Journal of Applied Pharmaceutical Science Vol. 6 (12), pp. 233-238, December, 2016
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2016.601234
ISSN 2231-3354

An Overview about the chemical composition and Biological Activity of Medicinal species found in the Brazilian Amazon

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ARTICLE INFO

Article history:
Received on: 20/05/2016
Revised on: 14/09/2016
Accepted on: 11/11/2016
Available online: 28/12/2016

Key words:
Biological activity, chemical composition, Brazilian Amazon, folk medicine.

ABSTRACT

This paper presents an overview on the chemical composition and biological activity of plants found in the Brazilian Amazon – *Bauhinia variegata, Cecropia obtusa, Cecropia palmata, Connarus perrottetti* var. *angustifolius, Chrysobalanus icaco* and *Mansoa alliacea*. The lack of information regarding these species, along with their importance given their pharmacological and nutritional use in Latin American folk medicine, justifies the demand for this study. However, various interesting and important actions, as antioxidant, antibacterial, cytotoxic, hypoglycemic, antifungal, antiangiogenic, antitumor, anti-inflammatory, antiulcer, and chemopreventive have been modestly reported so far. In other words, these species can play a very important role in terms of biological and chemical activity, but their pharmacology is still poorly investigated. Accordingly, the discovery of molecules that could play a role against the major diseases of modern society could be achieved by paying more attention to plants used daily in some regions of our country.

INTRODUCTION

The growing use of herbal medicine in recent decades, associated with the intense demand for biotech products, has attracted strong interest in pharmaceutical, cosmetic and food industries. About 30% of drugs available in the world market are currently derived from natural sources. This biological diversity translates into structural diversity, enabling the discovery of new classes of compounds and bioactive substances with therapeutic potential (Paracampo, 2011). The search for new medicinal molecules plays a paramount role on the global biotechnology industry development (Benini *et al.*, 2010). In Brazil, many factors contribute to this scenario, such as the diversity of plants considered therapeutic and the reduced cost associated with their acquisition. Furthermore, there is an incentive for the use of herbal products by the Unified Health System (SUS) of this country. The Amazon rainforest is house to approximately 50% of the global biodiversity, and 70% of its area is located in Brazilian territory. Consequently, Brazil is the country with the greatest potential for plant research (Port's *et al.*, 2013). Recent data show that the Brazilian Amazon region has at least 45.000 different species of plants and many of them are rich in active ingredients (Rodrigues *et al.*, 2010). However, the genetic resources of this vast biodiversity are still poorly explored, what is very surprising, given that they represent excellent sources of bioactive compounds, such as alkaloids, triterpenes and flavonoids that are able to protect the organism against damage caused by oxidative stress induced by free radicals (Neri-Numa *et al.*, 2013). More than 50.000 species of plants naturally occurring in Brazilian Amazon have already been cataloged, representing nearly 20% of the world's total (Lopes and Link, 2011).

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In this sense, various genera have been identified in this ecosystem, from which stand out: *Bauhinia*, *Cecropia*, *Connarus*, *Chrysobalanus* and *Mansoa*, which are extensively reported in the literature by their pharmacological activity and nutritional properties, mostly recognized in the folk medicine.

The *Bauhinia variegata* is a leafy canopy of the legume family (Caesalpinioidae). Besides having white flowers and pod-fruits, its leaves are similar to a "paw-of-cow" or "ox-nail", which gave rise to the popular name of the genus. This species is mainly found in tropical regions of the world and is widely used as a remedy in folk medicine (Bianco and Santos, 2003; Pizzolatti *et al.*, 2003).

The species *Cecropia obtusa* and *Cecropia palmata* belong to the family Moraceae (Sposito and Santos, 2001; Luengas-Caicedo, 2005) are popularly known as embaúva, imbaúba, imbaúva, umbaúba, umbaúva, ambaúba, embaíba, imbaíba, and toré. They are also recognized as the tree-of-laziness, since their leaves and fruits are commonly consumed by sloths. The species of the genus *Cecropia* can reach a height of fifty feet and are considered pioneer in the Atlantic Forest (Homma, 2003).

