# A review of the traditional uses, phytochemical compounds, and pharmacological activities of *Vallesia glabra* (Cav.) Link (Apocynaceae)

José G. Gavidia-Valencia, Alejandrina M. Llaure-Mora, Edmundo A. Venegas-Casanova, Luz A. Suárez-Rebaza Felipe R. Rubio-López, Maritza Rodrigo-Villanueva, Rainer W. Bussmann and Mayar L. Ganoza-Yupanqui

**Correspondence**

**José G. Gavidia-Valencia[1], Alejandrina M. Llaure-Mora[2], Edmundo A. Venegas-Casanova[3], Luz A. Suárez-Rebaza[2,3], Felipe R. Rubio-López[3], Maritza Rodrigo-Villanueva[3], Rainer W. Bussmann[4,5] and Mayar L. Ganoza-Yupanqui[2]***

[1]Departamento de Bioquímica, Facultad de Farmacia y Bioquímica, Universidad Nacional de Trujillo, Trujillo 13011, Perú.
[2]Grupo de Control de Calidad de Plantas Medicinales, Facultad de Farmacia y Bioquímica, Universidad Nacional de Trujillo, Trujillo 13011, Perú.
[3]Departamento de Farmacotecnia, Facultad de Farmacia y Bioquímica, Universidad Nacional de Trujillo, Trujillo 13011, Perú.
[4]Department of Botany, State Museum of Natural History Karlsruhe, 76133 Karlsruhe, Germany.
[5]Department of Ethnobotany, Institute of Botany, Ilia State University, 0105 Tbilisi, Georgia.

*Corresponding Author: mganoza@unitru.edu.pe

**Ethnobotany Research and Applications 24:27 (2022)**

## Review

## Abstract

*Background*: *Vallesia glabra* (Cav.) Link (Apocynaceae) is traditionally used in dermatological infections and as a desinflammatory. This review aims to collect information on its traditional uses, phytochemical compounds, and pharmacological activities.

*Methods*: The scientific literature was searched in the databases Scopus, Web of Science, Alicia Repository, ScienceDirect and PubMed Central; 38 documents were selected (26 original articles, 2 review articles, 4 books and 2 theses) from 1939 to 2022.

*Results*: *V. glabra* is traditionally used for pain relief, in infections and inflammations, and as an antifungal. Seventeen indole alkaloids of *V. glabra* have been identified, several of these alkaloids present important pharmacological activities as antimalarial and bactericidal agents demonstrated in *in vitro* assays.

*Conclusions*: The traditional use of *V. glabra* in infections has been pharmacologically demonstrated in *in vitro* assays, being the terpenoid indole alkaloids, which confer the activity.

*Keywords*: Traditional uses, phytochemical compounds, pharmacological activities, *Vallesia glabra*.

Manuscript received: 16/10/2022 – Revised manuscript received: 24/10/2022 - Published: 24/10/2022
http://dx.doi.org/10.32859/era.24.27.1-15

## Background

Apocynaceae comprises tropical plants with approximately more than 5500 species, distributed in 410 genera (Van Beek *et al.* 1984). The genera of this family are characterized by being a source of alkaloids, triterpenoids and cardenolics, with valuable pharmacological activities. Some of the reported genera are *Alstonia, Catharanthus, Kopsia, Rauvolfia, Vallesia*, among others (Bhadane *et al.* 2018, Bussmann & Sharon 2006, Van Beek *et al.* 1984). Among the 19 species that genus has got *Vallesia* Ruiz & Pavon is found *Vallesia glabra* (Cav.) Link. (Fig. 1).


Figure 1. *Vallesia glabra* (Cav.) Link (Apocynaceae), Peru (Photo: Bussmann, Herbarium specimen).

This species grows wild along the coast, in arid and semi-arid soils between 0 to 1000 masl reaching approximately 5 m in height (Bussmann & Sharon 2016, López 1954, Muriel 2008). It is known as a water indicator plant, it contributes to stop the advance of deserts and dry forests, because it has tolerance to water stress (Arhuire Ossio 2020). It is distributed in the coastal areas of several Latin American countries, from Mexico (Lower California) to Northern Argentina, being reported in the USA, Cuba, Colombia, Jamaica, Ecuador, Peru, Paraguay, Bolivia, and Argentina (Fig. 2) (Castañeda 2018).

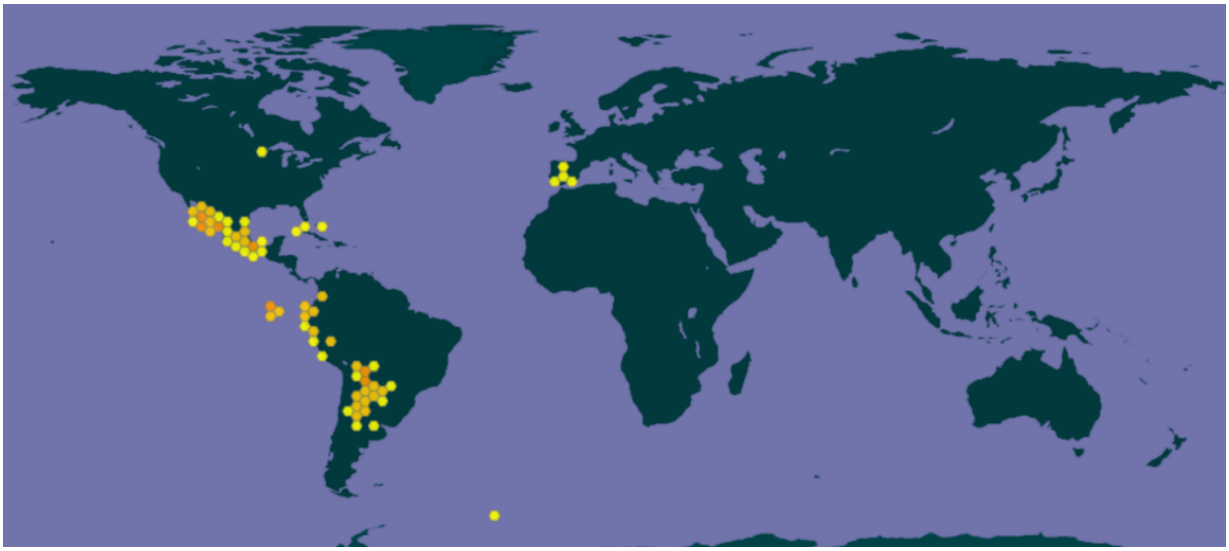

Figure 2. Geographic distribution of *Vallesia glabra* (Cav.) Link in the world (Photo: Global Biodiversity Information Facility).

