



Use of three peruvian medicinal plants and their scientific support

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ABSTRACT: Medical sciences have evolved in terms of understanding the origins of different diseases and the development of their treatments. However, people from some Peruvian communities still prefer the use of medicinal plants as the first alternative to improving their health. Even though this cultural practice seems to have positive results, the properties attributed to herbs are transmitted orally, often without any scientific argument to support them. Thus, some native plant species of Peru used for medicinal purposes have been of interest in the study of effectiveness, in view of their cultural use, showing results of great importance for medical, pharmaceutical, anthropological and agronomic sciences. In this sense, the present review collected the scientific information currently available on plants used for medicinal purposes in Peru, thus responding to the hypothesis that there is a scientific explanation about the medicinal properties of many Peruvian plants, mainly in biological sciences. To this end, different sources of information in the areas of anthropology, medicine and plant physiology were consulted, found with the help of academic search engines according to previously determined identifiers. The texts were chosen considering the journal's impact factor, the strength of the evidence found and the contribution to responding to the objective of the present review. In this way, it was found that some medicinal properties, for which some plant species are used by Peruvians, are supported by medical science and that secondary metabolites are mainly responsible for their benefits. Due to the usefulness of this information, it is recommended to continue studies on the large number of medicinal plant species existing in Peruvian lands.

Key words: alternative medicine, traditional use, secondary metabolites, *Achyrocline alata*, *Minthostachys mollis*, *Sambucus peruviana*.

Uso de três plantas medicinais no Peru e seu sustento científico

RESUMO: As ciências médicas têm evoluído no conhecimento sobre a origem de diferentes doenças e no desenvolvimento dos seus tratamentos. Contudo, pessoas de algumas comunidades peruanas ainda preferem o uso de plantas medicinais como primeira alternativa para a melhora da sua saúde. Ainda que essa prática cultural pareça ter resultados positivos, as propriedades atribuídas às ervas são transmitidas de forma oral, muitas vezes, sem nenhum argumento científico que as suporte. Assim, algumas plantas nativas do Peru usadas com fins medicinais têm sido de interesse no estudo da efetividade, tendo em vista o seu uso cultural, mostrando resultados de grande importância para as ciências médicas, farmacêuticas, antropológicas e agronômicas. Neste sentido, a presente revisão tem como objetivo coletar a informação científica atualmente disponível sobre plantas usadas com fins medicinais no Peru, respondendo assim à hipótese de que existe explicação científica sobre as propriedades medicinais de muitas plantas peruanas, principalmente nas ciências biológicas. Para tanto, diferentes fontes de informação das áreas de antropologia, medicina e fisiologia vegetal foram consultadas, encontradas com o auxílio de buscadores acadêmicos segundo identificadores previamente determinados. Os textos foram escolhidos considerando o fator de impacto da revista, a força da evidência encontrada e da contribuição na resposta ao objetivo do presente trabalho. Desse modo, foi encontrado que algumas propriedades medicinais, pelas quais algumas espécies vegetais são usadas pelos peruanos, são suportadas pela ciência médica e que os metabolitos secundários são os principais responsáveis pelos seus benefícios. Pela utilidade desta informação, recomenda-se continuar os estudos sobre o grande número de espécies de plantas medicinais existentes em terras peruanas.

Palavras-chave: medicina alternativa, uso tradicional, metabolitos secundários, *Achyrocline alata*, *Minthostachys mollis*, *Sambucus peruviana*.

INTRODUCTION

Peru is considered one of the megadiverse countries in the world (RODRÍGUEZ & YOUNG, 2000), due to the different edaphoclimatic conditions present in its eight natural regions, (PULGAR, 1987) or 84 ecoregions (ZAPPI et al., 1994), thus allowing the presence of high diversity in

fauna and flora throughout the territory. For this reason, Peru is home to 12% of vertebrate fauna (CARRILLO & ICOCHEA, 1995; PACHECO et al., 1995; RODRÍGUEZ, 1996; RODRÍGUEZ & YOUNG, 2000), 9% of invertebrates (SILVA, 1996; RAMIREZ, 1996; RODRÍGUEZ & YOUNG, 2000) and 10% of the world's plant species (BUSSMANN & SHARON, 2016).