Connarus perrotteti var. *angustifolius* is believed to originate in America, being found mainly in North and Center-West Brazil, where it is popularly called marassacaca or muraçacaca, pajurana or pajujurana, and raparigeira (Forero and Kamino, 2010). According to the regional population of Pará, this plant presents many healing effects, which may be obtained through various forms of extraction, such as maceration, tea or syrup. The most used part of this species are the barks, where the highest concentration of active compounds is found (Coelho-Ferreira, 2009).

Chrysobalanus icaco L., popularly known as icaco, agirú, ajiru, and abajeru, belongs to the Chrysobalanaceae family, which consists of 17 genera and 450 species. It consists of a medium-sized shrub with oval leaves, native to coastal areas of southern Florida, Bahamas and Caribbean. It is also found in Africa, and South and Central America, including Mexico, Ecuador and northern Brazil (Fernandes *et al.*, 2003). Besides possessing medicinal activity, its fruits are edible and are commercialized in some countries, either as a candy or canned (Fernandes *et al.*, 2003; Ugent and Ochoa, 2006).

The *Mansoa alliacea*, in turn, is popularly known as garlic vine, because of the strong garlic odor exhaled when its leaves, stems, flowers and fruits are macerated. This similarity results on this plant being easily counterfeited, what is a very serious issue to the market of herbal medicinal products. *Mansoa alliacea* belongs to the Bignoniaceae family, which includes eleven other species, and is mainly found in the forests of Brazil, Argentina, and southeastern Mexico. This species is usually cultivated away from water bodies, in shaded areas and with low vegetation density, since it is not able to grow in flooded areas or open fields (Zoghbi *et al*., 2009).

The medicinal actions of plants are attributed, at least partially, to the presence of secondary metabolites in their composition (Parekh *et al.*, 2006). Therefore, we aimed to describe the phytocompounds already identified in species, as well as their predicted biological activities, relating one another.

POPULAR USE, CHEMICAL COMPOSITION AND BIOLOGICAL ACTIVITY

Works regarding the chemical composition of the species reviewed in this study are summarized in Table 1 while biological activities reported in the literature concerning the species reported in this study are summed up in Table 2.

The majority of the studies found in literature concerning these plants are related to *Bauhinia variegate* (Table 2) while other genera and species reported in this survey are far less explored.

Bauhinia variegata is popularly used by its hypoglycemic, diuretic, anti-inflammatory (Duarte *et al.*, 2007), antibacterial, healing and expectorant activity (Mishra *et al.*, 2013; Bansal *et al*., 2015). Several studies demonstrating the biological activity of Bauhinia variegata are found in the literature (Table 2). Amongst them, we can highlight the tests carried out by Mishra *et al.*, (2013) showing the potential antibacterial, antioxidant and antitumoral roles of the leaf extracts of this plant. The analysis conducted by the authors acknowledged the presence of various classes of phytocompounds, such as terpenes, phenols, flavonoids, tannins, saponins, anthraquinones and alkaloids. The antimicrobial activity attributed to this plant might be related to the presence of alkaloids, tannins and flavonoids in its composition. The latter compounds also contribute to the antioxidant and anticancer capability of this plant extracts, alone or in combination with anthraquinones and saponins.

Many species of the Bauhinia genus are widely used in folk medicine as hypoglycemic agents (Silva and Cechinel Filho, 2002; Saravanamuttu and Sudarsanam, 2012). This medicinal action was previously confirmed, as the *Bauhinia variegata* leaf extracts lowered blood glucose in rats (Thiruvenkatasubramaniam and Jayakar, 2010). This effect can be attributed to the presence of flavonoids in its composition (Saravanamuttu and Sudarsanam, 2012). Accordingly, kampferol, quercetin, and rutin, were identified by previous studies presented (Rao, 2008; Silveira *et al.*, 2015) (Table 1).

There is a lack of studies investigating the species *Bauhinia variegata* var. *alboflava*. However, the literature reports presence of caffeic acid, rutin, and quercitrin in its composition (Silveira *et al.*, 2015).

