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Ocotea quixos essential oil: A systematic review about the ethno- medicinal uses, phytochemistry and biological activity

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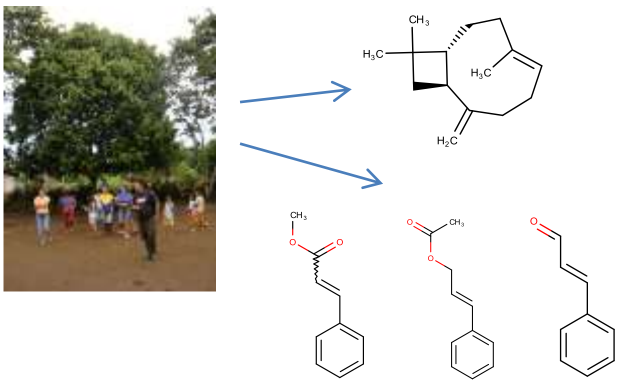
Graphical Abstract

Ocotea quixos



Main biological activities
Antiplatelet, antithrombotic, anti-inflammatory, antioxidant, antifungal and antimicrobial activities.

Abstract.

In the Ecuadorian Amazon region, Ocotea quixos is a well-known as well as an important plant used as a spice and as a folk medicine ingredient. Besides the traditional knowledge, only a few bioprospecting and pharmacological experiments have been carried out and some promising findings have been done. Essential oil from calices (OQCO) and from leaves (OQLO) have been investigated furthermore showing a remarkable difference. In the case of floral calyx oil the main components were trans-cinnamaldehyde and methylcinnamate while the leaves essential oil presented β-caryophyllene, cinnamyl acetate, sabinene, geranial and finally trans-cinnamaldehyde. Both essential oils have shown to possess useful biological activities, as antiplatelet, antithrombotic, anti-inflammatory, antioxidant, antifungal and antimicrobial activities. These findings open new research prospects and promising applications as functional fragrances for both oils.

Introduction

Recent reviews about research trends and scientific development clearly suggest that natural products will still be for a long time indispensable as sources of new drugs [1,2].

In the context of the novel therapeutic strategies and bio prospecting, the Amazonian region has to be considered an essential source of natural molecules, traditional medicine and ancestral knowledge. Tropical belt includes 17 "Mega diverse Countries" [3,4] and Ecuador is part of this important guild and has a notable ranking for its high biological diversity. As reported by Sierra *et al*., (2002) and Lessmann *et al*, (2014), considering the relationship between land area and number of species Ecuador seems to be the most biodiverse country on the planet [5,6]. In the American continent, the mega-diverse countries are Ecuador, Brazil, Colombia, Peru, Venezuela, Mexico and the United States. Other relevant countries for biodiversity in the world are Australia, New Guinea, Madagascar, Democratic Republic of Congo, South Africa, Indonesia, India, Philippines, Malaysia and China. Ecuador is the smallest country in territorial area among the mega-diverse countries, Thus, could be considered one of the richest areas for biodiversity [7].

Considering the above-mentioned biodiversity, Ecuador can provide a large number of bioactive molecules and essential oils that have been increasingly studied in order to understand their applications. Recent findings have allowed demonstrating different uses as a food preservative, for cosmetic formulation and for pharmaceutical preparations [2,8-13].

In the last decade *Ocotea quixos* essential oils have been studied in order to update the knowledge about this plant. For several years, *Ocotea quixos* was considered native to Ecuador and endemic of the local rainforest, nevertheless, deepened studies described the presence of this species also in Peru and Colombia, therefore in any case *Ocotea quixos* represents an emblematic tree of the Ecuadorian Amazonian Region [14,15]. Even if the findings about *O. quixos* are few, the promising data regarding the recent *in vitro* and *in vivo* studies and the aromatic properties mentioned since the Inca's age [16] encourage new researches on this species.

Hence, the aim of this review paper was to collect an up to date and exhaustive critical study about *Ocotea quixos* essential oil scientific literature, covering its traditional ethno-medicinal uses, phytochemistry and biological activities.

Materials and Methods

The present systematic review was achieved adopting the following electronic databases: Scifinder, Pubmed, ISI-Web of Science, Google Scholar, Scielo and Scopus. Data was independently extracted from six reviewers and the final papers selections were completed avoiding duplication of data. The following keywords were selected: *Ocotea quixos*, ishpingo, ishpink, canela amazónica.

