Biochemical and Biophysical Research Communications 750 (2025) 151328

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Andean medicinal plants and their secondary metabolites: Connections between Aymara traditional medicine and modern pharmacology

Ivania Cortés [a], Francisco Ceric [b], Hellen Navarrete [c], Maité Rodríguez-Díaz [d], María Carolina Otero [c,*]

[a] Escuela de Tecnología Médica, Facultad de Medicina, Universidad Andrés Bello, Santiago, Chile
[b] Laboratorio de Neurociencia Afectiva, Facultad de Psicología, Universidad del Desarrollo, Santiago, Chile
[c] Escuela de Química y Farmacia, Facultad de Medicina, Universidad Andrés Bello, Santiago, Chile
[d] Carrera de Química y Farmacia, Facultad de Ciencias Naturales, Matemáticas y Medio Ambiente, Universidad Tecnológica Metropolitana, Santiago, Chile

ARTICLE INFO

Keywords:
Aymara traditional medicine
Secondary metabolites
Healthcare
Azorella
Centaurium
Amaranthus

ABSTRACT

This review examines Aymara traditional medicine, which is deeply rooted in cultural perceptions of health and disease, and its utilization of medicinal plants rich in secondary metabolites—such as flavonoids, alkaloids, and saponins—to support immune function, emphasizing the synergy between ancestral knowledge and modern scientific research. Adhering to PRISMA 2020 guidelines, this review incorporates empirical studies from 2013 to 2024 on secondary metabolites and Aymara medicine, with a focus on the immunomodulatory effects of plants, while excluding non-indexed or irrelevant studies. Potential limitations include publication bias and reliance on secondary data.

Three key plant genera—*Azorella*, *Centaurium*, and *Amaranthus*—were identified for their traditional medicinal uses, highlighting their pharmacological benefits, such as anti-inflammatory, antioxidant, and hepatoprotective effects. Specifically, xanthones, a class of secondary metabolites found in *Centaurium*, exhibit notable antioxidant, anti-inflammatory, antitumoral, and cardioprotective properties, which support their traditional use in treating hypertension and related ailments. *Centaurium spp.* is characterized by its bioactive compounds (secoiridoids, flavonoids, phenolic acids, and xanthones), offering valuable immunomodulatory, anti-inflammatory, digestive, and antimicrobial properties recognized in both scientific and traditional Aymara medicine for treating diseases and maintaining physical and spiritual balance.

Overall, the study of secondary metabolites in Andean medicinal plants like *Azorella*, *Centaurium*, and *Amaranthus* underscores their diverse bioactive compounds with pharmacological properties, highlighting the Aymara community's integration of traditional and modern medicine through holistic practices that promote health, balance, and resilience against disease, while emphasizing the potential of these practices to enhance contemporary healthcare.

1. Introduction

Different cultures around the world shape their cultural perceptions to define body, health, and disease. These practices are rooted in the populations that have once suffered some type of illness, discomfort, or ailment. This phenomenon is recognized in the field of anthropology as a cultural syndrome or sociocultural epidemiology. The study of representations and subjectivities is crucial to thoroughly understanding the conceptualization that underlies these perceptions. It also allows us to understand lived experiences of different populations and cultures, as well as the human dimensions related to knowledge, techniques, beliefs, customs, norms, experiences, symbols, and values, which shape the perceptions of the body, health, and disease. Likewise, the experiences that these populations and/or cultures have lived bring into practice human dimensions related to knowledge, techniques, beliefs, customs, norms, experiences, symbols, and values [1].

Among these ancient cultures are the Aymara people, who belong to the group known as the Andean people of South America and, along with Quechuas and Guaranís, are one of the three largest indigenous groups in the continent. Currently, there are around 1.500.000 Aymaras. Most

* Corresponding author.
E-mail address: maria.otero@unab.cl (M.C. Otero).

https://doi.org/10.1016/j.bbrc.2025.151328
Received 29 September 2024; Received in revised form 10 January 2025; Accepted 12 January 2025
Available online 13 January 2025

of them, approximately 1.150.000, live in the Republic of Bolivia. In Peru, there are about 350,000 Aymaras, nearly all of whom live in the southern department of Puno. A few thousand Aymaras live in northern Chile, in what is known as the First Region (Fig. 1) [2].

The Aymara people are situated in different ecological zones within the northern regions of Chile, such as the highland, valleys, ravines, and the coast [3]. This group is characterized as an ancient Andean society that bases its order on its beliefs, which are directed towards the Holy Mother Earth, *Pachamama*, as the creator of fauna, flora, and humans. The Aymara worldview consists of three spiritual spaces: *Arajpacha, Akapacha*, and *Manqhapacha. Arajpacha* is the world that includes the sun, the moon, the Milky Way, stars, saints, angels, and virgins, representing the "above" world. *Akapacha* is the center, or "this world of ours" referring to the world where the Aymara people live. Finally, *Manqhapacha,* or the "below" world, encompasses the spirits of the mines, devils, and the condemned, which the community associates with darkness, evil, and rebellion [4,5].

Overall, ancient medicine holds considerable historical and practical significance, embodying the collective wisdom of cultures regarding health, the human body, and its connection to nature [6]. It serves as the foundation for many contemporary medical principles and continues to impact current practices, particularly in integrative medicine and community health [7].

This traditional medicine is regarded as the foundation of modern medicine, as many ancient practices and remedies laid the groundwork for pharmacology and even contemporary surgical techniques [6]. The use of medicinal plants continues to be significant in the search for new therapeutic agents [8]. From a holistic viewpoint, ancient traditions typically adopt a comprehensive approach that acknowledges the interconnectedness of the mind, body, spirit, and environment, a concept that is increasingly recognized by modern medicine [8]. Furthermore, these traditions emphasize sustainability through the responsible utilization of natural resources and the conservation of ecosystems. The significance of Andean Aymara medicine is deeply rooted in its connection to the natural environment and its distinct worldview, which fosters an integrative and interconnected perspective involving "Pachamama", the cosmos, the community, and the individual. This approach not only promotes environmental awareness but also emphasizes a communal aspect of health care. Additionally, the Aymara pharmacopoeia consists of a diverse array of local plants known for their healing properties [9].

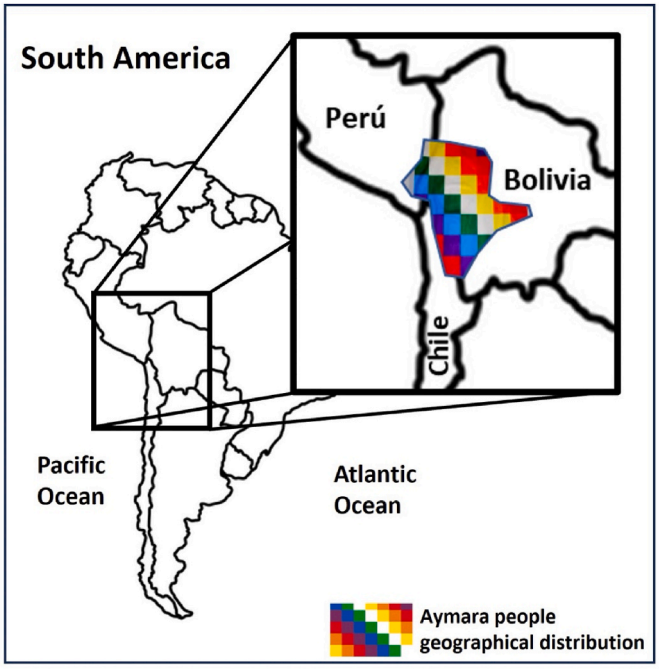

Fig. 1. Distribution of Aymara People. Map illustrates the geographical distribution of the Aymara people.

Traditional andean medicine is one of the cultural aspects that stands out in this community, characterized by a different perception of health and disease. Their concept of health is not limited to physical and psychological well-being but also encompasses the social balance and well-being of the person, that is, if they are in harmony with their family and community, their ancestors, protective spirits, and Mother Earth. This type of ancestral medicine is practiced by a relevant figure within the community, known as *Yatiri*, which means "wise" in English and refers to the person who knows, predicts, cures diseases, and guides people to heal the spirit or soul, thereby restoring balance within the community [10–12].

The Aymara conception of health is linked to work. For this culture, health has a direct relationship with work, thus, the ability to work is an indicator of a person's health. Specifically, work is directly proportional to health. For these populations, being healthy (*k'umara*) physically means being capable of working [12](13). According to the testimony of a community member from Jach'a Titilaca district of Platería (Puno, Peru), it means "being well and being able to carry out work (the farm) normally." However, health is also related to natural nutrition. Another important point to highlight is their beliefs and their relationship with divinities, which is also an expression of good health. In Andean culture specifically, health is a product of nurturing the harmony of biodiversity elements. Reinforcing this idea. Chambi states: "Health comes to build the fruit of the harmonization of the natural community, there will be illness if the rest of the components of the natural community (rivers, plants, animals, hills, stones, etc.) are unwell [13]. That is why harmony is always nurtured at every moment as it suits the Pachamama".

In the Aymara culture, understanding how the immune system functions is deeply intertwined with their worldview, beliefs, and traditional medical practices. The Aymara, like many other Indigenous peoples, view health as a holistic balance that encompasses body, mind, spirit, and environment [5,14]. Within Aymara medicine, the immune system is seen as intrinsically linked to the harmony between these elements. To strengthen the immune system, they focus on maintaining this balance through practices such as proper nutrition, plant-based medicine, physical exercise, meditation, and connecting with nature.

The Aymara emphasize the consumption of natural foods rich in antioxidants, vitamins, and minerals to support immune function. They also incorporate medicinal plants and herbs with immunomodulatory properties, such as garlic, quinoa, coca, and muña, into their diet. These plants are rich in secondary metabolites—such as alkaloids, flavonoids, terpenoids, and saponins—which play a vital role in enhancing immune function. Secondary metabolites, while not essential for growth, are crucial for plants' defense and ecological interactions, and they exhibit immunomodulatory effects in humans as well [15,16].

Flavonoids, recognized for their antioxidant and anti-inflammatory properties, play a vital role in reducing oxidative stress, a major contributor to immune cell damage. By minimizing inflammation and enhancing immune cell function, flavonoids bolster body's defenses. Quercetin and kaempferol, present in various fruits and vegetables, are particularly effective at protecting cells from damage and modulating immune responses [17].

Alkaloids, such as berberine—found in many Aymara medicinal plants—also demonstrate anti-inflammatory and antimicrobial effects, promoting immune balance [18]. Similarly, terpenoids like ursolic acid and carnosol, which are found in several herbs, help regulating immune responses by reducing inflammation and activating specific cells [19,20].

Tannins, found in green tea and red wine, provide notable immune benefits. Their antioxidant and astringent properties help fortify the intestinal mucosa and enhance the intestinal immune barrier, thereby reducing systemic inflammation [21]. These examples illustrate how Aymara medicinal plants, while culturally significant, are also

supported by modern scientific research, which confirms the beneficial effects of secondary metabolites on immune function.

For instance, saponins exhibit immunostimulant properties, enhancing the immune system by boosting antibody production, thereby strengthening the body's defense against infections [22]. Glycosides, in contrast, can modulate the immune response through their anti-inflammatory and antioxidant effects. For instance, cardiac glycosides like digoxin are known to have specific modulatory impacts on immune function [23].

Then, the general objective of this review is to analyze the use of medicinal plants in traditional Aymara medicine, focusing on identifying the secondary metabolites present in specific species such as *Azorella spp.*, *Centaurium spp.*, and *Amaranthus* spp., exploring their pharmacological, immunological, and cultural properties. This research aims to integrate ancestral knowledge with modern scientific evidence to understand their relevance in promoting health and well-being within the community.

1.1. Methodology

This review was structured according to the general PRISMA 2020 guidelines, ensuring compliance with the overall checklist system [24].

Eligibility criteria: This study is based on literature that includes scientific articles published in the last 10 years based on immunology, secondary metabolites, and Aymara medicine, in both English and Spanish. Studies without empirical results, unavailable in full text, or not indexed were excluded.

