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Original Article

Providing added value to local uses of paparahua (*Artocarpus altilis*) in Amazonian Ecuador by phytochemical data review

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ABSTRACT

Artocarpus altilis (Parkinson ex F.A.Zorn.) Fosberg, Moraceae, is a native tree of Southeast Asia introduced to South America at the beginning of the 19th century. It has been used by several indigenous communities. This paper aims to preserve the traditional knowledge at risk of loss and to validate some of the applications found. Current ancestral practices were documented, by interviews in a scarcely contacted Amazonic Kichwa community from the Bobonaza River (Ecuador). The findings were compared with bibliographic citations from other Amazonian cultures. A bioinformatics literature survey of articles that report experiments on the chemical constituents was executed. The major findings are that some uses given in this population may be considered surprising, but the molecular profile of this species justifies its local value. It has cycloartenol (terpenoid), artoindonesianin F (stilbenoid), and different groups of flavonoids (chalcones, prenylflavones, oxepinoflavones, pyrano-flavones, xanthones). This information can prove effective in a search for novel drugs, focused to merge potential innovative uses of the plant.

Introduction

Amongst the medicinal plants used by the indigenous Ecuadorians, the family Moraceae play a substantial role having 108 useful species. *Ficus* (42) and *Perebea* (12), are the most diverse genera while *Artocarpus*, is just represented by *Artocarpus altilis* (Parkinson ex F.A.Zorn.) Fosberg, Moraceae (de la Torre et al., 2008). It is a monoecious tree, that produces big anthocarps (Zerega, 2005). It was introduced in South America at the beginning of the 19th century (Acero Duarte, 1998), from a South Eastern asiatic ancestor, *A. camansi* Blanco (Basantes-Andrade, 2010). Nowadays it has one seedless variety that is vegetatively multiplied and one seeded variety of autonomous propagation (Zerega, 2005); it has reached a pantropical distribution, ranging in the neo tropics from the Southern United States to Peru. It has a cultural role in different parts of the world (Box 1) (Ragone and Cavaletto, 2006).

Regarding Ecuador (www.tropicos.org), it can be found below an altitude of 1200 m in some coastal and mainly in Amazonic provinces. It is an introduced plant that has not become an industrial crop but has been domesticated as a source of carbohydrates in the diet and employed as medicinal or raw material for mestizo, Kichwa, Tsa'chi, Cofan, Secoya, and Shuar indigenous communities (de la Torre et al., 2008; Vargas-Vera, 2011) as summarized in Box 2.

In isolated regions, where traditional knowledge is very often in risk of extinction, the loss of local ecological knowledge impacts negatively on the resilience of socio-ecological systems and affects bioprospecting efforts (Nemoga Soto, 2013; de Brito et al., 2017). This is specially heavy in the case of the Amazon (Convention on Biological Diversity, 2010), and in the case of the plants producing latex, because latex contains pharmacological active compounds (Ujwala and Karpagam, 2013). We consider particularly interesting an aim to contribute to ethnobiological conservation providing a degree of support rationale toward the validation of some new applications that should require it. We have selected a latex plant, *Artocarpus altilis*, and a remote indigenous amazonian community to make evident the relation between chemical composition and traditional knowledge, and to propose new research areas based in pharmacological innovation. With this background our work has an ethnopharmacological frame (Heinrich, 2014) transdisciplinary between socio-cultural and the natural-medical sciences.

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Box 1
Uses of *Artocarpus altilis* in different regions of the world.

Oceania	Leaves are used as plates for serving food, as well as for making organic fertilizers and animal fodder	Ragone (1997)
Oceania	Bark to make out the cloth "tapa"	Ragone and Cavaletto (2006)
Oceania	Ornamental tree for providing shade, which also yields good-quality wood for fuel and timber	Ragone (1997)
Oceania	Burning of dried male flowers acts as a repellent for flying insects	Ragone (1997)
Oceania	Latex is used as a chewing gum, glue for catching birds, sealer of canoes	Ragone (1997)
Oceania	Externally applied for fractures, sprains, wounds, mycosis, ulcers, diarrhea, malaria, hypertension and diabetes	Heuzé et al. (2017)
Oceania	Bark and leaves against headaches and ear infections	Campos Florián (2013)
Perú	Root is cooked to prepare mouth rinses. It is applied onto hernias	Mejía and Reginfo (2000)
Perú	Fractures, burns, and insect bites	Molina-Ayme (2011)
Perú	Malaria, hypertension, anemia	Acostupa et al. (2013)
Perú	Diarrhea	Medina Larico (2018)
Venezuela	Sedative	Delgado et al. (1994)
Venezuela	Shade for coffee and cocoa plantations	Herrera et al. (1987)
Colombia	Medicinal	Valencia Herrera et al. (2010)
Bolivia	Material for colorants, ferments, paper, and cloths	Killeen et al. (1993)
Bolivia	Root: diarrhea, rheumatism, beriberi, and numbness of the legs. Fresh flowers have been considered emollient; the seeds, digestive and genitourinary stimulants; the crushed fruits external suppurative and the latex a remedy against herniated children	Calzavara (1987)

The specific objective of this paper is to give added value to local uses of paparahua (*Artocarpus altilis*) in Amazonian Ecuador by phytochemical data review.