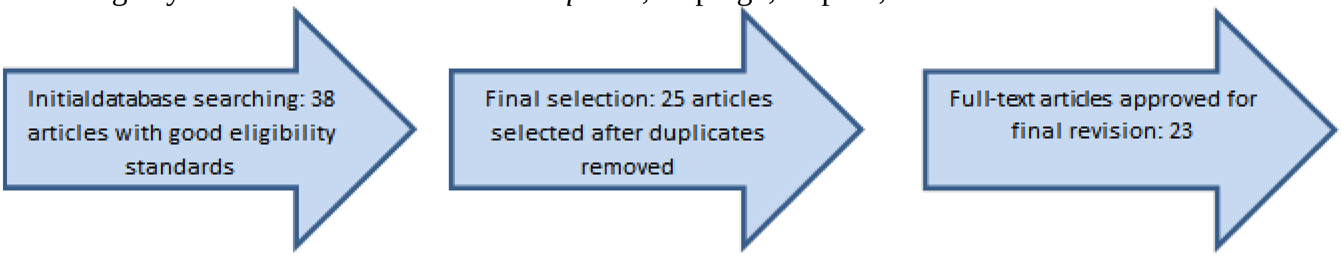


Figure 1. Selection strategy for eligible articles

All key words were searched individually and in combination. The reviewers selected articles in English and Spanish language, finally data from patents, symposiums and congress abstracts was excluded.

The oldest selected articles is dated 1981 and some key papers for the first three chapters were also considered.

As described in Fig. 1, the above-mentioned criteria allowed selecting 38 eligible articles. The second step allowed eliminating duplicated papers, resulting in 25 articles. Finally, two papers, which did not satisfy the selection methodology, were rejected because of the lack of clarity in their procedures.

Results and Discussion

2.1 Botanical description, historical information and folk medicine.

Ocotea quixos (Lam.) Kosterm. (*Lauraceae*) belongs to the *Lauraceae* family. The *Ocotea* genus incorporates about 350 tropical and subtropical trees and shrubs characterized for the presence of aromatic volatile compounds. The genus *Ocotea* is widespread within the American continent and in Southern Africa [17]. In Ecuador *O. quixos* is known with different common names, including: cannelloni, canela amazónica and ishpink or ishpingo [18,19].

The species: *O. quixos* was considered for a long time as endemic for Ecuador; it belongs to the *Lauraceae* family and it is a perennial tree 2-5 m tall with leaf blade and white-greenish color flowers. Due to its persistent and characteristic smell of cinnamon it is usually named "American cinnamon" [20,21].

As described by Naranjo (1969), Naranjo *et al*., (1981) and Fernandez de Oviedo (1959), *O. quixos* was known since the Incas age for its aromatic properties [16,21,22] and the local anesthetic and disinfectant uses. The same authors reported that in 1540 Pizarro and Orellana started an expedition from de Andes to the Amazonian region looking for a famous "cinnamon trees" with the hope to identify *Cinnamomum zeylanicum* Blume trees, an appreciated and well-known spice that was very important for the European market. In addition, in the Humbolt and Bonpland's 1800 expedition the presence of cinnamon-smell trees was reported. Due to its typical fragrance, *O. quixos* dried chalices were described as "Flor de Canela" and it is traditionally used for infusions and beverages or as a spice or flavoring for foods [23]. Nowadays, *O. quixos* is an essential ingredient for the recipe of "Colada Morada", a typical beverage that local people used to drink during the Day of the Dead; the essential oil is also used for aromatherapy [24-26]. Moreover, *O. quixos* essential oil and spice (powdered chalices) were mentioned respectively as ingredients for cosmetics and tisanes, these products are part of the proposal of Mashi Numi, an Ecuadorian network of 14 community-based organizations / companies producing natural ingredients and medicinal plants [27].

2.2 Phytochemistry

2.2.1 Leaves

Sacchetti *et al*. (2006) have studied samples of *Ocotea quixos* leaves oil (OQLO) from Morona Santiago (Ecuador) by means of gas chromatography coupled to mass spectrometry (GC-MS), the above-mentioned essential oil contains sixty-one compounds, representing the 93.6% of the total detected. The main constituents were β-Caryophyllene (15.1%), trans-Cinnamyl acetate (11.4%), Sabinene (7.6%), Geranial (5.6%) and trans-Cinnamaldehyde (5.1%). The authors highlighted the presence of a predominant sesquiterpene fraction (35.6%) followed by 2 minor fractions: the oxygenated monoterpenes (24.8%) and the monoterpenic hydrocarbons (21.7%), respectively. The essential oil scent was defined as, sweet-spicy, persistent cinnamon-like, warm and with a soft lemon-scented note. Trans-Cinnamyl acetate and cinnamaldehyde are the source of the cinnamon-like taste of the essential oil. The authors mentioned the high terpenic and sesquiterpenic abundance as responsible of slightly inferior odor profile, which can explain why a massive exploitation of *O. quixos* has never been observed [28].

