

## Lauraceae's Family: A Brief Review of Cardiovascular Effects

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### ABSTRACT

Lauraceae is a large family of woody plants (except the herbaceous parasite, *Cassytha*) with about 50 genera and 2500 to 3000 species distributed throughout tropical to subtropical latitudes. Twenty two genera are found in Brazil, distributed in rain forests as well as in restingas and cerrados. Lauraceae plants have the extremely important economic value. Previous studies showed that some species of the Lauraceae family were found to exhibit useful biological activities such as antispasmodic, antipyretic, antitumour, anticonvulsant, antibacterial, fungicidal, cytotoxic, and cruzain inhibitory activities and antiviral. Besides these biological activities, the Lauraceae plants are characterized by having various steels on the cardiovascular system, based on that, this study aimed to develop a literature review in order to address all the studies on the cardiovascular effects of the species of this family.

**Key words:** Lauraceae family, biological effects, cardiovascular effects, medicinal plants.

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### INTRODUCTION

The last decades have been a period of important changes in Brazilian population's life and health quality. Such interrelated changes have emerged a defiant health-illness standard for public health managers<sup>1</sup>.

Several illnesses, such as dyslipidemias, atherosclerosis as well as arterial hypertension, present alterations on endothelial function in their origin and/or function system. Hence, the endothelial dysfunction, characterized for a lesser production and/or bioavailability of nitric oxide (NO), is one of the elements which contribute for cardiovascular illnesses arise<sup>2</sup>.

Brazil, with its wide coastline, its flora diversity and considering it as the owner of the planet's largest muggy equatorial rain forest, cannot abdicate of its calling for natural products<sup>3</sup>. Our country has the most biodiverse environment in the world, rated in along 20% of planet's specimen. This great genetic patrimony, which is in lack on economically rich countries, nowadays has a priceless economic-strategic value in several activities, although it is in new medicines field that it is its greatest potentiality<sup>4</sup>. After centuries of disordered exploitation in Amazon region, Lauraceae family specimen still arise market interests, although with few chemical and pharmacological studies. On Amazon biodiversity, there are some specimen of Lauraceae family's which have never been studied, among the 400 ones presented in Brazil (organized in 25 genders)<sup>5</sup>. Among the specie that were chemically studied while the long period of researches in 1970's, few of them were studied by their extracts on pharmacological tests, mainly for cardiovascular illnesses.

In this way, the aim of this paper is to present the Lauraceae family's specie and genders which demonstrate biological effects on cardiovascular system.

### METHODOLOGY

It was carried on an indexed literary revision on *Scielo*, *PubMed* and Web of Science data bases, as well as literary sources on pharmacological field, from January 2002 to March 2012. It was applied the following research tags: "família Lauraceae", "efeitos cardiovasculares", "espécies de Lauraceae". It was analyzed issues on English, Portuguese and Spanish languages. The references cited in this paper also based the present study.

The issue approached the following points: I—Lauraceae family, II—Cardiovascular system, III—Biological effects.

From the number of the found issues, were selected those ones which presented methodological criteria approaching effects on cardiovascular system.

#### *Lauraceae Family*

Lauraceae is a large family of woody plants (except the herbaceous parasite, *Cassytha*) with about 50 genera and 2500 to 3000 species distributed throughout tropical to subtropical latitudes<sup>6</sup>. Twenty two genera are found in Brazil, distributed in rain forests as well as in restingas and cerrados<sup>7</sup>. The floristic mapping held in the Adolpho Ducke Reserve (Amazonas State, Brazil) cataloged so far 13 genera and 99 species<sup>8</sup>. Lauraceae plants have the extremely important economic value. A great number of them are important resource in the construction timber, spice, essential oil, and medicinal plants<sup>6</sup>. Most of the family members are characterized by a woody habit and are of great economic importance worldwide, as they

provide valuable timber, aromatic oils and important substances that are widely employed in the pharmaceutical and food industries, with emphasis on the genera *Aniba*, *Licaria*, *Nectandra*, *Ocotea*<sup>9</sup>.