Materials and methods

Selection of the area, voucher specimens, and permissions

The selected area to perform the field study (01° 39′ 07″S, 77° 36′11″W) was the Kichwa community of Pakayaku (Bobonaza River, Pastaza, Ecuador) only accessible by 5–6 h canoe rafting (Fig. 1). One of the authors (CXLQ) was affiliated with the Pindo Mirador Biological Station in the northern Bobonaza river basin and had been in charge of programs involving the local population, since 2008–2016. The vegetation of Pakayaku is dominated by lowland evergreen primary forest of Tigre-Pastaza (Sierra, 1999) with great arboreous plants with tabular roots as *ceibos* (*Ceiba pentandra*), big palms (*Oenocarpus batatua)* and tall trees (*Otoba glycicarpa*, *Pouruma* sp. pl., *Chorisia insignis*), full of orhidaceae and bromeliaceae, and an arboreal understory where we find large monocots (*Philodendron*, *Calathea*), ferns (*Cyathea*, *Danaena*) and vines (*Clidemia*). Families live scattered in the forest, there is no treated water, electric supply/electronic devices. It is a community that stays with little contact with outside. Specific permissions to access to the original territories of the indigenous community are obligatory and interpreters in Kichwa language are essential.

Ethnobotanical survey

Collective written research consent was obtained for C.X. Luzuriaga from the Assembly of Pakayaku and signed by Mrs. Luzmila Gayas, the community president. Prior verbal individual consents were obtained from the persons taking part in our survey. Our investigation consisted of a series of planned residential visits and treks accompanied by Kichwa interpreters and the local inhabitants of Pakayaku. The interviews were semi-structured and included a series of open questions aimed to encourage discussion. All the interviews were recorded. Four men and four women knowledgeable elders (26–46) of the Pakayaku community acted as informants and agreed to reveal their knowledge on the paparahua tree. The informants answered freely on several topics, including the common name in Kichwa, part of the plant used, description of usage, harvest season, storage (if any), preparation, and the target of the treatment. After the fieldwork, the data were entered into an MS Excel 2013 spreadsheet, that contained the units of the selected Classification of Plant Uses (Luzuriaga-Quichimbo, 2017), summarized (Box 3), and compared with the previous information on the ethnobotanical knowledge of the plant (Boxes 1 and 2).

Bibliographic survey

A bibliographic survey following (Amaral and Fierro, 2013) searching strategy was performed to provide scientific evidences for the medicinal uses of the plant. Databases accessed were: Academic Search Complete, Agricola, Agris, Biosis, CABS, Cochrane, Cybertesis, Dialnet, Directory of Open Access Journals, Embase, Espacenet, Google Patents, Google Academics, Medline, PubMed, Science Direct, Scopus, Teseo, and ISI Web of Science. The main keywords used were "*Artocarpus*" "chemical composition" "activity" and the common names of the plants ("árbol del pan, frutipan, breadfruit, aire, panatote, pitiu, and paparahua"). A critical reading was made and the most relevant information was selected. A synthetical box of chemical components (Box 4) was prepared. References for validation were included in the bibliographic section.

Results and discussion

The specific ethnobotanical uses reported by the fieldwork and the main chemical components selected from bibliography are summarized in Boxes 3 and 4. More than 70 components derived from the phenylpropanoid pathway have been reported as components of *A. altilis* (Sikarwar et al., 2014). They offer a valuable foundation for validating the medicinal activities collected during our fieldwork. But first we must emphasize on the importance of placing the discussion into the frame of the Biological Diversity Convention (2010).

