Natural Resources for Human Health

visaga publishing house

Original Research

View Article Online

Check for updates

Received 07 January 2023
Revised 20 January 2023
Accepted 21 January 2023
Available online 07 February 2023

Edited by Balamuralikrishnan Balasubramanian

KEYWORDS:
Yawar Panga
Aristolochia didyma
ethnomedicine
drug addiction
emesis

Natr Resour Human Health 2023; 3 (2): 248-258
https://doi.org/10.53365/nrfhh/159613
eISSN: 2583-1194
Copyright © 2023 Visagaa Publishing House

Ethnomedical uses of Yawar Panga (*Aristolochia didyma*) in a therapeutic community dedicated to the treatment of drug addiction in the Peruvian Amazon

Matteo Politi [1,*], Nahuel Simonet [2], Eric Kube [3], Tereza Rumlerová [4], Edilberto Chuquilín Bustamante [5], Gary Saucedo Rojas [1], Fabio Friso [1], Gokhan Zengin [6], Luigi Menghini [7,*], Claudio Ferrante [7]

[1]Center for Drug Addiction Treatment and Research on Traditional Medicines - Takiwasi, Prolongación Alerta 466, Tarapoto, Peru
[2]Independent Researcher, Route de la Poudrière 27, Fribourg, Switzerland
[3]School of Public Health, University of Texas, 7000 Fannin St, Houston, TX 77004, United States
[4]Department of Psychology, Palacky University, Vodární 6, Olomouc, Czech Republic
[5]Faculty of Renewable Natural Resources, Universidad Nacional Agraria de la Selva, Carretera Central km 1.21, Tingo Maria, Peru
[6]Department of Biology, Science Faculty, Selcuk University, Konya 42300, Turkey
[7]Department of Pharmacy, University of Chieti-Pescara, Via Vestini 31, Chieti Scalo, Italy

ABSTRACT: *Aristolochia didyma* (Yawar Panga) and other Aristolochia species are used as traditional herbal remedies with potent emetic properties. Scientific data for such Yawar Panga species, however, are scarce in the literature. The aim of this study was to describe the use of Yawar Panga within the context of the therapeutic community Takiwasi, in which the plant is used as part of the protocol for the rehabilitation of individuals with drug addiction. Fieldwork with experts in the administration of Yawar Panga at Takiwasi Center, as well as a retrospective qualitative analysis of experiences with this plant remedy in a residential inpatient population were performed. *In-silico* analysis of the main constituents of *A. didyma* as represented in the literature was completed in order to identify its putative pharmacological targets. The therapists interviewed consider Yawar Panga to be the most potent purga at Takiwasi and consider it especially useful in attenuating addiction withdrawal syndrome. From the patient's perspective, this plant induces strong physical effects, and commonly precipitates effects in the oneiric and emotional dimensions. GABA B seems to be the receptor involved in the emesis induced by the phytochemicals contained in this plant species. Despite some relevant concerns related to the safety of the genus Aristolochia in modern western pharmacopoeias, some species, including *A. didyma*, are routinely used in the context of traditional herbal medicine in the Peruvian Amazon. Further phyto-pharmacological investigations would be helpful to elaborate this species' medical utility, especially within the context of addiction treatment.

1. INTRODUCTION

1.1. The genus *Aristolochia*: between poison and medicine

The genus *Aristolochia* includes about 500 species which are mainly distributed throughout tropical regions; the genus has attracted great interest due to its relevant biological activities and unique constituents (Kuo et al., 2012). Various species of *Aristolochia* have been used globally in folk and traditional medicines, and written records of their use are well documented in ancient Ayurvedic, Chinese and European traditional medicine texts (Scarborough & Fernandes, 2011). Nowadays this genus seems to be of interest mainly due to its toxicological aspect (Grollman & Marcus, 2016; Han et al., 2019), however several *Aristolochia* species still persist in herbal formulas, particularly those of eastern pharmacopoeias (Shaw, 2010; Tripatara et al., 2012).

According to local traditional medicines, the general indications attributed to the different *Aristolochia* species and preparations stem from their tonic, depurative and, above all, anti-inflammatory properties. *Aristolochia* is used especially in

* Corresponding authors.
E-mail addresses: matteo.politi@takiwasi.com (Matteo Politi), luigi.menghini@unich.it (Luigi Menghini)

This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

cases of gout, arthritis, rheumatism, and skin diseases, and can also be used to treat snakebites (Gifford et al., 2017; Perry & Metzger, 1980). A recent review on biological activities of the *Aristolochia* genus recognizes an even larger spectrum of effects of traditional preparations from different species, including anticancer, antibacterial and antiparasitic activities, among others (Lerma-Herrera et al., 2022). The phytochemistry of the genus has been widely investigated but lacks a systematic approach, usually including various organs from different plant species.

The chemical composition of different species in this genus indicates the presence of many chemical classes of secondary metabolites, such as aristolactams, aporphines, protoberberines, isoquinolines, benzylisoquinolines, amides, flavonoids, lignans, biphenyl ethers, coumarins, tetralones, terpenoids, benzenoids, and steroids (Kuo et al., 2012). A typical feature present in most of the species is a class of metabolites sharing a common phenanthrene origin, classed as aristolochic acids and esters. This class of metabolites includes a group of substituted nitrophenanthrene carboxylic acids mainly represented by 3,4-methylenedioxy-8-methoxy-10-nitrophenanthrene-1-carboxylic acid, known as aristolochic acid I, and the demethoxylated derivative, aristolochic acid II. Their presence is reported in all plant organs and is often combined with aristolactams, a pool of phenanthrene cyclic amides.

Aristolochic acids are reported to exert their toxicological effects as phytotoxins through the common use of *Aristolochia* as an ingredient in formulations to reduce body weight, nowadays called aristolochic acid nephropathy (Gifford et al., 2017). Relevant literature confirms the toxicological profile of aristolochic acids, which are recognized as highly carcinogenic and toxic metabolites with potential health implications both directly, in their interactions in culinary and medicinal uses, as well as indirectly, in the form of environmental pollutants (Lukinich-Gruia et al., 2022). Many countries do not allow the use of *Aristolochia* as herbal medicines or food supplements due to the toxicity of aristolochic acid constituents. Certain homeopathic preparations are allowed, however, due to high dilutions which can be considered below the risk of toxicity. Nonetheless, *Aristolochia* species continue to be used in local medicines around the world, such as in traditional Chinese medicine (Agency, 2005). Despite the risk of nephropathy linked to the use of some species of the genus *Aristolochia*, about one hundred species are used medicinally worldwide, especially for gastrointestinal problems (Heinrich et al., 2009).

1.2. The study site and the concept of emesis

Takiwasi, located on the outskirts of the city of Tarapoto, in the Amazonian basin of Peru, is a therapeutic community recognized by the Ministry of Health of Peru which combines the use of psychotherapy and medicinal plants for the treatment of mental health and, more specifically, addiction (Berlowitz et al., 2017). The novel addiction treatment protocol implemented at Takiwasi has been presented in several studies (Berlowitz et al., 2017; Giovannetti et al., 2020; Giove, 2002; Politi et al., 2018), as have the different medicinal plants used in it (Cervi et al., 2019; Horák, 2013; Politi et al., 2018). Takiwasi welcomes patients from Peru (42%), other Latin American countries (34%) and North America / Europe (24%) (Berlowitz et al., 2020a). Patients mainly suffer from dependence on cannabis (72%), alcohol (52%), and cocaine / coca paste (48%), among other substances. Several studies have shown how the use of multiple substances or polydrug addiction is a common characteristic in those seeking treatment, affecting 84% of Takiwasi patients (Berlowitz, Torres, et al., 2020; DM, 2018).