Noriega and Dacarro (2008) have studied others samples of OQLO from Ecuador, these authors obtained sixty-two compounds which concern the 83.89% of the detected molecules. The β-Caryophyllene (19.0%) was found to be the main component, moreover, α-Humulene (14.3%), Eremophylene (11.4%) and Methyl cinnamate (7.0%) were also detected in relevant amount [29].

In another study on Ecuadorian OQLO [30], the β-Caryophyllene (28.2%) as major constituent was identified, followed by Methyl cinnamate (19.5%) β-Selinene (10.4%), α-Humulene and (10.1%) Δ-Cadienene (3.1%).

A research performed by Rolli *et al.* (2014) revealed again the presence of β-Caryophyllene (10.1%) and trans-Cinnamyl acetate (10.0%) as the mayor components, adding also 1,8-Cineole (8.2%), β-Selinene (5.0%) Sabinene (4.6%) and α-Pinene (4.3%) [31].

A study carried out by Scalvenzi *et al.* (2016) in Pastaza province (Ecuador), described the determination of fifty compound, including trans-Cinnamaldehyde (16.6%) as main component. Trans-Methylisoeugenol (11.9%), β-Caryophyllene (10.6%) and α-Pinene (9.4%) were also detected in decreasing amounts [32].

Finally, a preliminary study accomplished on the OQLO confirmed the presence of trans-Cinnamaldehyde into the essential oil and the presence of alkaloids, tannins coumarines flavonoids y quinones [33].

The composition of the mayor compounds reported by cited studies is detailed in Table 1.

Table 1. Mayor compounds of QOLO reported.

Main compounds	Composition (%)	Reference
β-Caryophyllene	15.1 19.0 28.2 10.1 10.6	[28] [29] [30] [31] [32]
trans-Cinnamaldehyde	5.1 16.6	[28] [32]
trans-Cinnamyl acetate	11.4 10.0	[28] [31]
Δ-Cadienene	3.1	[30]
1,8-Cineole	11.4	[29]
Eremophylene	8.2	[31]
Geranial	5.6	[28]
α-Humulene	14.3 10.1	[29] [30]
trans-Methylisoeugenol	11.9	[32]
Methyl cinnamate	7.0 19.5	[29] [30]
α-Pinene	4.3 9.4	[31] [32]
Sabinene	7.6 4.6	[28] [31]
β-Selinene	10.4 5.0	[30] [31]

2.2.2 Flower chalices

The first pioneering study on *O. quixos* flower chalices oil (OQCO) was mentioned in the 1981 [21]. For the first time Cinnamaldehyde, o-Methoxycinnamaldehyde, Cinnamic acid and Methyl cinnamate were reported.

A deepener study performed by Bruni *et al.* (2004) showed a chemical composition in which the main components detected, in a set of fourty-four compounds, were trans-cinnamaldehyde (27.0%), methylcinnamate (21.6%), 1,8-cineole (8.0%), benzaldehyde (3.6%), and β-selinene (2.1%) [34].

2.3 Biological Activity

2.3.1 Antimicrobial and antifungal activity

The inhibitory effects of OQLO were examined using the *in vitro* agar well diffusion method [29]. The study considered the growth of several causal agents of intestinal and epidermis infections in humans, such as *Escherichia coli*, *Staphylcoccus aureus*, *Staphylococcus epidermidis*, *Streptococcus mutans*, *Streptococos piogenes* and *Candida albicans*.

A similar research was performed by Scalvenzi *et al*., (2016) on the phytopathogenic fungi *Aspergillus oryzae*, *Cladosporium cladosporioides*, *Fusarium solani*, *Rhyzopus stolonifer*, *Moniliophthora roreri and Phytophthora sp*. OQLO, showing an inhibition rate average included on a range between 89% and 95%, at the concentration of 500 μL.mL^{-1}[32].

Bruni *et al.* (2004) reported the antimicrobial and antifungal activity of OQCO. The assay carried out showed higher MIC values (> 0.12 mg/ml) against *Staphylococcus aureus*, *Enterococcus foecalis* and *Escherichia coli*, while results were less efficient against *Pseudomonas aeruginosa* (0.049 mg/ml). All results were comparable with the effect of *Thymus vulgaris* essential oil, a natural product well-known for its antimicrobial and antifungal activity. Comparing again the results with *T. vulgaris* essential oil (0.049 mg/ml), the OQCO showed a lower activity against *Saccharomyces cerevisiae* and *Candida albicans* (0.024 mg/ml). Finally, the growth inhibition percentage against *Trichophyton mentagrophytes* Var. and *Pythium ultimum* where tested for OQCO and *T. vulgaris* oil at 500 mg/ml.

