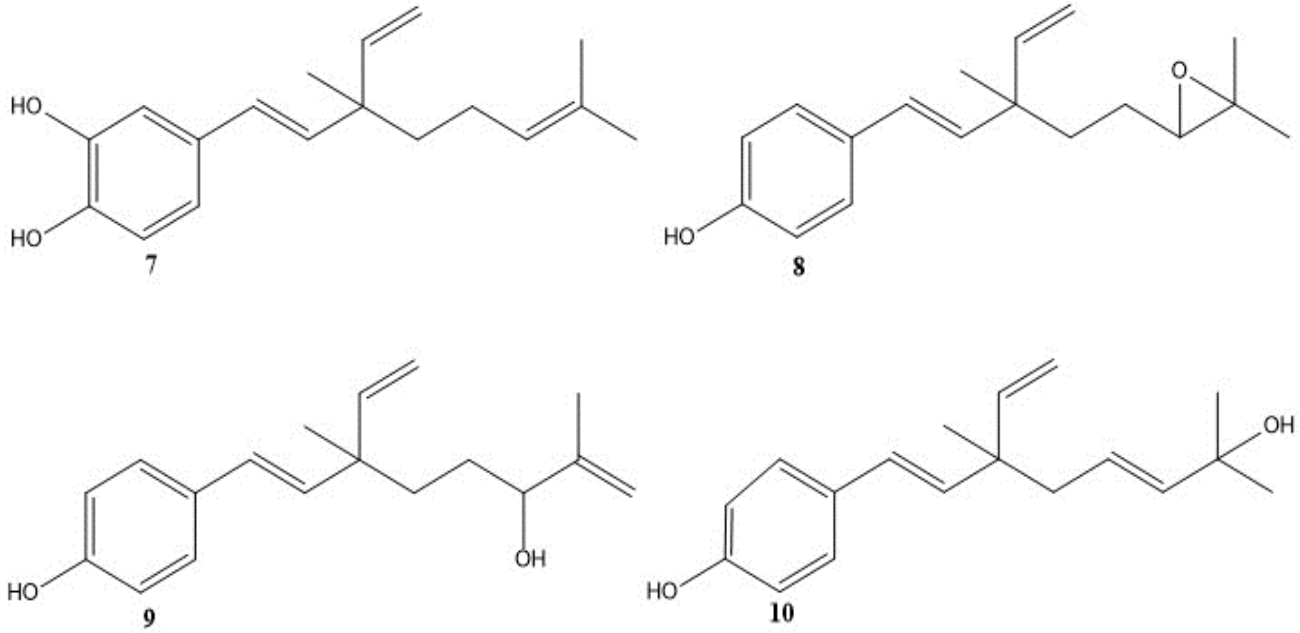

Figure No. 6
Meroterpenes derived from bakuchiol isolated from culén

In the following decade, for the first time, the chemical composition of the protective resin of the culén leaves collected in the locality of Lo Orozco, Casablanca, Valparaíso Region, Chile was studied for the first time, identifying meroterpenes **1**, **7** and **9**, plus a new diterpene called Kuchiol (**11**) (Madrid *et al*., 2013), which is illustrated in Figure No. 7.

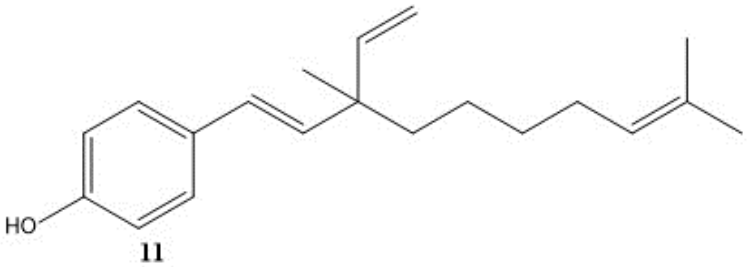

Figure No. 7
Diterpene isolated from the resinous exudate of *P. glandulosa*

On the other hand, Becerra *et al.* (2010), reported the chemical composition of the essential oil obtained by hydrodistillation from fresh leaves of culén collected in the Bio-Bio Region, Chile. This oil contained hydrocarbons, terpenes, and phenols. These include the following metabolites: caryophyllene (**12**), naphthalene (**13**), ledol (**14**), phytol (**15**), octadecane (**16**) and eicosane (**17**), which are illustrated in Figure No. 8.

The literature review reveals the presence of a total of 17 identified metabolites, including volatile compounds, present in the essential oil of culén leaves. These compounds have been classified into furanocoumarins, phenols, sesquiterpenes, diterpenes, hydrocarbons and mostly meroterpenes. Among them, the active compound that predominates in all parts of the plant is bakuchiol (**1**), a meroterpene that is present in different species of *Psoralea* and which is characterized by a series of potent biological activities (Koul *et al.*, 2019).