*V. glabra* is known to have several common names, these depend on the locality, region, and Country. In Argentina it is known as samañic, ancoche, ancochi, ancuchi, coquillo, tetilla or teta de gata. In Bolivia with the name of marguillo, leche leche, mataco, chulu chulu, arakuarembiu. In Mexico as otatabe, citabaro, huevito citabaro, tonóopa, timóopa, palo verde, cacarahue, frutilla, huelatave, huevito, otátave, sitavaro. In Peru as perlillo, cun-con, cuncún, cuncush or calato, cuncuno, cun cun (Castañeda 2018).

Six synonymies have been reported for *V. glabra* among them *Vallesia cymbifolia* Ortega, *Vallesia chiococcoides* Kunt, *Vallesia pubescens* Andersson, *Vallesia glabra* var. pubescens (Andersson) Wiggins, *Vallesia dichotoma* Ruiz & Pav., *Rauwolfia glabra* Cav. (Castañeda 2018).

*V. glabra* is a shrub with a slender, straight, and rough stem. The seed is ovoid with a longitudinal groove 6 to 8 mm long, 2.5 to 3 mm in diameter and varies in color from light brown to whitish. The leaf is lanceolate in shape, 8 cm long and 2 cm wide; it has a small petiole of 5-8 mm, its stipules are small and triangular, their color varies from dark green to emerald green and they do not present hairs on any face. The flowers are hermaphrodite, tubular in shape and with a stellate edge. The calyx has 5 short, oval, and triangular sepals, without glands at the base; the coralline tube is 3 to 5 mm long, widened at the base and in the region of the stamens, external glabrous and internal pubescence. It has a bicarpel gynoecium, bilocular ovary and 4 ovules in each locule. It is small, odorless, and greenish white. The fruit is translucent pearl-colored, oblong-shaped drupes measuring 2.54 cm long and containing 1-2 seeds (Fig. 3, Fig. 4, Fig. 5) (Castañeda 2018, Ezcurra 1981, Guadalupe & Albornoz 2013, Mora-Costilla *et al.* 2020).

In traditional medicine, *V. glabra* is known to possess healing properties in inflammation, diabetes, pain, stomach discomfort, and infections (Castañeda 2018, Mostacero & Fukushima 2005). Its biocidal capacity makes it an excellent alternative against dermatological infections and pests that attack plant species as in the case of potato (Castañeda 2018). The properties vary according to the country or region where they are located, for example, the Isoceño-Guaraní people (Bolivia) use "cuncuno" as an anti-inflammatory and in Mexico it is used against rheumatic pain (Bourdy *et al.* 2004, Dimayuga *et al.* 1998). In Peru consumption of the decoction of the leaves with 10 "fuque" seeds is used in cases of snakebite and drinking the extract of the leaves is used to treat diabetes (Bussmann & Sharon 2016).

This review aims to organize the scientific information of the traditional uses, pharmacological activities and phytochemical compounds involved of *Vallesia glabra* (Cav.) Link.

Figure 3. *Vallesia glabra* (Cav.) Link (Apocynaceae), Peru (Photo: Bussmann).

Figure 4. *Vallesia glabra* (Cav.) Link (Apocynaceae), Peru (Photo: Bussmann).


Figure 5. Morphology of *Vallesia glabra* (Cav.) Link (Apocynaceae).

## Materials and Methods

Documents reported from 1939 to 2022 were considered, *Vallesia glabra* and its synonymies were used as search terms in 5 databases. Duplicate documents were eliminated, registering 38 documents including original articles, review articles, books, and theses (Fig. 6).

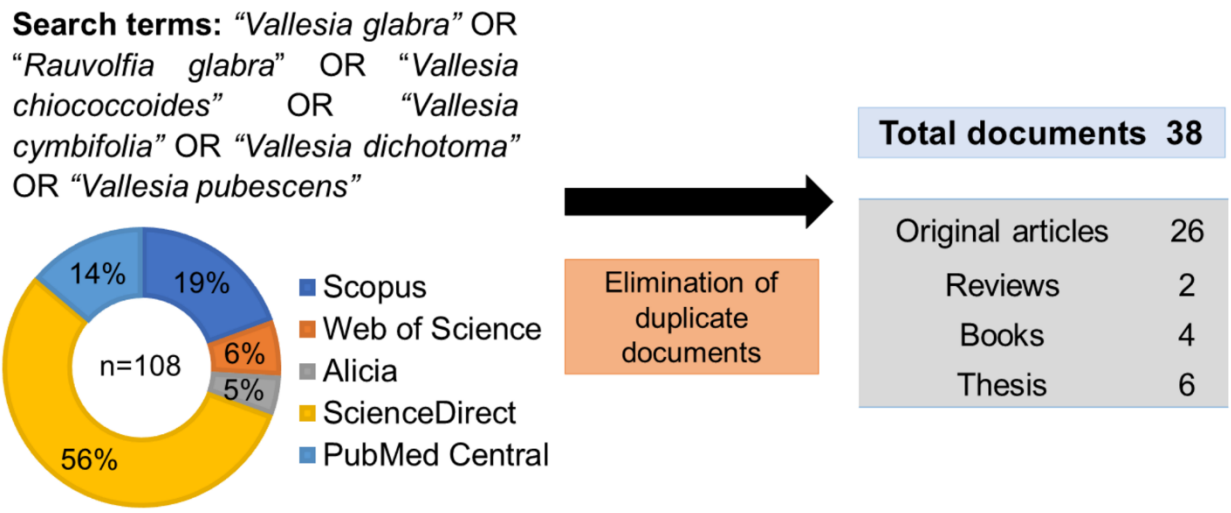


Figure 6. Information search scheme of *Vallesia glabra*.

## Results and Discussion

### Traditional uses

*V. glabra* is used in different Latin American countries mainly for its anti-inflammatory and anti-infectious capacity (Castañeda 2018). It is known by different vernacular names, such as "cuncuno", "otatabe", "ancoche", among others (Table 1).

