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Phytochemical and Pharmacological Profiles of the Genus *Odontonema* (*Acanthaceae*)

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Authors' contributions

This work was carried out in collaboration between all authors. Author LPL designed the study, wrote the protocol and wrote the first draft of the manuscript. Author NMM managed the analyses of the study and performed the spectroscopy analysis. Author HS managed the experimental process and author PMC corrected the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Odontonema is a group of tropical plant species used in folklore medicine because of its wide range of pharmacological properties. These plants are known to be anti-bacterial, anti-inflammatory, anti-hypertensive, anti-viral, hepatoprotective, sedative and anti-oxidant. Furthermore, some species have been reported to induce child birth and trigger bronchodilatation. Since this group of plants is associated with a plethora of pharmacological properties, a review of reported medicinally-relevant investigations is warranted. Herein, we review the ethnopharmacology, bioactivity reports, and phytochemistry of the plant species belonging to the genus *Odontonema*. To compile this review, an extensive literature search was conducted using Google Scholar, SciFinder, ScienceDirect, Web of Science, and Scielo web sites, updated to May 2015. Although there are a number of pharmacological and ethnopharmacological reports on the

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four species of *Odontonema* covered in this review, phytochemical profiling of this group of plants is quiet limited. *Odontonema strictium* was found to be the most phytochemically profiled showing the presence of phytosterols and flavonoids.

Keywords: Phytomedicine; phytochemical; pharmacological; bioactivity; Odontonema.

1. INTRODUCTION TO THE GENUS *Odontonema*

The genus *Odontonema* belongs to the Acanthaceae family which is composed of about 346 genera with almost 4300 species, widely distributed in tropical regions of the world but are poorly represented in temperate regions. This family flourishes on four main geographical epicenters including Indo-Malay (*Strobilanthes* and *Andrographis*), Africa (*Barleria*), Brazil (*Ruellia*) and generally tropical regions (*Aphellandra* and *Odontonema*). These plants show a wide variety in habitat-preference and biological types. Most of them are shrubs or herbs, climbing plants; xerophytes and marshy plants are also very common. Trees are rare in the family [1,2]. *Avicenniaceae, Justiciaceae, Mendonciaceae, Meyeniaceae, Nelsoniaceae* and *Thunbergiaceae* are the principal sub families of *Acanthaceae*. The family *Acanthaceae* is widely used in folk medicine to treat several diseases and to stabilize conditions such as depression and epilepsy. Some compounds isolated from this family have demonstrated a wide spectrum of pharmacological activities such as anti-cancer, anti-microbial, anti-infertility, anti-inflammation, bronchodilatation, vasodilatation / anti-hypertension, anti-viral, depressors, sedatives, pain killer et cetera [3,4].

Justicia is the largest subfamily of *Acanthaceae*, with approximately fifteen genera comprising of 600 species that are found in pantropical and tropical regions [5]. Because of the diversity and morphological variation of *Justicia*, knowledge of *Acanthaceae* phylogenetics will benefit greatly from an improved understanding of patterns of relationships within this lineage. According to Lucinda, the genus *Odontonema* belongs to the *Justicia* lineage [6].

The genus *Odontonema* includes flowering plants of the *Acanthaceae* family, native to America. *Odontonema strictium*, also called *Fire spike* (tip fire) in English or *Cardinal Guard* (custody of cardinal) or *Scarlet Flame* (flame scarlet), is a plant belonging to the dicotyledonous angiosperm subclass of *Asteridae*, order of *Scrophulariales*, family of *Acanthaceae*, sub family *of justiciaceae* and genus *Odontonema*. There are many species in the genus *Odontonema*. The most known are: *O. callistachyum* (Schltdl. & Cham.) Kuntze; *O. cuspidatum* (Nees.) Kuntze; *O. tubiforme* (Bertol.) Kuntze and *Odontonema strictum* (Bertol.) Kuntze (Fig. 1) [7].