As part of the therapeutic protocol of Takiwasi, several plants with emetic effects are offered to patients in order to provide physical cleansing, and to combine with this physical cleansing additional purported effects on an energetic or spiritual level. Herbal preparations with emetic activity are considered relevant therapeutic tools from both cultural and clinical perspectives within the context of Amazonian medical traditions (Fotiou & Gearin, 2019; Politi et al., 2021; Sanz-Biset & Cañigueral, 2013). One such major example is the liquid preparation of Tobacco, especially Nicotiana rustica L. (Berlowitz, Walt, et al., 2020). Emesis is considered a detoxification strategy within medical traditions other than those of Amazonia, including one Buddhist drug rehabilitation program in Thailand (Barrett, 1997). In the modern biomedical approach, emesis sits on a subtle border between being considered either a problem or a solution: gastric lavage, for example, is used only in cases of severe and acute poisoning, and neither as a prevention tool, nor as a "cure" for chronic poisoning. It is noteworthy to mention, however, the role of emesis as a key protective reflex of the body which involves multiple systems, including the respiratory, gastrointestinal, and abdominal muscles, and which can serve as a potential therapeutic option (Chai et al., 2016).

At Takiwasi, emetic plants are considered to act on precise somatic zones which have their own symbolic correspondences (Politi et al., 2018): we can observe that Rosa Sisa (*Tagetes erecta* L.) is used in cleansing the mind of excessive rationalization; Azucena (*Lilium candidum* L.) is considered useful for sexual cleansing and balance; Verbena (*Verbena litoralis* Kunth) acts on the liver and the anger symbolically linked with it; Sauco (*Sambucus peruviana* Kunth) is beneficial for cleansing the respiratory system. Yawar Panga (*Aristolochia didyma* S.Moore) is considered to be the most important emetic/purgative plant in the Takiwasi addiction treatment protocol (Mabit et al., 2014), since it offers deep cleansing and proves very useful in disabling the withdrawal syndrome in the first phase of the treatment for drug addiction (Politi et al., 2018).

Between the 1980s and 2000s, due to increased civil unrest and narcotics trafficking, illicit drug consumption and substance use disorders became a prominent problem in the San Martín region in which Takiwasi is located (Fotiou & Gearin, 2019; Mabit & Mariscal, 2013). The use of psychotropic plants for ceremonial purposes in Latin America has been documented for thousands of years with no report showing the presence

of notable addictive behaviors in traditional societies (Politi et al., 2018). The spread of addiction during the second half of the 20^{th} century therefore represented a relatively new phenomenon. Traditional healers in several regions of Peru responded by returning to methods linked to traditional ethnomedicine, similarly as in the case of the use of the mescaline cactus to treat alcoholism (Costa & M, 1976; Seguín, 1979).

Takiwasi was founded in 1992, drawing inspiration from such examples, and following 6 years of preliminary research centered in active observation of the work of Amazonian healers, especially those employing ancient plant remedies in the treatment of drug addiction (Mabit & Mariscal, 2013; Politi et al., 2018). Yawar Panga was introduced as part of Takiwasi's therapeutic protocol as a potent detoxifying plant following the indications of traditional healers from the *Kichwa Lamista* ethnic group of the Chazuta valley, located 50 km to the southeast of Tarapoto. Between 1987 and 1993, one of Takiwasi's founders, Dr. Jacques Mabit, completed an apprenticeship in traditional Amazonian medicinal practices in the Chazuta valley, becoming apprentice to several renowned master healers (Mabit & Mariscal, 2013). These healers included Don Aquilino Chujandama and Don Guillermo Ojanama (Villarreal & A, 2012), whom have both now passed away; the latter pioneered the traditional use of Yawar Panga at Takiwasi both before its foundation as well as during the first years of the center's activities (1989-1995). Ojanama utilized Yawar Panga to treat indigenous people who suffered from addiction to cocaine paste as a consequence of working as macerators of coca leaves for drug trafficking organizations. The Huallaga valley where Chazuta is located was, at that time, the main region for drug production in Peru.

The use of Yawar Panga (in this case spelled "Yawar Panka") by traditional healers in the Chazuta area as a therapy for the rehabilitation of individuals with tobacco and cocaine addiction has been recorded by Sanz-Biset and Cañigueral (Sanz-Biset & Cañigueral, 2013), who identified this plant as the species cognate *Aristolochia leuconeura* Linden and noted its use as a treatment for cough and bronchitis, and as a depurative and laxative. Again in the Chazuta area, Sanz-Biset et al. (Sanz-Bizet et al., 2009) identified "Yawar Panka macho" (male) as *Aristolochia fosteri* Barringer, and documented its use as an emetic, as well as for cough and bronchitis. Jauregui et al. (Jauregui et al., 2011) identify "Yawar Panga" as *Aristolochia cauliflora* Ule in the area of Pucallpa, Ucayali region, and describe its uses within the Shipibo-Konibo ethnic group as a potent emetic and detoxifying medicinal plant that is used for purification and cleansing. The authors themselves testify that "[…] the end of the sessions brings with it a profound sensation of wellbeing, lightness, mental clarity and a tranquil and relaxed countenance that lasts for two or three days".

1.3. Yawar Panga (*Aristolochia didyma*) state of the art

Within the context of Takiwasi Center, the plant known with the common name Yawar Panga has been identified as *Aristolochia didyma* S.Moore (family Aristolochiaceae). This identification was made taking into account the Field Museum (Field Museum, 2022) isotype; the legitimate scientific name was verified in Tropicos (Tropicos & Org, 2022), which is up to date with the APG IV Group. A synonym of *A. didyma* is *Aristolochia rodriguesii* Hoehne Moore (2022); Tropicos and Org (2022), although according to González and Pabón-Mora (F. González & Pabón-Mora, 2018), the accepted name is actually *Aristolochia trilabiata* Glaz and its synonyms are *A. didyma* and A. rodriguesii. In World Flora Online (Online, 2022), however, only *A. didyma* appears as an accepted name and has no synonymy, whereas A. trilabiata has not yet been considered.

Wanke et al. (2006) mentions *Aristolochia leuconeura* Linden in their analysis of the Aristolochioideae, however does not include *A. didyma*. Both species, however, have a morphological resemblance: both have seeds with glutinous aril and glabrescent leaves, for example, among other similarities. These two species, furthermore, are found in the same habitat or type of forest. The previously mentioned studies by Sanz-Biset and Cañigueral (Sanz-Biset & Cañigueral, 2013) and Sanz-Biset (Sanz-Bizet et al., 2009) describing the utilization of *Aristolochia leuconeura* Linden in cocaine and tobacco addiction were performed in the Chazuta valley, an area nearby to Takiwasi and similar in habitat. In this sense, *A. didyma* is probably within the same group of the subgenus *Aristolochia*, so it likely shares a phylogenetic and metabolic relationship with *A. leuconeura*. Despite these two *Aristolochia* species being well known locally and additionally being used as important plant remedies, scientific studies on both plants are rare. Apart from Júnior et al. (2002) and Pacheco and De Oliveira (2009), as far as we know, no other phytochemical data on *A. didyma* are present in the literature.

2. MATERIALS AND METHODS

2.1. Fieldwork with experts in Yawar Panga purge

Direct information about the Yawar Panga purge as practiced at Takiwasi was acquired through fieldwork performed between April and July 2021 as part of an ethnobotanical survey on purging plants at Takiwasi, authorized by the national authority "SERFOR" (authorization code AUT-IFL-2021-024). This research task was based on a participant-observation approach aimed at collection of plant material for botanical identification as well as descriptions of the method of preparation and administration of the Yawar Panga purge at Takiwasi.