To ensure the rigor of the review, studies were included based on the following Criteria.

Inclusion: Published in the last 11 years (2013–2024), empirical studies providing data on secondary metabolites and their pharmacological effects, particularly immunomodulatory effects, articles focusing on the use of medicinal plants by the Aymara or other Andean communities, or peer-reviewed articles indexed in the selected databases.

Exclusion: Studies without empirical results or clinical relevance, non-indexed articles, unpublished materials, or grey literature, or duplicate studies across databases and those lacking full-text access.

Information sources: search included academic databases such as PubMed, Scopus, and Web of Science, and used terms like "immunomodulation," "saponins," "glycosides," "immune response," and "ancestral medicine."

Search strategy: This study it is particularly focusing on secondary metabolites and their immunological properties. The review also aimed to contextualize these findings within the broader cultural and traditional practices of Aymara medicine. Literature search was conducted across three major academic databases: PubMed, Scopus, and Web of Science, covering articles published between 2013 and 2024. Both English and Spanish language publications were included to ensure comprehensive coverage of the topic.

Selection process: The search terms utilized were specific to the research goals and included combinations of keywords such as "immunomodulation," "secondary metabolites," "saponins," "flavonoids," "Aymara traditional medicine," and "immune response." Additional sources, including specialized books and articles focused on Aymara medicine from Chile, Peru, and Bolivia, were also reviewed to integrate both scientific literature and culturally significant perspectives.

Data collection process: For each selected study, relevant data were extracted and tabulated, focusing on:

1. Plant species used by Aymara communities (e.g., *Azorella* spp., *Centaurium spp.*, *Amaranthus* spp.).
2. Identified secondary metabolites, such as flavonoids, alkaloids, terpenoids, and saponins.
3. Biological activities associated with these compounds, particularly their immunomodulatory and pharmacological effects.
4. Cultural and traditional uses of these plants within Aymara medicine, integrating indigenous practices and holistic health concepts.

Additionally, a comparative analysis was conducted to correlate traditional knowledge with modern pharmacological findings, particularly focusing on the plants' roles in modulating the immune system and their therapeutic applications in managing common diseases in Aymara populations, such as inflammatory conditions and chronic illnesses.

1.2. Limitations

A potential limitation of the study is publication bias, as only studies indexed in major scientific databases were included, potentially excluding valuable insights from non-indexed indigenous knowledge sources. Furthermore, the reliance on secondary data may limit the direct applicability of findings, although efforts were made to integrate relevant clinical and cultural literature to provide a holistic understanding.

2. Results

2.1. Identification of key plant species

One of the key findings of this study was the identification of essential plant species used in traditional Aymara medicine. By reviewing both scientific and ethnobotanical literature, three primary plant genera were highlighted: *Azorella* spp., *Centaurium spp.*, and *Amaranthus* spp. These plants hold not only cultural and ritual significance within the Aymara worldview but also possess valuable medicinal properties, attributed to their secondary metabolites with well-documented pharmacological benefits.

1. *Azorella* spp.

Description: Commonly known as Yareta, this is a perennial plant that grows in the high Andes, particularly at altitudes above 3000 m. It has slow growth and a cushion-like appearance, which allows it to adapt to extreme climates.

Uses in Aymara medicine: Azorella has traditionally been used by Aymara communities to treat respiratory, rheumatic and digestive ailments. It is commonly used in infusions and poultices. In Chile, Azorella is found mainly in the high plateau and Andean puna areas [25], covering the northern regions, such as Arica and Parinacota, Tarapacá, Antofagasta, and to a lesser extent in the Atacama region [25,26]. It grows in arid and rocky terrain at high altitudes (3000 to 5000 m above sea level) [9].

It is a plant adapted to extreme climates, with low temperatures and high solar radiation.

Secondary Metabolites: Research has revealed a significant presence of terpenoids, flavonoids, and alkaloids in its extracts. The diverse chemical compounds found in plant-derived natural products have substantially contributed to the discovery and development of new medications. Many of these compounds, after being employed for years in traditional medicine, are currently under investigation for their potential therapeutic applications. The identification and exploration of these substances have led to the creation of new drugs and treatments for various diseases and health conditions. These compounds have shown anti-inflammatory, antioxidant, and antimicrobial properties, reinforcing their traditional applications in the treatment of inflammatory and respiratory disorders. Furthermore, the structural diversity of secondary metabolites across different species has resulted in a wide range of molecular mechanisms, influenced by the interactions between functional groups and their biological targets [27].

One of the species of the genus *azorella is Azorella* compacta, also known for its cushion-like growth form, is a characteristic plant of the Andean regions that has been widely used in traditional Aymara

medicine. The following image (Fig. 2) illustrate different aspects of this species. In image (A), the irregular cushion growth form is shown, while image (B) displays the surface of the male cushion, highlighting the morphological characteristics that have been the focus of botanical and ecological studies. Fig. 2 also depicts azorellanol (C) and mulinane (D), two diterpenoids found in *Azorella compacta*, which exhibit notable biological activities.

2. *Centaurium spp.*

Description: Known in traditional medicine as Cachanlahua, this herbaceous plant grows in temperate and cold regions of the Andes. It has small pink flowers and is known for its characteristic bitter taste.

Uses in Aymara medicine: This plant has historically been used to treat digestive and liver problems and to stimulate appetite. It is also employed as a general tonic, in infusions to alleviate fevers, and as a hypotensive agent. In Chile, species of *Centaurium spp.* are located in regions near the Andes Mountain range, particularly in areas with temperate conditions and moist soils that support their growth [28]. For instance, in the central region, these plants can be found on the slopes of the Andes. Their typical altitudes range from 500 to 1500 m above sea level in Valparaíso, Metropolitana, and O'Higgins regions, where a Mediterranean climate with humid soils prevails. They have also been identified in the Maule and Biobío regions at similar elevations, as well as in the Araucanía region near the Andes [28].

Secondary metabolites: Secoiridoids, flavonoids, and phenolic acids have been identified in this species. Secoiridoids are particularly important for their hepatoprotective and digestive properties, while flavonoids and phenolic acids offer antioxidant and anti-inflammatory effects, supporting its use in treating digestive disorders and inflammatory diseases.

In addition to its chemical composition, the morphology of *Centaurium cachanlahuen* has also been studied due to its importance in the identification and collection of the plant for medicinal uses. Fig. 3 shows the image of the *Centaurium cachanlahuen* species (A), whose botanical characteristics contribute to its recognition as a valuable source of secoiridoids (B), xanthones (C), flavonoids, and phenolic acids.

3. *Amaranthus* spp.

Description: The Amaranthus genus, known as Kiwicha or Amaranth, includes several species cultivated for both their nutritious grains and medicinal properties. It is characterized by its striking, colorful inflorescences and adaptability to diverse altitudes.

Uses in Aymara medicine: In Aymara culture, Amaranthus has been used to improve nutrition, treat anemia, and as a digestive remedy. Amaranth grains are rich in protein and have been essential to the diet of Andean communities. The genus Amaranthus spp. encompasses a variety of herbaceous plants that are widely distributed across the globe. Its origin and geographical range span multiple regions [29,30]. Most species of Amaranthus are indigenous to the Americas, particularly in tropical and subtropical areas [29]. Certain species, such as Amaranthus hypochondriacus and Amaranthus caudatus, originate from Mexico and the Andes, where they have been cultivated for food. In the Andes, these plants can be found at elevations of up to 3500 m above sea level. While they prefer warm or temperate climates, many species are resilient, tolerating drought conditions, poor soil quality [31], and high altitudes.

Secondary metabolites: *Amaranthus* spp. contains a high concentration of saponins, polyphenols, and flavonoids, which have been shown to possess antioxidant, hypocholesterolemic, and immunomodulatory properties. These compounds are crucial in preventing cardiovascular diseases and enhancing immune response, validating its use in both diet and traditional medicine.

In addition to its nutritional and medicinal properties, the distinctive appearance of *Amaranthus caudatus* makes it easily identifiable, especially due to its striking inflorescences. Fig. 4 shows the *Amaranthus caudatus* plant in its entirety (A), while image (B) provides a close-up of the flower, highlighting characteristics recognized in both botany and traditional use. Fig. 4 (C) presents the general structure of flavonoids, a class of secondary metabolites widely found in the genus *Amaranthus*.

The identification of these plants not only confirms their importance in Aymara medicine but also reveals how their use is supported by the pharmacological properties of their secondary metabolites. The ancestral knowledge about these species, passed down through generations, correlates with modern scientific studies that highlight their health benefits, particularly in strengthening the immune system and preventing chronic diseases.

These results underscore the importance of continuing research on plants used by traditional Aymara medicine, as their metabolites may offer new opportunities for developing pharmacological treatments based on natural compounds.

The analysis of secondary metabolites responsible for the biological activity of the Andean medicinal plants is of relevance for traditional medicine and pharmacognosy. These secondary metabolites include a variety of chemical compounds that can exhibit therapeutic effects [33]. Some of the most relevant secondary metabolites in these plants and their biological activity are presented below:

2.2. Genus Azorella spp

This genus is recognized within traditional Andean medicine for its effectiveness in treating a range of ailments. The secondary metabolites found in *Azorella* include:

- **Alkaloids:** Compounds known for their anti-inflammatory, analgesic, and antispasmodic properties [34].
- **Flavonoids:** Compounds with antioxidant, anti-inflammatory, and antitumoral activities. Flavonoids are characterized by protecting cells from oxidative damage [33,35].
- **Terpenoids:** Terpenoids are known for their anti-inflammatory, antimicrobial, and antitumoral properties [36].

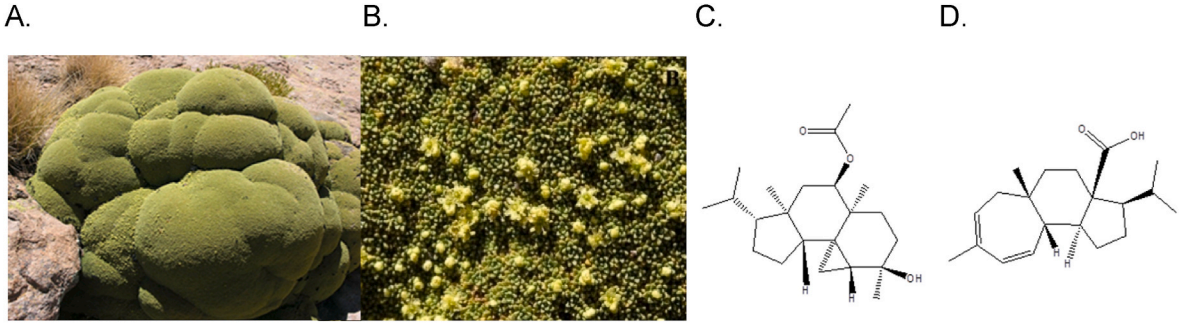

Fig. 2. *Azorella compacta*. (A) irregular cushion form of growth (B) surface of male cushion (C) diterpenoid Azorellanol (D) diterpenoid Mulinane [25].

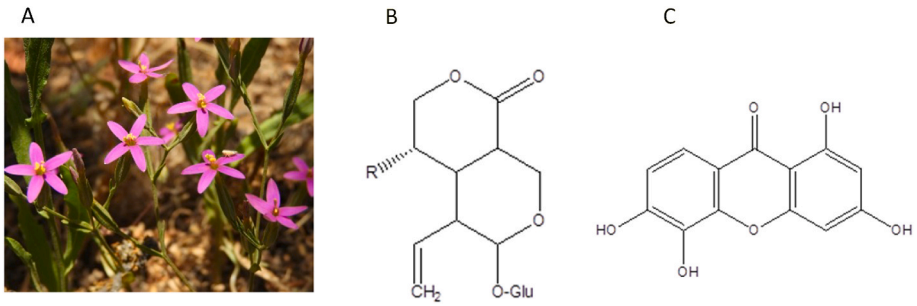

Fig. 3. (A) *Centaurium cachanlahuen*. (B) General structure of the secoiridoids from the genus *Centaurium*. (C) Chemical structure of a common xanthone (1,3,5,6-tetrahydroxyxanthone) found in the genus *Centaurium* [26].