Plants from the genus *Odontonema* are shrubs (Fig. 1), with an upright stem and they flourish in the tropical regions. The leaves are deciduous, green, shiny, simple, ovate, wavy margined, pinnately veined and measure 10 to 15 centimeters long. Flowers are red, axillary or terminal, tubiform, hermaphrodite, in long panicles and erect. Fertilization is mediated by butterflies and the proboscis of hummingbirds. The propagation of the species is usually achieved by cuttings.

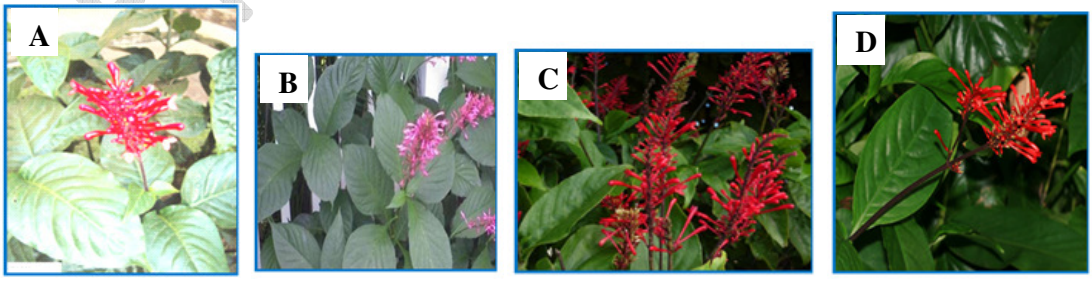

Fig. 1. Species of the genus *Odontonema*: *O. strictium* (A); *O. callistachyum* (B); *O. tubiforme* (C); and *O. cuspidatum* (D)

2. SEARCH AND ASSESSMENT METHODOLOGY

An extensive search in original and review articles was carried out to compile this review article. The keywords used for this review were *Odontonema, Justicia, Acanthaceae* and Medicinal plants. The search was performed using Google Scholar, SciFinder, ScienceDirect, Web of Science, and Scielo web sites, updated to May 2015.

2.1 Ethnopharmacological Reports on *Odontonema*

Three species of the genus *Odontonema* are used in folklore medicine. However, the similarities observed in the genus are a source of confusion. For instance, *Odontonema tubiforme (Bertol.) Kuntze, Odontonema strictum* and *Odontonema cuspidatum* seem to be synonyms for naming one species. This could explain why the taxonomy of species in the genus *Odontonema* is flexible.

The ground leaves and stem of *Odontonema callistachyum* (Fig. 1) are applied on open wounds in order to heal them in Sierra Mazateca (Mexico) [8]. The leaves of the species *Odontonema tubiforme (Bertol.) Kuntze* (Fig. 1) are also used by the Kuna, Ngöbe-Buglé, and Teribe Indians as an anti-inflammatory and for inducing child birth [9]. The aqueous extracts of the leaves of *Odontonema strictum* (Fig. 1) are used in Burkina Faso for the treatment of hypertension [10]. Additionally, toxicological investigations have demonstrated low toxicity of such aqueous extracts in mice (LD_{50} = 1825 mg/kg after 24 hours of observation) [11].

2.2 Bioactivity Reports on *Odontonema*

The bioactivity evaluation of the *Odontonema* species has been documented by a number of authors. Ouedraogo and co-workers investigated the water, ethyl acetate, and methanolic extracts of *Odontonema strictium* for vascular activity in isolated rat tail and pig coronary arteries. The ethyl acetate fraction appeared to contain the active principle and, therefore, this extract was thus recommended for further investigations [10].

More recently, researchers from central Africa have evaluated the antibacterial activity of the species *O. strictium* (leaves) using five bacterial strains (*Klebsiella, Shigela, Salmonella, Escherichia coli* and *Staphylococcus aureus*). *O. strictium* seemed to be active against both gram negative and gram positive bacteria. The Activity Index (AI) values of *O. strictium* were determined using chloramphenicol as a positive standard antibiotic. The results showed that *O. strictium* is four fold more bactericidal than the standard antibiotic on *Klebsiella* [12].

The total methanolic extracts including different fractions from the extracts of *O. cuspidatum* (Fig. 1) have been shown to exhibit anti-oxidant and hepatoprotective activities on the carbon tetrachloride-induced hepatotoxicity in rats [13].