Peru, the birthplace of the Inca empire, was admired by the Spanish for, among other things, considerable advances in medicine (LASTRES, 1951). The worldview of pre-Inca and Inca cultures understood the need to preserve harmony in the universe, if this was not achieved, disasters and diseases would occur (VÉLIZ, 2006). Thus, for the human being to be healthy, there must be internal harmony, between the body, the soul and the forces within it, and external harmony, with its surroundings: nature, other people and spiritual beings (BAUD, 2019). In this way, diseases could be caused by supernatural, emotional, religious, natural, personal and cultural reasons (ONOFRE, 2013), being avoided by conserving the internal “flame” in a preventive way (ARANA, 2009). This demonstrated the prevalence of prophylactic medicine within the Andean culture, mainly through food (ONOFRE, 2013).

In case of illness, one should first discover where the harmony was broken, through conversations with the patient, family and acquaintances or with divine beings. In some cases, the spirits were consulted through the coca leaf, passing the egg or guinea pig (*cuy* in Spanish, from Quechua *quwi*) over the patient's body, until diagnosing the reason and place of the disease (QUEVEDO & RAMOS, 2016). Once this was discovered, the doctor of that time defined a therapeutic treatment, which depended on the origin and nature of the disease, in addition to the person's social status (MONIGATTI et al., 2013; ARANA, 2009). In some cases, rituals were performed to scare away evil spirits, so the healer was also a type of witch. To this day, this person is called “chamán”, but, in Inca times, he was known as ichuri - differentiating between ‘Comasca’ and ‘Amauca’, depending on whether he was for the commoner or for the nobility (LASTRES, 1951). In pre-Inca times, the name depended on the culture, for example, in the Paracas culture, the surgeon was called Sir Kah (MARINO & GONZALES-PORTILLO, 2000).

Even today, there are places where similar rituals are carried out, but it is uncommon. However, the use of medicinal plants is common in both rural and urban areas, without the need for a medical prescription. The use of some plant species for medicinal purposes is not only of historical and cultural, but also of economic and social importance, as some people, especially women, found on collection and commercialization a form of family income (GONZÁLES DE LA CRUZ et al., 2014). In this regard, ethnobotanical studies have been essential for identifying the diverse uses of various plant species by humans (BABACAN et al., 2022; BALOS, 2023;

BÖLÜKBAŞI & ARAS, 2022). Finding that native species are not only valued in the countryside, where they constitute 50% of sales of medicinal plants on the market (BUSSMANN & SHARON, 2009), but also abroad (MADALENO, 2017), causing the export of the material used for the production of various food supplements and pharmaceuticals.

To date, 1,400 plant species with medicinal use have been identified in Peru (BRACK, 2004), which are used individually or in preparations made with several of them (BUSSMANN & SHARON, 2006). The part of the plant used and the type of administration (topically, orally or as an infusion) depend on both the plant and the disease/symptom to be treated. Knowledge has been acquired from previous generations verbally and also within a commercial context (AGAPITO & SUNG, 2004), but without any scientific basis.

The anti-inflammatory, antispasmodic, analgesic and anti-diuretic properties of some plants are attributed to the high content of steroids, tannins, terpenes and saponins, known secondary metabolites (TAIZ & ZEIGER, 2009; SAVITHRAMMA et al., 2011). Secondary metabolites arise from the evolution of some plant species as protection against abiotic and biotic stresses (SHARMA et al., 2018). Therefore, the concentration of them in the plant is affected both by the environmental conditions in which it develops and the phenological state (LI et al., 2020; ALHAITHLOUL et al., 2019), in such a way that, in some cases, plants could be toxic for human consumption.