There are numerous species of the Connarus genus with promising pharmacological activities, and a wide range of phytocompounds have been identified in these plants. However, only recently the *Connarus perrottetti* var. *angustifolius* species became a target of investigation (Paracampo, 2011). Surprisingly, this plant is widely used by local population with medicinal purposes (Roman and Santos, 2006; Coelho-Ferreira, 2009). This species was analyzed by Coelho-Ferreira (2009), who evaluated its action on the treatment of genitourinary infections in women, cystic ovaries, vaginal discharge, gastric diseases, headaches, flu, cough, and congestion.

Table 1: Major compounds isolated from species of interest found in the Brazilian Amazon and the respective characterization methods employed.

Species	Isolated major compounds	Method of characterization
Bahunia variegata	Chlorogenic acid, ferullic acid, rutin, quercetin Flavonoids (canferol), terpenes Phenolic compounds, tannins, proanthocyanidins Terpenes: (lupeol, α-amyrin caprylate), fatty acids Alkaloids	HPLC-PAD[a] (Silveira *et al.*, 2015) RMN[b] 1H e 13C; ESI-MS[c] (Rao *et al.*, 2008) Phytochemical analysis (Ahmed *et al.*, 2012) Spectroscopic analysis (Saha *et al.*, 2011) Spectrophotometry (Martinez *et al.*, 2011)
Bauhinia var alboflava	Cafeic acid, rutin, quercitrin	HPLC-PAD[a] (Silveira *et al.*, 2015)
Cecropia obtusa	Caffeic acid, *p*- coumaric acid, resveratro*l*	HPLC-PAD[a] (Silveira *et al.*, 2015)
Cecropia palmata	Chlorogenic acid, caffeic acid, resveratrol, rutin, *p-coumaric acid*, ferulic acid, catechin Terpenes: ursolic acid, α-amyrin, β-amyrin, lupeol, pomolic acid, coumarin (scopoletin), steroids	HPLC-PAD[a] (Silveira *et al.*, 2015) IR spectroscopy[d], 1H and 13C NMR[b] (Pinheiro, 1999)
Connarus perrottetti var. angustifolius	Saponin, coumarin, flavonoids, tannins, glycoside cardiotonics Gallic acid, caffeic acid, Catechin, rutin	Phytochemical analysis (Oliveira, 2013) HPLC-PAD[a] (Silveira *et al.*, 2015 Capillary Electrophoresis-CZE with UV detection[e] (Müller *et al.*, 2016)
Chrysobalanus icaco	Gallic acid, quercetin, miricitin betulinic, oleanolic, pomolic acids myricetin derivatives Anthocyanins Pomolic acid, 7-O-methyl kaempferol	HPLC-DAD[f] (Port's *et al.*, 2013) GC/MS[g], 1H and 13C NMR[b] (Fernandes *et al.*, 2003) HPLC-DAD[f] and HPLC/MS[h] (Barbosa *et al.*, 2006) Chromatography paper and Spectrophotometry UV/VIS[i] (Vargas-Simón *et al.*, 2002) GC/MS[g](Vargas *et al.*, 2010) Column chromatography, HPLC (reverse phase) GC/MS[g], 1H and 13C NMR[b] (Castilho and Kaplan, 2011)
Mansoa alliacea	Tannin, flavonoids, terpenes, alkaloid, cumarin, saponin *p*-coumaric acid, ferulic acid, resveratrol Sulfur compounds	Phytochemical analysis (Patel *et al.*, 2013; Ribeiro, 2008; Ribeiro *et al.*, 2009; Oliveira, 2013) HPLC-PAD[a] (Silveira *et al.*, 2015) GC/MS[g] (Zoghbi *et al.*, 2002; Zoghbi *et al.*, 2009)

[a] High-performance liquid chromatography with Pulsed Amperometric Detection; [b] Nuclear magnetic resonance; [c] electrospray ionization-mass spectrometry; [d] Infrared spectroscopy; [e] Capillary zone electrophoresis with ultraviolet detection; [f] High-performance liquid chromatography-diode array detection; [g] Gas chromatography-mass spectrometry; [h] High-performance liquid chromatography-mass spectrometry; [i] Ultraviolet/Visible; [j] High-performance liquid chromatography.