2.3 Phytochemistry of *Odontonema*

Although there has been limited phytochemical investigation of the species of *Odontonema*, the species *O. strictium* has been subjected to a number of phytochemical studies. A group of chemists from Burkina Faso investigated the ethyl acetate fraction of the leaves of *O. strictium* and identified flavone-type of flavonoids. According to the same reports, *C*-heterosides and *O*-heterosides (Fig. 2) were shown to be present in 0.37% and 1.13% respectively [14].

A qualitative phytochemical screening of the extracts obtained from the leaves of *O. strictium* indicated the presence of flavonoids (type of flavones), saponins, glycosides, tannins, steroids and terpenoids. Consequently, two phytosterols (stigmasterol and *β*-sitosterol, Fig. 2) were isolated as a mixture [15]. Furthermore, Luhata and his colleagues have reported the isolation and identification of a tiliroside (Fig. 2) from the leaves of *O. strictium* using chromatographic, physical and NMR methods [16].

A summary of the different species of *Odontonema* with corresponding synonyms, geographical distribution, phytochemical information, known biological activity, and references is captured in Table 1. Table 1 also sheds more light on the similarities in synonyms across the different species.

3. DISCUSSION

The plethora of therapeutic properties mentioned in the literature above is indeed noteworthy. Despite the confusion in the taxonomic identification of different species of *Odontonema*, we can note some biologically relevant properties among the different species. For instance, the different species of the genus *Odontonema* seem

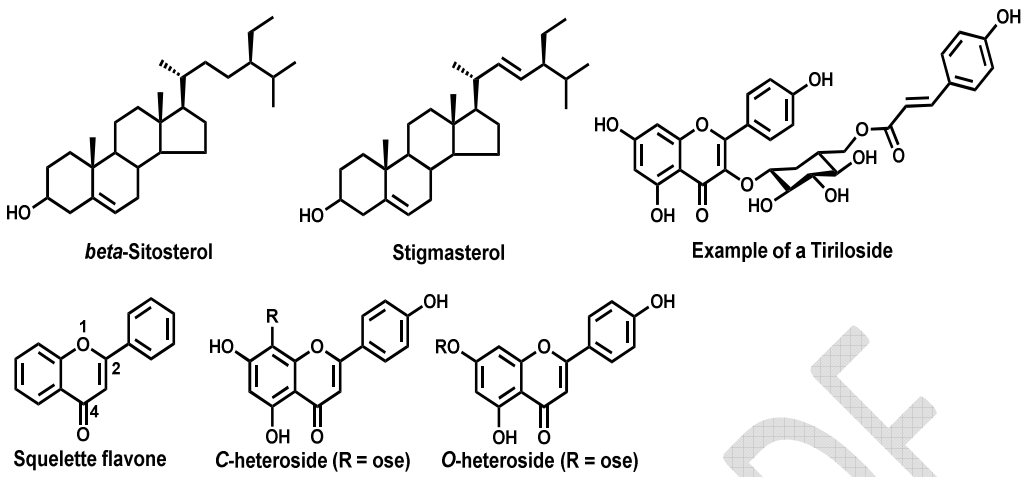

Fig. 2. Chemical structures of compounds isolated from *O. strictum*

Table 1. Scientific names, synonyms, and geographical distribution of the species of *Odontonema* with previous phytochemical and biologically relevant information

Species	Synonyms	Geographical distribution	Phytochemical information	Biological activity	References
O. callistachyum	Purple Firespike, Naktam ay	Central America, Central Africa	No	Yes/Heal open wounds	[6]
O. tubiforme	Bois indien ou bois genou, Firespike, Bwa kwapo, chapantye gwan bwa	Central America, Central Africa	No	Yes/Anti-inflammatory, induction of child birth	[7]
O. strictum	Firespike	Central America, Central Africa	Yes	Yes/Anti-hypertension, anti-bacterial	[9,10,12,13, 23]
O. cuspidatum	The mottled toothed thread, the Cardinal's guard or the firespike	Central America, Central Africa	No	Yes/ Hepatoprotective, antioxidant	[11]

to exhibit the following pharmacological properties: anti-inflammatory, anti-bacterial, anti-oxidant, anti-hypertensive, uterine contraction (see the mode of action of prostaglandins E2 (PGE2) and F2 (PGF 2)).