Several studies from other countries have extracted secondary metabolites and demonstrated their medicinal function in medicinal plants, such as *Achyranthus bidentata* Blume in China (LI & HU, 2009), six plant species in Sudan (DIRAR et al., 2019) and *Scoparia dulcis* L. in Brazil (FREIRE et al., 1991). In addition to being used directly, many of these plants are cultivated in vitro to obtain secondary metabolites and for use in the pharmaceutical production industry (SANCHITA, 2018). However, information on the properties of medicinal plants in Peru is still scattered.

In view of the above, this review article collected ethnobotanical reports, medical studies and existing physiological information regarding three medicinal plants used in Peru: *Achyrocline alata* (Kunth), *Minthostachys mollis* (Benth.) Griseb and *Sambucus peruviana* Kunth, with the aim of concentrating the existing information on this ancestral practice and demonstrating the scientific bases that support it. Furthermore, the aim is to encourage research into the secondary metabolites

present in Peruvian medicinal plants, which would be of great contribution to different areas of knowledge, such as agronomy, bioeconomy and pharmacy.

METHODOLOGY

This ethnobotanical survey was carried out between April 2021 and June 2024 and searched for articles published in the last 20 years, mainly through the Redalyc, Scielo and NCBI platforms. The descriptors used were: 'traditional medicine', 'medicinal plants' and 'alternative medicine'. From these articles, the three native species of peruvian medicinal plants with the highest number of citations were chosen. Subsequently, on the same platforms and with the descriptors '*Achyrocline alata*', '*Minthostachys mollis*' and '*Sambucus peruviana*', texts were selected that met the following inclusion criteria: (1) contain a cultural description of the species, (2) mention its use as a medicinal plant, (3) present biochemical analyses, (4) have biomedical studies with extracts or oils obtained from these plants.

DEVELOPMENT

The ancient Peruvians considered the body as a support for two opposing and complementary forces (hot and cold) and illnesses meant an imbalance towards one of these forces. For this reason, in order to re-establish balance and harmony in the body, the healer applied treatment opposite to the nature of the disease. For example, the flu, a cold illness, would need treatment with hot elements for the person to achieve balance again (DE FEO et al., 2003; GONZALES DE LA CRUZ et al., 2014).

All of this was described by specific people who had knowledge of their surroundings and beliefs specific to the culture of the time, but it is currently known that the medicinal properties of some plants are due to organic compounds produced by their secondary metabolism. Next, the article describes the cultural use, secondary metabolites found and medical studies of some plant species native to Peruvian territory and which, since ancient times, have been used for medicinal purposes by Peruvians.

Achyrocline alata

It is a plant from the Asteraceae family that grows spontaneously both in the upper part of the mountains and in the valleys, commonly known as ishpingo blanco (Bolivar region), wilca-wilca, wilawaq'ta (Ancash), male pirca (Canta), arnica (Jauja) (MONIGATTI et al., 2013; GONZALES

DE LA CRUZ et al., 2014; TELLO-CERON et al., 2019). It can also be found in Argentina, Paraguay and Southwestern Brazil, where it is known as jatei-ka-ha or jatei-kaá (DEMARQUE et al., 2015; ROSA et al., 2021) and in Colombia, with the name viravira (BUENO-SANCHEZ et al., 2009). As it is considered a hot plant, it is used in baths against the cold of the body, in case of rheumatic pain and bruises, taken as tea or "agua de tiempo" to regulate or de-inflate the digestive system, as an emmenagogue or sedative. In cases of blows or wounds, the leaves and flowers of this species are used together with Chupasangre, Verbena and Chuculucuy or with urine, Perejil, Yawarshujo. It is also used by shamans for "cleans" in case of "scare" (loss of spirit) (SIMÕES et al., 1999; MONIGATTI et al., 2013; GONZALES DE LA CRUZ et al., 2014; TELLO-CERON et al., 2019).