With the ratification of the Nagoya Protocol (Convention on Biological Diversity, 2010) there has been a strengthening of the recognition and value of traditional knowledge that indigenous populations have acquired over their long coexistence with the jungle. This is the case of Pakayaku community, in whose world view; lessons from nature are acquired through verbal transmissions, songs, and dreams. They maintain an ancestral bond with the forest and use plants as part of their daily lives. Their respect for nature (Pacha mama) is part of their cultural identity. This is expressed as a collective aspiration: the Sumak Kawsay (=Good Living), is living in harmony with the environment (GADP-Pastaza, 2013). These rely on approaching and understanding the reality

Box 2
Ethnobotanical knowledge on *Artocarpus altilis* retrieved from indigenous communities of Ecuador based on bibliographic reports under predefined categories Classification of Plant Uses (Luzuriaga-Quichimbo, 2017).

Categories	Part used	Preparation	Traditional knowledge	Native community – province of Ecuador
Human consumption form				
Edible fruits or sweet fruits	Fruit		To prepare pudding	Pichincha, Azuay – *Mestizo*, Sucumbíos – *Secoya, Kichwa of Eastern Ecuador*, Orellana – *Kichwa of Eastern Ecuador*, Napo – *Shuar, Unidentified ethnicity*, Pastaza – *Kichwa of Eastern Ecuador*, *Shuar*, Morona Santiago – Unidentified ethnicity, Guayas, Coastal Region – *Mestizo, Unidentified ethnicity*
	Seed	Fried with salt, eggs, and cooked like peanuts	For making cakes	Pichincha – *Tsa'chi;* Sucumbíos – *Cofan, Secoya, Kichwa of Eastern Ecuador* Napo – *Kichwa of Eastern Ecuador, unidentified ethnicity* *Unidentified ethnicity-* El Oro
Non-alcoholic beverages		Seeds are ground and mixed with cooked cassava (*Manihot esculenta*) and left to ferment	Ingested as a drink	
Animal fodder				
Fruits/sweet fruits	Fruit		Used as a pig fodder	*Unidentified ethnicity*-Guayas, Coastal Region
Building				
Houses, buildings, and agricultural facilities			Timber	*Unidentified ethnicity-* Coastal Region
Medicine				
Digestive system	Latex		To relieve toothaches	Pichincha – *Tsa'chi*, *mestizo*, Napo – *Kichwa of Eastern Ecuador*, Sucumbíos, Pastaza – *Kichwa of Eastern Ecuador*, Orellana – *Shuar*, *Unidentified ethnicity*
Endocrine-metabolic system	Leaves	The leaf infusion is ingested	Treatment of obesity (fat-burning) Treatment of high cholesterol Treatment of diabetes	Pichincha – *Tsa'chi*, *Mestizo*, Azuay, Chimborazo – *Unidentified ethnicity*
Immune system	Latex	In the form of pills	Treating inflamed lymph nodes	Napo – *Kichwa of Eastern Ecuador*,
Skin and subcutaneous tissue	Latex		Treating warts	Pichincha – *Tsa'chi*, *Mestizo*, Napo, Sucumbíos, Pastaza – *Kichwa of Eastern Ecuador*, Orellana – *Shuar*, Unidentified ethnicity – Coastal Region
	Fruit pulp	Maturing plasters	Treating boils	Unidentified ethnicity – Coastal Region
Muscular and skeletal systems	Latex		Treating dislocations	Pichincha – *Tsa'chi*, *Mestizo*, Napo, Sucumbíos, Pastaza – *Kichwa of Eastern Ecuador*, Orellana – *Shuar*, *Unidentified ethnicity* – Coastal Region
Tumor diseases	Latex		For shrinking tumors	Pichincha – *Tsa'chi*, *Mestizo*, Napo, Sucumbíos, Pastaza – *Kichwa of Eastern Ecuador*, Orellana – *Shuar*, *Unidentified ethnicity* – Coastal Region
Infectious and parasitic diseases	Latex		Treatment of mumps	Pichincha – *Tsa'chi*, *Mestizo*, Napo, Sucumbíos, Pastaza – *Kichwa of Eastern Ecuador*, Orellana – *Shuar*, *Unidentified ethnicity*-Coastal Region
	Latex	Applied onto the affected area	Used to remove larvae from inside the skin	Napo – *Kichwa of Eastern Ecuador*
Symptoms and states of undefined origin	Latex		Has fortifying and energizing properties	Orellana – *Kichwa of Eastern Ecuador*

of indigenous communities, respecting their mentality, envisaging their customs as part of a wider cultural wealth, and highlighting their knowledge as sustainable sources for human development.

