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Folk uses and pharmacological properties of *Casearia sylvestris*:

a medicinal review

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ABSTRACT

Folk uses and scientific investigations have highlighted the importance of *Casearia sylvestris* extracts and their relevant bioactive potential. The aim of this work was to review the pharmacological properties of *C. sylvestris*, emphasizing its anti-ulcer, anti-inflammatory, anti-ophidian and antitumor potentialities. Ethanolic extracts and essential oil of their leaves have antiulcerogenic activity and reduce gastric volume without altering the stomach pH, which corroborates their consumption on gastrointestinal disorders. Leaf water extracts show phospholipase A₂ inhibitory activity that prevents damage effects on the muscular tissue after toxin inoculation. This antiphospholipasic action is probably related to the use as an anti-inflammatory, proposing a pharmacological blockage similar to that obtained with non-steroidal anti-inflammatory drugs on arachidonic acid and cyclooxygenase pathways. Bioguided-assay fractionations lead to the identification of secondary metabolites, especially the clerodane diterpenes casearins (A-X) and casearvestrins (A-C), compounds with a remarkable cytotoxic and antitumor action. Therefore, the *C. sylvestris* shrub holds a known worldwide pharmacological arsenal by its extensive folk utilization, exciting searches for new molecules and a better comprehension about biological properties.

Key words: *Casearia sylvestris*, folk uses, pharmacological properties.

INTRODUCTION

The phytotherapeutic use has increased in developing and in developed countries as an additional way to treat and prevent diseases, particularly chronic illnesses, such as cardiovascular and neurodegenerative dysfunctions (World Health Organization 2003, Ferreira et al. 2008). These natural products are represented by teas, powders, extracts, infusions and other sorts of formulations (Balu...
The Brazilian territory embrace the major diversity of plant species in the world, but less than 10% have been evaluated with respect to their biological characteristics and fewer than 5% have been subjected to detailed phytochemical studies (Luna et al. 2005). Nowadays, the curative principle of plants is more disseminated in rural areas due to the lack of efficient laboratorial and clinical facilities, where medical services are problematical, complex and financially more expensive (Holetz et al. 2002, Ferreira et al. 2009).

**TAXONOMY OF Casearia sylvestris**

Traditionally, *Casearia sylvestris* Swartz, 1860 (Synonymous: *Samyda parviflora* L., *Casearia parviflora* L., *Anavinga samyda* Gaertn. F.) belongs to the Flacourtiaceae family, which has 89 genus and 1300 species distributed in tropical and temperate regions around the world. *Casearia* genus includes almost 180 species (Little and Wadsworth 1964, Torres and Yamamoto 1986).

Recently, molecular, ecological, chemical and morphological studies associated with phylogenetic approaches of several families, including Flacourtiaecae and Salicaceae, led to the birth of the Angiosperm Phylogeny Group (APG), leading to the Flacourtiaecae family extinction and permutation of the majority of its genus to the Salicaceae family, including *Casearia* (Souza and Lorenzi 2005).

**DISTRIBUTION AND ANATOMIC DESCRIPTION OF Casearia sylvestris**

Commonly widespread in the Americas, *C. sylvestris* is found in Cuba, Antilles and Porto Rico to Mexico, Brazil, Bolivia, Peru and Argentina (Little and Wadsworth 1964, Instituto de Botanica Darwinion 2002). In Brazil, it is distributed practically throughout the entire territory extension from Amazonas (Tapajós river region) to Rio Grande do Sul states (Torres and Yamamoto 1986, Hack et al. 2005).

Anatomically, its vegetative and reproductive structures are characterized by crystalline inclusions and glandular cells full of essential oils. The leaves are assimetric, smooths or rough, peciolated, lanceolate, brilliant, with 6-12 cm length and 3-5 cm wide. It presents radiate and protostelic root and the stem is siphonotelic and ectophloic, distinguished by prismatic crystals and druses, mainly in the cortical phloem (Aisy and Scavone 1973).