Biochemical analyzes have shown the presence of polyphenols in the composition of raw extracts from the aerial part of the species, mainly flavonoids, such as flavones, flavonols and caffeic compounds (BROUSSALIS et al., 1988). TOFFOLI-KADRI et al. (2014) identified isoforms A and C of isochlorogenic acid, in addition to chalcone, flavonol and other secondary metabolites belonging to phenylpropanoids. In most cases, thymol, recognized for its antimicrobial activity (ANDRADE-OCHOA et al., 2021), was the majority compound (24%) found in *A. alata* essential oils (BUENO-SANCHEZ et al., 2009; ZAPATA, 2010) which explains its beneficial use for wounds.

Secondary metabolites, mainly polyphenols, have been recognized by medical science as highly beneficial compounds for human health, as their phenolic group accepts electrons from free radicals, thus preventing cellular oxidation (CLIFFORD, 2000). Thus, they function as protection against various degenerative processes in the human body, such as cancer, diabetes, cardiovascular problems and aging (PANDEY & RIZVI, 2009). In fact, an antioxidant and free radical scavenging activity of the raw extract of *A. alata* was confirmed (GRASSI-ZAMPIERON et al., 2009). This explained the properties found by ancient Peruvian communities, which have also been demonstrated by some medical studies.

Some authors have reported antiproliferative activity in cancer cells (CARRAZ et al., 2015; ROSA et al., 2021), anti-inflammatory, antihyperalgesic (TOFFOLI-KADRI et al., 2014), healing, promoting re-epithelialization and collagen remodelling effects (PEREIRA et al., 2017). In this way, the uses for de-inflammation as an ointment become scientific confirmed.

Conversely, essential oils obtained from this species showed bacteriostatic activity against *Mycobacterium tuberculosis*, the causative agent of tuberculosis (BUENO-SÁNCHEZ et al., 2009) and activity against *Aspergillus fumigatus*, a saprophytic fungus present in the atmospheric air, identified as a threat in hospitals (ZAPATA et al., 2010). Furthermore, the purified extract of *A. alata* was active against *Streptococcus mutans*, the main bacteria that causes cavities (DEMARQUE et al., 2015). From what has been described, this species is promising in medical practice or even for the pharmaceutical industry in the mentioned specialties.

Minthostachys mollis

It is a species belonging to the Lamiaceae family, known by the Quechua name muña (all of Peru), ishmuña (Ancash), and by the Hispanic names vento, tinto, champca (Bolívar region), poleo (Amazon region) or peperina, in Argentina. Its natural ecosystem is the Andean cloud forest, both in the upper part and in the valley. Considered a very hot plant, it was used by indigenous Peruvians in conjunction with chilca to fracture bones. The branches and leaves are consumed in the form of tea, for flu, cough, bronchitis, headaches, altitude sickness, gastritis, stomach or intestinal spasm and as a digestive. In case of strong symptoms, it is recommended to bathe in hot water with the branches or directly apply a type of ointment made with leaves, either macerated with pisco or cooked in a pan with animal fat. In the province of Bolívar, it is also used as incense in cases of “scare” (DE LA CRUZ et al., 2006; SCANDALIARIS et al., 2007; MONIGATTI et al., 2013; GONZALES DE LA CRUZ et al., 2014; CASTRO-ALAYO et al., 2019). An experiment conducted in rats, has demonstrated the analgesic activity and gastroprotection of *M. mollis* infusion (VELARDE-NEGRETE et al., 2022). The use of this plant species as a repellent for different insects in crops, warehouses and livestock was also reported (MAGUERA et al., 2009), like *Aedes aegypti* adults (SOLDÁN et al., 2023).