The first one achieved a lower activity compared with the second one, reaching the 40% and 85% of activity, respectively [34].

2.3.2 Phytotoxic activity

Rolli *et al.* (2014) tested the phytotoxic activity of OQLO against *Solanum lycopersicum* seeds and seedlings, in order to find new potential natural herbicides. The OQLO was able to extend the germination time in a pre-emergence effects test but showed a low damage rate in a post-emergence effects test on the same species, in both assays essential oils were applied at 1 ml/l on *S. lycopersicum* plant [31].

2.3.3 Antioxidant activity

As reported by Bruni *et al*. (2004) and Amilia Destryana *et al*., (2014), the β-Carotene Linoleic Acid Bleaching Test and the DPPH Radical Scavenging Assay were performed on the OQCO and on the OQLO respectively. In the DPPH test, the oil revealed a promising scavenging effect, also in comparison with Trolox and *T. vulgaris* essential oil, respectively, a synthetic and a natural antioxidant. The assay showed that OQCO have stronger antioxidant activity than Trolox but weaker than *T. vulgaris,* which means in any case a remarkable result. The same assay was performed on OQLO in comparison with another anti-oxidant agent, butylated hydroxytoluene (BHT), showing an irrelevant antioxidant activity [30,34].

For both oils, the β-Carotene Linoleic Acid Bleaching Test showed negligible results.

2.3.4 Anti-inflammatory activity

OQLO was studied in order to appreciate the suppression of prostaglandin E2 (PGE2) by lipopolysaccharide (LPS-stimulated RAW264.7 Macrophage System) and the nitric oxide (NO) concentration, both pro-inflammatory predictive assays [30]. The results obtained showed that OQLO inhibited NO and PGE-2 production, suggesting promising usages as anti-inflammatory compound. By means of in vitro and in vivo models, similar studies were performed by Ballabeni *et al.* (2010) [17] on OQCO and its main components: trans-cinnamaldehyde and methyl cinnamate. Using dexamethasone as positive control, OQCO and trans-cinnamaldehyde were able to significantly reduced LPS-induced NO release from J774 macrophages, showing in addition a non-toxic concentration between 1 and 10 μg/ml. Methyl cinnamate was not effective. At the concentration of 10 μg/ml OQFC and trans-cinnamaldehyde exhibited a strong and quite strong ability to inhibit the nitrite (NO) production, showing the 66% and 30% of inhibition activity, respectively. Moreover, OQCO, but not trans-cinnamaldehyde and methyl cinnamate, was able to significantly increased the levels of CAMP in forskolin-stimulated SK-N-MC cells, suggesting that the phytocomplex presented synergic effects that are not ascribable to a single constituent of the essential oil. OQCO could also inhibit the LPS-induced COX-2 expression according to a dose-dependently (1–10 μg/ml) mechanism.

2.3.5 Antiplatelet and antithrombotic activities

The antiplatelet activity and the inhibition of clot in guinea pig and rat plasma by 24 different essential oil were recently screened [35]. OQLO showed potent antiplatelet activity against ADP, Arachidonic Acid and the Thromboxane A2 agonist U46619, moreover a good ability to destabilize clot retraction was observed. The findings seems to be associated to the presence of phenylpropanoids content, like trans-cinnamaldehyde and methyl cinnamate.

A similar study on OQCO and its main components was performed; the trans-cinnamaldehyde and the methyl cinnamate, were considered in rodent and human plasma, respectively. The study showed that OQCO, probably due to the presence of trans-cinnamaldehyde, owns a strong antithrombotic activity not accompanied by pro-hemorrhagic side effect. The findings were supported by the *in vitro* research on inhibition of arachidonic acid-U46619-, ADP-, phorbol12-myristate13-alcetate, collagen-induced platelet aggregation and thrombin-induced clot retraction in human and rodent plasma. Moreover, in *in vivo* study on mice, it was found that OQCO and trans-cinnamaldehyde could reduce the contraction induced by thromboxane A2 receptor agonist U46619 in rat isolated aortic ring and prevented acute thrombosis induced by collagen-epinephrine intravenous injection [17].

Conclusions

Essential oils from *O. quixos*, obtained from leaves (OQLO) and from calices (OQCO), respectively showed interesting activity, especially as antiplatelet, antithrombotic and anti-inflammatory bio-compound. Considering also the antioxidant, antifungal and antimicrobial activities, both oils and their main components may be an attractive and promising source of new functional fragrances.

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