The flowers are small, green, actinomorphic, hypogone and hemaphrodite. They produce imperceptible odor, nectar of easy access and have exposed sexual organs. The plant flourishies in June and August and its fruits ripen from September to November. These fruits are septicidal capsules with seeds involved by red aril (Aisy and Scavone 1973, Torres and Yamamoto 1986).

Under good conditions, *C. sylvestris* is capable to flower and fruit in the second year of life, when it reaches about 1 meter in stature (Little and Wadsworth 1964).

In Panamá, these species flower even in dry season between August and December (Croat 1978). With a moderate rate of growth, the plant lives at least 20 years. Its natural and artificial propagation usually occurs through seeds and its wood is used as fuel and suitable to build fence, posts, stakes, rustic carpentry and handle tools (Torres and Yamamoto 1986).

Acquainted with the medical importance of several parts of *Casearia sylvestris*, this work aims to review its folk pharmacological uses, emphasizing its anti-ulcer, anti-inflammatory, anti-ophidian and antitumor potentialities.

**PHARMACOLOGICAL PROPERTIES**

In Brazil, *C. sylvestris* is popularly known as “guaca-tonga”, a word originated from “Tupi-Guarani” language, which indicates its ancient exploitation by native communities. Other folk names are “erva-de-lagarto”, “lingua-de-tiu”, “cafezinho-do-mato”, “corta-lengua”, bugre herb and wild-coffee (Hoehne 1939, Little and Wadsworth 1964). The Karajá Indian tribe habitually makes a bark maceration to treat diarrhea; other Brazilian tribes crush its roots to care for wounds, leprosy and as anti-ophidian. Natives from the Shipibo-Combo tribe (Peru) utilize bark decoction for flu and chest colds (Hoehne 1939). Certainly, the antimicrobial action against pathogens as fungi (*Aspergillus niger*, *Saccharomyces cerevisiae*, *Candida albicans*, *Candida tropicalis*) (Carvalho et al. 1998, Oberlies et al. 2002, Da Silva et al. 2008b) and bacteria (*Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Salmonella enteriditis*) (Chiappeta et al. 1983, Mosaddik et al. 2004, Da Silva et al. 2008b) explains the uses to treat wounds, skin ulcerations and diarrhea.

In the last years, *C. sylvestris* has been exploited in the development of creams against herpes and commercialized in mixed formulations with other plants to commercialize the use of plant species in the world.
prepare teas and infusions with therapeutical purposes (Camargo et al. 1993, Alves 2000, Simões et al. 1999). An infusion can be easily obtained (20 g of dried leaves per 1 L of water) for oral consumption (2-3 times/day) together with meals, in case of gastric ulcers or for topical treatment of wounds, burns, rashes, eczema and vitiligo (Blanco 2010).

Table I displays some therapeutic properties of *C. sylvestris* and Table II shows the biological activities already mentioned by the scientific community.

### Anti-ulcer activity

Ethanolic extracts of *C. sylvestris* leaves have revealed anti-ulcer properties, a finding that corroborates its wide use in gastrointestinal disorders (Hoehne 1939, Fialho et al. 2010). Basile et al. (1990) showed that ethanolic extract significantly decreases stomach volume (42%) in a more efficient way (when compared to misoprostol, 26%) and chloride acid (HCl) production in absence of gastric pH changes, an excellent finding since protein digestion is largely activated in the stomach by pepsin enzymatic action. The pepsin generation from its inactive precursor pepsinogen requires acid pH (between 1.6-3.2) and its catalytic activity also needs acid environment. Therefore, alkalinization softly up to pH 5 causes enzyme inactivation (Constanzo 2004). Leaf ethanolic extract do not interferes in the aminoacid absorption, displaying an additional advantage when compared to some synthetic drugs as atropine and cimetidine, molecules that arouses gastric pH alterations (Torregrosa 1997).