Fig. 4. *Amaranthus caudatus* (Amaranth). (A) Whole plant of *Amaranthus caudatus.* (B) Detail of the *Amaranthus caudatus* flower. (C) General structure of flavonoids [32].

2.3. Secondary metabolites of the genus Azorella of the Terpenoid type

Terpenoids contained in the genus *Azorella* exhibit various biological and pharmacological properties, making them relevant to human health. Terpenoids are an extensive class of organic compounds derived from isoprene units which can be divided into several subclasses, such as monoterpenes, sesquiterpenes, diterpenes, triterpenes, and tetraterpenes, among others.

Terpenoids, also known as terpenes, are the largest group of secondary metabolites, encompassing more than 40,000 different molecules. They are chemically heterogeneous biomolecules but physically similar, consisting of units of 5 carbon atoms or "isoprene" units, hence they are also called isoprenoids. These biomolecules are usually insoluble in water and compatible with slightly polar organic solvents such as dichloromethane and chloroform. Initially, terpenes were identified as hydrocarbons originally found in turpentine oil and composed solely of alkenes. However, the presence of various functional groups such as aldehydes, ketones, esters, and carboxylic acids in their structure led to the term terpenoids [37].

Diterpenoids possess the capability to cross the blood-brain barrier (BBB) and affect the central nervous system. Transmembrane diffusion is the primary method by which drugs traverse the blood-brain barrier. Certain diterpenes can promote GLUT4 translocation and activate signaling pathways that involve phosphoinositide 3-kinase (PI3K) and AMP-activated protein kinase (AMPK). Additionally, diterpenoids may reduce the expression of inflammatory markers such as NLRP3 and interleukin (IL)-6. They also have the potential to enhance joint health by modifying various pathways involved in arthritis. In terms of antiviral and antibacterial effects, these compounds can inhibit bacterial growth, influence the gene expression associated with virulence factors, and reduce the expression of those same factors [38].

Especially in the *Azorella genus*, terpenoids of the diterpene type are produced. Mulinane- and azorellane-type diterpenoids are exclusive constituents of medicinal plants belonging to the *Azorella* spp, *Laretia* spp, and *Mulinum genera*. These diterpenoids exhibit medicinal properties, including antimicrobial, antiprotozoal, spermicidal, gastroprotective, and anti-inflammatory, among others [28]. The structure of the diterpenoids azorellanol and mulinane is shown in Fig. 2C and D respectively.

2.4. Genus Centaurium

The genus *Centaurium*, commonly known as centaury, is recognized for its digestive and hepatoprotective properties. Also, this plant has been used to treat asthma, fever, intestinal parasites, hypertension, spasms of gastrointestinal musculature, edemas, and rheumatism, among others [39]. Plant extracts have exhibit clinical properties such as sedative, antipyretic, antihelmintic, anti-inflammatory, analgesic, diuretic, antidiabetic, and antioxidative agents [39].

The secondary metabolites present in this genus include:

- **Secoiridoids:** These compounds are known for their digestive and hepatic properties, aiding digestion and protecting the liver [40].
- **Flavonoids:** As in the genus Azorella, these compounds possess anti-inflammatory and antioxidant effects [32].
- **Phenolic acids:** These compounds are characterized by their antioxidant and anti-inflammatory properties, contributing to protection against oxidative stress [32](39).

In Chile, various species belonging to the genus *Centaurium,* such as *Centaurium cachanlahuen, Centaurium littorale,* and *Centaurium pulchellum*, are distributed throughout the country. The Aymara community uses this native species as a medicinal plant by preparing an infusion characterized by its bitter taste. It has been demonstrated that this infusion might exhibit different properties such as hypotensive, hypoglycemic, sudorific, antipyretic, and might be protective for liver and digestive affections [39,41].

Various species belonging to the genus Centaurium are used as medicinal plants due to their biological activities in treating different types of diseases. Consequently, numerous studies have identified different secondary metabolites such as alkaloids, xanthones, and iridoids, which contribute to the characteristic bitter taste of the Cachanlahua infusion. Among these metabolites, xanthones are noteworthy for their limited distribution within various species families and significant biological

activity identified through phytochemical studies.

Secoiridoids are bioactive compounds that exhibit a range of biological activities, including anti-inflammatory, anti-cancer, and neuroprotective effects (Fig. 3B). These compounds regulate the production of inflammatory cytokines and nitric oxide in macrophage cells. They also inhibit the phosphorylation of MAPK, STAT3, and I-κB.

Furthermore, secoiridoids can generate reactive oxygen species (ROS), which can impede cell division and induce cell death. They may also work synergistically with other chemotherapeutic agents to suppress tumor cell proliferation. Specifically, the secoiridoid oleanolic acid has the potential to protect against the effects of diabetes by reducing oxidative stress and promoting histological regeneration [42].

2.5. Secondary metabolites of the genus Centaurium: xanthones

Xanthones are a class of secondary metabolites found in various plants, including some species of the genus *Centaurium* (Fig. 3C). Renowned for their varied biological and pharmacological effects, xanthones are a valuable focus in both pharmaceutical research and traditional healing practices. The biological and pharmacological properties of xanthones of the genus *Centaurium* include antioxidant, anti-inflammatory, antitumoral, antimicrobial, and hepatoprotective properties [43].

Xanthones are also characterized as a subgroup of phenolic compounds generally found in two plant families, *Clusiaceae* and *Gentianaceae*. These secondary metabolites exhibit antioxidant properties and provide pigmentation to some plant species. In the organism, they are notable for their antioxidant, anti-inflammatory, hypotensive, anti-allergic, and antitumoral properties.

Xanthones have the ability to inhibit pro-inflammatory cytokines, enhance the production of anti-inflammatory cytokines, and shield normal tissues from cellular harm. Additionally, they can regulate NF-κB and MAPK signaling pathways, modulate eosinophil recruitment, and hinder the proliferation, adhesion, and invasion of melanoma cell lines.

The biological activity of xanthones, which exhibit numerous structural variations, is influenced by factors such as the degree of oxidation of the C-ring, the presence of functional groups, and other structural elements [44].

Scientific studies have demonstrated that the plant species *Centaurium cachanlahuen* contains a group of xanthones responsible for its hypotensive and cardioprotective biological properties, utilized by the Aymara community in treatments for arterial hypertension. *Centaurium cachanlahuen* is recognized by the Aymara culture for its properties and benefits in treating specific ailments and pathologies. Consequently, through its uses and research, the population supports the cardioprotective property of this plant and uses it routinely [45].

2.6. Genus Amaranthus

The species of the genus *Amaranthus* are known for their medicinal and nutritional properties. The secondary metabolites present in this genus include:

- **Saponins:** Saponins are known for their antimicrobial, immunomodulatory, and hypocholesterolemic activities. These compounds might reduce cholesterol levels and improving cardiovascular health [48].
- **Polyphenols:** Polyphenols are antioxidant compounds that protect against oxidative damage and possess anti-inflammatory [46] and antitumoral properties [34].
- **Betalains:** These are pigments with anti-inflammatory and antioxidant properties, contributing to cellular protection [47].

The genus *Amaranthus* was first classified by Linnaeus in 1753 and encompasses around 70 species, the majority of which are indigenous to the Americas, while the remaining species are found in Asia, Australia, Africa, and Europe. In Chile, various species such as *Amaranthus caudatus*, *Amaranthus cruentus*, and *Amaranthus hypochondriacus* exist [48]. *Amaranthus caudatus* is cultivated in the Andean region and primarily sold as an ornamental plant in Europe and North America. *Amaranthus Cruentus* is native to Mexico and Central America, where it is grown primarily for its grain. It is also consumed as a vegetable. *Amaranthus Hypochondriacus* originating from central Mexico, it is also grown for its grain [49].

Amaranth primarily contains high levels of proteins, fiber, niacin, squalene, and tocotrienols, which have recently shown positive effects in reducing total cholesterol levels. Phytochemical research has demonstrated that extracts from *Amaranthus caudatus* contain tocotrienol and tocopherol, substances that regulate cholesterol metabolism. Additionally, this plant species has been identified to contain a range of secondary metabolites like polyphenols and flavonoids. Numerous studies have demonstrated that these compounds exhibit a wide range of biological and clinical properties, including the ability to lower cholesterol levels and offer antioxidant, antidiabetic, cardioprotective, and hepatoprotective benefits. Therefore, the Aymara community uses amaranth seeds, which have the highest concentration of these bioactive components, to complement a healthy diet and maintain good control of blood cholesterol levels [50].

Saponins possess various mechanisms of action, including the activation of immune cells and the release of cytokines via signaling pathways such as TLRs, NF-κB, and MAPK, among others. These processes initiate innate immune responses and enhance antigen-specific immune responses. Additionally, saponins can promote autophagy, which is frequently linked to tumor growth. However, the activation of autophagy may also stimulate T-cell cytotoxicity, thereby inhibiting the growth of cancer cells [51].

2.7. Secondary metabolites of the genus Amaranthus: flavonoids

Flavonoids are a class of secondary metabolites widely present in the genus *Amaranthus* (Fig. 4C). These compounds possess biological and pharmacological properties that make them valuable in medicine and nutrition. Main properties of these flavonoids form *Amaranthus* include anti-inflammatory, antioxidant, antimicrobial, antitumoral, cardioprotective, and neuroprotective properties [52](53).

Phenolic compounds or polyphenols are bioactive secondary plant metabolites that are widely distributed in different species and plant-based foods, such as amaranth. Flavonoids are one of the main subgroups of phenolic compounds, characterized by having one or more phenol groups in their chemical structure. They are recognized for their electron-donating capacity and their ability to stop chain reactions. Flavonoids are composed of 15 carbons and two aromatic rings connected by a three-carbon bridge [54,55]. Rutin, naringenin, isoquercetin, quercetin, myricetin, kaempferol, apigenin, hyperoside, and catechin are the main flavonoids and derivatives compounds found in the *Amaranthus* Genera. For decades, natural products research has focused on the study of polyphenols, emphasizing their antioxidant and anti-inflammatory potential, especially as protectors of chronic diseases such as cancer, cardiovascular and neurodegenerative diseases [56].

The primary role of flavonoids is their involvement in inflammation. Flavonoids inhibit the activity of enzymes that produce eicosanoids, including cyclooxygenases, lipoxygenases, and phospholipase A2. They also suppress the production of various cytokines, such as IL-1β, IL-6, IL-8, and TNF-α. Furthermore, flavonoids influence the expression of pro-inflammatory genes, including nuclear factor kappa-light chain enhancer of activated B cells (NF-κB), activator protein-1 (AP-1), and intercellular adhesion molecule-1 (ICAM).

Additionally, flavonoids counteract reactive oxygen species by donating electrons and hydrogen atoms. They also enhance the activity of endogenous antioxidant enzymes and chelate transition metal ions [57].

2.8. Secondary metabolites Comparision

Table 1 shows secondary metabolites comparation of terpenoid, xanthomonas and flavonoids, including characteristics of their chemical structure, pharmacological properties, applications and how they are used in Aymara medicine. Terpenoids have properties such as anti-inflammatory, antioxidant, antitumoral and antimicrobial among others, their applications are estimated in uses such as pharmaceutical products, aromatherapy and food. It is estimated that for the Aymara people their use is through essential oils mixed with carrier vegetable oils to support headaches, relaxation and stress. As shown in Table 1, terpenoids exhibit anti-inflammatory, antioxidant, antitumoral, and antimicrobial properties, among others.

Xanthomonas are used by the Aymara people in infections, as they are attributed with antifungal, antibacterial and antiviral properties. On the other hand, flavonoids with their antioxidant, anti-inflammatory and cardioprotective properties among others have been used by these cultures by infusions and preparations to be drunk [48].

Xanthones included in these plants are used by Aymara people for infections, attributed to their antifungal, antibacterial, and antiviral properties [62]. At the same time, flavonoids—known for their antioxidant, anti-inflammatory, and cardioprotective benefits—have been utilized by these cultures in various infusions and beverages [62].