Table 2: Biological activity from species of interest in the Brazilian Amazon.

Species	Popular name	Biological activity
Bauhinia variegata	"Paw-of-cow" "Nail-of-cow" "Hull-of-cow"	*Antitumor (Rajkapoor *et al.*, 2003; Mishra *et al.*, 2013) *Antiulcer (Rajkapoor *et al.*, 2003) *Chemopreventive and cytotoxic (Rajkapoor *et al.*, 2006) *Anti-inflammatory (Rao *et al.*, 2008) *Hypoglycemic (Thiruvenkatasubramaniam and Jayakar, 2010) *Antioxidant (Ahmed *et al.*, 2012; Mishra *et a.*, 2013) *Cytotoxic (Martinez *et al.*, 2011) *Hepatoprotective (Gupta *et al.*, 2015) * Antibacterial (Parekh *et al.*, 2006; Mishra *et al.*, 2013)
Cecropia obtuse and *C. palmata*	"White Embaúba " and "Red Embaúba"	*Antioxidant (Silva *et al.*, 2007)
Connarus perrottetii var. *angustifolius*	"Barbatimão"	*Cytotoxic (Suffredini *et al.*, 2007) *Inhibition of histamine release - Antiallergic (Oliveira, 2013)
Chrysobalanus icaco	"Abajeru" "Agiru" "Ajiru"	*Antiangiogenic (Paulo *et al.*, 2000) *Antitumor (Fernandes *et al.*, 2003) *Antibacterial (Castilho and Kaplan, 2011) *Antioxidant (Port's *et al.*, 2013)
Mansoa alliacea	"Garlic vine or D'garlic vine"	*Antifungal (Freixa *et al.*, 1998) *Antiviral (Khurana and Bhargava, 1970; Zoghbi *et al.*, 2009) *Antibacterial (Araújo, 2010) *Suppression of tumor growth (Towne *et al.*, 2015) *Inhibition of histamine release- Antiallergic (Oliveira, 2013) *Anti-inflammatory (Dunstan *et al.*, 1997; Zoghbi *et al.*, 2009) *Antioxidant (Desmachelier *et al.*, 1997; Zoghbi *et al.*, 2009)

Moreover, Oliveira (2013) demonstrated the anti-allergic property of *Connarus perrottetti* var. *angustifolius*, due the inhibition of histamine production by its leaf and bark extracts. This activity, which is more effective in bark extracts, is attributed to the presence of flavonoids, catechins, and tannins, which were identified by phytochemical analysis. Another study detected gallic acid, catechin, caffeic acid, and rutin employing high-performance liquid chromatography and capillary electrophoresis (Silveira *et al.,* 2015; Muller *et al.*, 2016).

Species of Cecropia genus are commonly used to treat respiratory diseases, such as cough and asthma, as an expectorant and to treat hypertension. The species show anti-inflammatory, antimicrobial and diuretic activity (Arend *et al.,* 2006; Costa *et al.,* 2011). One can evidence a shortage of biological studies regarding the chemical composition of *Cecropia palmata* (phenolic acids, flavonoids, resveratrol) and *Cecropia obtusa* (phenolic acids and resveratrol) (Silveira *et al.,* 2015) (Table 1). Silva et al., (2007) discussed the antioxidant potential of C. palmata and suggested that more studies are needed. Pinheiro (1999) isolated and identified ursolic acid terpenes, α-amyrin, β-amyrin, lupeol, pomolic acid, and phytol in samples of *Cecropia palmata.*