*C. sylvestris* extracts were also capable to prevent early establishment of gastric lesions in stressed rats with efficacy similar to cimetidine and misoprostol, though these drugs have demonstrated greater protection against severe lesions, especially necrotic and hemorrhagic injuries (Aboin et al. 1987). Esteves et al. (2005) demonstrated a decrease in gastric volumes without physiological alterations in H⁺ concentration, emphasizing that essential oils as well as crude extracts of “guaçatonga” leaves have anti-ulcer properties.

Quantitative analyses of the ethanolic extract indicated traces of terpenes (triterpenes and sesquiterpenes), cumarines, tannins (flavonoids) and some volatile oils that play an important role in mucosa protection (Sertié et al. 2000). Flavonoids are phenolic compounds with antioxidant action and strong capacity to inhibit the production of both nitric oxide and the TNF (tumoral necrosis factor) mediators (Kawada et al. 1998). In fact, the antioxidant potential was showed by Menezes et al. (2004) and among all bioactive compounds found...
TABLE II

Biological activities from different parts of *Casearia sylvestris*.

<table>
<thead>
<tr>
<th>Part of the plant</th>
<th>Biological activity</th>
<th>Extract, compound or preparation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaves</td>
<td>Antitumor</td>
<td>Ethanolic extract,</td>
<td>Itokawa et al. (1988, 1990)</td>
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<tr>
<td></td>
<td></td>
<td>Casearins (A-F)</td>
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<td></td>
<td></td>
<td>Gallic acid derivatives</td>
<td>Da Silva et al. (2009)</td>
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<tr>
<td></td>
<td><em>In vitro</em> cytotoxicity on normal and/or tumor cells</td>
<td>Casearins (A-X)</td>
<td>Morita et al. (1991), Wang et al. (2009), Ferreira et al. (2010), Santos et al. (2010)</td>
</tr>
<tr>
<td></td>
<td>Antiviral against <em>Herpes simplex</em></td>
<td>Casearvestrins A, B and C</td>
<td>Da Silva et al. (2009c)</td>
</tr>
<tr>
<td></td>
<td>Anti-inflammatory</td>
<td>Ethanolic extract</td>
<td>Camargo et al. (1993)</td>
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<td></td>
<td>Infusion</td>
<td>Ruppelt et al. (1991)</td>
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<td></td>
<td></td>
<td>Hydroalcoholic extract</td>
<td>Almeida (2000)</td>
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<td>Decoction 5%</td>
<td>Sassiotto et al. (2004)</td>
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<td></td>
<td></td>
<td>Essential oil</td>
<td>Esteves et al. (2005)</td>
</tr>
<tr>
<td></td>
<td>Antibacterial</td>
<td>Not described</td>
<td>Hoehne (1939), Chiappeta et al. (1983)</td>
</tr>
<tr>
<td></td>
<td>Antifungal</td>
<td>Methanolic extract</td>
<td>Alves (2000)</td>
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<td></td>
<td></td>
<td>Casearins G, S and T</td>
<td>Carvalho et al. (1998)</td>
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<td></td>
<td></td>
<td>Casearins A, B and C</td>
<td>Orefies et al. (2002)</td>
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<td></td>
<td>Phospholipase A₂ inhibition</td>
<td>Gallic acids</td>
<td>Da Silva et al. (2008b), Borges et al. (2000, 2001), Cavalcante et al. (2007)</td>
</tr>
<tr>
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<td></td>
<td>Water extract</td>
<td>Basile et al. (1990), Sertie et al. (2000), Fialho et al. (2010)</td>
</tr>
<tr>
<td></td>
<td>Anti-ulcer</td>
<td>Ellagic acid derivatives</td>
<td>Da Silva et al. (2008a)</td>
</tr>
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<td></td>
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<td>Ethanolic extract</td>
<td>Basile et al. (1990), Sertie et al. (2000), Fialho et al. (2010)</td>
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<td>Molluscicide</td>
<td>Essential oil</td>
<td>Esteves et al. (2005)</td>
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<td>Antioxidant</td>
<td>Methanolic extract</td>
<td>Alves (2000)</td>
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<td>Water extract</td>
<td>Menezes et al. (2004)</td>
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<tr>
<td></td>
<td>Against <em>Leishmania donovani</em>, <em>Trypanosoma cruzi</em> and <em>Plasmodium falciparum</em></td>
<td>Ethanolic and hexane extracts</td>
<td>Mesquita et al. (2005, 2007)</td>
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<td>Analgesic</td>
<td>Hydroalcoholic extract</td>
<td>Mattos et al. (2007)</td>
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<td>Hypcholesterolemic</td>
<td>Methanolic extract</td>
<td>Schoenfelder et al. (2008)</td>
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<td>Stem</td>
<td>Against <em>L. donovani</em> and <em>T. cruzi</em></td>
<td>Ethanolic and hexanic extracts</td>
<td>Mesquita et al. (2005)</td>
</tr>
<tr>
<td></td>
<td>Against <em>Aedes aegypti</em></td>
<td>Hexane extract</td>
<td>Rodrigues et al. (2006)</td>
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<tr>
<td></td>
<td>Against <em>P. falciparum</em></td>
<td>Hexane extract</td>
<td>Mesquita et al. (2007)</td>
</tr>
<tr>
<td>Roots</td>
<td>Analgesic</td>
<td>Bark infusion with leaves</td>
<td>Ruppelt et al. (1991)</td>
</tr>
<tr>
<td></td>
<td>Against <em>T. cruzi</em></td>
<td>Clerodane diterpen</td>
<td>Espindola et al. (2004)</td>
</tr>
<tr>
<td></td>
<td>Against <em>L. donovani, T. cruzi</em> and <em>P. falciparum</em></td>
<td>Ethanolic and hexane extracts</td>
<td>Mesquita et al. (2005, 2007)</td>
</tr>
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</table>