Simultaneously, as their crowns are spacious, they have immense ecological value for virescence and environment protection. Boasting of various kinds and widespread distribution, Lauraceae plants are known to have an ancient origin with a fossil record dating back to the mid-Cretaceous period<sup>6</sup>.

Previous studies showed that some species of the Lauraceae family were found to exhibit useful biological activities such as antispasmodic, antipyretic, antitumour, anticonvulsant, antibacterial, fungicidal, cytotoxic, and cruzain inhibitory activities and antiviral<sup>10,11,12,13,14,15,16,17</sup>. They contained interesting classes of natural products, such as alkaloids, monoterpenes and sesquiterpenes, triterpenes and sterols, 2-pyrone, flavonoids, benzophenones and arylpropanoids (including lignans and neolignans)<sup>18</sup>. In addition, compounds from the medicinal plants of this family have been found to show antioxidant activities<sup>19,20</sup> which can promote antiproliferation of the human cancer cells<sup>21</sup>.

Besides these biological activities, the Lauraceae plants are characterized by having various steels on the cardiovascular system, based on that, this study aimed to develop a literature review in order to address all the studies on the cardiovascular effects of the species of this family.

#### *Lauraceae Family And Action On Cardiovascular System*

Cardiovascular illnesses, according to World Health Organization (WHO) (2011)<sup>22</sup>, are the first cause of death in the world: each year more people die by cardiovascular illnesses than by any other cause. It is estimated that 17.3 million people have died by cardiovascular illnesses in 2008; it represents 30% of all global deaths. From those deaths, it is rated that 7.3 million occurred because coronary illnesses and 6.2 million were by cerebral vascular accident. Low-and middle-income countries are disproportionately affected: more than 80% of deaths by CVI occur in Low-and middle-income countries furthermore, they occur almost equally on men and women. According to Ministério da Saúde (2011)<sup>23</sup>, in 2030, it will be almost 23.6 million of deaths due cardiovascular illnesses, mainly heart disease and stroke. Cardiovascular illnesses are also the main cause of death in Brazil, concerning 29.4% of the declared deaths, counting 308.000 cases in 2007. The mortality rate due this kind of illness has decline 26% in 11 years, dropping from 284 per 100.000 inhabitants, in 1996, to 206 per 100.000 inhabitants in 2007<sup>23</sup>. One reason for this outcome is a more elevated population's level of information as well as the prevention policies, such as reduction of smoking, promoting of healthy diet and incentive of physical activities practice. Cardiovascular illnesses embed a group of illnesses comprise the heart diseases (cardiomyopathy, ischemic heart dysfunction, congestive heart failure) and of the blood vessels (coronary artery disease, hypertension and atherosclerosis)<sup>24</sup>.

Mechanisms and signaling pathways involved in pathological functional and structural changes of the vessel walls focus of intensive resource, because they can promote the identification of potential therapeutic targets for developing new pharmacological strategies<sup>25</sup>. Hence, join up popular and scientific knowledge searching for phytotherapeutic medicines is one of the pathways for succeed on searches in medicinal plants field<sup>26</sup>, that aims to evaluate biological activity of plants and its elements and chemical systems, organs and tissues in order to discover substances that can be potentially used in therapeutics and/ or as pharmacological tools.

Lauraceae distinguish among the other branches also for its medicinal importance. Following are listed some genera and species with their respective effects on the cardiovascular system.

#### *Gender Aniba*

*Aniba canelilla* (H.B.K.) Mez (Lauraceae) [Syn. *A. Elliptica* A.C. SM., *Cryptocarya canelilla* Kunth] is an aromatic herb which is abundant in Amazon areas, where it is well-known as precious shell. The precious shell's trunk wood and thin stems and leaves of the shell are used as spice, smelling and sachets. In popular science, its *A. canelilla*'s shell decoction is generally used in antispasmodic action and digestive stimulant<sup>27</sup>.

Its shell stalk has an essential oil tenor equal to 1% in dry weight. The odor principle of *A. canelilla*'s sheets, shell and wood is 1-nitro-2-feniletano, which is reason of its smell; Metileugenol also is an important *A. canelilla*'s volatile constituent<sup>28</sup>.

The *A. canelilla*'s essential oil presented cardiovascular effects either in normotensive and spontaneously hypertensive mice, such effects were attained because of its main constituents in isolated way.