The collection of botanical samples and the preparation of voucher specimens were performed at the Botanical Garden of the Takiwasi Center, Tarapoto, Peru. The vouchers were then sent and deposited at the Herbarium HTIN of the Universidad Nacional Agraria de la Selva, Tingo María, Peru, for botanical identification. The identification of the species was carried out using the taxonomic keys of Gentry and Vásquez (Gentry, 1993), Vásquez and Rojas (Martínez & González, 2004), and Mostacero et al. (León et al., 2017), and their classification was determined according to the APG IV (Group et al., 2016).

Certificate C-011-2021-HTIN-FRNR-UNAS was issued as a result of this identification process.

The information regarding the practice of the Yawar Panga purge at Takiwasi was collected through semi-structured interviews, lasting an average of 1.5h each, with 7 different therapists, healers, and an ethnobotanist of the Center, who are considered experts in this traditional Amazonian herbal practice. These individuals will hereafter be referred to as informants. All interviews were performed in Spanish and recorded and subsequently transcribed verbatim to be used for the analysis. Formal approval by the Institutional Review Board for Research of the Takiwasi Center was acquired for this research task (document of approval CIRICT0012021), and all informants signed written informed consent. Some of the questions given to the informants included: How is the Yawar Panga purge prepared? Why and when is it used? How is it administered? What are the effects and benefits recognized by therapists and healers?

2.2. Retrospective study

This research task analyzed experiences of the Yawar Panga purge among residential inpatients being treated for addiction at Takiwasi. We specifically examined written records of psychotherapy sessions held with patients following the purge. These data are stored in the Takiwasi clinical data management system (Rojas et al., 2018). Formal approval by the IRB of Takiwasi Center was acquired for this task (document of approval CIRICT0012021). Takiwasi is an accredited therapeutic community recognized by the Ministry of Health of Peru (resolution Nº039-DG-DIRES/SM-96). In accordance with article 15 of Law No. 29765 (Decreto Supremo Nº006-2012-SA), all care received by patients of therapeutic communities must be registered in a clinical history, which includes, among other elements, a psychological sheet. The psychological sheet of Takiwasi patients who received the Yawar Panga purge was consulted for the purpose of this analysis. The maintenance of the clinical history is audited by the Ministry of Health periodically. The analysis of this clinical data is intended to provide descriptive support to the interviews and participant observation and has no claim to be clinical research of any sort.

Participants came from 19 different countries; the most frequently represented countries were Peru (56), France (11), and Spain (10). All patients were male (n=114), as Peruvian law for therapeutic communities requires that all patients be of the same biological sex (Decreto Supremo Nº006-2012-SA). Patients' average age was 31 years. The goal of this analysis was to outline the subjective effects of the Yawar Panga purge and to specify its relevance within the context of addiction treatment.

Psychotherapy sessions during which patients recounted their experience were held within one week following the purge. Patients were questioned in an open-ended format, allowing them to highlight whichever parts of their experience were most notable. The psychotherapy sessions were conducted in Spanish and later summarized and uploaded by the psychotherapists into Takiwasi's internal online archive. All patients sign an authorization form for the use of their de-identified data for research purposes at the beginning of treatment (Rojas et al., 2018).

The data was analyzed using Microsoft Excel and Atlas.ti 9. The analysis was conducted using conventional content analysis, which permits derivation of representative categories directly from written texts without placing strong emphasis on the source of the material (Hsiesh & Shannon, 2015). This method is useful when little is known about the topic under investigation. The examined data was gathered between 2008 and 2021. A total of 664 Yawar Panga purges were administered to residential inpatients during this period, which resulted in a total of 194 written testimonies that were then subjected to a preliminary reading. Those that did not provide substantive information were excluded. The final number of testimonies utilized was 172.

Analysis of this data consisted of an initial review of each testimony during which lexical descriptions were given to each entry. The testimonies were then reviewed a second time, utilizing the descriptions from the first analysis as guidelines to assist in the derivation of representative codes. After being assigned codes, the testimonies were reviewed once more so as to corroborate the accuracy of each code as it pertained to each testimony. From these codes emerged the final categories which represent common effects and experiences perceived as a direct result of the Yawar Panga purge. The reports given by psychotherapists varied in both length and content, so it was usual for each testimony to be assigned more than one representative category. The results include those categories which appeared more than 20 times.

2.3. *In silico* analysis

Putative targets were identified through the bioinformatics method described by Gu et al. (2020). Briefly, chemical structures were prepared and converted into canonical "Simplified Molecular Input Line Entry System" (SMILES) using ChemSketch software (12.0 version).

The SMILES were then processed by the SwissTargetPrediction (http://www.swisstargetprediction.ch/) and SwissADME (http://www.swissadme.ch/index.php) platforms to predict putative targets and pharmacokinetic profile, respectively. The names of identified targets were normalized in accordance with the UniProt database (https://www.uniprot.org/). Finally, Cytoscape software (3.8 version) was used to create a component-target network.

3. RESULTS

3.1. Preparation and administration of Yawar Panga purge

The Yawar Panga purge is prepared using fresh leaves which are ground mechanically in a hand-operated grinder until a liquid extract comes out. The liquid is then recollected and filtered. The plant extraction is always prepared on the same day as the purge ceremony.

The administered dose for one person is one tablespoon of the recollected liquid. The liquid is then diluted with some water to facilitate its intake. The plant preparation is administered thereafter in a ritualistic context, in the so-called ceremonia de purga (purge ceremony). The context in which the plant is administered is considered to be crucial by Takiwasi informants and includes the use of some Traditional Amazonian Medicine (TAM) tools. Such tools may include chanting sacred melodies (icaros), blowing tobacco smoke on specific parts of the body such as the hands, chest, or top of the head (soplada), or sucking out the illness-causing agent (chupada) J. González et al. (2022); Mabit (2006).

During the ceremony, which lasts 2 to 3 hours, the Yawar Panga preparation is ingested and followed by 5-8 liters of water, which is consumed to facilitate absorption of the plant and to induce vomiting. The Yawar Panga purge is not pleasant; it induces strong and persistent vomiting which may last for several hours. After the ceremony the participants are advised to take a shower without soap and rest until the next morning without eating or drinking, save for an herbal tea if necessary.

Yawar Panga was the first emetic plant to be administered to patients when Takiwasi first opened as a therapeutic community in the 1990s. Currently, however, after several decades of experience, Takiwasi therapists may choose to give newly admitted patients a less demanding emetic plant (see introduction) to begin treatment and to allow them to work their way up to Yawar Panga.

According to the informant accounts, the Yawar Panga purge must be administered with care. One informant told of a person who died taking Yawar Panga: "I heard cases of the brother of a patient who died. He died taking Yawar Panga, for example. An alcoholic patient went to take a purge with a curandero, that curandero did not check the patient's background and gave him a purge. The most potent one. This patient who was a relative of a patient here in Tarapoto died". At Takiwasi, therapists strongly emphasize the importance of the medical evaluation (health declaration) and the patient interviews before any treatment is considered. Nevertheless, there was one instance of a Takiwasi patient being brought to the hospital following a Yawar Panga purge. The process during the ceremony went well for this individual, but intense nausea persisted afterwards. The medical doctor and curandero attended to him, but as soon as he manifested pain in the stomach, they brought him to the hospital for precautionary reasons. It was later revealed that this patient had been traveling extensively before arriving at Takiwasi and had maintained an improper dietary regimen before the ceremony which included spicy food, ceviche, grilled chicken and other strongly flavored foods. Yawar Panga, like other ceremonially-used plants, can manifest its toxic qualities in the absence of appropriate preparatory conditions on the part of the participant. Following a strict dietary regimen before and after ingesting the plant is one such condition. This situation properly exemplifies the principle of pharmakon, whereby a substance can act as a poison or medicine depending on the context of its use.