in the ethanolic extract of *C. sylvestris*, the therapeutic effects of essential oils have been attributed to the biciclogermacrene, a sesquiterpene with anti-inflammatory activity (Abreu Gonzaga et al. 2003). An enriched fraction of diterpenes extracted from leaves of *C. sylvestris* presented antulcerogenic action in rats in a dose of
MEDICINAL PROPERTIES OF *Casearia sylvestris*

15.5 mg/kg/day, inhibiting ulcer formation up to 100%. The clerodane diterpenes casearins B, D, O, X and caseargrewiin F (Fig. 1) presented the same action in a dose of 1.68 mg/kg/day. Casearin X was called initially as Casearin U (FAPESP et al. 2003, Santos 2008).

Besides protecting the stomach mucosa, the ethanolic extract shows a LD$_{50}$ value of 1842 mg/kg (Basile et al. 1990), a value considered slightly toxic according to toxicity categories established for humans by Hodge and Sterner (1949). Some subacute toxicity assays exhibited promising outcomes, since doses 2.5 fold higher (143.9 mg/kg/day of body weight) show effectiveness as anti-ulcer agent without altering physiological parameters, such as water and food intake, body weight gain and key organ relative weights after thirty days of ethanolic extract oral administration (Basile et al. 1990). Oral acute toxicity (30, 65 and 172 mg/kg/day) with the compound Casearin X also did not indicate corporal or behavioral changes, despite the fact that 172 mg/kg/day is a dose 100-fold higher than ED$_{100}$ (maximum effective dose) necessary to obtain antiulcerogenic action (1.68 mg/kg/day) (FAPESP et al. 2003, Santos 2008).

### Anti-inflammatory activity

Researchers have emphasized the anti-inflammatory potential of substances extracted from “guacatonga” leaves, attracted by its economical appealing, practical handling and easy folk preparations (Hoehne 1939, Ruppelt et al. 1991).

In some carrageenan-induced inflammation models, the essential oil of *C. sylvestris* leaves inhibited paw edema formation. This proposes a blockage of inflammatory cascade mediators from the arachidonic acid and inhibition of cyclooxygenase (COX) catalytic activity, a property comparable to indomethacin (a non-selective and non-steroidal COX inhibitor). On the other hand, this oil does not interfere on vascular permeability (Esteves et al. 2005) probably due to its failure in antagonizing mastocyte and/or basophile degranulation and discharging of active pharmacological substances (histamine and serotonin, for example) (Tamura et al. 2002).