2.9. Comparative table of Azorella, Centarium, and Amaranthus plants

The use of medicinal plants has now become an optimal alternative for the treatment and control of different diseases. The secondary metabolites present in most plants have demonstrated in recent studies biological functions that generate a positive impact on health due to their bactericidal, antioxidant, anticancer, antihyperglycemic, vasodilatory effects, among others. In the Aymara population, diabetes mellitus, arterial hypertension, and dyslipidemia are significant health concerns within the population, not only due to their prevalence in daily life but also because of their considerable impact on overall health and well-being. These diseases are treated through different treatments offered by the territory due to the richness and diversity of the ecological floors of the region that contribute to a traditional Andean medical system specialized in this type of pathologies [68].

Table 2 describes the plants of the genera *Azorella, Centarium*, and *Amaranthus*, including their botanical description, immunological properties, and most common preparations used by the Aymara medicine [66]. As shown in the table, both *Azorella* and Amaranthus are mostly attributed to their antioxidant properties and are commonly used in infusions by the Aymara community [69].

Based on Table 2, several relevant findings about the use and properties of Azorella, Centarium, and Amaranthus plants in Aymara medicine can be exposed:

2.9.1. Immunological properties and therapeutic uses

Azorella: This plant, with its anti-inflammatory and antioxidant properties, is primarily used to treat respiratory and rheumatic problems, making it a valuable remedy for chronic and painful diseases. It is normally used by infusions and poultices highlighting its significance in traditional Aymara medicine.

Centarium: Its properties as an immune system stimulant including its digestive benefits position this specie as a key plant for treating digestive disorders stimulating appetite. This underscores its importance where digestive diseases are prevalent, with teas and liquid extracts being the preferred methods of preparation.

Amaranthus: In addition to being rich in nutrients, it has potent antioxidant properties that enhance immune responses. It is commonly used for nutrition, treating anemia and digestive issues. It is prepared in the form of flours, infusions, and poultices.

2.9.2. Diversity of preparations

The preparations vary depending on the plant; however they all share a focus on traditional methods such as infusions, poultices, and liquid extracts. This highlights a strong connection between the Aymara medicine and the use of simple yet effective techniques to extract medicinal benefits from plants [64].

2.9.3. Impact on the population's health

All three plants are recognized for their immunological effects, including antioxidant, anti-inflammatory, and immune-stimulating properties, highlighting their importance in enhancing overall health and preventing common diseases in the region.

For the Aymara people, plants are considered gifts from Pachamama, with Azorella holding special significance in ancestral medicine for restoring bodily and spiritual balance and promoting the holistic well-being of the community. The following table (Table 3) provides a detailed overview of the *Azorella* spp. genus, emphasizing key aspects such as its chemical composition, immunological properties, therapeutic applications, and its role in traditional Aymara medicine. This compendium synthesizes insights from both scientific research and ancestral knowledge, offering a comprehensive perspective on the use and benefits of these plants in traditional and modern medicinal practices.

Centaurium, formerly known as Erythraea, is a group of genera of the *Gentianiaceae* family, which contains approximately 50 species of plants that are part of the Chironieae tribe. In Chile, there are different species belonging to the *Centaurium genus*, such as *Centaurium cachanlahuen*, *Centaurium littorale*, *Centaurium pulchellum,* among others, which are distributed throughout the country [59]. The Aymara community uses this native species as a medicinal plant by preparing an infusion that is characterized by its bitter taste. This preparation has different properties and clinical uses such as hypotensive, hypoglycemic, sudorific, febrifuge and is also used for liver and digestive problems [74].

Table 4 describes the *Centaurium genus* characteristic, detailing its chemical composition, medicinal properties, and therapeutic applications from a immunological and holistic perspective. Additionally, it analyzes its role in traditional Aymara medicine, as well as scientific evidence and its use in Western medicine (Table 3). This table highlights how the *Centaurium spp.* genus is valued both for its chemical composition and medicinal properties, as well as for its role in traditional Aymara practices. From a scientific perspective, emphasis is placed on the bioactive compounds that offer healing properties and its ability to

Table 1
Comparative table of secondary metabolites: Chemical structure, pharmacological properties, applications, and use by the Aymara medicine.

Metabolite Type	Chemical Structure	Pharmacological Properties	Applications	Uses by Aymara Medicine	Reference
Terpenoids	Hydrocarbons with isoprene units	Anti-inflammatory, antioxidant, anticancer, antimicrobial	Pharmaceutical, aromatherapy, food additives	Essential oils mixed with carrier vegetable oils for headaches, relaxation, and stress relief	[1,36, 58–60]
Xanthones	Phenolic compounds with two aromatic rings	Antifungal, antibacterial, antiviral	Pharmaceutical, traditional medicine	Used in infections for their antifungal, antibacterial, and antiviral properties	[61–63]
Flavonoids	15 carbons, two aromatic rings, 3-carbon bridge	Antioxidant, anti-inflammatory, cardio-protective	Pharmaceutical, dietary supplements, beverages	Infusions and preparations for drinking due to their antioxidant, anti-inflammatory, and cardioprotective properties	[65,73], [35,67]

Table 2
Comparative table describing Azorella, Centarium, and Amaranthus plants.

Genus	Botanical Description	Immunological Properties	Use in Aymara Medicine	Common Preparations	References
Azorella	Perennial plant with low growth, small and aromatic leaves	Anti-inflammatory and antioxidant properties	Treatment of respiratory and rheumatic problems	Infusions, poultices	[53,63]
Centarium	Herbaceous plant with pink flowers, also known as lesser centaury	Immune system stimulant, digestive properties	Treatment of digestive disorders, appetite stimulant	Teas, liquid extracts	[39,61]
Amaranthus	Plant with colorful inflorescences, nutrient-rich grains	Antioxidant properties improve immune response	Nutrition, treatment of anemia and digestive problems	Flours, infusions, poultices	[48]

Table 3
Table for the Genus *Azorella spp* characteristics.

Aspect	Scientific Description	Immunological Description	Holistic Aymara Description	References
Chemical Composition	Contains terpenoids, flavonoids, alkaloids, and other bioactive compounds	Bioactive compounds can modulate the immune response and reduce inflammation	Plants are seen as a gift from Pachamama, used in harmony with nature	[53]
Medicinal Properties	Anti-inflammatory, antioxidant, antimicrobial, and anticancer properties	Improves defense against pathogens, modulates inflammation, and strengthens the immune system	Used in traditional medicine to restore bodily and spiritual balance	[70]
Therapeutic Applications	Studies have demonstrated its efficacy in inflammatory and microbial diseases	Helps in treating infections and chronic immune system diseases	Used in rituals and spiritual practices to promote integral health	[70]
Scientific Evidence	Limited but promising clinical studies, pharmacological research	Evidence of immunological modulation and pathogen load reduction	Based on ancestral knowledge and traditional Andean practices	[70]
Role in Traditional Medicine	Common ingredient in natural treatments for its healing properties	Plants used to strengthen the immune system and prevent diseases	Part of healing rituals, including offerings to Pachamama and cleanses	[71]
Usage Practices	Extraction of compounds for use in medicines and supplements	Use of extracts and preparations to strengthen the immune response	Traditional preparations, infusions, and ointments used by healers	[72]

Table 4
Table for the Genus *Centaurium spp characterization.*

Aspect	Scientific Description	Immunological Description	Holistic Aymara Description	Reference
Chemical Composition	Contains secoiridoids, flavonoids, phenolic acids, and xanthones	Bioactive compounds can modulate the immune response and reduce inflammation	Plants are seen as a gift from Pachamama, used in harmony with nature	[39,61, 74]
Medicinal Properties	Digestive, hepatoprotective, antioxidant, anti-inflammatory, and antimicrobial properties	Improves defense against pathogens, modulates inflammation, and strengthens the immune system	Used in traditional medicine to restore bodily and spiritual balance	[39,61]
Therapeutic Applications	Studies have demonstrated its efficacy in digestive and liver diseases, inflammatory and microbial diseases	Helps in treating infections and chronic immune system diseases	Used in rituals and spiritual practices to promote integral health	[75]
Scientific Evidence	Limited but promising clinical studies, pharmacological research	Evidence of immunological modulation and pathogen load reduction	Based on ancestral knowledge and traditional Andean practices	[76]
Role in Traditional Medicine	Common ingredient in natural treatments for its healing properties	Plants used to strengthen the immune system and prevent diseases	Part of healing rituals, including offerings to Pachamama and cleanses	[75,77]
Usage Practices	Extraction of compounds for use in medicines and supplements	Use of extracts and preparations to strengthen the immune response	Traditional preparations, infusions, and ointments used by healers	[77]

Table 5
Table for the Genus *Amaranthus* spp *characterization*.

Aspect	Scientific Description	Immunological Description	Holistic Aymara Description	Reference
Chemical Composition	Contains flavonoids, saponins, alkaloids, and polyphenols	Bioactive compounds can modulate the immune response and reduce inflammation	Plants are seen as a gift from Pachamama, used in harmony with nature	[79–81]
Medicinal Properties	Antioxidant, anti-inflammatory, anticancer, antimicrobial, and hypocholesterolemic properties	Improves defense against pathogens, modulates inflammation, and strengthens the immune system	Used in traditional medicine to restore bodily and spiritual balance	[82]
Therapeutic Applications	Efficacy in preventing chronic diseases, cardiovascular diseases, infections, and cancer	Helps in treating infections and chronic immune system diseases	Used in rituals and spiritual practices to promote integral health	[83,84]
Scientific Evidence	Limited but promising clinical studies, pharmacological research	Evidence of immunological modulation and pathogen load reduction	Based on ancestral knowledge and traditional Andean practices	[52]
Role in Traditional Medicine	Common ingredient in natural treatments for its healing properties	Plants used to strengthen the immune system and prevent diseases	Part of healing rituals, including offerings to Pachamama and cleanses	[71,79]
Usage Practices	Extraction of compounds for use in medicines and supplements	Use of extracts and preparations to strengthen the immune response	Traditional preparations, infusions, and ointments used by healers	[74]

strengthen the immune system. From the Aymara perspective, this plant has a deep spiritual meaning and is used in balance with nature to restore bodily and spiritual health.

Finally, *Amaranthus caudatus* or amaranth or kiwicha is a fast-growing plant species with cylindrical branches that sprout from the base, a central stem that reaches 2–2.5 m in height, broad green leaves and flowers that gather in long red or purple clusters whose pigmentation is due to its high content of betacyanins which considerably enhances its visual appeal. It is distributed in the low and high regions of Peru, Ecuador, Argentina, Bolivia and Chile, where it easily adapts to different environments and grows at altitudes of more than 3000 m above sea level [78].

Table 5 provides a detailed characterization of the *Amaranthus* spp. genus from multiple perspectives: scientific, immunological, and holistic Aymara. It explores key aspects such as its chemical composition, medicinal properties, and therapeutic applications, highlighting the importance of this plant in both traditional Aymara medicine and modern scientific research. Table 5 synthesizes data from clinical and pharmacological studies, as well as ancestral knowledge, illustrating the comprehensive value of this plant.

2.10. Most relevant characteristics for the genus Centaurium spp are

2.10.1. Chemical and immunological composition

Centaurium spp contains bioactive compounds such as secoiridoids, flavonoids, phenolic acids, and xanthones, which can modulate the immune response reducing inflammation. These compounds not only strengthen the immune system but also play an important role in the inflammatory treatment and microbial diseases [39,61].

2.10.2. Medicinal properties

Plants of this genus have digestive, hepatoprotective, antioxidant, anti-inflammatory, and antimicrobial properties [39]. From a immunological perspective, they help improving defense against pathogens strengthening the immune system, while in traditional Aymara medicine, they are used to restore bodily and spiritual balance.