In the same work that evaluated *Connarus angustifolius*, Oliveira (2013) examined *Mansoa alliacea* leaf extracts, which also inhibited the release of histamine, but only in high concentrations. Therefore, the latter species showed a smaller potential antiallergic activity than the former. The presence of coumarins in *Mansoa alliacea* composition, along with its phenolic content, is associated with the medicinal actions attributed to this plant, as reported in the literature (Gonsior *et al.,* 1979; Choi and Yan, 2009; Santos, 2012). Tudela-Talavera (2016) and Zoghbi, *et al.,* (2009) cited several popular uses of *Mansoa alliacea* for the treatment of cough, nausea, fever, flu, diarrhea, rheumatic pains, among others. Zoghbi *et al.*, (2009) state that the essential oil of this species is composed by various sulfur compounds, which showed antinflammatory and antimicrobial activity and may be responsible for the medicinal actions of the plant. Other classes of secondary metabolites and specific compounds were identified in the species and are referenced in Table 1. Antifungal (Freixa *et al*., 1998) and antibacterial activity (Araujo, 2010) are also reported. However, the lack of studies showing the compounds responsible for such actions emphasizes the need to deeply explore the potential of this plant.

Chrysobalanus icaco is popularly used on the control the blood glucose levels (Presta *et al*., 2007; Coelho-Ferreira, 2009).The infusions of fruits, leaves, barks or roots are employed in the treatment of chronic diarrhea, bleeding and leukorrhea. Additionally, leaves of this plant are used as diuretic and hypoglycemic (Paulo de *et al.*, 2000). Port's *et al.*, (2013) found relevant phenolic compounds in *Chrysobalanus icaco*, which are directly associated with the antioxidant activity of the extract obtained by infusion of leaves of this plant (Table 1). Furthermore, Castilho and Kaplan (2011) reported the antibacterial activity of *Chrysobalanus icaco* extracts and of 7-O-methylkaempferol, isolated from this species, against microorganisms such as *Staphylococcus aureus* and *Streptococcus pyogenes*.

The antitumor activity was observed for all species, except the ones of Cecropia genus (Table 2). Rajkapoor *et al.*, (2003) verified the antitumor action of *Bauhinia variegata* against Dalton's ascitic lymphoma, since the extract was able to increase the average survival time of the mice assessed. Also, fractions of *B. variegata* leaves showed pronounced cytotoxic effect against different tumor cell lines such asprostate, lung, ovary, breast and leukemic (Mishra *et al.*, 2013).

Triterpenes as betulinic, pomolic and oleanolic acids were isolated from leaves of *Chrysobalanus icaco*, and were able to inhibit the growth and apoptosis of leukemic tumor cells (Fernandes *et al.*, 2003). Suffredini *et al.,* (2007) assessed the cytotoxicity of *Connarus perrottetti* leaves in cancer cells and also observed that they were able to inhibit their growth. Similarly, Towne *et al.,* (2015) observed this effect for *Mansoa alliacea* leaves, highlighting the antitumor potentiality of such species.

CONCLUSION

This work has analyzed and compiled information regarding the species *Bauhinia variegata*, *Cecropia obtusa*, *Cecropia palmata*, *Connarus perrottetii* var. *angustifolius*, *Chrysobalanus icaco*, and *Mansoa alliacea*. These common species of the Brazilian Amazon region, widely used in folk medicine, show antioxidant, antibacterial, cytotoxic, hypoglycemic, antifungal, antiangiogenic, antitumor, anti-inflammatory and antiallergic activity. However, many studies regarding the biological activity of such plants pay little attention to the constituents responsible for their medical actions. Therefore, more examination is required regarding both biological and chemical activity. Such investigations could lead to the discovery of new compounds and confirm these pharmacological effects. Based on the outcomes of these studies, the evaluated plants may become potential herbal products.

Financial support and sponsorship: Nil.

Conflict of Interests: There are no conflicts of interest.

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How to cite this article:

Pires FB, Dolwitsch CB, Prá VD, Mônego DL, Schneider VM, Loose RF, Schmidt MEP, Bressan LP, Mazutti MA, Rosa MB. An Overview about the chemical composition and Biological Activity of Medicinal species found in the Brazilian Amazon. J App Pharm Sci, 2016; 6 (12): 233-238.