Decoction of *C. sylvestris* leaves was capable to decrease bone formation possibly because of the presence of anti-inflammatory phytochemical compounds and prostaglandin synthesis inhibition, which may cause inability in macrophage chemotaxis, fibroblast activation and collagen fiber arrangement and formation, with noticeable inhibitory effects on osteogenesis (Sassioto et al. 2004).

### Anti-ophidian activity

In many countries, plant extracts have been traditionally used in the treatment of snake bite poisoning (Martz 1992). Water extract of *C. sylvestris* leaves shows great inhibitory effects on the toxic, enzymatic, hemorrhagic and anticoagulant activities exhibited by various venoms, particularly against those belonging to the PLA$_2$ I (Phospholipase A$_2$) (Elapidae Family), II (Viperidae Family) and III (bee) types (Borges et al. 2000, 2001).

Neuromuscular junction is the main target of snake venoms, some of which possessing strong pre-synaptic neurotoxins, such as the Crototox (CTX), a heterotrimeric Asp49-PLA$_2$ complex found in the *Crotalus durissus terrificus* venom (Kini 2003). The PLA$_2$ enzyme activity of CTX is critical for blockage of signal transmission at the endplate. The *C. sylvestris* anti-ophidian property seems to be related to the capacity of PLA$_2$ inhibition (Borges et al. 2000, 2001), which is an enzyme largely activated after venom administration/inoculation. Aqueous extract of the leaves diminishes injures on skeletal muscle fibers via the prevention of edema formation within endomise (connective tissue) and reduces the muscle blockage, findings responsible by tissue damage protection and enhanced survival rates in extract-pretreated animals depending on the venom class (Cavalcante et al. 2007).

The anti-venom activities of the extract on myotoxins (*Bothrops* and *Crotalus* genus) is attributed to their antiphospholipasic action, explaining, at least partially, the anti-inflammatory potential in some clinical circumstances in which there are synthesis and release of prostaglandins and leukotrienes and failure to prevent chronic responses (Esteves et al. 2005). It could be a plausible proposal to assume that the mechanism of action of these compounds may be analogous to non-steroidal anti-inflammatory drugs.

In view of the fact that the water extract was more efficient in neutralizing hemorrhagic metalloproteinases

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Fig. 1 –...
from bothropic venoms than neutralize serina-proteases, it is proposed that this extract may act as a metal natural chelating (Borges et al. 2001). Other possibility would be linkage of the active compound, present in the extract, to the enzyme catalytic site which could avoid coupling of the substrate to the enzyme in a covalent or non-covalent interaction way. Highly reactive tannins presented in the leaves can bind to biological polymers and enzymes, allowing the electron transportation and obstructing the enzymatic activity (Abdulla and Gruber 2000, Delfino and Canniatti-Brazaca 2010).

Four ellagic acid derivatives from aqueous extracts of *C. sylvestris* were isolated, characterized and tested against actions of both total venom and PLA₂ (Asp 49 BthTX-II) from *Bothrops jararacussu* venom. The isolated compounds were ellagic acid, 3′-O-methyl ellagic acid, 3,3′-di-O-methyl ellagic acid and 3′-O-methyl-3′,4′-methylenedioxy ellagic acid. The constant inhibition values for enzymatic activity as well the IC₅₀ values found in the edematogenic and myotoxic activities indicate that the ellagic acid is the best inhibitor of these activities. The results show that the presence of hydroxyl at position 3 or 3′ increase the capacity of these derivatives in inhibiting toxic effects. However, the existence of methoxyl groups at position 3 or 3′ reduced but did not completely inhibit the capacity of compounds on reducing all the toxic effects studied (Da Silva et al. 2008a).