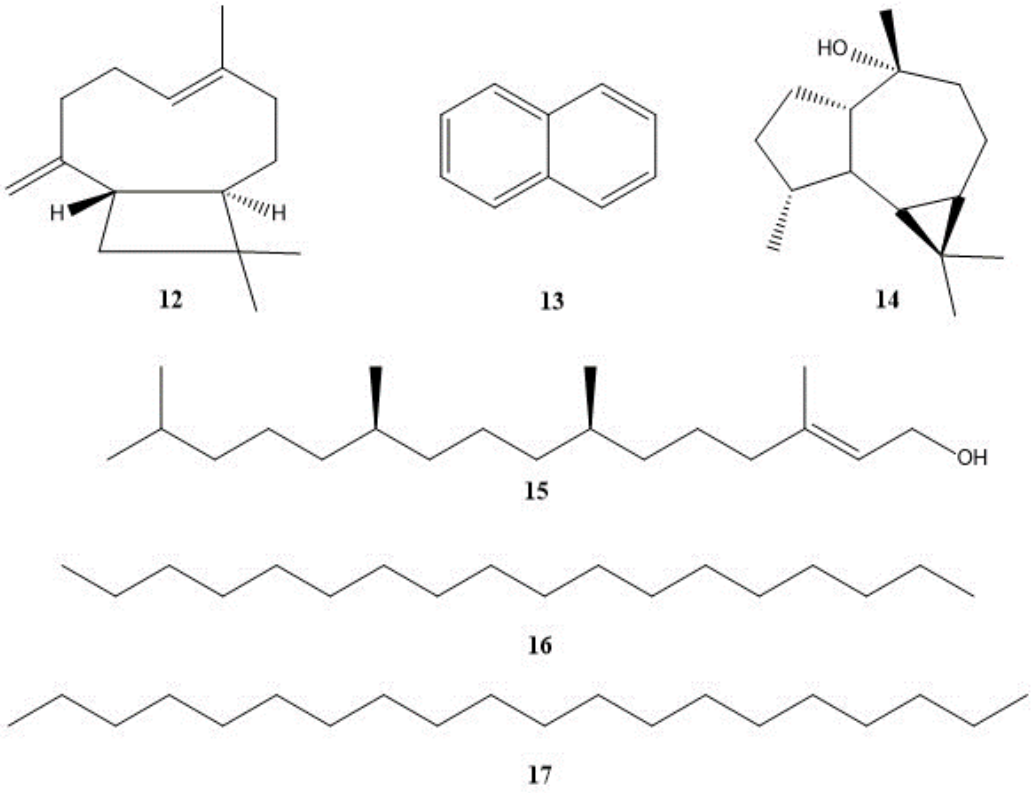

Figure No. 8
Metabolites identified in the essential oil of *P. glandulosa*

Pharmacological activities

The culén medicinal shrub has received enormous attention over the years due to its bioactive principles that possess remarkable pharmaceutical properties.

Antibacterial activity

The antibacterial activity of extracts (successive extraction with petroleum ether, dichloromethane and methanol) of culén leaves was reported by Erazo *et al*. (1997). The results of this study indicated that the petroleum ether extract was the most active and only showed activity against Gram-positive bacteria with minimum inhibitory concentration (MIC) values of 12.5 µg/mL for *Staphylococcus aureus, S. epidermis, Micrococcus flavus* and 25.0 µg/mL for *Bacillus pumilus*. In addition, it was demonstrated that the activity of this extract is largely due to the presence of bakuchiol (**1**), the most abundant metabolite of the plant, which showed a strong antibacterial activity against Gram-positive bacteria with MIC values of 5-10 µg/mL and very low activity against Gram-negative bacteria with MIC values of >100 µg/mL for *Escherichia coli* and *Pseudomonas aeruginosa*.

Anti-inflammatory activity

The activity was evaluated on petroleum ether, dichloromethane, and methanol extracts of the aerial parts of culén. The petroleum ether extract was found to be more active, which was fractionated to obtain compounds **1**, **4**, **5** and **6**. It was demonstrated that the activity was given by bakuchiol (**1**), which inhibits degranulation in human neutrophils and decreases cell migration, eicosanoid levels and myeloperoxidase activity in mice. In addition, compounds **5** and **6** were shown to increase anti-inflammatory activity by nearly 15% over their biogenetic precursor **1**, due to their cyclic nature, thus confirming the anti-inflammatory potential of this shrub (Backhouse *et al.,* 2001).

Antipyretic activity

Rabbits were used as animal model and *Escherichia coli* endotoxin (13 ng/kg) as pyrogen, petroleum ether, dichloromethane and methanol extracts of the aerial parts of culén were reported to possess antipyretic activity. The antipyretic effect (21.7%) of the petroleum ether extract was due to the compound bakuchiol present in the extract. The maximum antipyretic effect (68%) was observed at a dose of 17 mg/kg (Backhouse *et al*., 2001), supporting the febrifuge effect reported for this shrub.