Table 1. Traditional medicinal uses of *Vallesia glabra* in Latin American countries.

| Country | Vernacular name | Traditional use | Plant part | Way of use | Reference |
|---|---|---|---|---|---|
| Argentina | Samañic | Anti-acne and against pimples | Fruit | Skin wash | (Martínez & Barboza 2010) |
| | Ancoche, ancochi, ancuchi, coquillo, tetilla, teta de gata | Anti-acne | Fruit | Skin wash juice | (Castañeda 2018) |
| | | Against pimples, against pediculosis and against scabies | Branches | Infusion for skin washing | |
| | | Against fleas | Leaves | Cleaning house floors | |
| | | Against heartache | Leaves | Tonic | |
| | | Stops blood vomiting | Leaves | Tonic | |
| | | Against eye infections | Fruit | Juice for ophthalmic use | |
| | | Against rheumatic pain | Leaves and stems | Mixture of infusion with animal fat | |
| | | | Leaves | The macerate for body bath | |
| | | Bladder and gallbladder desinflammatory | Leaves | NR | |
| | NR | Wound healing | Leaves | NR | (Svetaz *et al.* 2010). |
| | Amarguillo, arakuarembiu | Faced with cardiovascular complications in Chagas disease | Leaves | NR | (Salm *et al.* 2021) |
| | NR | Against dermatosis | Leaves | Ashes are applied locally | (Bourdy *et al.* 2004). |
| Mexico | Otatabe | Against warts, against rheumatism, against the bite of "lopon" *Scorpaena* sp. and ray | Branches | NR | (Dimayuga *et al.* 1998) |
| | Citabaro, huevito citabaro, otatabe, tonóopa, timóopa, palo verde | Ocular desinflammatory, against measles, against rheumatism, against muscle pain | Fruits and leaves | NR | (Robles-Zepeda *et al.* 2013) |
| | Cacarahue, frutilla, huelatave, huevito, otátave, sitavaro | Against indigestion | Fruit peel and leaves | Decoction | (Castañeda 2018) |
| | | Reduces stomach acidity | Fruit | Raw | |
| | | Against the evil eye (pink eye) | Fruit | Juice for ophthalmic use | |
| | | Reduce ulcers | Branches | Infusion | |
| | | Relieves discomfort caused by ant bites | Leaves | Leaves are burned and applied to affected areas | |
| | | Relieves skin rashes | Leaves | Powdered burnt leaves for topical use | |
| | | Against measles | Root | Cataplasm | |
| Peru | Perlillo, cun-con, cuncún, cuncush o calato | Germicide for wounds and any dermatological infection | Leaves | NR | |
| | | Lower the fever | Leaves | Extract of the ground leaves | |
| | | Against varicella | Leaves | The infuse for body baths | |

| | | | | |
|---|---|---|---|---|
| | Anti-allergic and against rash | Whole plant | For body baths | |
| | Antifungal | Fruit | Poultice | |
| | Deflamant in the treatment of acne | Whole plant | Crushed plant | |
| Cuncuno | Relieves symptoms caused by snakebite | Leaves | NR | (Bussmann *et al.* 2010). |
| Cuncuno, Cun Cun | Against diabetes | Leaves | Oral | (Bussmann & Glenn 2011) |
| Cun Cun | Lower the fever | Leaves | Liquid from ground leaves | (Raymundo 2015) |
| | Against varicella | | Cooking for body baths | |
| | Against fungi | Fruit | Poultice | |
| | Against rash and antiallergic | Whole plant | Cooking for body baths | |
| | Anti-acne and pimple deflamant | | Crushed | |
| Perlillo, cun cun | Bactericide, against ocular inflammation and serious gastrointestinal disorders (ulcers) | NR | NR | (Whaley *et al.* 2010) |
| | Fungicide | | Infusion-broth | |

NR: Not reporting

The use and consumption of traditional preparations based on the parts of *V. glabra* contribute to the reduction of infections and inflammations, as reported in Table 1. These preparations are mainly aimed at curing dermatological infections; the infusion of the leaves or whole plant, the juice of the fruit and the ashes of the leaves counteract the problems of acne, pimples, scabies, rash, chickenpox and measles.

The infusion of the leaves of *V. glabra* is used against recurrent inflammatory skin diseases (acne) (Table 1). Acne is caused by increased sebum production, bacterial infection, and hyperkeratosis (Cong *et al*. 2019). The metabolites found in the infusion are phenolic compounds (PCs) and alkaloids, both of which are considered important in reducing inflammation and infection (Sindhu *et al*. 2021). Based on the action of both compounds, the topical use of the infusion to reduce acne can be substantiated; through the antioxidant capacity of the PCs, reactive oxygen species (ROS) released by neutrophils responsible for the progression of inflammation can be reduced (Briganti & Picardo 2003, Prasad *et al*. 2020, Zielinski *et al*. 2014). Added to this is the biocidal power of alkaloids on the infection-causing bacteria *Cutibacterium acnes*, *Staphylococcus epidermidis* and *Propionibacterium acnes*. Alkaloids from the genera *Tabernaemontana* and *Rauvolfia* belonging to the same family as *V. glabra* have been shown to inhibit bacterial growth in *in vitro* assays (de Almeida *et al*. 2010, Naidoo *et al*. 2021).

According to a scientific report, the leaves, and fruits of *V. glabra* present proteolytic enzymes. This type of enzymes in dermatology are considered exfoliating, as they have the ability to break down skin proteins, favoring the elimination of skin scars (González-Velázquez *et al*. 2021, Trevisol *et al*. 2021).

The use of vegetable ashes is not yet substantiated, but it is known that they contain calcium, magnesium, sodium, iron, copper, zinc, among other minerals that are part of the composition of skin care products (Gutiérrez *et al*. 2014, Polefka *et al*. 2012). To treat diabetes, the consumption of the cold extract of the fresh leaves in the mornings for 30 days is reported, and as an antidote in snakebite, the decoction of the leaves is consumed, with Faique seeds and oil for two days, morning and evening (Bussmann & Sharon 2016).

**Phytochemical compounds**

*V. glabra* in a source of several important secondary metabolites, such as coumarins, saponins, flavonoids, PCs, tannins, anthocyanins, terpenes, sterols, and alkaloids (Flores & Ibáñez 2022, Quintanilla Carhuamaca & Guerrero Lezama 2018), identified by staining and precipitation reactions. Alkaloids are the secondary metabolites that could be elucidated by mass spectrometry and magnetic resonance analysis (Zeches *et al*. 1995) (Table 2).

Investigations on chromatography and spectrometry analysis have reported the presence of alkaloids in the leaves, bark, and stems of *V. glabra* (Table 2). Alkaloids are nitrogenous secondary metabolites produced by plants in response to environmental changes and pathogenic microorganisms (Debnath *et al*. 2018). The alkaloids found in *V. glabra* are terpenoid indole alkaloids (TIAs), which are characteristic of several species pertaining to the Apocynaceae family, as well as being the only metabolites identified and characterized so far in *V. glabra* (Mohammed *et al*. 2021).

The biosynthesis of TIAs in plant cells is based on the production of tryptamine, secologanin and strictosidine (Zhu *et* al. 2015). Through the shikimate pathway, the amino acid L-tryptophan loses a $CO_2$ molecule by the action of the enzyme tryptophan decarboxylase thus forming tryptamine in the cytosol. L-tryptophan is essential for indole alkaloid formation, reason why it is absent in *V. glabra* (Hedhili *et al*. 2007, Moran-Palacio *et al*. 2014b, Panjikar *et al*. 2012). Secologanin is formed in plastids via the terpenoid pathway (non-mevalonate pathway) (Hedhili *et al*. 2007, Oudin *et al*. 2007). The fusion of tryptamine and secologanin catalyzed by the enzyme strychosidine synthase will give me as result to precursor of most TIAs, strychosidine (Fig. 7) (Runguphan *et al*. 2009).