**Antitumor activity**

Most of the compounds isolated from *Casearia* leaves are represented by a series of oxygenated tricyclic clerodane diterpenes in which the tetrahydrofuran ring is C-acylated at positions C-18 and C-19 (Fig. 1). The diacetic ring is a highly oxygenated structure rarely seen in natural molecules, being a protected dialdehyde (Santos et al. 2007). Bioguided fractionation assays have regularly revealed that clerodane diterpenes, predominantly those rich in oxygen atoms, possess anti-fungal, antibacterial, insecticidal, antifeedant and cytotoxic properties (Morita et al. 1991, Merrit and Ley 1992, Oberlies et al. 2002, Vieira-Junior et al. 2009).

Twenty eight clerodane diterpenes typical of *Casearia* were isolated from *C. sylvestris*: casearins A-X (Carvalho et al. 1998, Itokawa et al. 1990, Morita et al. 1991, Wang et al. 2009, Santos et al. 2010) and caseargrewiin F (Santos et al. 2010), isolated from leaves; casearvestrins A-C, isolated from leaves and branches (Oberlies et al. 2002); and rel-19S-acetoxy-18R-butanoxyloxy-18,19-epoxy-6S-hydroxy-2R-(2-methylbutanoyloxy)-5S, 8R, 9R, 10S- cleroda-3,13(16),14-triene, isolated from roots (Espindola et al. 2004) (Fig. 1).

Casearins and their biological activities show structure-activity relationship largely attributed to the diterpene skeleton substitutions at positions C-2 (R¹), C-6 (R²), C-7 (R³), C-18 (R⁴) and C-19 (R⁵). Figure 1 describes the cytotoxic activity of the casearins in Chinese hamster V-79 cells. Casearins G, H and L, whose structures are characterized by the oxygen-bearing functionality absence at C-6, showed the highest antiproliferative activity, followed by the diterpenes J, K, L and M, whose structures present hydroxyl moiety at C-6 or C-7. Other casearins, as N, O, P, Q and R have weaker activity, which seems to be determined by methoxyl, hydroxyl or oxygen substituents of R¹. Derivatives converted from the casearins A and D by inducement of acyl substituent at C-6 exerted decrease in the cytotoxicity (Morita et al. 1991), demonstrating that bulkiness at C-6 has the highest influence on the bioactivity. Such cytotoxicity on cancer cells was also found in the *C. sylvestris* leaf oil (Da Silva et al. 2008c), whose composition previously reported exhibits two well characterized cytotoxic sesquiterpenes (β-caryophyllene e α-humulene) (Tatman and Mo 2002, Esteves et al. 2005, Sylvestre et al. 2005). Although the cytotoxic mechanism is unclear, Carvalho et al. (1998) reported that clerodane diterpenes G, S and T can cause acetylating on DNA molecule. Recently, this toxicity on DNA molecules was confirmed by Ferreira et al. (2010) who showed that Casearin X causes DNA and nuclear fragmentation, phosphatidylserine externalization, activation of the effector caspases 3/7 and mitochondrial depolarization in leukemia cells, all evidences of apoptosis cell death. Caspases, cysteine-proteases with ability to cause cleavages on laminin and changes on DNA structure triggered by DNAses lead to cytoskeleton and nuclear destabilization and chromatin fragmentation and condensation. Eventually, cells become divided in apoptotic bodies full of organelles and/or nuclear material surrounded by integral plasma membrane. Immediately, the largest part of the bodies is engulfed by macrophages. Thus, since there is no...
intracellular factor releasing, apoptosis occurs without immune system activation (Strasser et al. 2000).

Ethanolic extract phytochemical investigations of C. sylvestris leaves reported strong antitumor activity on Sarcoma 180 transplanted mice (100 mg/kg/dia), with tumor growth inhibition rates higher than 80% (Iokawa et al. 1988). Bioguided studies led to the isolation of six pharmacologically active compounds, the casearins A, B, C, D, E and F. Additional in vivo experiments (15 mg/kg/day) confirmed the antineoplastic action of these clerodanes, though casearin C has showed better antiproliferative effects. The main structural difference among these six diterpenes is the presence of a casearin C decanoate substituent at C-7 (Fig. 1), which could explain its higher cytotoxicity on V-79 cells (Iokawa et al. 1990) likely based on its remarkably larger hydrophobicity and facility to penetrate cytoplasm membrane cell.