Antifungal activity

Madrid *et al*. (2012a), conducted a study in which the *in vitro* antifungal activity of bakuchiol (**1**) and 3-hydroxybakuchiol (**7**) obtained from the resinous exudate of the aerial parts of culén was evaluated, showing MIC80 ranging from 4-16 and 0.125-16 µg/mL respectively, against various clinical isolates of *Candida* spp. strains. The overall results obtained from this investigation provided important information for the potential application of culén in the therapy of severe infections and skin diseases caused by clinical yeasts, thus confirming the anti-yeast potential of this shrub.

In a subsequent study carried out on culén leaves, the inhibitory effect of the resin and the isolated compounds bakuchiol (**1**), psoralen (**4**), 3-hydroxybakuchiol (**7**) and 12-hydroxysobakuchiol (**9**) on the mycelial growth of the phytopathogens *Botrytis cinerea* Pers: Fr. and *Phytophthora cinnamomi* Rands was evaluated *in vitro*. The resinous exudate inhibited the mycelial growth of both pathogens, while **1** showed an inhibitory effect on mycelial growth of *B. cinerea* of up to 94% at a concentration of 150 mg/L and 4 reduced mycelial growth of *P. cinnamomi* up to 80% at a concentration of 150 mg/L. The resin and the analyzed compounds demonstrated the ability to block the development of mycelial growth and can be used as potential biopesticides in the agricultural sector (Madrid *et al.,* 2014), further supporting the antimicrobial capacity reported for this shrub.

Antioxidant activity

The first study was carried out by preparing sequential extracts of increasing polarity (n-hexane, dichloromethane, ethyl acetate and ethanol) from the leaves, stems, bark and root of culén. Subsequently, the antioxidant activity of the different extracts was evaluated by *in vitro* DPPH·, H_2O_2, iron reducing power III (FRAP) and total antioxidant capacity (TRAP) assays. Of the extracts tested only the leaf extracts expressed very strong scavenging activity, reducing the DPPH· radical (IC_{50} = 1.00 mg/mL to 1.61 mg/mL) and neutralizing H_2O_2 (IC_{50} = 34.29 mg/mL to 64.87 mg/mL). Likewise, the dichloromethane extract of the leaves showed a remarkable FRAP (2.71 mM) and TRAP (1.19 mM). The results suggest a strong antioxidant potential of dichloromethane and ethyl acetate extracts of culén leaves would be partially explained by the levels of phenolic compounds (1.65 mg GAE/g dry extract) and flavonoids (55.34 mg QE/g dry extract) respectively (Madrid *et al*., 2012b). In a subsequent

study, the antioxidant activity of the resinous exudate and its major compounds (**1**, **7**, **9** and **11**) was evaluated by three antioxidant methods DPPH·, FRAP and TRAP. The results obtained from these assays led to the following conclusion: compound 7 possesses potent antioxidant activity compared to the control compounds (hydroxybutylanisole (BHA) and α-tocopherol) antioxidants used in the food industry. The antioxidant activities of the compounds decrease as follows **7** > resin > **1** > **11** > BHA > α-tocopherol > **9** (Madrid *et al.*, 2013).

Anticancer activity

Culén, through a series of studies, has been shown to possess unique bioactive compounds with anticancer properties. In this field, the only study conducted to date was carried out on A2058 melanoma cells using the resinous exudate of culén, demonstrating in this study that it can inhibit the growth of cancer cells after 48 h of treatment. These experiments confirmed the anticancer potential of culén, which can be attributed to the presence of bakuchiol, 3-hydroxy-bakuchiol and 12-hydroxy-isobakuchiol (Madrid *et al*., 2015).

Toxicity

To date, only the toxicity test on *Artemia salina* conducted by Erazo *et al*. (1997), has been reported. In this study, the toxicity of extracts of (petroleum ether, dichloromethane, and methanol) culén leaves and bakuchiol (**1**) was evaluated, which showed a mean lethal dose LD_{50} ranging from <10 to 500 µg/mL and <2 µg/mL, respectively. After 24 hours of the test, the small crustaceans had lost their motility and were assumed dead, however, when transferred to pure seawater, the crustaceans moved and swam again, suggesting that the effects exerted by bakuchiol only affected the motility of the crustaceans, but this effect was not lethal.

CONCLUSIONS

The medicinal culén shrub (*Psoralea glandulosa*) has great potential to cure various diseases. Although preclinical studies have yielded promising results, further studies are needed to explore in depth the molecular mechanisms responsible for the above pharmacological activities and to test the efficacy of the isolated metabolites. In addition, long-term toxicity studies and drug interaction data are also needed to establish the safety profile of the extracts before initiating clinical trials. In conclusion, culén is a promising species for further research from a phytochemical (flowers, fruits, and roots), pharmacological (antibacterial, anticancer, and antiviral), silvoagricultural (antioomycetes, herbicide and insecticide) and industrial (development of products and commercial crops), so its conservation is key to keep alive the cultural tradition of this Chilean medicinal plant.

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