The TIAs found in *V. glabra* have varied structures, this is due to the various rearrangements of strictosidine when it loses its sugar. The action catalyzed by the enzyme strychosidine glucosidase by removing glucose from C-21, generates chiral centers at C-15 and C-3 of the strychosidine aglycone producing type I, II and III alkaloids (Szabó 2008). In relation to chemotaxonomic studies, it can be assumed that the *V. glabra* TIAs plotted are type II and III (Fig. 8) (Singh 2016).

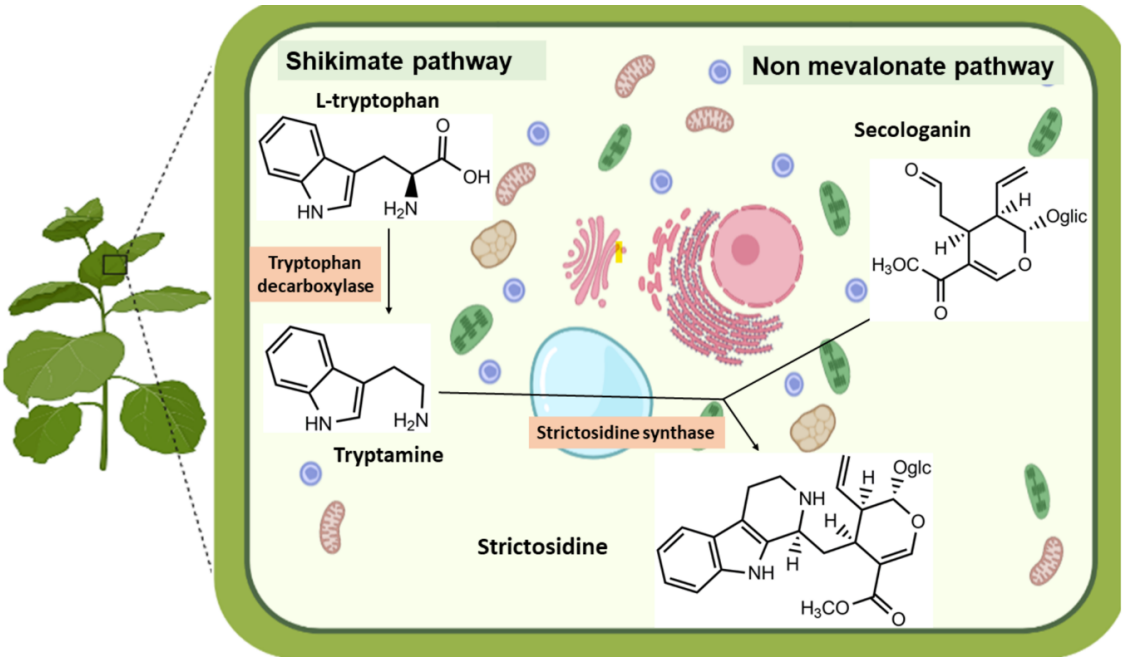


Figure 7. Strictosidine production mechanism, precursor of terpenoid indole alkaloids.

**Pharmacological activities**

Table 3 shows four activities presented by the extracts and essential oil of *V. glabra*; *in vitro* assays have demonstrated the biocidal power of this species. The most important activities are antibacterial and antimalarial (Bourdy *et al.* 2004, Quintanilla Carhuamaca & Guerrero Lezama 2018).

Table 3 and Figure 8 show the TIAs that have been determined so far from *V. glabra* and its synonym *V. dichotoma* Ruiz et Pav, several of them have reported *in vitro*, *in vivo* and *in silico* activity, forming part of extracts and isolates of other plant species belonging to the Apocynaceae family. Some of the alkaloids with *in vitro* activity are vallesine (antimalarial), aspidospermine (antimalarial), rhazilinilam (tumor cell inhibitor), tubotaiwine (analgesic and anti-inflammatory), apparicine (analgesic, antimalarial, anti-inflammatory), apparicine (analgesic, antimalarial inhibitor) and tubotaiwine (antimalarial, anti-inflammatory), antimalarial, xanthine oxidase inhibitor and inhibit Polio III activity), haplocidine (antiparasitic), vincadifflormine (antimalarial), reserpine (antimycobacterial), vallesamine (analgesic) (Albeshri *et al.* 2021, Begum *et al.* 2012, Chierrito *et al.* 2014, Ghosh *et al.* 2021, Ingkaninan *et al.* 1999, Komalasari *et al.* 2019, Mitaine-offer *et al.* 2002, Mustofa *et al.* 2006, Reina *et al.* 2011, Shang *et al.* 2010, Shi *et al.* 2019); *in vivo*, reserpine (antihypertensive) (Zhu *et al.* 2019) and *in silico,* condylocarpine is considered a possible anticancer (Obaid *et al.* 2017).

Within the reported pharmacological studies, antimalarial, antifungal, antibacterial and antioxidant activities are shown (Table 3). However, research has not reported the molecule or molecules involved in such activity. However, the presence of alkaloids in the extracts tested has been identified.

The antimalarial activity of the hydroalcoholic extract of *V. glabra* has been achieved by two forms of inhibition (Table 3). The first is the *in vitro* inhibition of the growth of *Plasmodium falciparum*, according to reports that vallesine, aspidospermine, apparicine and vincadifformine, isolated from the genus *Aspidosperma* (Apocynaceae) have the ability to reduce the growth of the parasite. The mechanism by which the growth inhibition is generated is not yet known, but it was suggested that it is different from that performed by chloroquine. On the other hand, the extract also achieved the inhibition of the biocrystallization of ferriprotoporphyrin IX (FP) or *β*-hematine, this substance when not converted into hemozoin inside the food vacuole of the parasite, exits to the cytosol and adheres to the parasite membranes leading to death (de Villiers & Egan 2021, Ginsburg & Golenser 2003).