Recently, two gallic acid-derived compounds isolated from C. sylvestris leaves – isobutyl gallate-3,5-dimethyl ether (IGDE) and methyl gallate-3,5-dimethyl ether (MGDE) – showed significant chemotherapeutic potential against Ehrlich and Lewis lung cancer ascite tumor cells and increased animals’ survival by approximately 90%, though IGDE possesses a slightly superior activity when compared to MGDE (Da Silva et al. 2009). Hydroxybenzoic acids, such as gallic and ellagic acids as well as other polyphenolic molecules possess cytotoxic activity on human cancer cells (Zhang et al. 2005, Veluri et al. 2006). In addition, other researches have reported that plants with polyphenolic substances (for instance, flavonoids) protect the cells against injury caused by X-rays, block the progression of the cell cycle and prostaglandin synthesis, inhibit mutations and prevent carcinogenesis in experimental animals (Abdulla and Gruber 2000). Detailed studies revealed that MGDE and IGDE induce higher levels of splenic natural killer (NK) cell in tumor-bearing mice (Da Silva et al. 2009). During Ehrlich ascites tumor growth, the level of NK cell activity in the spleen frequently decreases, which is important for tumor proliferation, since NK cells and cytokines (interleukin-2 and interferon-γ) inhibits the growth of this murine tumor model (Valadares et al. 2003). Moreover, evidences show role of interferon-γ in macrophage-mediated regulation of host anti-tumor responses (Yamamoto et al. 1995). Then, the anticancer potential exhibited by MGDE and IGDE might be related to the modulation of the immunologic system as a result of enhancement in NK cell activity in tumor-bearing mice. Therefore, many researches have highlighted the in vitro and in vivo antiproliferative capacity from clerodane diterpenes of C. sylvestris on tumor cells, very important discoveries that emphasize this plant as an important natural source of leading molecules.

Besides this antitumor potentiality, different parts of the plant also exhibit activity against Leishmania donovani promastigotes (Mesquita et al. 2005), Trypanosoma cruzi amastigotes (Espíndola et al. 2004, Mesquita et al. 2005), Plasmodium falciparum strains resistant to chloroquine (Mesquita et al. 2007) and Aedes aegypti larvae (Rodrigues et al. 2006). Leaf methanolic extract shows anti-hyperlipidemic properties, decreasing serum triglycerides and lipases (Schoenfelder et al. 2008) and the water extract displays neuromodulatory effects on central nervous system by the interference on enzymatic action of the purinergic and cholinergic systems since it inhibits Na+/K+/ATPase and 5′-nucleotidase activities (Silva et al. 2006). Additionally, the hydroalcoholic extract has antinociceptive capability likely due to the inhibition of an inflammatory mediator and/or by the activation of opioid cascade (Mattos et al. 2007).

**CONCLUSION**

Several reports have highlighted the medicinal value of extracts and compounds isolated from Casearia sylvestris, underscoring a worthy pharmacological arsenal to this plant, bringing evidence to its worldwide popular use and encouraging further searches for novel bioactive molecules and a better comprehension about its bioactivities.

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RESUMO

Usos populares e pesquisas científicas têm destacado a importância dos extratos da planta *Casearia sylvestris* e seu grande potencial bioativo. Neste trabalho, objetiva-se revisar as propriedades farmacológicas de *C. sylvestris*, enfatizando sua potencialidade antitumoral, antiinflamatória, antiofídica e antitumoral. O extrato etanólico e o óleo essencial das folhas possuem atividade antitumoral. Assim, a planta *Casearia sylvestris*, com seus componentes químicos, representa um interesse a ser explorado para o desenvolvimento de novas fórmulas farmacológicas.

Palavras-chave: *Casearia sylvestris*, uso popular, propriedades farmacológicas.

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