3.2. Informants' accounts on Yawar Panga purge effects

According to the informant accounts, Yawar Panga is considered the strongest of all purging plants, as it can clean deep into the bottom of the stomach and internal organs. This purge is believed to work principally on three levels: the physical-biochemical, the psychological-emotional, and the energetic-spiritual. The latter is described at Takiwasi as a non-metaphorical plane of reality populated by both good and evil spirits (DM, 2018), and is considered a central component in the center's concept of illness etiology. Furthermore, the psychological effects induced by the purge can be subdivided into three distinct levels: the cerebral-cortical, the limbic and the brainstem. The purge can influence all three of these levels, leading, respectively, to effects on one's cognitive processes, affective responses, and autonomic mechanisms such as temperature regulation.

If taken in the absence of proper oversight and without following the prescribed restrictions, adverse reactions up to and including death have been known to occur. In addition to administering an appropriately sized dose, the ritualized context plays an important role in controlling the external environment and regulating the internal state of the participants. Furthermore, the ritual framework potentiates the effects of the purge, enabling greater influence on the psychological-emotional and energetic-spiritual levels. The ritualized context gives a structured framework within which the plant can work without transgressing the desired effects of the purge.

Yawar Panga is considered unpleasant to drink but is at the same time a versatile and efficient purge, as it can detoxify an individual from different loads, whether they be energetic-spiritual, psychological-emotional or physical in origin. This powerful cleansing effect, however, can be difficult to endure because it induces strong vomiting. Some informants report patients having vomited several hours into the night, sometimes until 3am. Some patients report expelling bile in which can be smelled odors of drugs and chemical products or undigested food from previous days. Occasionally, participants may persist with nausea and vomiting for hours after the ceremony ends. In such cases the patient may be given a small piece of ginger to chew on, like a small caramel. The ginger juice alleviates the emetic effect of the plant and reduces nausea, calming the patient.

Informants report that the positive effects of the purge are often only felt the day following the ceremony. Many patients may say "never again" after completing the purge only to realize the next day how valuable the effects of the plant can be.

Informants report that patients who have been using drugs for many years have a saturation of the substance in their circulatory system. After having cleansed their blood and the cardiovascular system with Yawar Panga, patients tend to experience fewer withdrawal symptoms. Afterwards they may hold a better disposition toward continuing treatment, as their symptoms of physical dependence on the drug have weakened. Informants say that the multifaceted cleanse offered by Yawar

Panga, detoxifying the body on the physical, psychological, and spiritual level helps patients to understand more clearly their reasons for seeking addiction treatment. Due to the intensity of the purge, patients might also experience an intense state of awareness or have vivid dreams about their relationship with drug consumption. The Yawar Panga purge is additionally considered helpful when one is very anxious or irritable: it can offer emotional stabilization and help to recalibrate a sense of balance within the individual. This effect can become well known during the course of treatment, and the patients even joke around with it. When one is very irritable or agitated, other patients respond "Te falta una Yawar Panga" ("You need a Yawar Panga") or "Ah te viene una Yawar Panga" ("ah you will get a Yawar Panga").

3.3. Yawar Panga names and symbolism

The name Yawar Panga consists of two words from the Quechua language. "Yawar" means blood and "Panga" signifies leaf. The Yawar Panga's sap is as red as blood and among locals this name stands for its ability to purify the blood. Different names for this plant are used in other parts of the Amazon. The Asháninka ethnic group, for example, call the plant Huancahui Sacha. Huancahui refers to a falcon bird (*Herpetotheres cachininans*) that hunts poisonous snakes. Another name used in the Amazon is Machacuy Huasca. Machacuy (machaco or *Bothrops bilineatus*) is a poisonous snake and huasca refers to its characteristic of being a climbing plant.

At Takiwasi a symbolic connection is found between Yawar Panga and the elements of nature: Yawar Panga is mainly considered an "earth plant" but contains, however, certain characteristics from other elements, such as air (Mabit et al., 2014). Therapists at Takiwasi relate that Yawar Panga can be used to eliminate poisoning, witchcraft, or other negative energies particularly on the spiritual level. Herein lies the connection with the bird Huancahui, as Yawar Panga is considered to have the ability to "see" where there are bad energies and bad spirits and eliminate them (Mabit et al., 2014). Yawar Panga thus demonstrates its dual symbolic nature: in its healing aspect, when used with proper knowledge and in a ritualized context, it possesses the power of air (bird) that dominates the venomous snake; in its destructive aspect it represents the power of earth (snake) that is poisonous and can kill (Mabit et al., 2014).

3.4. Insights from the retrospective study

3.4.1 Physical Effects

Physical effects were the most common effect of the purge. This category includes all immediate or persistent bodily sensations other than vomiting, as vomiting was the intention of the therapy and was ubiquitous. Very strong or notable incidences of vomiting were, however, included in this category. General physiological effects were described in one testimony as, "Difficult, he vomited for a long time, didn't feel anything particularly special, he slept poorly (nausea, having to go to the bathroom every so often". Many entries described powerful emetic reactions: "...strong, difficult, he drank four jars [of water], vomited a lot, cried a lot, something very deep came out." One testimony described, "shakes, shivers came to him", with the patient going on to say, "...'although it was coming out and coming out, I no longer felt like vomiting". An irrepressible urge to vomit which lasted into the night was common: "He drank four jars of water [and] vomited until 1 am." The strong emetic effect may persist into the night, however it is usually resolved by the following morning. This testimony went on to say, "'...it left me well, it's always good'. He wants to purge it every once in a while".

3.4.2 Cleansing

Cleansing, or a feeling of having cleared or purged negative contents from the body or mind, was a very common event (n=76). Sometimes this feeling manifested itself in a broad or general sense: "He did not comment on anything special. It was not overly strong. He was able to vomit well and had the feeling of having cleaned quite a bit." Other times the feeling was more specific: "He feels he cleansed some of his anxiety and fear of death, and was able to sleep well. It cleaned his stomach, heart, and sexuality." The purge seems to have worked on different levels for different patients, as some describe the effects more physically while others describe them more energetically. One testimony described the purge as "Very strong, it went very deep. He felt it worked on the energetic level and took things out". Another patient illustrates a similar experience: "He felt the plant go deep into his body. He says it's the best purge he's had in his life. For him Yawar Panga is a Christ-like plant because it eliminates everything that blocks the Christian light at the cellular level. The day before [the purge] he was angry but after the purge he was feeling much better in spirit."

3.4.3 Sleep/Dreams

An effect on sleep and dreams (n=40) was a common experience after the purge. Some patients found the effects of the plant last into the night and interfere with their sleep (n=8), however a greater number of patients (n=14) found that the exhaustive effects of the purge allowed them to sleep profoundly. One testimony describes, "Vomited until 3am and since 5am was not able to sleep." Another states, "Slept from 6pm until 4am. Woke up very well, relieved." These differences were found to vary both between patients as well as within successive purges by the same patient.

Numerous patients (n=18) had meaningful dreams the night following the purge. One patient states, "Yawar Panga always leaves me like this, with dreams of dieting." Although dreams are an important component of the therapeutic work at Takiwasi, they are recorded in a separate section of the protocol which was not taken into account for the purposes of the present work.