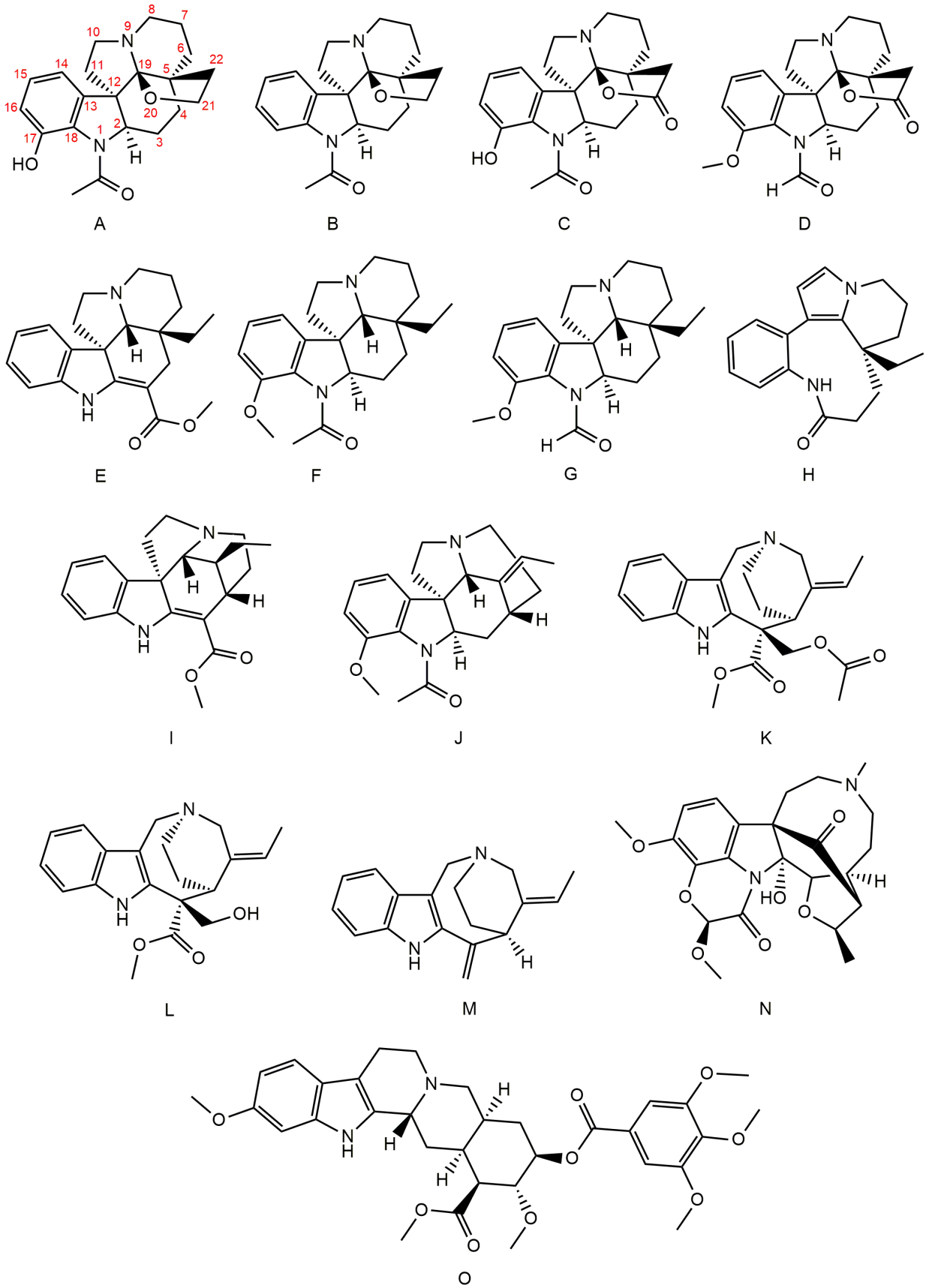


Figure 8. Terpenoid indole alkaloids identified in *V. glabra* extracts; A: 1-acetyl-17-hidroxyaspidoalbidine, B: 1-acetylaspidoalbidine, C: 18-oxohaplocidine, D: dichotamine, E: vincadifformine, F: aspidospermine, G: vallesine, H: rhazinilam, I: tubotaiwine, J: aspidospermatine, K: *O*-acetylvallesamine, L: vallesamine, M: (-)-apparicine, N: 11-methoxydichotine, O: reserpine

Table 2. Phytoconstituents of *Vallesia glabra* and in its synonym *Vallesia dichotoma* Ruiz et Pav.

| Synonymy | Phytoconstituents | Analyzed part | Identification technique | Reference |
|---|---|---|---|---|
| *Vallesia glabra* (Cav.) Link | Vallesine, aspidospermine, 11-methoxydichotine, (-)-rhazinilam, (-)-apparicine, aspidospermatine, haplocidine, 18-oxohaplocidine, tubotaiwine, vincadifformine, condylocarpine | Leaves and stems | UV, IR, MS, NMR | (Zeches *et al.* 1995) |
| *Vallesia dichotoma* Ruiz et Pav | Dichotamine, 1-acetyl-17-hydroxyaspidoalbidine (haplocidine), 1-acetylaspidoalbidine | Bark | UV, MS | (Brown *et al.* 1963) |
| | Vallesamine, *O*-acetylvallesamine | Stems | UV, NMR, MS | (Walser & Djerassi 1964) |
| | Reserpine | Leaves and branches | MS | (Holker *et al.* 1959) |
| | Aspidospermine, vallesine, dichotamine | Leaves and branches | | |

UV: Ultraviolet spectrophotometry; IR: Infrared spectroscopy; MS: Mass spectrometry; NMR: Nuclear magnetic resonance spectroscopy.

Table 3. Pharmacological activities of *Vallesia glabra.*

| Pharmacological Activities | Plant part | Extract | Metabolites | Description of the activity | References |
|---|---|---|---|---|---|
| Antimalarial | Bark | Hydroalcoholic | NR | Inhibition of the growth of *Plasmodium falciparum* and the biocrystallization of ferriprotoporphyrin IX with $IC_{50}$ 3.75 ± 1.06 and 0.18 ± 0.10 mg/ml. | (Bourdy *et al.* 2004) |
| Antifungal | NR | Hydroalcoholic | NR | MIC<500 µg/ml for *Trichophyton rubrum* C 113 and *Epidermophyton floccosum* C 114.<br>MIC=1000 µg/ml for *Microsporum gypseum* C 115 and *Trichophyton mentagrophytes* ATCC 9972. | (Svetaz *et al.* 2010) |
| Antibacterial | Leaves | Ethanolic | Coumarins, saponins, alkaloids | Inhibition of the growth of *Staphylococcus aureus* at a concentration of 50% and 100%. | (Quintanilla Carhuamaca & Guerrero Lezama 2018) |
| | Leaves | Hydroalcoholic | NR | Growth inhibition of 48% for methicillin-resistant *Staphylococcus aureus* and 44.83% for *Pseudomonas aeruginosa*. | (Mogollón & Rodríguez 2019) |
| | | Essential oil | | Growth inhibition of 28% for methicillin-resistant *Staphylococcus aureus* and 24.14% for *Pseudomonas aeruginosa*. | |
| | Leaves and bark | Ethanolic | NR | MIC=64 mg/ml for *Escherichia coli*.<br>MIC=16 mg/ml for *Staphylococcus aureus*. | (Bussmann *et al.* 2010) |
| | | Aqueous | | MIC=32 mg/ml for *Escherichia coli*. | |
| | Leaves | Hydroalcoholic | Alkaloids, flavonoids, saponins, phenolic compounds, tannins, anthocyanins | Inhibition of the growth of *Streptococcus pyogenes* at concentrations of 12.5, 25, 50 and 100 µg/ml. | (Flores & Ibáñez 2022) |
| Antioxidant | Leaves | Methanolic | Alkaloids, polyphenols, terpenes, tannins, sterols | DPPH inhibition in 57.70%. | (Moran-Palacio *et al.* 2014a) |