In this case we find ourselves faced with the cultivar of a species, possibly introduced in the Bobonaza River Basin region, through Canelos, Sarayaku, or Montalvo, after 1887, the year in which the French Dominican missionaries (García, 1999) and other European nationalities started to inhabit the regions around this river source (Luzuriaga-Quichimbo, 2017). Technical dossiers (Borgtoft et al., 1998; Alvarez, 2006; GADP-Pastaza, 2013; Santi Gualinga, 2015) have cited it as a tree growing near the residences of the inhabitants, somehow forming a part of the emerging strata of the tropical low forest. Although the plant has been used in Amazonian Ecuador (Box 1), no further specific information from the huge unexplored area of the Bobonaza River Basin (Pastaza) had been recorded.

The Pakayaku community thereby had access to certain non-autochthonous cultivars, and in turn developed their own traditional knowledge. The consumption of fruit pulp and seeds is similar to that practiced by the inhabitants in other regions of South America. This is important from a nutritional point of view, since the plant has a high protein content, which is approximately 20% in the seeds (Liu et al., 2015). In addition, the plant proteins have a good balance of essential amino acids and are particularly rich in methionine (7.5 g per 100 g of plant protein), which produces health benefit. It is also rich in calcium, iron, potassium, and phosphorus. The protein intake of these communities depends

Fig. 1. Location of the field study in Ecuador.

on hunting and fishing. These activities are currently declining due to the environmental impacts of the oil extractive industry in the territory (GADP-Pastaza, 2015). Therefore, in a first approach, the introduction of the edible protein-rich plant *A. altilis* has been of convenience to the Pakayaku community, and the techniques of preparation and cultivation should be preserved. We present this as a good demonstrating case of best practice that should be replicated to improve the nutritional condition of the population. Very interesting from the pharmaceutical-nutritional and agroforestal point of view.

Another perspective deals with the medicinal uses of this plant. As we have already exposed, it has many applications in Ecuador and other regions of the world, our contribution is focused in latex.

The medicinal uses of its latex diarrhea and for killing the human bot fly ("tupe") are noteworthy. It is highly valued by the community owing to its effectiveness against it, since the local climatic conditions promote the breeding of a diversity of insects and is a perfect habitat for the dipteran species that causes myiasis. The people of the village commonly suffer from these diseases, and have access to neither the Medical Office nor the commonly used western medicines (Luzuriaga-Quichimbo, 2017). The effectiveness of latex against "tupe" is genuinely satisfactory, and this activity can be considered as validated taking in consideration the chemical constituents of *A. altilis*, that we have summarized in Box 4. In three chemical groups: terpenoid, stilbenoid, and flavonoid, the latter divided in chalcone, prenylflavone, oxepinoflavone, pyranoflavone or xanthone or subgroups, respectively. The structures can be compared in Box 4, column shows biological activity experimentally demonstrated for each molecule. In many cases it is referred as cytostatic, and we must outline that an international patent US 9,486,490 B2 of Korean origin on an anti-cancer drug is based on the extracts of this species and recent studies have analyzed the potential of *A. altilis* against prostate cancer (Jeon et al., 2015). This cytostatic, anti-inflammatory (Fakhrudin et al., 2015) and haemostatic (Bhagyashri et al., 2015; Singh et al., 2015) properties justify its wound-healing attributes. This can be explained by the fact that latex is rich in cysteine proteases (Ujwala and Karpagam, 2013; Soares et al., 2015).

Apart from this, the extracts of the plant have been described as anti-diabetic (Indrowati et al., 2017), *in vivo* antioxidant (Tiraravesit et al., 2015), antimicrobial (Medina-Medina, 2014; Ravichandran et al., 2016), hypolipidemic (Fajaryanti et al., 2016), hepatic and renal protectant (Adaramoye and Akanni, 2016).

On the other hand, in silico analysis of flavones on leishmanial enzyme targets (Scotti et al., 2015) revealed good results for structures that are present in *A. altilis*. The lectin, artin M, extracted from *A. heterophyllus* (Souza et al., 2013), has been shown to be effective against leishmaniasis, and suggests the potential of furthering research on the immunomodulatory effects of lectins of *A. altilis* and their applications.

In conclusion, studies on the bioactivity of the chemical constituents of *A. altilis* provide a degree of support/rationale for efficacy of the plant in traditional medicine, and this information can prove effective in the search for novel drugs having larvicidal, antihelmintic, or leishmanicidal activities.