3.4.4 Emotion

Emotion, defined here as the welling up or expulsion of affective contents occurred frequently during or after the purge

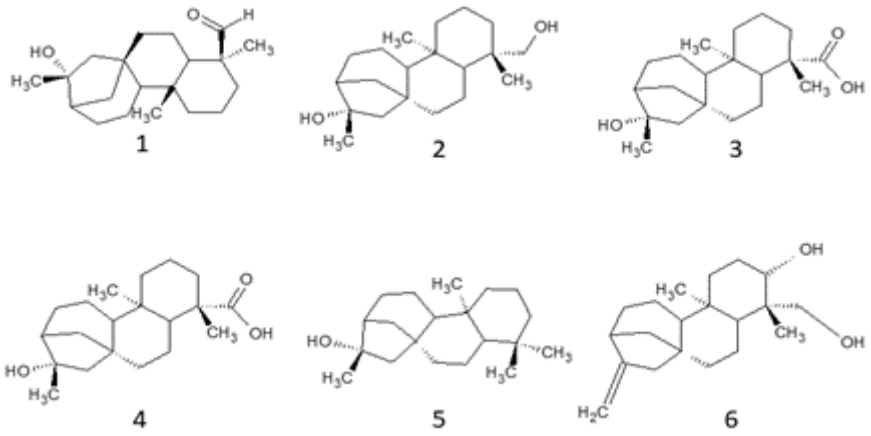

Figure 1. Terpene compounds present in *A. didyma* (Pacheco & De Oliveira, 2009): ent-Kauran-16β-ol [(–)-kauranol] (1); ent-Kauran-16β,19-diol [ent-16β,19-dihydroxykaurane] (2); [ent-16β,17-Dihydroxy-(–)-kauran-19-oic acid (3); ent-16ß,17-Dihydroxy-(–)-kauran-19-oic acid (4); ent-Kauran-16ß-ol [(–)-kauranol] (5); [ent-3ß,18-dihydroxykaur-16-ene] (6).

(n=35). Patients experienced an array of affective events which varied in intensity. Some events were relatively less intense: "I connected a lot with anger during the purge, I was able to get it out", one patient described. Another testimony stated, "He purged Yawar Panga before ayahuasca, which allowed him to throw away all of his anger." Other patients had more powerful experiences:

"A very strong experience in which a wall that disconnected him from his emotions was broken. He was able to cry (for the first time since he was 5 years old), he cried after the purge for "all of his life", connected a lot with emotional pain, memories of his infancy and of a sadness and loneliness that 'surpassed his life', which 'came from something even older'. The crying felt like the first cries of a newborn child. He felt that he was born there. The next day he felt much better inside, with a huge discharge and liberation, 'newly born'. He seemed much more embodied and present."

3.4.5 *Energizing*

Many patients experienced an energizing effect (n=30), characterized as a persistent feeling of motivation, energy, or well-being. One testimony recounts that, "After the purge he commented having felt himself with more energy and more desire, and that he purged contents of his life's history." This effect generally manifested after a night's sleep: "Yesterday he took Yawar Panga - it was 'long' [and] 'terrible', [but] upon getting up at night to use the bathroom, he felt 'an incredible peace', a lot of tranquility that he had never known before, as if he were 'recently born'. In the morning he felt more animated and saw life 'in another form'. He slept very well." One patient describes his relationship with the plant after having purged it a few times: "I have a lot of respect for [Yawar Panga] because it makes me throw away all the negative things that I hold and wake up all the good things. When I take Yawar Panga it's as if I were recharging my batteries. It moves me quite a lot. I'm scared of it but when I drink it, it does me good."

3.4.6 *Reflection*

Some participants experienced reflections (n=20), defined as voluntary or involuntary contemplation of past life events, either during or after the purge. Memories of childhood or adolescence, relationships with others, and recollection of past actions or states of mind were all common experiences. Many found these thoughts related to their past transgressions or substance abuse: "Negative thoughts. He realizes what he's done in order to get drugs and what he's lost. He has robbed and he's been scammed." Many patients thought about their past and were able to garner insight into their behavior: "It was a very strong purge for him. 'Yesterday I felt responsibility for the first time in my life.' There was a strong de-structuring of himself in that purge, rationalized defenses fell and he felt enormous guilt for violence and wrongs committed, especially toward his wife." One patient found the reflecting effect became stronger with each purge: "He feels that each time [he purges] he becomes more calm, he remembers more and more things from his life, it makes him reflect."

3.4.7 *Consumption*

Numerous patients (n=20) had experiences during or after the purge which were directly related to substance use or their current treatment at Takiwasi. Some of these experiences were related to one specific substance, whereas others were broader in their reach. One testimony states, "It took away all of his desire to smoke cigarettes, no longer even being able to bear the smoke." Other effects were felt more generally: "After the Yawar Panga, his craving to consume went down in an important way. Furthermore, before the purge he asked that his cravings diminish". Another patient recounts: "'It helped me concentrate more on my needs, process, and treatment."'

Other testimonies describe experiences that occurred during the act of purging: "He felt that he threw up a piece of marijuana". Another states, "...he was throwing up dark balls [which] he thinks were the drugs". Another patient recounted

his insight into his treatment process: "'Every vomit or pain was a lesson to be learned from that moment and I remembered something that I still think: in that moment that Dr. Jacques told me, 'your body is clean, care for it, don't mistreat it', that came to my head, nothing else. I get angry when I remember that in a moment when I drink alcohol or smoke cigarettes."'

3.5. *In silico* analysis

An *in silico* study was conducted in order to predict putative targets and pharmacokinetics of characteristic phytochemicals of this plant. According to the study previously published by Pacheco and De Oliveira (2009), the *in silico* prediction considered the following terpenoid compounds: ent-Kauran-16β-ol [(–)-kauranol] (1); ent-Kauran-16β,19-diol [ent-16β,19-dihydroxykaurane] (2); [ent-16β,17-Dihydroxy-(–)-kauran-19-oic acid (3); ent-16ß,17-Dihydroxy-(–)-kauran-19-oic acid (4); ent-Kauran-16ß-ol [(–)-kauranol] (5); [ent-3ß,18-dihydroxykaur-16-ene] (6) (Figure 1).

The structures of the above-mentioned compounds were run on the bioinformatics platforms SwissTargetPrediction and SwissADME, in order to predict putative targets and pharmacokinetics, respectively. Most of *A. didyma* terpenes were predicted to interact with various targets involved in steroid hormone pathways (Figure 2); however, only ent-Kauran-16β-ol [(–)-kauranol] could bind to GABA B receptor.

Recently, the GABA B receptor agonist baclofen has been showed to inhibit emesis stimulus, in shrew (Konno et al., 2022). The pharmacokinetics predictions also pointed to a high probability of gastrointestinal absorption and blood-brain barrier permeation for ent-Kauran-16β-ol [(–)-kauranol]. This is consistent, albeit partially, with pharmacological data available for the kaurene diterpene compound steviol, which can be absorbed in the colon only in the aglycon form (Mohammed et al., 2022). Overall, the present in silico and literature data would make rational and probable the absorption of ent-Kauran-16β-ol [(–)-kauranol] and the involvement of GABA B receptor in mediating the emetic effects induced by *A. didyma* preparations, in Takiwasi-assisted patients.

Future studies should look to unravel the bioavailability of such compounds and to elucidate the molecular interactions between ent-Kauran-16β-ol [(–)-kauranol] and GABA B receptor, aimed at a final goal of verifying whether the compound affinity toward the receptor is consistent, albeit partially, with plasma concentrations following oral administration.