There is no consensus among different authors on the biochemical composition of *M. mollis* vegetable oil. However, all authors agree that the compounds belong to the terpene group and, in ca. 78% of the literature consulted, the presence of monoterpenes like pulegone and menthone were found. (ROJAS & USUBILAGA, 1995; FUERTES & MUNGUÍA, 2001; CANO et al., 2008; MAQUERA et al., 2009; ZAPATA et al., 2009; OLIVERO-VERBEL et al., 2010; TORRENEGRA-ALARCON

et al., 2016; CASTRO-ALAYO et al., 2019; ROJAS-MOLINA et al., 2024).

The presence of these secondary metabolites gives *M. mollis* essential oils antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* (TORRENEGRA-ALARCON et al., 2016), *Helicobacter pylori* (CARHUAPOMA et al., 2009; FUERTES et al., 2001), *Salmonella enterica*, *Pseudomonas aeruginosa* (ROJAS-MOLINA et al., 2024), *Proteus* spp., *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Enterococcus faecalis* and *Enterobacter* spp. (VELARDE et al., 2024). Petroleum ether and dichloromethane fractions of *M. mollis* essential oil have been described as responsables for bacterial growth inhibition of *Streptococcus mutans*, *Enterococcus faecalis*, *Porphyromonas gingivalis* and *Lactobacillus acidophilus* (SÁNCHEZ-TITO & COLLANTES-DIAZ, 2021). As *L. acidophilus* is a beneficial bacterium for nutrient assimilation, the proper administration of this essential oil should be pursued to avoid harm from excess use.

Furthermore, essential oils from this species inhibited Aflatoxin B1 (AFB1), a mycotoxin, (CADENILLAS et al., 2023), resulting in antifungal activity against *Candida albicans* (CANO et al., 2008; TORRENEGRA-ALARCON et al., 2016; HUAMANÍ et al., 2021), *Aspergillus fumigatus*, *Aspergillus flavus*, *Candida krusei*, *Candida parapsilosis* (ZAPATA et al., 2009), *Microsporium canis*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans* (CANO et al., 2008) and *Botrytis cinerea* (LEÓN-MARROU et al., 2023).

However, antioxidant activity of *M. mollis* essential oil was dependant on the analytical method and its concentration. In this way, TBARS and DPPH methods didn't show antioxidant activity, while through FRAP and ABTS methods, it was high (OLIVERO-VERBEL et al., 2010; GRANADOS et al., 2012; ROJAS-MOLINA et al., 2024).

Even though there is a concern of the quality of this plant in terms of toxic metals, a study has revealed no significant non-carcinogenic health risk to drinkers of infusion of muña that became from two sectors of Huancayo province (ZÁRATE-QUÍÑONES et al., 2021). Still, *M. mollis* essential oils hasn't shown non cytostatic nor cytotoxic effect against different tumor cell lines (VACA et al., 2024).

Based on the above, *M. mollis* can be considered a potential species for the development of drugs and for the disinfection of hospital environments, but it is important to perform a biochemical analysis of the plants used in order to check the concentration of terpenes in its composition.

Sambucus peruviana

It is a tree belonging to the Adoxaceae family, which grows naturally in the Andean cloud forest and is known by the Quechua names sambucu or samucu and the Hispanic names sauco and tilo. In traditional medicine, it is considered a cold plant. The leaves and branches are used in the form of tea mixed with urine to treat inflammation of the kidneys, bladder or prostate. Furthermore, the leaves can be boiled to use as a rinse to combat oral infections or can be chopped to apply to the breast ducts. Finally, when mixed with hot animal fat, they are used as an ointment for wounds, nerves, bad breath or “scare”. Inflorescence tea is drunk in case of urinary tract infections, as a depurative, antirheumatic or aphrodisiac, nasal congestion, bronchitis and respiratory problems. (HAMMOND et al., 1998; NETO et al., 2002; DE LA CRUZ et al., 2006; MONIGATTI et al., 2013; GONZALES DE LA CRUZ et al., 2014).

Studies and literature point out this species was taken to Peru by Spanish conquerors on times of Huayna Capac, being *S. nigra* synonym of *S. peruviana* (GALÁN DE MERA et al., 2020).