2.10.3. Therapeutic applications

Scientific studies have demonstrated the effectiveness of *Centaurium spp* in the treatment of digestive issues, liver diseases, inflammatory conditions, and microbial infections. Additionally, in traditional Aymara medicine, these plants are used in rituals and spiritual practices to promote holistic health, suggesting an application in both physical and spiritual level.

2.10.4. Scientific evidence

Although clinical studies are limited, pharmacological research is promising. There is evidence supporting the ability of *Centaurium spp* to modulate the immune system reducing pathogens burden. This validates its use in natural treatments in both traditional and modern medicine.

2.10.5. Role in traditional medicine

Centaurium spp is a common ingredient in natural treatments due to its healing properties. Plants are used not only to strengthen the immune system and prevent diseases but also as part of healing rituals, including offerings to Pachamama and spiritual cleansings.

2.10.6. Usage practices

In Aymara medicine, traditional preparations include infusions and ointments made by healers, reflecting ancestral knowledge passed down through generations.

These results highlight the relevance of *Centaurium spp* both in modern medicine and in Aymara traditional medicine, emphasizing its ability to treat a variety of diseases and its role in maintaining spiritual and physical balance.

Now, regarding the perception and etiology of what is known by the term “disease,” these are extremely important aspects for addressing the world of Aymara medicine. While it is true that illness is a category of medicine, it is also a category of anthropology because it responds to a sociocultural construction. It is more advantageous to know and directly interpret the medical systems of any culture; it is also beneficial to understand the knowledge and practices of a specific human group in relation to the care and techniques that should be applied to individual when it is affected by a pathology (disease, discomfort, ailment, condition, injury, or illness) [1].

Regarding the causality of the disease in the western medical system, it is still claimed that bacteria, fungi, viruses and microbes would be the main pathogens, however, this theory has evolved because it has already been identified and confirmed that there are other factors that can cause diseases, including poor nutrition, intoxication, stress, social conflicts, drug addiction, rape, poverty, alcoholism, work, worries, anxiety, etc. Even now, climate change has become another factor in diseases. Thus, for example, disease is now understood as the loss of an organism’s ability to adapt to environmental changes within normal limits [85].

This quote implies that disease would not only be a consequence of extrinsic factors, but rather, because of intrinsic factors. That is, human organism does not respond efficiently to the demands of the environment. Which means that the quality of life of the human body depends, in any case, on the way of life. Moreover, in the Aymara conception we find other variants that would influence the acquisition of diseases, these variables are more of a social, cultural and cosmogonic nature [1,86].

3. Discussion

The study of secondary metabolites in Andean medicinal plants like *Azorella*, *Centaurium*, and *Amaranthus* reveals a rich diversity of bioactive compounds with significant pharmacological properties. These plants play a crucial role in traditional medicinal practices, particularly within Aymara culture, reflecting not only their therapeutic potential but also their cultural and historical significance [52].

While the concept that plants possess healing properties is ancient, indigenous communities have traditionally focused on the effects of these plants, using them for nutrition, healing, and socio-cultural purposes. Over the years, research has advanced in evaluating the pharmacological properties of native species to scientifically support their folklore uses, and the active compounds responsible for their biological effects have been characterized.

For instance, in *Azorella*, flavonoids are known for their antioxidant properties, which help protect against oxidative damage—a key factor in combating chronic and degenerative diseases. These flavonoids also exhibit anti-inflammatory and antitumor activities [65]. Terpenoids and alkaloids present in *Azorella* are particularly noted for their analgesic, antispasmodic, and anti-inflammatory properties, making them effective in treating rheumatic and respiratory conditions. Terpenoids also demonstrate antimicrobial, anti-inflammatory, and antitumor effects, further justifying their use in Aymara traditional medicine.

Similarly, species from the genus *Centaurium* contain bioactive compounds such as xanthones, flavonoids, phenolic acids, and secoiridoids [29]. Xanthones are valued for their antioxidant and cardioprotective properties, and studies highlighting their efficacy in reducing hypertension support the Aymara community’s use of *Centaurium* in managing cardiovascular diseases.

In *Amaranthus*, secondary metabolites like saponins, polyphenols, and flavonoids are prevalent. Saponins stand out for their cholesterol-lowering, antimicrobial, and immunomodulatory effects. The use of *Amaranthus* in reducing cholesterol and improving cardiovascular health is well-supported by the presence of these compounds [84]. Flavonoids, known for their potent antioxidant capabilities, neutralize free radicals, protect cells from oxidative damage, and help prevent chronic and degenerative conditions like cancer and cardiovascular disease. They also possess anti-inflammatory properties, reducing inflammation and alleviating symptoms of conditions such as arthritis.

Their antitumoral activities, including inducing cell apoptosis inhibiting angiogenesis, are significant for cancer prevention. In Aymara medicine, flavonoids are commonly used in infusions aimed at improving cardiovascular and digestive health, underscoring their importance in promoting well-being.

In traditional Aymara medicine, terpenoids are primarily applied in essential oils for pain and stress relief, highlighting their pharmacological significance. Though the use of xanthones in ancestral medicine is less documented, their potential in treating infections is recognized [87].

Further exploration of these plants and their bioactive compounds could significantly enrich our understanding and expand their applications in both traditional and modern medicine. It is well-established that many secondary metabolites in these species share common biosynthetic pathways. However, the structural diversity of compounds found in various extracts and preparations used by the Aymara community contributes to their wide-ranging effects. The synergistic interactions among these components result in a spectrum of pharmacological activities, rather than effects being attributable to any single compound. This intricate interplay of traditional knowledge and medicinal plant use is particularly evident in the health practices of the Aymara people, who rely on their deep-rooted medicinal traditions alongside an evolving understanding of modern healthcare.

Aymara medicine, deeply rooted in the cultural practices of the Aymara people, faces several limitations when integrated into modern clinical applications. These limitations can be categorized into four main areas: sustainable large-scale extraction, regulatory issues, pharmaceutical forms, and routes of administration.

3.1. Sustainable large-scale extraction

The sustainable extraction of medicinal plants central to Aymara medicine presents significant challenges. Many traditional remedies depend on local flora, which is often not cultivated sustainably. Rising demand for these plants risks overharvesting, jeopardizing biodiversity and disrupting the ecological balance of their habitats. Furthermore, the absence of robust infrastructure to support sustainable cultivation and harvesting practices hinders efforts to scale production while adhering to modern pharmaceutical standards. This tension underscores the difficulty of integrating traditional knowledge and practices into contemporary healthcare systems without compromising ecological integrity or cultural heritage [88].

3.1.1. Regulatory issues

Regulatory frameworks frequently fail to accommodate traditional medical practices such as those of the Aymara. The lack of recognition and integration within national health policies creates significant barriers to the formal acceptance of Aymara medicinal practices in clinical settings. For example, the Chilean healthcare system has faced criticism for its inability to provide culturally appropriate care, highlighting systemic issues that marginalize indigenous health traditions. Addressing these challenges requires a more inclusive approach to policy-making that respects and integrates traditional knowledge into modern healthcare systems while ensuring equitable access for indigenous communities [90,92]. Furthermore, regulatory bodies may require extensive scientific validation for traditional remedies, which can be difficult to achieve given the qualitative nature of much traditional knowledge and practice [91].

3.1.2. Pharmaceutical forms

The transition from traditional herbal remedies to standardized pharmaceutical forms involves numerous challenges. Aymara medicine often relies on whole plants or complex mixtures, which may not easily align with the single active pharmaceutical ingredients (APIs) typically required by modern regulatory frameworks. This inherent complexity makes it difficult to develop consistent dosage forms that adhere to contemporary pharmacological standards [6]. Additionally, issues related to bioavailability—the efficiency with which a drug is absorbed and utilized in the body—frequently emerge when transforming these traditional remedies into modern pharmaceutical formats. These obstacles underscore the need for innovative approaches to bridge the gap between traditional practices and modern medical requirements [89].

3.1.3. Routes of administration

The routes of administration for Aymara medicinal preparations are typically oral or topical, relying on herbal infusions or poultices. However, modern medicine often emphasizes different routes (e.g., intravenous or intramuscular) that may not align with traditional practices. The reluctance among Aymara people to accept invasive procedures reflects a cultural preference for less invasive treatments that respect bodily integrity [90].

This cultural perspective can sometimes hinder the acceptance of modern medical interventions, particularly those perceived as invasive or potentially harmful. In conclusion, while Aymara medicine provides valuable insights and practices deeply rooted in indigenous knowledge, its integration into modern clinical applications faces several challenges. These include sustainability concerns, regulatory barriers, difficulties in standardizing pharmaceutical formulations, and cultural preferences for traditional routes of administration. Overcoming these limitations demands a collaborative approach that respects and preserves traditional practices while addressing the complexities and requirements of modern healthcare systems [93].

Compared to other indigenous populations, the Aymara adopt a balanced approach by integrating native plants like *Amaranthus* and *Azorella* with modern medicine, effectively addressing health challenges such as anemia, digestive disorders, and inflammation. Although they face similar barriers to healthcare access as other ancestral communities, their continued reliance on traditional remedies plays a vital role in maintaining their overall health. The combination of their nutrient-rich dietary practices, which include grains like *kiwicha*, with the pharmacological benefits of their native plants, bolsters their long-standing resilience against chronic and infectious diseases [94,95].

The Aymara's holistic perspective—viewing health as an integration of physical, spiritual, and environmental well-being—offers a unique insight into the potential of natural compounds in promoting long-term health [96].

4. Conclusion

The study of secondary metabolites in Andean medicinal plants such as *Azorella*, *Centaurium*, and *Amaranthus* uncovers a wealth of bioactive compounds with important pharmacological properties and traditional medicinal uses. In *Azorella*, terpenoids, alkaloids, and flavonoids offer antioxidant, anti-inflammatory, and antitumoral benefits, particularly in treating rheumatic and respiratory diseases. In *Centaurium*, xanthones, flavonoids, and secoiridoids provide antioxidant and cardioprotective properties, making the plant effective in managing cardiovascular health. Meanwhile, *Amaranthus* contributes hypocholesterolemic, antimicrobial, and immunomodulatory effects, along with potent antioxidant protection against oxidative damage, which prevents chronic and degenerative diseases and offers antitumor properties.

The comparison between Western and Aymara Andean medicine reveals distinct differences in therapeutic approaches, preparation methods, and cultural practices. Western medicine, grounded in scientific evidence and clinical studies, ensures effective and safer treatments. In contrast, Aymara medicine, rooted in ancestral knowledge and the Andean worldview, integrates spiritual and holistic practices, addressing disease with a holistic approach that considers multiple causes simultaneously.

Similar to other indigenous communities, the Aymara encounter challenges related to access to modern healthcare and health issues

stemming from changes in diet and lifestyle. However, they manage to maintain a relatively strong balance between their traditional practices and Western medicine, which allows them to sustain a more stable state of health compared to many other indigenous populations.

For the Aymara, health is seen as a balance between the body, mind, spirit, and nature, with immune health maintained through harmony with Pachamama. Rituals and spiritual practices, combined with the use of medicinal plants, are essential to strengthen the immune system.

Integrating traditional Aymara medicinal knowledge with modern scientific approaches offers a comprehensive perspective on health promotion and disease prevention. This fusion underscores the importance of valuing ancestral practices while expanding our understanding of their benefits in contemporary medicine.

While the Aymara community continues to encounter challenges in accessing modern healthcare, their reliance on traditional medicine has enabled them to maintain a relatively robust foundation of health. Preserving their traditional health practices, alongside efforts to enhance access to contemporary healthcare, will be crucial for ensuring their long-term well-being.

Traditional Aymara medicine embodies a deep understanding of medicinal plants and their uses, which have been cultivated over generations. This knowledge, rooted in cultural practices and a holistic view of health, offers valuable insights that can enhance modern medical practices. By bridging the gap between traditional wisdom and scientific research, we can explore new therapeutic avenues improving public health outcomes, while also respecting and preserving the cultural heritage of the Aymara people. Collaborative efforts that honor and integrate both systems of knowledge can lead to innovative health solutions that benefit diverse communities.