4. CONCLUSIONS

Yawar Panga belongs to the *Aristolochia* genus and is used as a traditional medicine in the San Martin region of the Peruvian Amazon. While a previous ethnobotanical survey in the Chazuta valley identified "Yawar Panka" as *A. leuconeura* (Sanz-Biset & Cañigueral, 2013) for the treatment of Tobacco and cocaine addiction, the present work performed at Takiwasi, in the nearby city of Tarapoto, identified "Yawar Panga" as the species *A. didyma*; both species, however, share common morphological features and possible metabolic pathways. Despite the *Aristolochia* genus being contentious in current western pharmacopoeias, due mostly to its toxicological profile, there are written records of use of various *Aristolochia* species in ancient Ayurvedic, Chinese and European traditional medicine texts (Scarborough & Fernandes, 2011). The present work outlines the current use of *A. didyma* within the context of Takiwasi's therapeutic protocol for drug addiction rehabilitation, in which a fresh-leaf extract is administered within a ritualized context for, principally, detoxification purposes. After having cleansed the blood with Yawar Panga, patients tend to experience fewer withdrawal symptoms from their addiction. Due to the intensity of the emesis not only as a cleanse of the physical body, but also of the psycho-emotional and energetic-spiritual bodies, patients report experiencing heightened clarity into their relationship with drug consumption and gaining awareness into their addiction disorders. An in-silico analysis predicting putative targets and pharmacokinetics of characteristic phytochemicals described in the literature for *A. didyma* (Pacheco & De Oliveira, 2009) indicates the possible involvement of the GABA B receptor in mediating its emetic effects.

The objective of this research was to describe the use of the identified botanical species *A. didyma* within the context of the therapeutic community Takiwasi; literature data on this and other similar species known locally as Yawar Panga is scarce. This research therefore represents an important input into the use of Yawar Panga and will hopefully inspire further investigations into the species, especially given its relevance within the Amazonian herbal tradition. The evaluation and discussion of possible pharmacological targets through the network pharmacology analysis might also serve to stimulate further phytochemical and in-vivo assays which remain, however, outside the scope of the present work.

Despite the risk of toxicity linked to the use of some species of the genus *Aristolochia*, this research provides one more example of the use of an *Aristolochia* species (*A. didyma*) and, in this case, within a recognized clinical context with 30 years of documented use following the traditional indications derived from local herbal experts. Despite the well-known toxicity of *Aristolochia* alkaloids, such ethnopharmacological fieldwork testifies to the possibility of using *Aristolochia* species in a safe and effective way. It has already been specified elsewhere that, "The etymology of the word "pharmakon" from ancient Greek means at the same time "poison" and "drugs"; this remarks the subtle line between being a problem or a solution and the pharmacist's ability to convert a potential poison into an effective drug" (Politi et al., 2021). This same concept, which represents one of the pillars of pharmacology, has also been noted previously (Politi et al., 2018). Tresca et al. (Tresca et al., 2020) challenged the very same concepts of quality, safety, and efficacy, key components in Good Manufacturing Practice, in their relation to traditional and modern herbal medicines. It appears evident that modern ethnopharmacology should not only verify the quality, safety, and efficacy of traditionally used medicinal plants using laboratory experiments, but should

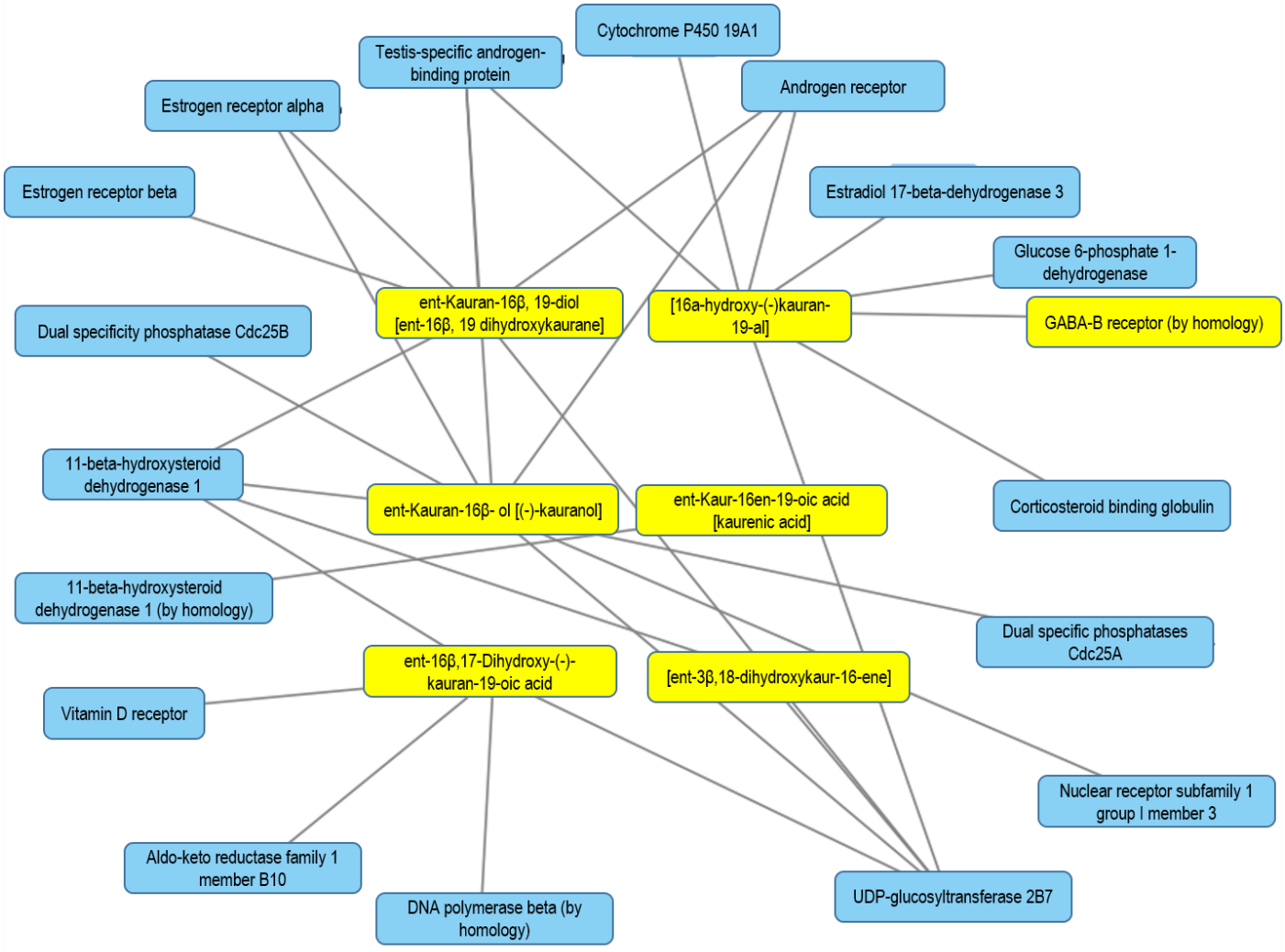

Figure 2. Pharmacological profile of phytocompounds identified in *Aristolochia didyma*. Molecular target and pharmacokinetic profile were predicted through SwissTarget Prediction (http://www.swisstargetprediction.ch/) and SwissADME (http://www.swissadme.ch/index.php) platforms, respectively. Finally, a component-target analysis was carried out through Cytoscape software (3.8 version).

also be open to integrating the traditional indications for the preparation and use of these herbal remedies in order to provide a more comprehensive understanding of their therapeutic potential.