These observed biological activities can be attributed to the presence of certain biologically active secondary metabolites some of which are mentioned above. Admittedly, there is still much work to be done in order to have a very broad understanding of the Phytochemistry across the different species. Of all the species belonging to the genus *Odontonema*, only *O. strictium* has been the subject of phytochemical investigations [15]. From the phytochemical studies conducted so far, it has been shown that *O. strictium* contains steroids, flavonoids, tannins, terpenoids and glycosides. Among these groups of molecules, the steroids and flavonoids exhibited biological activities. The importance of plant sterols in human health is well established. The European Foods Safety Authority [16] recommends consumption of about 1.5 - 2.4 g/day of phytosterols and/or stanols in order to reduce blood cholesterol. Furthermore, the Food and Drug Administration (FDA) has approved the incorporation of phytosterol esters into low saturated fat and cholesterol-based diet in an attempt to reduce the risk of heart disease.

This includes consumption of at least 1.3 g/day of sterols, twice a day [17]. The anti-bacterial activities of stigmasterol and *β*-sitosterol have been reported in many studies [18,19]. Research has indicated that stigmasterol may be useful in prevention of certain cancers, including ovarian, prostate, breast, and colon cancers. It also possesses potent anti-oxidant, hypoglycemic and thyroid inhibiting properties [20]. Corfuff and Benedi have also reported the laxative properties of stigmasterol while *β*-sitosterol is used as an anti-oxidant and an anti-diabetic agent [21].

The work of Kini et al. [14] attributed the anti-hypertensive property of the ethyl acetate fraction of *O. strictium* to the presence of flavonoids. Refaey et al. [13] confirmed two biological properties of the methanolic extract of *O. cuspidatum*: hepatoprotection and anti-oxidation. According to the authors, the méthanolic extract of *O. cuspidatum* has the ability to minify the rate of lipid peroxidation, promote the anti-oxidant defense stature, and conserve against the pathological changes of the liver induced by CCl_4 intoxication. The hepatoprotection observed may be due to its anti-oxidant activity which minimizes free radical damage of hepatocytes.

Polar compounds such as flavonoids (tilirosides), glycosides, tannins, and some alkaloids are normally extracted using methanol as solvent [16]. The isolation and identification of a glycosidic flavonoid (a tiriloside) in the methanol extract of leaves of *O. strictium* confirm the theory [22]. Tirilosides are glycosidic flavonoids known for their anti-diabetic and anti-hyperlipidemic properties [23]. The anti-viral and cytotoxic activities of this class of molecules have also been confirmed [24]. Goto et al. [25] revealed that tirilosides ameliorate obesity-induced metabolic disorders in mice. In addition, Kaempferol-3-O-β-D (6-O-transp-cinnamoyl) glucopyranoside (*trans*-tiliroside,), an example of a tiriloside, demonstrated significant anti-hyperglycemic effects when compared with phenethyldiguanide in alloxan mice. As a part of a *trans*-tiliroside, kaempferol-3-O-β-D-glucopyranose and related analogues showed weak anti-diabetic activity. Furthermore, the anti–inflammatory, anti-rheumatic, anti-microbial and anti-oxidant properties of tilirosides have also been reported in other studies [26–28].

4. CONCLUSION

Although the phytochemical knowhow around the genus *Odontonema* is limited, the genus appears to be a rich source of structurally diverse molecules that have a wide array of pharmacological and therapeutic properties. The phytosterols (stigmasterol, and *β*-sitosterol) maybe the molecules responsible for the antibacterial property in the leaves of *O. strictium*. Flavonoids (flavones type) maybe partly responsible for the anti-hypertensive activity and tilirosides may impart anti-oxidant and hepatoprotective properties. The anti-inflammatory, anti-bacterial, anti-oxidant, anti-hypertensive and uterine contraction properties must stimulate phytochemical research interests into this genus which could, one day, lead to development and commercialization of a drug from this natural source.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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