Plants discussed in the article—Azorella, Centaurium, and Amaranthus—demonstrate significant drug potential due to their pharmacological properties and secondary metabolites. Azorella, in particular, is rich in terpenoids, flavonoids, and alkaloids, making it a strong candidate for anti-inflammatory drugs aimed at chronic conditions like rheumatoid arthritis. Its terpenoids can help reduce inflammation and pain, while its flavonoids may be beneficial in therapies targeting oxidative stress related to degenerative diseases such as Alzheimer's. Centaurium is rich in xanthones, secoiridoids, and flavonoids, all noted for their antioxidant and hepatoprotective properties. It shows promise for treating hypertension, as xanthones with cardioprotective effects could be developed into hypertension medications and drugs to prevent cardiovascular diseases. Additionally, secoiridoids may be formulated to protect the liver from toxins and liver diseases. Amaranthus contains saponins, polyphenols, and flavonoids, offering antioxidant and immune-modulating benefits. Potential applications include using saponins to lower LDL cholesterol and prevent cardiovascular conditions, while polyphenols could be developed into supplements to enhance immune function and prevent infections and autoimmune diseases.

Each of these plants has applications in traditional medicine and, through scientific research, their metabolites can contribute to developing treatments for modern diseases, bridging ancestral knowledge with contemporary science. Traditional Aymara medicine provides valuable insights into medicinal plants. By merging this wisdom with modern science, we can uncover new treatments, enhance health outcomes, and preserve the cultural heritage of the Aymara people.

Funding

This research was funded by Núcleo UNAB DI-03-23/NUC and Núcleo UNAB DI-02-22/NUC.

CRediT authorship contribution statement

Ivania Cortés: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. **Francisco Ceric:** Writing – review & editing, Supervision, Methodology. **Hellen Navarrete:** Writing – original draft, Investigation, Conceptualization. **Maité Rodríguez-Díaz:** Validation, Supervision, Conceptualization. **María Carolina Otero:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

I am writing to declare that I have NO personal, financial, or professional interests related this publication that could be perceived as a conflict of interest. I am committed to maintaining transparency and integrity in all my professional engagements.

References

[1] Mamani Onofre, Medicina tradicional Aymara, perú. Comunicación, Rev. Int. Invest. Comunicación Desarro. 4 (1) (2013). https://mail.comunicacionunap.com/index.php/rev/article/view/40.

[2] P.J.M. van den Berg, 'La tierra no da así no más': los ritos agrícolas en la religión de los Aymara-cristianos de los Andes. Version of the Following Full Text: Latin American Studies, 1989. Publisher's version Downloaded from: http://hdl.handle.net/2066/113147Downloaddate:2024-09-18.

[3] Milano Bárbara, Robellodo Francico, Castro Natalia, Olavarría Rodrigo, Zañartu Carolina, Unidad de coordinación de asuntos indígenas del ministerio de desarrollo social y familia, Chile. https://www.conadi.gob.cl/, 2022.

[4] J.J.M.M. Van Kessel, Yatiris y Ch'amakanis del Altiplano Aymara; Sueños, Testimonios y Prácticas Ceremoniales. Gerardo Fernández Juárez, Abya Yala, Quito, Ecuador, Chungará (Arica) 37 (1) (2005) 91–95, https://doi.org/10.4067/S0717-73562005000100008.

[5] Adimelia Moscoso García, Vásquez Acosta, María, Pulido Iparraguirre, Cristóbal, Relaciones sociales de mujeres aymara translocales: una explicación desde la presencia/ausencia del Suma Qamaña, Diálogo andino (65) (2021) 321–331, https://doi.org/10.4067/S0719-26812021000200321.

[6] Losada Guerra, Jorge Luis, Hernández Navarro, V. Elena, Salvat Quesada, Miguel, Losada Hernández, Omar José, Evolución histórica del razonamiento clínico, Medisan 23 (6) (2019) 1164–1180. Epub 20 de diciembre de 2019. Recuperado en 01 de enero de 2025, de, http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192019000601164&lng=es&tlng=pt.

[7] R.K. Wallace, Ayurgenomics y medicina moderna, Medicina (Kaunas) 56 (12) (2020 Nov 30) 661, https://doi.org/10.3390/medicina56120661. PMID: 33265906; PMCID: PMC7760374.

[8] J.T. Zhang, New drugs derived from medicinal plants, Therapie 57 (2) (2002 Mar-Apr) 137–150. PMID: 12185962.

[9] Serena Caroselli, El dolor de los pacientes aymara de la comuna de putre: prácticas terapéuticas y políticas de salud intercultural, Diálogo andino (42) (2013) 89–104, https://doi.org/10.4067/S0719-26812013000200008.

[10] Valentina B. González-Garrido, Jiménez-Baltierra, Diego A. Orellana, Renán, Manuel E. Cortés, Plantas medicinales chilenas: desde el saber ancestral a la comercialización poco regulada, Rev. Med. Chile 150 (2) (2022) 275–276, https://doi.org/10.4067/S0034-98872022000200275.

[11] Mamani Onofre, Medicina tradicional Aymara, perú. Comunicación, Rev. Int. Invest. Comunicación Desarro. 4 (1) (2013). https://mail.comunicacionunap.com/index.php/rev/article/view/40.

[12] F. Mamani, El rol del yatiri en la cultura andina, Volveré 19 (4). https://www.iecta.cl/revistas/volvere_19/editorial.htm.

[13] Néstor y otros Chambi, Así no más nos curamos La medicina en los andes. Lima: Editorial Proyecto Andino de Tecnologías Campesinas, 1998.

[14] Melino Sáens, Sabiduría, Creencias, Valores y Prácticas en la Cosmovisión AndinaAcademia Nacional de Historia Ecuatoriana de Ciencias de la Ingeniería, Programa de Manejo del Agua y del Suelo PROMAS 37 (3) (2024). Universidad de Cuenca.

[15] N.M. Al Aboud, Unlocking the genetic potential: strategies for enhancing secondary metabolite biosynthesis in plants, J. Saudi Soc. Agric. Sci. 2024 (2024), https://doi.org/10.1016/j.jssas.2024.06.004. ISSN 1658-077X.

[16] P.A. Divekar, S. Narayana, B.A. Divekar, R. Kumar, B.G. Gadratagi, A. Ray, A. K. Singh, V. Rani, V. Singh, A.K. Singh, A. Kumar, R.P. Singh, R.S. Meena, T. K. Behera, Plant secondary metabolites as defense tools against herbivores for sustainable crop protection, Int. J. Mol. Sci. 23 (5) (2022) 2690, https://doi.org/10.3390/ijms23052690.

[17] F. Alrumaihi, S.A. Almatroodi, H.O.A. Alharbi, W.M. Alwanian, F.A. Alharbi, A. Almatroudi, A.H. Rahmani, Pharmacological potential of kaempferol, a flavonoid in the management of pathogenesis via modulation of inflammation and other biological activities, Molecules 29 (9) (2024 Apr 26) 2007, https://doi.org/10.3390/molecules29092007.

[18] M.A. Neag, A. Mocan, J. Echeverría, R.M. Pop, C.I. Bocsan, G. Crişan, A. D. Buzoianu, Berberine: botanical occurrence, traditional uses, extraction methods, and relevance in cardiovascular, metabolic, hepatic, and renal disorders, Front. Pharmacol. 9 (2018 Aug 21) 557, https://doi.org/10.3389/fphar.2018.00557.

[19] B. Ncube, J. Van Staden, Tilting plant metabolism for improved metabolite biosynthesis and enhanced human benefit, Molecules 20 (7) (2015 Jul 13) 12698–12731, https://doi.org/10.3390/molecules200712698.