In normotensive and non anesthetized mice, the *A. canelilla*'s essential oil promoted a dose-dependent reduction of the rate arterial pressure as well as of the heart frequency of these animals. This effect did not suffer a change after a ganglion blocking with hexamethonium, while it was partially reduced when applied L-NAME (inhibitor of nitric oxide synthesis) and a muscarinic receptor blockage agent<sup>29</sup>. This hypotension produced involves a vascular relaxation, functional endothelium-dependent embedding the NO/L-arginina via, such as inhibition of the calcium stream throughout voltage-dependent calcium canals<sup>29</sup>.

The isolated verification of one the *A. canelilla* essential oil's main components, 1-nitro-2-feniletanium, was carried on normotensive and spontaneously hypertensive animals. In these two kinds of animals, the *A. canelilla* essential oil main component induced a cardiovascular response featured by a vago-vagal bradycardia and a reflexor depressant, which apparently results from the stimulation of pulmonary vagal than the heart C afferent fibers. The second hypotensor response of the 1-nitro-2-phenylethane was in part because a strait effect on the vascular soft muscle<sup>30,31</sup>.

Other constituent of the essential oil of *A. canelilla* and several other plants, methyleugenol, in studies with non-anesthetized normotensive mice, promoted a drop in blood

pressure, probably through a vascular vasorelaxing process, it is credible that it is linked to an oxide nitric/L-arginine via<sup>32</sup>.

*Aniba panurensis*, another species of the genus *Aniba*, has as a synonym *Aniba gonggrijpii*, *Aniba but*, *Aydendron panurensis*. It is popularly known as Yellow Bay<sup>33</sup>. In phytochemical characterization of essential oil of *Aniba panurensis* sesquiterpene hydrocarbons were identified. In tests of antioxidant activity and platelet aggregation were required large amounts of essential oil in order to promote effects<sup>5</sup>.

The biological effects on the cardiovascular system are scarce, Assis (2012)<sup>34</sup> conducted studies with an isolated esterilpyrone of the of immature fruits, 6 – [(E) – esteril] – 2 – pyrone, in which in mice's superior mesenteric artery rings isolated, observed that this pyrone was able to promote an effect vasorelaxant, mediated in part by endothelium-dependent mechanisms is involving via eNOS /CGs. But also by mechanisms independent of the vascular endothelium and the ability to promote relaxation in vascular smooth muscle seems to act interferin with contract mechanisms subsequent to the entry of calcium, mainly by inhibiting the release of calcium from intracellular stores sensitive to IP3, and engagement channels sensitive potassium calcium.

#### Gender *Persea*

The avocado tree (*Persea americana* Mill) is a native American fruitful tree. The first navigators have found it from Mexico, Guatemala and other Central American countries till Equator, Venezuela, Columbia and Peru<sup>35</sup>. The avocado tree is a plant 6 to 20 feet tall, its leaves are alternate and its inflorescences are auxiliary. It has small, bisexual, and yellowish-green flowers. The fruit has form of pear, oval and presents a number of varieties. Its flesh has a high nutritional value, its rich in fats, proteins and vitamins<sup>35</sup>.

Former studies have shown that the leaves of *Persea americana*'s extract has a casting of pharmacological activities, including analgesic, anti-inflammatory, anti diabetic, hypoglycemic, hypotension and anti hypertensive properties<sup>36,37,38</sup>.

In isolated rat thoracic aorta, the aqueous extract of leaves of *Persea americana* promoted a vessel-relaxing dependent on a concentration response in the presence of functional endothelium, and when it is lack, the relaxing effect was attenuated, what proofs that the effects depends on the endothelium<sup>39</sup>. This relaxing process depends on the synthesis and release of endothelium relaxing derivate factors, such as the release of prostaglandin I2 (PGI2) and E2 (PGE2). The extract was also able to inhibit rings of thoracic aorta to calcium mobilization through the voltage dependents calcium channels and, with a minor effect on the channels operated by receptors<sup>39</sup>.