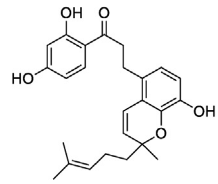
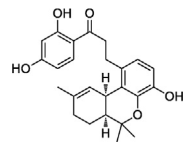
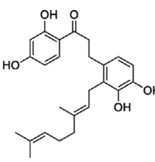
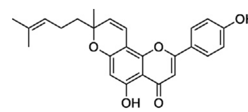
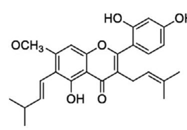
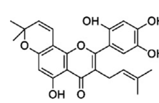
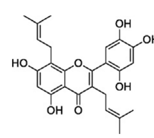
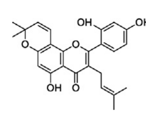
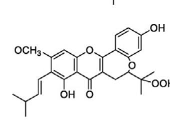
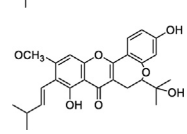
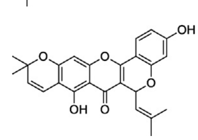
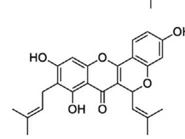
Authors' contributions

CXLQ (PhD student) contributed in collecting plant sample, getting into the community by canoe, doing the fieldwork, presenting the first analysis of the data and contributing to draft the paper. CCM contributed in plant identification, mounting herbarium specimens and fieldwork design. JBS did the bibliographic survey and

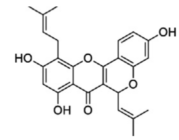
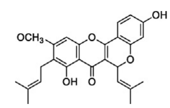
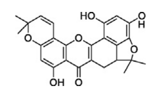
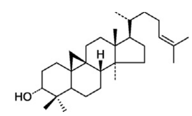
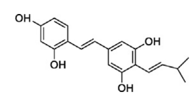
Box 3
Specific ethnobotanical uses of *Artocarpus altilis* reported in the fieldwork.

		Part of the plant used	Preparation	Method of usage/purpose of use
Consumption in human diet	Food	Fruit	The fruit is boiled in water *for twenty minutes.*	In the diet.
Human medicine	Digestive system	Latex obtained from the trunk	A diagonal cut is made on the trunk of the tree and "the milk" is collected in a woody fruit shell. *One spoonful is taken repeatedly* (*about every four hours*) *until the irregularity of the stool ceases.*	*Dysentery*
	Insect bites and other animal bites	Latex obtained from the trunk	The latex extracted from the plant is placed *directly where* ="*tupe*" (human bot fly) *has stung* (to help the extraction of larvae of Dermatobia)	Used against myiasis: "to kill the tupe"
	Additional information: It is cultivated in the chakra, or near the houses. It is collected throughout the year. It is not stored. It is used at present.			

Box 4
Artocarpus altilis: main chemical components and activities reported by different authors, based on Hafid et al. (2016), Hakim (2010), Hakim et al. (2007), and Sikarwar et al. (2014).

Class of compound		Name of compound	Structure	Activity	Reference
Flavonoid	Chalcone	1-(2,4-Dihydroxyfenyl)-3-(8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-yl-5-benzopyran)-1-propanone		Cytotoxic	Wang et al. (2007)
		1-(2,4-Dihydroxyfenyl)-3-{4-hydroxy-6,6,9-trimethyl-6a,7,8,10a-tetrahydro-6Hdibenzo(b,d) pyran-5-il}-1-propanone		Cytotoxic	Wang et al. (2007)
		2-Geranyl-2′,3,4,4′-tetrahydroxydihydrochalcone		Cytotoxic	Wang et al. (2007)
	Prenylflavone	Cycloaltilisin		Cathepsin inhibitor	Patil et al. (2002)
	3-Prenylflavone	Artocarpin		Cytotoxic Antitubercular Tyrosinase inhibitor, 5-α reductase inhibitor	Boonphong et al. (2007)
		Artonin E		Cytotoxic Antitubercular Antimalarial Antibacterial	Boonphong et al. (2007)
		Artonin V			Hano et al. (1994)
		Morusin		Cytotoxic Antitubercular Antimalarial	Boonphong et al. (2007)
	Oxepinoflavone	Artoindonesianin B		Cytotoxic	Boonphong et al. (2007)
		Chaplashin		Cytotoxic Antitubercular Antimalarial	Boonphong et al. (2007)
	Pyrano-flavone	Isocyclomorusin			Chen et al. (1993)
		Isocyclomullberin			Chen et al. (1993)

Box 4 (*Continued*)

Class of compound		Name of compound	Structure	Activity	Reference
		Cyclomulberin			Chen et al. (1993)
		Cycloartocarpin		Cytotoxic Antitubercular Antimalarial	Boonphong et al. (2007)
	Xanthone	Cycloartobiloxanthone		Cytotoxic Antitubercular Antimalarial	Boonphong et al. (2007)
Terpenoid	Terpenoid	Cycloartenol		No report	Altman and Zito (1976)
Stilbenoid	Stilbene	Artoindonesianin F		No report	Jagtap and Bapat (2010)

synthesis of the retrieved information. TRT designed the study, supervised the laboratory work and contributed to critical reading of the manuscript. All the authors have read the final manuscript and approved the submission.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bjp.2018.09.008.