Hydroalcoholic, ethanolic, and aqueous extracts were reported to have activity against *Staphylococcus*, *Streptococcus*, *Pseudomonas* and *Escherichia* bacteria. The hydroalcoholic and ethanolic extracts qualitatively reported the presence of PCs and alkaloids, known to have antibacterial capacity (Table 3). For example, the hydroalcoholic extract presents effect against *Streptococcus pyogenes* and *Pseudomonas aeruginosa*, it is suspected that PCs and alkaloids are the ones that contribute to this activity, through the inhibition of biofilm formation and action on the bacterial wall (Flores & Ibáñez 2022, Macé *et al.* 2017, Mogollón García & Rodríguez Haro 2019). The ethanolic extract has effect against *Staphylococcus aureus*, as found reserpine is an alkaloid identified in *V. glabra* with the ability to inhibit biofilm or biofilm formation, affects the formation of exopolymeric substances and alters virulence gene regulators (Quintanilla & Guerrero 2018, Parai *et al.* 2019).

## Conclusions

The systematic review of research reports the extensive traditional use of *V. glabra* against infections and inflammation. Terpenoid indole alkaloids are the main phytochemical compounds present in *V. glabra* and the possible responsible for its antimicrobial activity. Pharmacological studies are needed to confirm the *in vitro* activity of these alkaloids.

## Declarations

**Ethics approval and consent to participate:** Not applicable.
**Consent to publication:** Not applicable.
**Availability of data and materials:** Not applicable.
**Competing interests:** The authors declare that they have no competing interests to the topic described in this review.
**Funding:** M.L. Ganoza-Yupanqui acknowledges the financial support of the CONCYTEC-World Bank Project "Mejoramiento y Ampliación de los Servicios del Sistema Nacional de Ciencia Tecnología e Innovación Tecnológica" 8682-PE, through its executing unit PROCIENCIA [contract number 114-2018-FONDECYT-BM-IADT-MU].
**Authors' contributions:** MLG-Y, LAS-R and RWB conceived the work, JGG-V, AML-M, EAV-C and MLG-Y compiled the information and wrote the manuscript, LAS-R, FRR-L, MR-V and RWB reviewed the manuscript. All authors approved the final manuscript.

## Literature Cited

Albeshri A, Baeshen NA, Bouback TA, Aljaddawi AA. 2021. A review of *Rhazya stricta* Decne phytochemistry, bioactivities, pharmacological activities, toxicity, and folkloric medicinal uses. Plants 10(11):2508.

Arhuire Ossio M. 2020. Cuantificación del ahorro de agua que se puede lograr en la gestión de espacios verdes urbanos a través de la selección de especies y la modificación del suelo en un estudio comparativo. Universidad Científica del sur, Lima, Perú.

Begum S, Naqvi SQZ, Ahmed A, Tauseef S, Siddiqui BS. 2012. Antimycobacterial and antioxidant activities of reserpine and its derivatives. Natural Product Research 26(22):2084-2088.

Bhadane BS, Patil MP, Maheshwari VL, Patil RH. 2018. Ethnopharmacology, phytochemistry, and biotechnological advances of family Apocynaceae: A review. Phytotherapy Research 32(7):1181-1210.

Bourdy G, Oporto P, Giménez A, Deharo E. 2004. A search for natural bioactive compounds in Bolivia through a multidisciplinary approach: Part VI. Evaluation of the antimalarial activity of plants used by Isoceño-Guaraní Indians. Journal of Ethnopharmacology 93(2-3):269-277.

Briganti S, Picardo M. 2003. Antioxidant activity, lipid peroxidation and skin diseases. What's new. Journal of the European Academy of Dermatology and Venereology 17(6):663-669.

Bussmann RW & Glenn A. 2011. Traditional knowledge for modern ailments-plants used for the treatment of diabetes and cancer in Northern Peru. Journal of Medicinal Plants Research 5(31):6916-6930.

Bussmann RW, Malca-García G, Glenn A, Sharon D, Chait G, Díaz D, Pourmand K, Jonat B, Somogy S, Guardado G. 2010. Minimum inhibitory concentrations of medicinal plants used in Northern Peru as antibacterial remedies. Journal of Ethnopharmacology 132(1):101-108.

Bussmann RW & Sharon D. 2006. Traditional medicinal plant use in Northern Peru: tracking two thousand years of healing culture. Journal of Ethnobiology and Ethnomedicine 2(1):1-18.

Bussmann RW & Sharon D. 2016. Plantas medicinales de los Andes y la Amazonía-La flora mágica y medicinal del Norte del Perú. Ethnobotany Research and Applications 15(1):1-293.

Brown JKS, Budzikiewicz H, Djerassi C. 1963. Alkaloid studies XLII. The structures of dichotamine, 1-acetyl-aspidoalbidine and 1-acetyl-17-hydroxyaspidoalbidine: three new alkaloids from *Vallesia dichotoma* Ruiz et Pav. Tetrahedron Letters 4(25):1731-1736.

Castañeda N. 2018. *Vallesia glabra* (Cav.). Technical Report. Universidad Nacional Agraria La Molina 1-6.

Chierrito TP, Aguiar AC, de Andrade IM, Ceravolo IP, Gonçalves RA, de Oliveira AJ, Krettli AU. 2014. Anti-malarial activity of indole alkaloids isolated from *Aspidosperma olivaceum*. Malaria journal 13(1):1-10.

Cong TX, Hao D, Wen X, Li XH, He G, Jiang X. 2019. From pathogenesis of acne vulgaris to anti-acne agents. Archives of Dermatological Research 311(5): 337–349.

Debnath B, Singh WS, Das M, Goswami S, Singh MK, Maiti D, Manna K. 2018. Role of plant alkaloids on human health: A review of biological activities. Materials Today Chemistry 9:56-72.

de Almeida CL, da Silva AKA, Curcino VIJ, Mathias L, Braz-Filho R, Silva SS, Vieira-da-Motta O. 2010. *Rauvolfia grandiflora* (Apocynaceae) extract interferes with staphylococcal density, enterotoxin production and antimicrobial activity. Brazilian Journal of Microbiology 41(3):612-20.

de Villiers KA, Egan TJ. 2021. Heme Detoxification in the Malaria Parasite: A Target for Antimalarial Drug Development. Accounts of Chemical Research 54(11):2649-2659.