In normotensive rats, *Persea americana*'s induced a relaxing process in the door vein as aorta rings having endothelium, and caused hypotension in anaesthetized rats, normotensives and hyper tenses ones. The vessel relaxing process was largely responsible for the plant's hypotensive action, because it involves production of nitric oxide

depending on the endothelium and of the release of GMPc, does not involving muscarinic receptors<sup>40</sup>.

#### Gender *Ocotea*

Gender *Ocotea* includes more than 350 aromatic shrubs or trees, spread on the Americas and Africa. Most of them are important wood producer trees, being a great source of essential oils with a predominant via of phenylpropanoid and a number of them, such as *O. pretiosa*, *O. sassafrás*, *O. caudata* and *O. cymbarum*, has a renewed market position mainly in perfumery industry<sup>41</sup>.

In Brazil, several species of the genus *Ocotea* are applied in popular science for treatment of a number of illnesses. The chemical characterization of this plant has shown the presence of alkaloids of the branch of the benzyltetrahydroisoquinoline, which has as its main component the (S)-reticulín<sup>42</sup>.

(S)-reticulín component, reduces blood pressure and cardiac frequency in non-anesthetized normotensive rats, inhibiting the contractions induced by phenylephrine and KCL in rat's aorta rings, depending o the presence of the endothelium<sup>43</sup>. In the present study, (S)-reticulín prevented transient calcium-dependent contractions promoted by norepinephrine, but did not change the contractions induced by caffeine. Supposing that the calcium channels may be involved in the relaxing response produced by (S)-reticulín<sup>43</sup> (Dias et al., 2004).

Furthermore in the Medeiros and others' studies (2009)<sup>42</sup> on (S)-reticulín, it were observed the possible mechanisms of relaxing produced by the (S)-reticulín, that is isolated from the *Ocotea duckei* Vattimo, using patch clamp techniques and cells culture.

The study has shown a large characterization of the effects of (S)-reticulín. Some factors accept the assumption that (S)-reticulín inhibits calcium current (I<sub>Ca,L</sub>), probably because an interaction to the type L calcium channels, besides a minor participation of AMPc dependent mechanisms<sup>42</sup>.

*Ocotea quixos*, another species of the genus *Ocotea*, showed in BALLABENI<sup>44</sup> and others' studies that its essential oil is an antithrombotic phytochemical free of pro hemorrhagic side effects, in sub acute administration condition. The antithrombotic activity was reported by the ability to block platelet aggregation, the retraction of coagulum in rodents' plasma, and inhibit vesselconstriction property<sup>44</sup>. It is thought that the trans-cinnamaldehyde can be the essential oil's major constituent involved in these effects.

#### Gender *Cassytha*

*Cassytha filiformis* Linn is a parasitic plant that grows at lower altitudes. It is used in folk medicine in Taiwan as a diuretic and antibiotic agent<sup>45</sup>. Chemical studies on *C. filiformis* have shown the presence of a number of alkaloids and lignans components.

Several compounds of this species had their effects tested in rats' aorta rings, and some of them presented a vessel-relaxing potential. Considering the studied compounds, the alkaloids play a significant role on *C. filliformis*' vessel-relaxing effect<sup>45</sup> Gender *Cinnamomum*

*Cinnamomum cassia* has been shown as being secure for ingestion and has many pharmacological properties, such

as antioxidant activity and antimicrobial effects<sup>46</sup>. *C. cassia* is used to prevent several illnesses caused by insufficiency in microcirculation and blood stasis in the bloodstream, according to oriental medicine<sup>47</sup>.

Choi and others' studies (2009)<sup>47</sup> have shown that *C. cassia* and its active compound, cinnamic acid, promote the formation of new vessels, as well as the increase of the endothelium cells proliferation in bull's aorta. Both also induce quimiotatic mobility and formation of a kind of web on the endothelial cells. The angiogenesis induction mechanisms require the super expression of the vascular growth endothelium factor, as well as the expression of the Flk-1/ KDR receptor<sup>47</sup>.

## CONCLUSION

This study reveals that family Lauracea is an important family which has the world's flora species useful to man and relevant from an economic standpoint for the world population, with effects already featured on the cardiovascular system. several metabolites found relate to the effects therapeutic described for species of this family.

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