CONFLICTS OF INTEREST

Given their role as Editor-in-Cheif, Claudio Ferrante and Associate Editor, Gokhan Zengin has not been involved and has no access to information regarding the peer review of this article. Full responsibility for the editorial process for this article was delegated to Associate Editor Balamuralikrishnan Balasubramanian. All authors has no conflict of interest to declare.

ACKNOWLEDGMENTS

The present study is part of the third mission activity of the Botanic Garden “Giardino dei Semplici” of “G. d’Annunzio” University Chieti-Pescara.

ORCID

Matteo Politi	0000-0002-1185-8569
Nahuel Simonet	GWD-9303-2022
Eric Kube	0000-0002-6224-8322
Tereza Rumlerová	0000-0003-0202-0067
Edilberto Chuquilín Bustamante	0000-0002-7534-8269
Gary Saucedo Rojas	0000-0002-7235-3150
Fabio Friso	0000-0001-5427-956X
Gokhan Zengin	0000-0001-6548-7823
Luigi Menghini	0000-0002-7346-7395
Claudio Ferrante	0000-0001-9431-9407

AUTHOR CONTRIBUTIONS

Conceptualization, research inputs, coordination, writing (M.P.); Fieldwork, botanical voucher preparation, writing (N.S.); Botanical voucher preparation, retrospective analysis, writing and editing (E.K.); Retrospective analysis, writing (T.R.); Botanical identification, writing (E.C.B); Data extraction for retrospective analysis (G.S.R); Research inputs, coordination, writing (F.F.); Supervision, research inputs, writing (L.M.); Supervision, bioinformatics analysis, writing (C.F), (G.Z.); All authors have read and agreed to the published version of the manuscript.

REFERENCES

Agency, E.M., 2005. Public Statement on the risks associated with the use of herbal products containing Aristolochia species, EMEA/HMPC/138381/2005. . https://www.ema.europa.eu/en/documents/scientific-guideline/public-statement-risks-associated-use-herbal-products-containing-aristolochia-species_en.pdf

Barrett, M.E., 1997. Prevention programs: Wat Thamkrabok: A Buddhist drug rehabilitation program in Thailand. Substance Use & Misuse. 32, 435–459. https://doi.org/10.3109/10826089709039364

Berlowitz, I., Ghasarian, C., Walt, H., Mendive, F., Alvarado, V., Martin-Soelch, C., 2017. Conceptions and practices of an integrative treatment for substance use disorders involving Amazonian medicine: traditional healers' perspectives. Brazilian Journal of Psychiatry. 40, 200–209. https://doi.org/10.1590/1516-4446-2016-2117

Berlowitz, I., Torres, E.G., Walt, H., Wolf, U., Maake, C., Martin-Soelch, C., 2020. Tobacco Is the Chief Medicinal Plant in My Work": Therapeutic Uses of Tobacco in Peruvian Amazonian Medicine Exemplified by the Work of a Maestro Tabaquero. Frontiers in Pharmacology. 11, 594591. https://doi.org/10.3389/fphar.2020.594591

Berlowitz, I., Walt, H., Ghasarian, C., Shaughnessy, D.M., Mabit, J., Rush, B., Martin-Soelch, C., 2020. Who turns to Amazonian medicine for treatment of substance use disorder? Patient characteristics at the Takiwasi addiction treatment center. Journal of Studies on Alcohol and Drugs. 81, 416–425.

Cervi, F., Friso, F., Saucedo, G., Biolcati, R., Torres, J., Politi, M., 2019. La experiencia de la comunidad terapéutica" Centro Takiwasi" en el contexto de la medicina natural e integrativa. Medicina naturista. 13, 12–19.

Chai, D., Jiang, H., Li, Q., 2016. Induced vomiting: a therapeutic option. International Journal of Clinical and Experimental Medicine. 9, 17098–17105.

Costa, C., M., 1976. El empleo de alucinógenos en la psiquiatría folklórica. Boletín de la Oficina Sanitaria Panamericana (OSP). Boletín de la Oficina Sanitaria Panamerican. 81, 176–186.

DM, O., 2018. Takiwasi: addiction treatment in the "Singing House". http://dx.doi.org/10.4225/28/5a9dce00eafa6

Fotiou, E., Gearin, A.K., 2019. Purging and the body in the therapeutic use of ayahuasca. Social Science & Medicine. 239, 112532. https://doi.org/10.1016/j.socscimed.2019.112532

Gentry, A.H., 1993. A Field Guide to the Families and Genera of Woody Plants of Northwest South America, and others, (Eds.)., p. 920.

Gifford, F.J., Gifford, R.M., Eddleston, M., Dhaun, N., 2017. Endemic Nephropathy Across the World. Kidney International Reports, 282–292. https://doi.org/10.1016/j.ekir.2016.11.003

Giovannetti, C., Arce, S.G., Rush, B., Mendive, F., 2020. Pilot evaluation of a residential drug addiction treatment combining traditional Amazonian medicine, ayahuasca and psychotherapy on depression and anxiety. Journal of Psychoactive Drugs. 52, 472–481. https://doi.org/10.1080/02791072.2020.1789247

Giove, N., 2002. La liana de los muertos al rescate de la vida: Medicina tradicional Amazónica en el tratamiento de toxicomanías, R. Takiwasi, (Eds.). .

González, F., Pabón-Mora, N., 2018. Sinopsis actualizada de *Aristolochia* (Aristolochiaceae, Piperales) en Panamá. Acta botánica mexicana, 109–140. https://doi.org/10.21829/abm122.2018.1249

González, J., Lopez, J., Horák, M., 2022. Uso ritual de plantas en el tratamiento de drogadicción en el centro Takiwasi. Medicina naturista. 16, 27–40.

Grollman, A.P., Marcus, D.M., 2016. Global hazards of herbal remedies: lessons from *Aristolochia*: the lesson from the health hazards of *Aristolochia* should lead to more research into the safety and efficacy of medicinal plants. EMBO Reports. 17, 619–625. https://doi.org/10.15252/embr.201642375

Group, A.P., Chase, M.W., Christenhusz, M.J., Fay, M.F., Byng, J., Judd, W., Soltis, D., Mabberley, D., Sennikov, A., Soltis, P., 2016. An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG IV. Botanical Journal of the Linnean Society. 181, 1–20. https://doi.org/10.1111/boj.12385

Gu, L., Lu, J., Li, Q., Wu, N., Zhang, L., Li, H., Xing, W., Zhang, X., 2020. A network-based analysis of key pharmacological pathways of *Andrographis paniculata* acting on Alzheimer's disease and experimental validation. Journal of Ethnopharmacology. 251, 112488. https://doi.org/10.1016/j.jep.2019.112488

Han, J., Xian, Z., Zhang, Y., Liu, J., Liang, A., 2019. Systematic overview of aristolochic acids: nephrotoxicity, carcinogenicity, and underlying mechanisms. Frontiers in Pharmacology. 10, 648. https://doi.org/10.3389/fphar.2019.00648

Heinrich, M., Chan, J., Wanke, S., Neinhuis, C., Simmonds, M.S., 2009. Local uses of *Aristolochia* species and content of nephrotoxic aristolochic acid 1 and 2-A global assessment based on bibliographic sources. Journal of Ethnopharmacology. 125, 108–144. https://doi.org/10.1016/j.jep.2009.05.028

Horák, M., 2013. The house of song: Rehabilitation of drug addicts by the traditional indigenous medicine of the Peruvian Amazon.