Dimayuga RE, Virgen M, Ochoa N. 1998. Antimicrobial Activity of Medicinal Plants from Baja California Sur (México). Pharmaceutical Biology 36(1): 33-43.

Ezcurra C. 1981. Revisión de las Apocinaceas de Argentina. Universidad de Buenos Aires, Buenos Aires, Argentina.

Flores J, Ibáñez K. 2022. Efecto *in vitro* del extracto hidroalcohólico de hojas de *Vallesia glabra* sobre el crecimiento de *Streptococcus pyogenes*. Universidad Nacional de Trujillo, Trujillo, Perú.

Ginsburg H, Golenser J. 2003. Glutathione is involved in the antimalarial action of chloroquine and its modulation affects drug sensitivity of human and murine species of *Plasmodium*. Redox Report 8(5):276-279.

Ghosh P, Poddar S, Chatterjee S. 2021. Morphological features, phytochemical and ethnopharmacological attributes of *Tabernaemontana divaricata* Linn.: A comprehensive review. Journal of Pharmacognosy and Phytochemistry 10(6):31-36.

González-Velázquez DA, Mazorra-Manzano MA, Martínez-Porchas M. 2021. Exploring the Milk-Clotting and Proteolytic Activities in Different Tissues of *Vallesia glabra*: a New Source of Plant Proteolytic Enzymes. Applied Biochemistry and Biotechnology 193:389-404.

Guadalupe G, Albornoz PL. 2013. Anatomía foliar de *Vallesia glabra* (Apycynaceae), especie de importancia medicinal y en frugivoría. Lilloa 50(1):25-32.

Gutiérrez JMB, Ortiz AFL, Perea EM, Méndez JJ. 2014. Flora silvestre medicinal utilizada por los Kofan colombianos en el tratamiento de la leishmaniasis cutánea. Revista Cubana de Plantas Medicinales 19(4):407-420.

Hedhili S, Courdavault V, Giglioli-Guivarc'h N, Gantet P. 2007. Regulation of the terpene moiety biosynthesis of *Catharanthus roseus* terpene indole alkaloids. Phytochemistry Reviews 6(2):341–351.

Holker JSE. Cais M. Hochstein FA. Djerassi C. Holker JSE. Cais M. Hochstein FA. Djerassi C. Holker JSE. 1959. Alkaloid Studies. XXII.1 The Alkaloids of *Vallesia dichotoma* Ruiz et Pav. Journal of Organic Chemistry 24 (3):314-316.

Ingkaninan K, Ijzerman AP, Taesotikul T, Verpoorte R. 1999. Isolation of Opioid-active Compounds from *Tabernaemontana pachysiphon* leaves. Journal of Pharmacy and Pharmacology 51(12):1441-1446.

Komalasari O, Maryani S, Juairiyah O, Novriadhy D. 2019. Kearifan Lokal Masyarakat Desa Bakung dalam memanfaatkan Resam (*Gleichenia linearis*), Seduduk (*Melastoma malabathricum*) dan Tembesu (*Fagraea fragrans*) yang Tumbuh di Tanah Bergambut sebagai Obat Herbal. In Seminar Nasional Lahan Suboptimal 354-359.

López EA. 1954. Algunos aspectos de la obra de Ruiz y Pavón. In Anales del Jardín Botánico de Madrid 12(1):5-111

Macé S, Hansen LT, Rupasinghe HV. 2017. Anti-bacterial activity of phenolic compounds against *Streptococcus pyogenes*. Medicines 4(2):25.

Martínez GJ & Barboza GE. 2010. Natural pharmacopoeia used in traditional Toba medicine for the treatment of parasitosis and skin disorders (Central Chaco, Argentina). Journal of Ethnopharmacology 132(1):86-100.

Mitaine-Offer AC, Sauvain M, Valentin A, Callapa J, Mallié M, Zèches-Hanrot M. 2002. Antiplasmodial activity of *Aspidosperma* indole alkaloids. Phytomedicine 9(2):142-145.

Mohammed AE, Abdul-Hameed ZH, Alotaibi MO, Bawakid NO, Sobahi TR, Abdel-Lateff A, Alarif WM. 2021. Chemical diversity and bioactivities of monoterpene indole alkaloids (MIAs) from six Apocynaceae genera. Molecules 26(2):488.

Mogollón García MV, Rodríguez Haro IM. 2019. Efecto del extracto hidroalcohólico y aceite esencial de hojas de *Vallesia glabra* sobre el crecimiento de *Staphylococcus aureus* meticilino resistente y *Pseudomonas aeruginosa*. Pueblo Continente 30(1):299-306.

Mora-Costilla MM, López-Medina SE, Mostacero-León J, Gil-Rivero AE, López-Zavaleta A, Anthony J, Villena-Zapata L. 2020. Morfometría de frutos y semillas de *Vallesia glabra* "Cuncuno''. REBIOL 40(1):79-84.

Moran-Palacio E, Zamora-Álvarez L, Stephens-Camacho N, Yáñez- Farías G, Virgen-Ortiz A, Martínez-Cruz O, Rosas-Rodríguez J. 2014a. Antioxidant capacity, radical scavenging kinetics and phenolic profile of methanol extracts of wild plants of southern Sonora, Mexico. Tropical Journal of Pharmaceutical Research 13(9):1487.

Moran-Palacio E, Tortoledo-Ortiz O, Yañez-Farias G, Zamora-Álvarez L, Stephens-Camacho N, Soñanez-Organis J, Rosas-Rodríguez J. 2014b. Determination of Amino Acids in Medicinal Plants from Southern Sonora, Mexico. Tropical Journal of Pharmaceutical Research 13(4):601.

Mostacero LJ, Fukushima NM. 2005. Características edafoclimáticas y fitogeográficas de las plantas medicinales del dominio andino noroccidental del Perú, durante 1976 al 2004. Universidad Nacional de Trujillo. Trujillo, Perú.

Muriel P. 2008. La diversidad de ecosistemas en el Ecuador. In: de la Torre L, Navarrete H, Muriel P, Macía MJ, Balslev H. (eds). Enciclopedia de las Plantas Útiles del Ecuador. Herbario QCA & Herbario AAU. Pontificia Universidad Católica del Ecuador, Quito, Ecuador. Pp. 28-38.