References

Acero Duarte, L.E., 1998. Guia para el cultivo y aprovechamiento del arbol del pan: *Artocarpus altilis* (Park.) Fosberg. Bogotá.

Acostupa, R.J.H., Bardales, J.J.A., Teco, R.M.V., 2013. Uso de las plantas medicinales en la comunidad El Chino del área de conservación regional comunal Tamshiyacu-Tahuayo, Loreto Perú. Conoc. Amaz. 4, 77–86.

Adaramoye, O.A., Akanni, O.O., 2016. Modulatory effects of methanol extract of *Artocarpus altilis* (Moraceae) on cadmium-induced hepatic and renal toxicity in male Wistar rats. Pathophysiology 23, 1–9.

Altman, L.J., Zito, S.W., 1976. Sterols and triterpenes from the fruit of *Artocarpus altilis*. Phytochem. 15, 829–830.

Álvarez, C., 2006. In: Abya-Yala (Ed.), Historias desde el Aula. Quito Ecuador.

Amaral, L.F.G., Fierro, I.M., 2013. Profile of medicinal plants utilization through patent documents: the andiroba example. Rev. Bras. Farmacogn. 23, 716–722.

Basantes-Andrade, A., 2010. Estudio de factibilidad para la creación de una microempresa de industrialización y comercialización del fruti-pan (*Artocarpus altilis*) en la ciudad de Ibarra, provincia de Imbabura. Universidad Técnica del Norte, Ecuador.

Bhagyashri, A., Jogendra, C., Avinash, P.V., 2015. Plant latex: an inherent spring of pharmaceuticals. World J. Pharm. Pharm. Sci. 4,1781–1796.

Boonphong, S., Baramee, A., Kittakoop, P., Pakawan, P., 2007. Antitubercular and antiplasmodial prenylated flavones from the roots of *Artocarpus altilis*. Chiang Mai J. Sci. 34, 339–344.

Borgtoft, H.F., Fjeldsa, S., Øllgaard, J.B., 1998. People and biodiversity. Two case studies from the Andean foothills of Ecuador. Centre for research on cultural and biological diversity of Andean rainforests. DIVA Tech. Rep. 3, 1–190.

Calzavara, B.B.G., 1987. Fruticultura tropical: a fruta-pão (*Artocarpus altilis* (Park.)). Belem, Fôsberg.

Campos Florián, J., 2013. Hypolipidemic effect of aqueous extract from the leaves of *Artocarpus altilis* "breadfruit" in *Rattus norvegicus* induced hiperlipidemia. Sci. Agropecu. 4, 275–283.

Chen, C.C., Huang, Y.L., Ou, J.C., Lin, C.F., Pan, T.M., 1993. Three new prenylflavones from *Artocarpus altilis*. J. Nat. Prod. 56, 1594–1597.

Convention on Biological Diversity, 2010. CoP10 decisions, Decision adopted by the Conference of the Parties to the Convention on Biological Diversity at its tenth Meeting.

de Brito, C. de C., Da Silva, T.C., Albuquerque, U.P., Ramos, M.A., Ferreira Júnior, W.S., Barros, F.N., Costa Neto, E.M., de Medeiros, P.M., 2017. The use of different indicators for interpreting the local knowledge loss on medical plants. Rev. Bras. Farmacogn. 27, 245–250.

de la Torre, L., Navarrete, H., Muriel, P., Marcia, M., Balslev, H., 2008. Enciclopedia de plantas utiles del Ecuador, Herbario QCA de la Escuela de Ciencias Biológicas de la