[20] Zhijian Yao, Qian Wu, Wenbing Sheng, XuDong Zhou, Lidong Cheng, Tian Xing, Hanwen Yuan, Limin Gong, Wei Wang, Bin Li, Caiyun Peng, Flavonoidal alkaloids: emerging targets for drug discovery from Nature's bounty, Fitoterapia 177 (2024) 106099, https://doi.org/10.1016/j.fitote.2024.106099. ISSN 0367-326X.
[21] Zhifang Qin, Ran Tang, Juan Liang, Xiaoyi Jia, Berberine, a natural alkaloid: advances in its pharmacological effects and mechanisms in the treatment of autoimmune diseases, Int. Immunopharm. 137 (2024) 112422, https://doi.org/10.1016/j.intimp. ISSN 15675769, 2024.112422.
[22] N. Tiwari, V.K. Gupta, P. Pandey, D.K. Patel, S. Banerjee, M.P. Darokar, A. Pal, Adjuvant effect of Asparagus racemosus Willd. derived saponins in antibody production, allergic response and pro-inflammatory cytokine modulation, Biomed. Pharmacother. 86 (2017 Feb) 555–561, https://doi.org/10.1016/j.biopha.2016.11.087.
[23] Pallavi Sharma, Arti Tyagi, Pravin Bhansali, Shubhra Pareek, Vineeta Singh, Ashal Ilyas, Rajeev Mishra, Nitesh Kumar Poddar, Saponins, Extraction, bio-medicinal properties and way forward to anti-viral representatives, Food Chem. Toxicol. 150 (2021) 112075, https://doi.org/10.1016/j.fct.2021.112075. ISSN 0278-6915.
[24] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ 372 (2021) n71, https://doi.org/10.1136/bmj.n71.
[25] k Collao-alvarado, A. maldonado, L. gonzález, A. sandoval, M.E. de porras, A. zamora, G. arancio, Estudio de la relación polen-vegetación actual en el Norte de Chile, en el transecto Pozo Almonte-Salar de Huasco (20°15'S/69°06'O). Gayana, Botanica (Delhi) 72 (1) (2015) 125–136, https://doi.org/10.4067/S0717-66432015000100015.
[26] L.M. Orellana, Caracterización de humedales altoandinos para una gestión sustentable de las actividades productivas del sector norte del país. Flora y vegetación y región de Tarapacá, CIREN. Centro de Investigación de Recursos Renovables, FLORA Y VEGETACIÓN: REGIÓN DE TARAPACÁ 1 (2013).
[27] N. Chaachouay, L. Zidane, Plant-derived natural products: a source for drug discovery and development, Drugs Drug Candidates 3 (2024) 184–207, https://doi.org/10.3390/ddc3010011.
[28] Matteo Sartori, Plantas medicinales del sur de chile en la época colonial. una aproximación desde la historia ambiental hacia el conocimiento socionatural (1646-1732), Diálogo andino (67) (2022) 242–254, https://doi.org/10.4067/S0719-26812022000100242.
[29] Erick A. Aguilera-Cauich, Karen Z. Solís-Fernández, Ariadna Ibarra-Morales, Rolando Cifuentes-Velásquez, Ivonne Sánchez-del Pino, Amaranto: distribución y diversidad morfológica del recurso genético en partes de la región Maya (sureste de México, Guatemala y Honduras), Acta Bot. Mex. (128) (2021) e1738, https://doi.org/10.21829/abm128.2021.1738. Epub 16 de marzo de 2021.
[30] C. Kleier, T. Trenary, E.A. Graham, W. Stenzel, P.W. Rundel, Size class structure, growth rates, and orientation of the central Andean cushion Azorella compacta, PeerJ 3 (2015 Mar 17) e843, https://doi.org/10.7717/peerj.843.
[31] D Faina Valle, Compuestos bioactivos de especies medicinales endémicas de Chile bajo consideración de los saberes indígenas. Informe de práctica indígena. Universidad de Chile. Facultad de Ciencias Físicas y Matemáticas, Departamento de Ingeniería Química, Biotecnología y Materiales Santiago, Chile (2021) 91.
[32] Milano Bárbara, Robellodo Francico, Castro Natalia, Olavarría Rodrigo, Zañartu Carolina, Unidad de coordinación de asuntos indígenas del ministerio de desarrollo social y familia, chile. https://www.conadi.gob.cl/, 2022.
[33] J. Bórquez, Edward J. Kennelly, Mario J. Simirgiotis, Activity guided isolation of isoflavones and hyphenated HPLC-PDA-ESI-ToF-MS metabolome profiling of Azorella madreporica Clos. from northern Chile, Food Res. Int. 52 (Issue 1) (2013) 288–297, https://doi.org/10.1016/j.foodres.2013.02.055. ISSN 0963-9969.
[34] M. Heinrich, J. Mah, V. Amirkia, Alkaloids used as medicines: structural phytochemistry meets biodiversity-an update and forward look, Molecules 26 (7) (2021 Mar 25) 1836, https://doi.org/10.3390/molecules26071836.
[35] Bonilla Rivera Pablo Enrique, Toche Tuesta Analucía, Fernández Rebaza Gustavo Adolfo, Curioso Melo Dara Edith, Rayme Gutierrez Robert Leonardo, Soto Tantaraico Edith Celia, Balladares Quintana Alfonso David, Milla Guerra Geralda Ines, Kevin Angel Suarez Santa Cruz, Mamani Herrera Leslie Karina, Acuña Guzman Victor Anderson, Gongora Ariana Yasmeen Yui, Venegas Fiestas Gerardo Antonio, Chemical composition and flavonoids characterization of the methanolic extract of leaves of two types of Ruta Chalepensis L. Instituto de Investigación en Ciencias Farmacéuticas y Recursos Naturales "Juan de Dios Guevara", Facultad de Farmacia y Bioquímica, Universidad Nacional. Mayor de San Marcos. Lima – Perú, Revista Peruana de Medicina Integrativa ISSN, 2020, pp. 2415–2692, https://doi.org/10.26722/rpmi.2020.53.18.
[36] Tohfa Siddiqui, Mohammad Umar Khan, Vikram Sharma, Komal Gupta, Terpenoids in essential oils: chemistry, classification, and potential impact on human health and industry, Phytomedicine 4 (Issue 2) (2024) 100549, https://doi.org/10.1016/j.phyplu.2024.100549. ISSN 2667-0313.
[37] Fernanda Tomiotto-Pellissier, Manoela Daiele Gonçalves, Taylon Felipe Silva, Virgínia Márcia Concato, Bruna Taciane da Silva Bortoleti, Nilton Syogo Arakawa, Ivete Conchon-Costa, Wander Rogério Pavanelli, Carolina Panis, Chapter 2 - plant-derived diterpenes for breast cancer treatment: new perspectives and recent advances, Stud. Nat. Prod. Chem 74 (2022) 41–80, https://doi.org/10.1016/B978-0-323-91099-6.00011-6. ISSN 1572-5995, ISBN 9780323910996.
[38] Islam M. Torequl, C. Quispe, J. Herrera-Bravo, M.M. Rahaman, R. Hossain, C. Sarkar, M.A. Raihan, M.M. Chowdhury, S.J. Uddin, J.A. Shilpi, E. Marcelo de Castro, J. Sousa, A.A.C. Melo-Cavalcante, M.S. Mubarak, J. Sharifi-Rad, D. Calina, Activities and molecular mechanisms of diterpenes, diterpenoids, and their derivatives in rheumatoid arthritis, Evid Based Complement Alternat Med 2022 (2022 Mar 25) 4787643, https://doi.org/10.1155/2022/4787643. PMID: 35368757; PMCID: PMC8975657.
[39] Danijela Mišić, Branislav Šiler, Marijana Skorić, Milutin S. Djurickovic, Jasmina Nestorović Živković, Vladan Jovanović, Zlatko Giba, Secoiridoid glycosides production by Centaurium maritimum (L.) Fritch hairy root cultures in temporary immersion bioreactor. Process Biochem., 48(10),1587-1591, ISSN 1359-5113, doi: 10.1016/j.procbio.2013.07.0Evid.Bas.Complement.Alternat.Med.15.
[40] M.V. Ashraf, S. Khan, S. Misri, K.S. Gaira, S. Rawat, B. Rawat, M.A.H. Khan, A. A. Shah, M. Asgher, S. Ahmad, High-altitude medicinal plants as promising source of phytochemical antioxidants to combat lifestyle-associated oxidative stress-induced disorders, Pharmaceuticals 17 (8) (2024 Jul 23) 975, https://doi.org/10.3390/ph17080975.
[41] D. Mišić, Branislav Šiler, Marijana Skorić, Milutin S. Djurickovic, Jasmina Nestorović Živković, Vladan Jovanović, Zlatko Giba, Secoiridoid glycosides production by Centaurium maritimum (L.) Fritch hairy root cultures in temporary immersion bioreactor, Process Biochem. 48 (10) (2013) 1587–1591, https://doi.org/10.1016/j.procbio.2013.07.015. ISSN 1359-5113.
[42] A. Viljoen, N. Mncwangi, I. Vermaak, Anti-inflammatory iridoids of botanical origin, Curr. Med. Chem. 19 (14) (2012) 2104–2127, https://doi.org/10.2174/092986712800229005. PMID: 22414102; PMCID: PMC3873812.
[43] Smail Aazza, Soukaina El-Guendouz, Maria da Graça Migue, Screening for acetylcholinesterase inhibition, lipid peroxidation inhibition and antioxidant activity of medicinal plants from Morocco. Boletin latinoamericano y del caribe de plantas medicinales y aromáticas/ISSN 0717 7917, 2023, https://doi.org/10.37360/blacpma.23.22.1.1.
[44] N.V. Gunter, S.S. Teh, Y.M. Lim, S.H. Mah, Natural xanthones and skin inflammatory diseases: multitargeting mechanisms of action and potential application, Front. Pharmacol. 11 (2020) 594202, https://doi.org/10.3389/fphar.2020.594202.
[45] Gordana Tovilovic-Kovacevic, Nevena Zogovic, Dijana Krstic-Milosevic, Chapter, Secondary metabolites from endangered Gentiana, Gentianella, Centaurium, and Swertia species (Gentianaceae): promising natural biotherapeutics, Biodiversity and Biomedicine 2020 (2020) 335–384, https://doi.org/10.1016/B978-0-12-819541-3.00019-0.
[46] E. Bolat, S. Sarıtaş, H. Duman, F. Eker, E. Akdaşçi, S. Karav, A.M. Witkowska, Polyphenols: secondary metabolites with a biological impression, Nutrients 16 (15) (2024 Aug 3) 2550, https://doi.org/10.3390/nu16152550.
[47] M.G. Miguel, Betalains in some species of the amaranthaceae family: a review, Antioxidants 7 (4) (2018 Apr 4) 53, https://doi.org/10.3390/antiox7040053.
[48] Mmbulaheni Happiness Netshimbupfe, Jacques Berner, Frank Van Der Kooy, Olakunle Oladimeji, Chrisna Gouws, The importance and use of Amaranthus for crop diversification in the SADC region, South Afr. J. Bot. 152 (2023) (2023) 192–202, https://doi.org/10.1016/j.sajb.2022.11.039. ISSN 0254-6299.
[49] E.R.B. Morales, Efecto de dosis nitrogenadas en el contenido proteico y pigmentos en el crecimiento fisiológico del cultivo de amaranto (Amaranthus caudatus l), para uso agroindustrial, Revista Vínculos ESPE 2 (1) (2017).
[50] Jai Vidaurre Prem, R. Narel Paniagua& Mónica Moraes, Etnobotánica en los Andes de Bolivia. Herbario Nacional de Bolivia, Cota Cota, Campus Universitario, Calle 27 s/n. La Paz. Bolivia, Botánica Económica de los Andes Centrales Editores, Universidad Mayor de San Andrés, 2006, pp. 224–238.
[51] L. Shen, H. Luo, L. Fan, X. Tian, A. Tang, X. Wu, K. Dong, Z. Su, Potential immunoregulatory mechanism of plant saponins: a review, Molecules 29 (2024) 113, https://doi.org/10.3390/molecules29010113.
[52] U. Sarker, S. Oba, Polyphenol and flavonoid profiles and radical scavenging activity in leafy vegetable Amaranthus gangeticus, BMC Plant Biol. 20 (2020) 499, https://doi.org/10.1186/s12870-020-02700-0.
[53] N. López Carreras, M. Miguel, A. Aleixandre, Beneficial health properties of iridoids terpenes, Revi. Nutr Clínica Dieta Hosp. (2012) 211–6057. Año de publicación: 2012. Volumen: 32. Número: 3. Páginas: 81-91.
[54] Fernández Barrero Fernández, Plantas iberoamericanas, como fuente de terpenoides útiles en química fina. Programa CYTED, Secretaría Gen. 28015 (2005) 293.
[55] García Salman Jorge, Considerations on Natural and Traditional Medicine, the scientific method and the Cuban health system, Rev. Cubana Salud Publica 39 (3) (2013). Editorial Ciencias Médicas ISSN 1561-3127, https://revsaludpublica.sld.cu/index.php/spu/article/view/12/107.
[56] Umakanta Sarker, Shinya Oba, Riaz Ullah, Bari Ahmed, Ercisli Sezai, Skrovankova Sona, Adamkova Anna, Zvonkova Magdalena, Mlcek Jiri, Nutritional and bioactive properties and antioxidant potential of Amaranthus tricolor, A. lividus, A viridis, and A. spinosus leafy vegetables, Heliyon 10 (9) (2024) e30453, https://doi.org/10.1016/j.heliyon.2024.e30453. ISSN 2405-8440.
[57] P. Rathee, H. Chaudhary, S. Rathee, D. Rathee, V. Kumar, K. Kohli, Mechanism of action of flavonoids as anti-inflammatory agents: a review, Inflamm. Allergy - Drug Targets 8 (3) (2009) 229–235, https://doi.org/10.2174/187152809788681029.
[58] I. Faraone, D.K. Rai, D. Russo, L. Chiummiento, E. Fernandez, A. Choudhary, L. Antioxidant Milella, Antidiabetic, and anticholinesterase activities and phytochemical profile of azorella glabra wedd, Plants 8 (2019) 265, https://doi.org/10.3390/plants8080265.
[59] A. Ludwiczuk, K. Skalicka-Woźniak, M.I. Georgiev, in: Simone Badal, Rupika Delgoda (Eds.), Chapter. 2017. Terpenoids, Academic Press, Pharmacognosy, 2017, pp. 233–266. https://www.sciencedirect.com/science/article/pii/B9780128021040000111.
[60] N. López-Carreras, M. Miguel, A. Aleixandre, Propiedades beneficiosas de los terpenos iridoides sobre la salud Nutrición clínica dietética y Hospitalaria, Nutr. Clínica Dietética Hosp. 40 (1) (2012). https://revista.nutricion.org/revista.asp?id=10.