Mustofa M, Valentin A, Lewin, G. 2006. *In vitro* Antiplasmodial Activity and Cytotoxicity of Vincadifformine and Its Semisynthetic Derivatives. Indonesian Journal of Biotechnology 11(1):878-883.

Naidoo CM, Naidoo Y, Dewir YH, Murthy HN, El-Hendawy S, Al-Suhaibani N. 2021. Major bioactive alkaloids and biological activities of *Tabernaemontana* species (Apocynaceae). Plants 10(2):313.

Obaid AY, Voleti S, Bora RS, Hajrah NH, Omer AMS, Sabir JS, Saini KS. 2017. Cheminformatics studies to analyze the therapeutic potential of phytochemicals from *Rhazya stricta*. Chemistry Central Journal 11(1):1-21.

Oudin A, Courtois M, Rideau M, Clastre M. 2007. The iridoid pathway in *Catharanthus roseus* alkaloid biosynthesis. Phytochemistry Reviews 6(2-3): 259-276.

Panjikar S, Stoeckigt J, O'Connor S, Warzecha H. 2012. The impact of structural biology on alkaloid biosynthesis research. Natural Product Reports 29(10):1176-1200.

Parai D, Banerjee M, Dey P, Mukherjee SK. 2019. Reserpine attenuates biofilm formation and virulence of *Staphylococcus aureus*. Microbial Pathogenesis 138:103790.

Polefka TG, Bianchini RJ, Shapiro S. 2012. Interaction of mineral salts with the skin: a literature survey. International Journal of Cosmetic Science 34(5):416-423.

Prasad SB, Marimuthu S, Prasad GP, Mangal AK, Srikanth N. 2020. The Recent Advancements in Field of Medicinal Plant Research With special reference to Acne Therapy. International Journal of Ayurvedic Medicine 11(1):10-4.

Quintanilla Carhuamaca CD, Guerrero Lezama JA. 2018. Efecto antibacteriano del extracto etanólico de hojas de *Vallesia glabra* (cun cun) frente a cepas de *Staphylococcus aureus* y *Escherichia coli* estudio *in vitro*. Universidad Inca Garcilazo de la Vega, Lima, Perú.

Raymundo S. 2015. Etnobotánica de las especies del Monte Ribereño en el río Chira, Sullana. Universidad Nacional de Piura, Piura, Perú.

Reina M, Ruiz-Mesia W, Ruiz-Mesia L, Martínez-Díaz R, González-Coloma A. 2011. Indole Alkaloids from *Aspidosperma rigidum* and *A. schultesii* and their Antiparasitic Effects. Zeitschrift Für Naturforschung C 66(5-6):225-234.

Robles-Zepeda RE, Coronado-Aceves EW, Velázquez-Contreras CA, Ruiz-Bustos E, Navarro-Navarro M, Garibay-Escobar A. 2013. *In vitro* anti-mycobacterial activity of nine medicinal plants used by ethnic groups in Sonora, Mexico. Complementary and Alternative Medicine 13:329.

Runguphan W, Maresh JJ, O'Connor SE. 2009. Silencing of tryptamine biosynthesis for production of nonnatural alkaloids in plant culture Proceedings of the National Academy of Sciences of the United States of America 106(33):13673-8.

Salm A, Krishnan SR, Collu M, Danton O, Hamburger M, Leonti M, Almanza G, Gertsch J. 2021. Phylobioactive hotspots in plant resources used to treat Chagas disease. iScience 24(4):102310.

Shang JH, Cai XH, Feng T, Zhao YL, Wang JK, Zhang LY, Luo XD. 2010. Pharmacological evaluation of *Alstonia scholaris*: Anti-inflammatory and analgesic effects. Journal of Ethnopharmacology 129(2):174-181.

Shi BB, Chen J, Bao MF, Zeng Y, Cai XH. 2019. Alkaloids isolated from *Tabernaemontana bufalina* display xanthine oxidase inhibitory activity. Phytochemistry 166:112060.

Singh R. 2016. Chemotaxonomy: A Tool for Plant Classification. Journal of Medicinal Plants Studies 4(2):90-93.

Sindhu RK, Kaur P, Sanjana M, Kaur P, Goyal A, Bala R, Sandhu A. 2021. Phytochemicals: Extraction, isolation methods, identification and therapeutic uses: A review. Plant Archives 21(1):174-184.

Svetaz L, Zuljan F, Derita M, Petenatti E, Tamayo G, Cáceres A, Cechinel V, Giménez A, Pinzón A, Zacchino S, Gupta M. 2010. Value of the ethnomedical information for the discovery of plants with antifungal properties. A survey among seven Latin American countries. Journal of Ethnopharmacology 127(1):137-158.

Szabó LF. 2008. Rigorous biogenetic network for a group of indole alkaloids derived from strictosidine. Molecules 13(8):1875-96.

Trevisol TC, Henriques RO, Souza AJA, Furigo JA. 2021. An overview of the use of proteolytic enzymes as exfoliating agents. Journal of Cosmetic Dermatology 21(8):3300-3307.

Van Beek TA, Verpoorte R, Svendsen A B, Leeuwenberg AJM, Bisset NG. 1984. *Tabernaemontana* L. (Apocynaceae): A review of its taxonomy, phytochemistry, ethnobotany and pharmacology. Journal of Ethnopharmacology 10(1):1-156.

Walser A, Djerassi C. 1964. Alkaloid-Studien XLIX Die Strukturen von Vallesamin und *O*-Acetyl-vallesamin. Helvetica 47(7):2072-2086.

Whaley O, Orellana-Garcia A, Tenorio W. 2010. Plantas y vegetación de Ica, Perú- Un recurso para su restauración y conservación. Royal Botanic Gardens. 72.

Zeches M, Mesbah K, Richard B, Moretti C, Nuzillard M, Le Men-Olivier L. 1995. Alkaloids from leaves and stems of *Vallesia glabra*. Planta Medica 61(1):89-91.

Zhu GH, Sun XP, Li J, Pi L, Tang HQ, Gao HQ, Cong HL, Qu P, Lu XZ, Zhang XJ. 2019. No hay asociación entre el uso de dosis bajas de reserpina y la depresión en pacientes mayores hipertensos: resultado de un estudio transversal multicéntrico. Journal of Geriatric Cardiology 16(8):608.

Zhu J, Wang M, Wen W, Yu R. 2015. Biosynthesis and regulation of terpenoid indole alkaloids in *Catharanthus roseus*. Pharmacognosy Reviews 9(17):24-8.

Zielinski AAF, Haminiuk CWI, Nunes CA, Schnitzler E, van Ruth SM, Granato D. 2014. Chemical composition, sensory properties, provenance, and bioactivity of fruit juices as assessed by chemometrics: A critical review and guideline. Comprehensive Reviews in Food Science and Food Safety 13(3):300-316.