Pontífica Universidad Católica del Ecuador & Herbario AAU del Departameto de Ciencias Biológicas de la Universidad de Aarhus. Quito & Aarhus, Quito, Ecuador.
Delgado, R., Sanabria, M.E., González, R., Cumana, L.J., 1994. Plantas medicinales de Macuro, estado Sucre, Venezuela. Saber 6.
Fajaryanti, N., Nurrochmad, A., Fakhrudin, N., 2016. Evaluation of antihyperlipidemic activity and total flavonoid content of *Artocarpus altilis* leaves extracts. Int. J. Pharm. Clin. Res. 8, 461–465.
Fakhrudin, N., Hastuti, S., Andriani, A., Widyarini, S., Nurrochmad, A., 2015. Study on the antiinflammatory activity of *Artocarpus altilis* leaves extract in mice. Int. J. Pharmacogn. Phytochem. Res. 7, 1080–1085.
GADP-Pastaza, 2015. Plan de Desarrollo y Ordenamiento Territorial del Cantón Pastaza, 2015-2020. Puyo, Pastaza, Ecuador.
GADP-Pastaza, 2013. Estudio del Impacto Ambiental del Proyecto de Construcción del afirmado camino vecinal Latasas-Umupi, Parroquia Canelos, Provincia Pastaza, Puyo, Pastaza, Ecuador.
García, L., 1999. Historia de las misiones en la Amazonía ecuatoriana, Abya-Yala, Quito, Ecuador.
Hafid, A.F., Septiani, R.P., Fabriana, L.H., Febrianty, N., Ranggaditya, D., Widyawaruyanti, A., 2016. Antimalarial activity of crude extracts of *Artocarpus heterophyllus*, *Artocarpus altilis*, and *Artocarpus camansi*. Asian J. Pharm. Clin. Res. 9, 261–263.
Hakim, A., 2010. Diversity of secondary metabolites from genus *Artocarpus* (Moraceae). Nusant. Biosci. 2, 146–156.
Hakim, E.H., Achmad, S.A., Juliawaty, L.D., Makmur, L., Syah, Y.M., Aimi, N., Kitajima, M., Takayama, H., Ghisalberti, E.L., 2007. Prenylated flavonoids and related compounds of the Indonesian *Artocarpus* (Moraceae). J. Nat. Med.61.
Hano, Y., Inami, R., Nomura, T., 1994. Constituents of Moraceae plants. 20. A novel flavone, artonin V, from the root bark of *Artocarpus altilis*. J. Chem. Res. Syn. 9, 348–349.
Heinrich, M., 2014. Ethnopharmacology: Quo vadis? Challenges for the future. Rev. Bras. Farmacogn. 24, 99–102.
Herrera, R., Aranguren, J., Escalente, G., Cuenca, G., Accardi, A., Navidad, E., Toro, M., 1987. Coffee and cacao plantations under shade trees in Venezuela. Ser. Tec. Inf. Tec. - Cent. Agron. Trop. Investig. y Ensen.
Heuzé, V., Tran, G., Hassoun, P., Bastianelli, D., Lebas, F., 2017. Breadfruit (*Artocarpus altilis*) in Feedipedia - Animal Feed Resources Information System [WWW Document]. NRA, CIRAD, AFZ FAO, URL http://www.feedipedia.org/node/523.
Indrowati, M., Pratiwi, R., Rumiyati, Astuti, P., 2017. Levels of blood glucose and insulin expression of beta-cells in streptozotocin-induced diabetic rats treated with ethanolic extract of *Artocarpus altilis* leaves and GABA. Pakistan J. Biol. Sci. 20, 28–35.
Jagtap, U.B., Bapat, V.A., 2010. *Artocarpus*: a review of its traditional uses, phytochemistry and pharmacology. J. Ethnopharmacol. 129, 142–166.
Jeon, Y.J., Jung, S.N., Chang, H., Yun, J., Lee, C.W., Lee, J., Choi, S., Nash, O., Han, D.C., Kwon, B.M., 2015. *Artocarpus altilis* (Parkinson) Fosberg extracts and geranyl dihydrochalcone inhibit STAT3 activity in prostate cancer DU145 cells. Phyther. Res. 29, 749–756.
Killeen, T.J., Garcia, E.G., Beck, S.G., 1993. Guía de Arboles de Bolivia. Garden, Herbario Nacional de Bolivia & Missouri Botanical, B.
Liu, Y., Ragone, D., Murch, S.J., 2015. Breadfruit (*Artocarpus altilis*): a source of high-quality protein for food security and novel food products. Amino Acids 47, 847–856.
Luzuriaga-Quichimbo, C.X., 2017. Estudio etnobotánico en comunidades kichwas amazónicas de Pastaza, Ecuador. Extremadura, España.
Medina-Medina, M.C., 2014. Evaluación antimicrobiana y aislamiento de metabolitos secundarios de la especie Artocarpus altilis (Parkinson)Fosberg. "árbol de la fruta de pan" de la provincia de Zamora Chinchipe. Universidad Técnica Particular de Loja.