[61] Gordana Tovilovic-Kovacevic, Nevena Zogovic, Dijana Krstic-Milosevic, Chapter 2020. Secondary metabolites from endangered Gentiana, Gentianella, Centaurium, and Swertia species (Gentianaceae): promising natural biotherapeutics. Munir Ozturk, Dilfuza Egamberdieva, Milica Pešić, Biodiversity and Biomedicine, Academic Press, 2020, pp. 335–384, https://doi.org/10.1016/B978-0-12-819541-3.00019-0. ISBN 9780128195413.
[62] A. Sharma, S. Gautam, S. Wadhawan, Xanthomonas, in: Carl A. Batt, Mary Lou Tortorello (Eds.), Encyclopedia of Food Microbiology, second ed., Academic Press, 2014, pp. 811–817, https://doi.org/10.1016/B978-0-12-384730-0.00359-1. ISBN 9780123847331.
[63] Carla Maldonado, Narel Paniagua-Zambrana, Bussmann, W. Rainer, Freddy S. Zenteno-Ruiz, Alfredo F. Fuentes, La importancia de las plantas medicinales, su taxonomía y la búsqueda de la cura a la enfermedad que causa el coronavirus (COVID-19), Ecología en Boliv. 55 (1) (2020) 1–5. Recuperado en 08 de septiembre de 2024, de, http://www.scielo.org.bo/scielo.php?script=sci_arttext&pid=S1605-25282020000100001&lng=es&tlng=es.
[64] Zhijian Yao, Qian Wu, Wenbing Sheng, XuDong Zhou, Lidong Cheng, Tian Xing, Hanwen Yuan, Limin Gong, Wei Wang, Bin Li, Caiyun Peng, Flavonoidal alkaloids: emerging targets for drug discovery from Nature's bounty, Fitoterapia 177 (2024) 106099, https://doi.org/10.1016/j.fitote.2024.106099. ISSN 0367-326X.
[65] H.W. Lv, Q.L. Wang, M. Luo, M.D. Zhu, H.M. Liang, W.J. Li, H. Cai, Z.B. Zhou, H. Wang, S.Q. Tong, X.N. Li, Phytochemistry and pharmacology of natural prenylated flavonoids, Arch Pharm. Res. (Seoul) 46 (4) (2023 Apr) 207–272, https://doi.org/10.1007/s12272-023-01443-4.
[66] Bonilla Rivera Pablo Enrique, Toche Tuesta Analucía, Fernández Rebaza Gustavo Adolfo, Curioso Melo Dara Edith, Rayme Gutierrez Robert Leonardo, Soto Tantaraico Edith Celia, Balladares Quintana Alfonso David, Milla Guerra Geralda Ines, Kevin Angel Suarez Santa Cruz, Mamani Herrera Leslie Karina, Acuña Guzman Victor Anderson, Gongora Ariana Yasmeen Yui, Venegas Fiestas Gerardo Antonio, Chemical composition and flavonoids characterization of the methanolic extract of leaves of two types of Ruta Chalepensis L. Instituto de Investigación en Ciencias Farmacéuticas y Recursos Naturales "Juan de Dios Guevara", Facultad de Farmacia y Bioquímica, Universidad Nacional. Mayor de San Marcos. Lima – Perú. Revista Peruana de Medicina Integrativa (2020) 2415–2692, https://doi.org/10.26722/rpmi.2020.53.18. ISSN.
[67] María G.A. Franca, Ana Paula S. Oliveira, Daniele R. Lima, Fátima C.E. Oliveira, Cristiane F. Paiva, Cláudia Ó. Pessoa, Maria T.S. Trevisan, Maria G.V. Silva, Flavonoids composition, antioxidant, anticholinesterase, and cytotoxic activities of flowers extract of Senna cearensis, Afr. Fern, Nat. Prod. Res. 37 (11) (2023) 1892–1896, https://doi.org/10.1080/14786419.2022.2121922. ISSN 1478-6419.
[68] Víctor M. Loyola-Vargas, Patricia Sánchez-Iturbe, Blondy Canto-Canché, Luis C. Gutiérrez-Pacheco, Rosa M. Galaz-Ávalos, Oscar Moreno-Valenzuela, Biosíntesis de los alcaloides indólicos: Una revisión crítica, Rev. Soc. Quim. Mex. 48 (1) (2004) 67–94. Recuperado en 28 de septiembre de 2024, de, http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0583-76932004000100013&lng=es&tlng=es.
[69] Gordana Tovilovic-Kovacevic, Nevena Zogovic, Dijana Krstic-Milosevic, Chapter, Secondary metabolites from endangered Gentiana, Gentianella, Centaurium, and Swertia species (Gentianaceae): promising natural biotherapeutics, Biodiversity and Biomedicine 2020 (2020) 335–384, https://doi.org/10.1016/B978-0-12-819541-3.00019-0. ISBN 9780128195413.
[70] Nooshin Hashemi, Davood Ommi, Parya Kheyri, Faham Khamesipour, William N. Setzer, Marlene Benchimol, A review study on the anti-trichomonas activities of medicinal plants, Int. J. Parasitol.: Drugs Drug Resist. 15 (2021) (2021) 92–104, https://doi.org/10.1016/j.ijpddr.2021.01.002. ISSN 2211-3207.
[71] Ángel Fernando Ortega-Ocaña, Quiñónez Bedón, Mayra Fernanda, Echeverría Guevara, Mónica Paulina, Priscila Inés Masaquiza-Masaquiza, La medicina ancestral desde la cosmovisión andina en el desarrollo turístico, Salasaka, Tungurahua, Ecuador, Rev. Arbitr. Interdisciplinaria Koinonía 8 (Supl. 2) (2023) 619–641, https://doi.org/10.35381/r.k.v8i2.2930. Epub 19 de julio de 2024.
[72] I. Faraone, D.K. Rai, D. Russo, L. Chiummiento, E. Fernandez, A. Choudhary, L. Antioxidant Milella, Antidiabetic, and anticholinesterase activities and phytochemical profile of azorella glabra wedd, Plants 2019 (2019) 265, https://doi.org/10.3390/plants8080265.
[73] R. Vinet, M. Cortés, R. Álvarez, L. Guzmán, E. Flores, Centaurium cachanlahuen (Mol.) Robinson, a Chilean native plant with a vasodilatory effect. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas (Internet), Enero 11 (1) (2012) 61–65. Disponible en: https://www.redalyc.org/articulo.oa?id=85622229006.
[74] Gjoshe Stefkov, Biljana Miova, Suzana Dinevska-Kjovkarovska, Jasmina Petreska Stanoeva, Marina Stefova, Petrusevska Gordana, Svetlana Kulevanova, Chemical characterization of Centaurium erythrea L. and its effects on carbohydrate and lipid metabolism in experimental diabetes, J. Ethnopharmacol. 152 (1) (2014) 71–77, https://doi.org/10.1016/j.jep.2013.11.047. ISSN 0378-8741.
[75] S. Chabane, Amel Boudjelal, Souhila Bouaziz-Terrachet, Eleonora Spinozzi, Filippo Maggi, Riccardo Petrelli, Ghania Tail, Analgesic effect of Centaurium erythraea and molecular docking investigation of the major component swertiamarin, Nat. Prod. Res. 2023 (2023), https://doi.org/10.1080/14786419.2023.2278160. ISSN 1478-6419.
[76] Jakubska-Busse, A, Adrian Wysocki, Paweł Domagała, Anna Brudzińska-Kosior, Monika Sporek, Grzegorz Kosior. Expanding the boundaries in the face of global warming: a lesson from genetic and ecological niche studies of Centaurium erythraea in Europe, Sci. Total Environ., 2024, 176134, ISSN 0048-9697, doi: 10.1016/j.scitotenv.2024.176134.
[77] Carolina Villagrán, Marcela Romo, Victoria Castro, etnobotánica del sur de los andes de la primera región de Chile: un enlace entre las culturas altiplánicas y las de quebradas altas del Loa superior, Chungará (Arica) 35 (1) (2003) 73–124, https://doi.org/10.4067/S0717-73562003000100005.
[78] H.F. Hevia, D.M. Berti, E.R. Wilckens, C. Yévenes, Contenido de proteína y algunas características del almidón en semillas de amaranto (Amaranthus SPP.) cultivado en Chillán, Chile. Agro Sur (Internet). 31 de enero 2002, Disponible en: http://revistas.uach.cl/index.php/agrosur/article/view/3679, Consultado el 20 diciembre 2021.
[79] Danny E. García, Maria G. Medina, Composición química, metabolitos secundarios, valor nutritivo y aceptabilidad relativa de diez árboles forrajeros, Zootec. Trop. 24 (3) (2006) 233–250. http://ve.scielo.org/scielo.php?script=sci_arttext&pid=S0798-72692006000300004&lng=es&tlng=es.
[80] Sandra Lopez, Beatriz Lima, María Belén Agüero, María Liza Lopez, Hadad Martìn, Zygadlo Julio, Duilio Caballero, Raúl Stariolo, Eduardo Suero, Egly Feresin Gabriela, Tapia Alejandro, Chemical composition, antibacterial and repellent activities of Azorella trifurcata, Senecio pogonias, and Senecio oreophyton essential oils, Arab. J. Chem. 11 (Issue 2) (2018) 181–187, https://doi.org/10.1016/j.arabjc.2014.11.022. ISSN 1878-5352.
[81] S. Lopez, Beatriz Lima, María Belén Agüero, María Liza Lopez, Hadad Martìn, Zygadlo Julio, Duilio Caballero, Raúl Stariolo, Eduardo Suero, Egly Feresin Gabriela, Tapia Alejandro, Chemical composition, antibacterial and repellent activities of Azorella trifurcata, Senecio pogonias, and Senecio oreophyton essential oils, Arab. J. Chem. 11 (Issue 2) (2018) 181–187, https://doi.org/10.1016/j.arabjc.2014.11.022. ISSN 1878-5352.
[82] I.M. Madaleno, J. Delatorre-Herrera, Medicina popular de Iquique, Tarapacá, Idesia (Arica) 31 (1) (2013) 67–78, https://doi.org/10.4067/S0718-34292013000100009.
[83] Manish Pal Singh, Bharat Goel, Rakesh Kumar, Sandeep Rathor, Phytochemical and pharmacological aspects of genus Amaranthus, Fitoterapia 176 (2024) (2024) 106036, https://doi.org/10.1016/j.fitote.2024.106036. ISSN 0367-326X.
[84] T. Balasubramanian, M. Karthikeyan, K.P. Muhammed Anees, C.P. Kadeeja, K. Jaseela, Potential antidiabético y antioxidante de Amaranthus hybridus en Streptozotocin-Induced Diabetic Rats, J Dieta Suministro 14 (4) (2017) 395–410, https://doi.org/10.1080/19390211.2016.1265037. Epub 2017 Ene 27. PMID: 28129002.
[85] Brindis y Santiago Mendoza Mamani, Concepto de los aymaras sobre las enfermedades y sus causas. Puno: Instituto de Estudios Aymaras), 1981. Boletín Nº 08.
[86] Serena Caroselli, El dolor de los pacientes Aymara de la comuna de Putre: prácticas terapéuticas y políticas de salud intercultural, Diálogo andino (42) (2013) 89–104, https://doi.org/10.4067/S0719-26812013000200008.
[87] Valentina B. González-Garrido, Jiménez-Baltierra, Diego A. Orellana, Renán, Manuel E. Cortés, Plantas medicinales chilenas: desde el saber ancestral a la comercialización poco regulada, Rev. Med. Chile 150 (2) (2022) 275–276, https://doi.org/10.4067/S0034-98872022000200275.
[88] Scribbr, APA formatting and citation. Generator, seventh ed., 2020, June 11 template, examples, https://www.scribbr.com/apa-style/format/.
[89] Auckland University of Technology, APA 7th Referencing Style Guide, 2024, July 10. https://aut.ac.nz.libguides.com/APA7th.
[90] California State University, Dominguez Hills. (n.d.). APA seventh ed. - citation. Retrieved January 6, 2025, from https://libguides.csudh.edu/citation/apa-7(90).
[91] American Psychological Association. (n.d.). Reference examples - APA style. Retrieved January 6, 2025, from https://apastyle.apa.org/style-grammar-guidelines/references/examples (91).
[92] Purdue Online Writing Lab. (n.d.). General format - Purdue OWL. Retrieved January 6, 2025, from https://owl.purdue.edu/owl/research_and_citation/apa_style/apa_formatting_and_style_guide/general_format.html92.
[93] University of Alberta Library, APA Citation Style, seventh ed., 2015, July 17. https://guides.library.ualberta.ca/apa-citation-style93.
[94] Joseph W. Bastien, Herbal curing by qollahuaya andeans, J. Ethnopharmacol. 6 (1) (1982) 13–28, https://doi.org/10.1016/0378-8741(82)90069-1. ISSN 0378-8741.
[95] Manuel E. Cortés, Fernanda Calderón, Plantas medicinales chilenas: desde el saber etnobotánico a los efectos terapéuticos y las reacciones adversas, Rev. Med. Chile 147 (5) (2019) 673–674, https://doi.org/10.4067/S0034-98872019000500673.
[96] A. Caqueo-Urízar, K. de Munter, A. Urzúa, J.L. Saiz, Entre lo aymara y lo chileno: escala de involucramiento en la cultura aymara (eica). una aproximación interdisciplinar a la dimensión aymara en la vivencia intercultural de estudiantes de enseñanza básica del norte de chile, Chungará (Arica) 46 (3) (2014) 423–435, https://doi.org/10.4067/S0717-73562014000300007.