Hsiesh, H., Shannon, S.E., 2015. Three approaches to qualitative content analysis. Qualitative Health Research. 15, 1277–1288. https://doi.org/10.1177/1049732305276687

Jauregui, X., Clavo, Z.M., Jovel, E.M., Pardo-De-Santayana, M., 2011. Plantas con madre": Plants that teach and guide in the shamanic initiation process in the East-Central Peruvian Amazon. Journal of Ethnopharmacology. 134, 739–752. https://doi.org/10.1016/j.jep.2011.01.042

Júnior, S.F.P., Conserva, L.M., Corrêa, M.S., Guilhon, G.M.S., 2002. Constituents of *Aristolochia* species (Aristolochiaceae). Biochemical Systematics and Ecology. 7, 701–703. https://doi.org/10.1016/S2225-4110(16)30111-0

Konno, D., Sugino, S., Shibata, T.F., Misawa, K., Imamura-Kawasawa, Y., Suzuki, J., Kido, K., Nagasaki, M., Yamauchi, M., 2022. Antiemetic effects of baclofen in a shrew model of postoperative nausea and vomiting: Whole-transcriptome analysis in the nucleus of the solitary tract. CNS Neuroscience & Therapeutics. 28, 922–931. https://doi.org/10.1111/cns.13823

Kuo, P.C., Li, Y.C., Wu, T.S., 2012. Chemical Constituents and Pharmacology of the *Aristolochia* (□□□ mǎdōu ling) species. Journal of Traditional and Complementary Medicine. 2, 249–266. https://doi.org/10.1016/s2225-4110(16)30111-0

León, J.M., Coico, F.M., Rosas, D.G., Cruz, D.L., Castillo, J., 2017. Inventario taxonómico, fitogreográfico y etnobotánico de frutales nativos del norte del Perú. Scientia Agropecuaria. 8, 215–224. http://

dx.doi.org/10.17268/sci.agropecu.2017.03.04
Lerma-Herrera, M.A., Beiza-Granados, L., Ochoa-Zarzosa, A., López-Meza, J.E., Navarro-Santos, P., Herrera-Bucio, R., Aviña-Verduzco, J., García-Gutiérrez, H.A., 2022. Biological Activities of Organic Extracts of the Genus *Aristolochia*: A Review from 2005 to 2021. Molecules. 27, 3937. https://doi.org/10.3390/molecules27123937
Lukinich-Gruia, A.T., Nortier, J., Pavlović, N.M., Milovanović, D., Popović, M., Drăghia, L.P., Păunescu, V., Tatu, C.A., 2022. Aristolochic acid I as an emerging biogenic contaminant involved in chronic kidney diseases: A comprehensive review on exposure pathways. Chemosphere. 297, 134111. https://doi.org/10.1016/j.chemosphere.2022.134111
Mabit, J., 2006. A propos de la pratique des tabaqueros. Le Tabac, plante d'enseignement et de guérison, Actes du 2ème, 17–28.
Mabit, J., Mariscal, J.G., 2013. Towards a transcultural medicine: Reflections and proposals based on the experience in Takiwasi. Journal of Transpersonal Research. 5, 49–76.
Mabit, J., Rengifo, R., Hidalgo, J., 2014. Ceremonia ritual de la Yawar Panga. https://www.takiwasi.com/docs/arti_esp/yawar-panga.pdf
Martínez, R.V., González, R.R., 2004. Plantas de la Amazonía peruana: Clave para identificar las familias de Gymnospermae y Angiospermae. Plantas de la Amazonía peruana: clave para identificar las familias de Gymnospermae y Angiospermae. Trujillo, Perú. https://doi.org/10.5962/bhl.title.61812
Mohammed, A., Tajuddeen, N., Ibrahim, M.A., Isah, M.B., Aliyu, A.B., Islam, M.S., 2022. Potential of diterpenes as antidiabetic agents: Evidence from clinical and pre-clinical studies. Pharmacological Research. 179, 106158. https://doi.org/10.1016/j.phrs.2022.106158
Moore, S., 2022. Field Museum - *Aristolochia didyma*,.
Online, T.W.F., 2022. Aristolochia didyma S.Moore.
Pacheco, A., De Oliveira, P.M., 2009. 13C-NMR data of diterpenes isolated from *Aristolochia* Species. Molecules. 14, 1245–1262. https://doi.org/10.3390/molecules14031245
Perry, L.M., Metzger, J., 1980. Medicinal plants of east and southeast Asia: attributed properties and uses, and others, (Eds.). Massachusetts Institute of Technology Press, Massachusetts, p. 620.
Politi, M., Friso, F., Mabit, J., 2018. Plant based assisted therapy for the treatment of substance use disorders - part 1. The case of Takiwasi Center and other similar experiences. Revista Cultura y Droga,. 23, 99–126. 10.17151/culdr.2018.23.26.7
Politi, M., Tresca, G., Menghini, L., Ferrante, C., 2021. Beyond the Psychoactive Effects of Ayahuasca: Cultural and Pharmacological Relevance of Its Emetic and Purging Properties. Planta Medica. 88, 1275–1286. https://doi.org/10.1055/a-1675-3840
Rojas, G.S., Friso, F., Romero, J.T., Politi, M., 2018. Uso de tecnologías de la información en la gestión de un centro de medicina integrativa especializado en adicciones. Revista Peruana de Medicina Integrativa. 3, 123–131.
Sanz-Biset, J., Cañigueral, S., 2013. Plants as medicinal stressors, the case of depurative practices in Chazuta valley (Peruvian Amazonia). Journal of Ethnopharmacology. 145, 67–76. https://doi.org/10.1016/j.jep.2012.09.053
Sanz-Bizet, J., Cruz, J.C.D.L., Epiquien-Rivera, M.A., Canigueral, S., 2009. A first survey on the medicinal plants of the Chazuta valley (Peruvian Amazon). Journal of Etnopharmacology. 122, 333–362. https://doi.org/10.1016/j.jep.2008.12.009
Scarborough, J., Fernandes, A., 2011. Ancient medicinal use of *Aristolochia*: birthwort's tradition and toxicity. Pharmacy in history. 53, 3–21.
Seguín, C.A., 1979. Psiquiatría folklórica: shamanes y curanderos., and others, (Eds.). Peru: Ed. Ermar.
Shaw, D., 2010. Toxicological risks of Chinese herbs. Planta Medica. 76, 2012–2018. https://doi.org/10.1055/s-0030-1250533
Tresca, G., Marcus, O., Politi, M., 2020. Evaluating herbal medicine preparation from a traditional perspective: Insights from an ethnopharmaceutical survey in the Peruvian Amazon. Anthropology & Medicine. 27, 268–284. https://doi.org/10.1080/13648470.2019.1669939
Tripatara, P., Onlamul, W., Booranasubkajorn, S., Wattanarangsan, J., Huabprasert, S., Lumlerdkij, N., Akarasereenont, P., Laohapand, T., 2012. The safety of Homnawakod herbal formula containing *Aristolochia tagala* Cham. in Wistar rats. BMC complementary and alternative medicine. 12, 1–10. https://doi.org/10.1186/1472-6882-12-170
Tropicos, Org., 2022. Aristolochia didyma S. Moore. Missouri Botanical Garden, 15–15.
Villarreal, P., A., 2012. Chazuta y sus saberes maravillosos. Gobierno Regional de San Martín,. Peru: Ed., Lima
Wanke, S., González, F., Neinhuis, C., 2006. Systematics of pipevines: Combining morphological and fast-evolving molecular characters to investigate the relationships within subfamily Aristolochioideae (Aristolochiaceae). International Journal of Plant Sciences. 167, 1215–1227. https://doi.org/10.1086/508024