Medina Larico, R.A., 2018. Etnobotánica cuantitativa de las plantas medicinales en la comunidad nativa Nuevo Saposoa, provincia Coronel Portillo, Ucayali, Perú. Nacional de San Agustín de Arequipa.
Mejía, K., Reginfo, E., 2000. Plantas Medicinales de la Amazonía Peruana. Agencia Española de Cooperación Internacional, Lima, Perú.
Molina-Ayme, Y., 2011. Estudio etnobotánico y etnofarmacólogico de plantas medicinales de Tambopata, Madre de Dios Perú | Molina Ayme | Ciencia y Desarrollo. Rev. Mundo Nat. 4, 7–26.
Nemoga Soto, R., 2013. Globalizacion y transformacion de las formas juridicas: apropiacion de material genetico. Pensam. Juridico; Existe un nuevo derecho? 2357-6170 0122-1108.
Patil, A.D., Freyer, A.J., Killmer, L., Offen, P., Taylor, P.B., Votta, B.J., Johnson, R.K., 2002. A new dimeric dihydrochalcone and a new prenylated flavone from the bud covers of *Artocarpus altilis*: potent inhibitors of cathepsin K. J. Nat. Prod. 65, 624–627.
Ragone, D., 1997. Breadfruit. *Artrocarpus altilis* (Parkinson) Fosberg. In: Promoting the Conservation and Use of Underutilized and Neglected Crops. 10th International Plant Genetic Resource Institute, Rome, Italy.
Ragone, D., Cavaletto, C., 2006. Sensory evaluation of fruit quality and nutritional composition of 20 breadfruit (*Artocarpus*; Moraceae) cultivars. Econ. Bot. 60, 335–346.
Ravichandran, V., Vasanthi, S., Shalini, S., Ali Shah, S.A., Harish, R., 2016. Green synthesis of silver nanoparticles using *Atrocarpus altilis* leaf extract and the study of their antimicrobial and antioxidant activity. Mater. Lett. 180.
Santi Gualinga, F., 2015. Diagnóstico de la realidad socio-económica de las comunidades kichwa de la Cuenca del Bobonaza con enfoque de Género. Universidad de Cuenca, Ecuador.
Scotti, L., Ishiki, H., Mendonca, F.J.B., Da Silva, M.S., Scotti, M.T., 2015. In-silico analyses of natural products on Leishmania enzyme targets. Mini-Reviews Med. Chem. 15, 253–269.
Sierra, R., 1999. Propuesta preliminar de un sistema de clasificación de la vegetación para Ecuador Continental. Proyecto INEFAN/GEF y EcoCiencia, Quito, Ecuador.
Sikarwar, M.S., Hui, B.J., Subramaniam, K., Valeisamy, B.D., Yean, L.K., Balaji, K., 2014. A review on *Artocarpus altilis* (Parkinson) Fosberg (breadfruit). J. Appl. Pharm. Sci. 4, 91–97.
Singh, M.K., Usha, R., Hithayshree, K.R., Bindhu, O.S., 2015. Hemostatic potential of latex proteases from *Tabernaemontana divaricata* (L.) R Br. ex. Roem. and Schult. and *Artocarpus altilis* (Parkinson ex. F.A. Zorn) Forsberg. J. Thromb. Thrombolysis 39, 43–49.
Soares, E.F., Silva, A.C., da Queiroz, A.E.S. de F., Gomes, J.E.G., Herculano, P.N., Moreira, K.A., 2015. Potencial do latex da fruta pão (*Artocarpus altilis*) como agente coagulante do leite. Ciência Rural 45, 149–154.
Souza, M., Carvalho, F., Ruas, L., Ricci-Azevedo, R., Roque-Barreira, M., 2013. The immunomodulatory effect of plant lectins: a review with emphasis on artinM properties. Glycoconj. J., 641–657.
Tiraravesit, N., Yakaew, S., Rukchay, R., Luangbudnark, W., Viennet, C., Humbert, P., Viyoch, J., 2015. *Artocarpus altilis* heartwood extract protects skin against UVB in vitro and in vivo. J. Ethnopharmacol. 175, 153–162.
Ujwala, K., Karpagam, N., 2013. Potential therapeutical values of plant latices. Int. J. Med. Aromat. Plants 3, 317–325.
Valencia Herrera, W., Hernández Londoño, C., Montealegre Ramírez, Y., 2010. Plantas oleaginosas del Caquetá, amazonia colombiana. Ing. Amaz. 3, 28–39.
Vargas-Vera, P., 2011. Estudio técnico-economico para la producción y comercialización de torta de fruta de pan. Universidad de Guayaquil.
Wang, Y., Xu, K., Lin, L., Pan, Y., Zheng, X., 2007. Geranyl flavonoids from the leaves of *Artocarpus altilis*. Phytochem. 68, 1300–1306.
Zerega, N., 2005. Systematics and species limits of breadfruit (*Artocarpus*, Moraceae). Syst. Bot. 30, 603–615.