Although, this species is widely used as a medicinal plant in Peru, there is little consistent scientific evidence regarding its organic compounds and health benefits. Thus, the *S. peruviana* leaf extract did not show antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* (BUSSMAN et al., 2010). Conversely, antibacterial activity of this extract against the Gram-positive bacteria *Staphylococcus epidermidis* and *Staphylococcus aureus*, were observed (HERNÁNDEZ et al., 2000). Also, its efficacy against *Streptococcus bovis*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Streptococcus* spp., *Clostridium histolyticum* and *Corynebacterium diptheriae* was observed (NETO et al., 2002). Therefore, a selective antibacterial activity on the part of the *S. peruviana* extract is deduced.

S. peruviana leaf seems to have potential use for the management and prevention of diabetes complications, as it demonstrated roughly 50% of the inhibitory effect against rat lens aldose reductase (RLAR) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging (HWANG et al., 2019). At the same time, its abundance in chlorogenic acid, make this plant's leaves an important material for wound treatment (STUDZIŃSKA-SROKA et al., 2024), as it decreases the amount of reactive oxygen species, tumour necrosis factor alpha, interleukin-8 secreted by neutrophils and keratinocytes, interleukin-6 and interleukin-8 secreted by fibroblasts, besides the

impact its components have on the skin's enzyme activity (SKOWROŃSKA et al., 2024).

Silver nanoparticles using *S. nigra* leaf extract have shown to act as antimicrobial agents (KARAN et al., 2024). Also, extracts of sauco, specially of the fruits, have shown anti-inflammatory and antinociceptive activities, as well as inhibitory activity against virus replication, being; therefore, suitable for the treatment of pain, inflammation and for HSV-2 viral infections therapy (SEYMENSKA et al., 2023; SEYMENSKA et al., 2024).

Fruits, mainly the bagasse, have shown a high antioxidant activity through ABTS and DPPH methods (ROJAS-OCAMPO et al., 2021). The antioxidant capacity of the plant is due to the high concentration of total phenolic content (ROJAS-OCAMPO et al., 2021), like flavonoids (REYES et al., 2013) and phenolic acids in flower extract (SEYMENSKA et al., 2024), ferulic acid in leaf extract (KARAN et al., 2024) and rutin and chlorogenic acid in both (SEYMENSKA et al., 2023). Other authors have identified terpenes, amino acids, lactones, flavonoids and saponins as major compounds in leaves of this and other species of the *Sambucus* genus (REYES et al., 2013; LAUTIÉ et al., 2020), while in the fruit extracts were anthocyanins (SEYMENSKA et al., 2024).

Sauco fruit is widely used in the food industry. Even though it has not been cited as an ancestral therapeutic treatment, it is important to highlight the high amounts of antioxidants it contains, which may have been the active compounds of the medicinal treatment of Peruvian ancestors. However, its content can vary according to the juice extraction method (FLORES, 2017).

CONCLUSION

According to Peruvian ancestor classification, the three plant species studied here can be classified as hot (*A. alata* and *M. mollis*) and cold (*S. peruviana*). Hot plants were used in case of respiratory and digestive disease, while cold plants were used to cure urinary infections and all of them used to cure wounds. The two hot species were found to be rich in polyphenols and terpenes, while the cold species was found to be rich in phenols. The studies described variation in secondary metabolite concentration which can mask genetic association studies to identify the genomic regions responsible for the compounds accumulated. Therefore, it is our conclusion that further research is needed for the correct identification of compounds and their concentrations behind the hot and cold plants.

ACKNOWLEDGEMENTS

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) fellowship to R.E.G.A., Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) fellowship to A.C.O. This review was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brasil.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTIONS

R.E.G.A. conceived the idea, did the data curation and wrote the original manuscript. A.C.O. did the supervision and corrected the first version. A.C.O. and C.M.C. performed the review and approved the final version.

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