

## Chemical review and studies related to species from the genus *Tynanthus* (Bignoniaceae)

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Species from the Bignoniaceae Family, including the genus *Tynanthus*, are very prevalent in the tropical Americas, with specimens found in a large part of the Brazilian territory. These plants are commonly used in traditional medicine for several purposes, and some studies have described their chemical structure, in addition to other reports related to some species from this genus. This review aimed to gather information from published works concerning species of the genus *Tynanthus*, as well as to detect flaws in research related to these plants, which may have great biological and pharmaceutical importance. Also, this review points out some common chemical characteristics of these species, providing information that may help new researchers to improve their knowledge about these plants.

**Uniterms:** *Tynanthus*/pharmacognosy. *Tynanthus*/phytochemistry. *Tynanthus*/biological activity. Bignoniaceae/pharmacognosy. Bignoniaceae/phytochemistry. Medicinal plants.

As espécies da família Bignoniaceae possuem grande predominância na região da América tropical e entre elas, as espécies do gênero *Tynanthus*, com representantes em grande parte do território brasileiro. Estas plantas são comumente utilizadas na medicina tradicional para os mais diversos fins e algumas pesquisas já descrevem a constituição química além de outros estudos relacionados a alguns integrantes deste gênero. Este trabalho de revisão teve como objetivo reunir informações de trabalhos publicados a respeito das espécies do gênero *Tynanthus* e permitiu detectar a deficiência nas pesquisas relacionadas a estas plantas, que podem trazer consigo grande importância biológica e farmacológica. Além disto, este trabalho tornou possível apontar algumas características químicas em comum entre as espécies, trazendo informações que podem auxiliar novos pesquisadores que procuram melhorar seus conhecimentos acerca destas plantas.

**Unitermos:** *Tynanthus*/pharmacognosy. *Tynanthus*/phytochemistry. *Tynanthus*/biological activity. Bignoniaceae/pharmacognosy. Bignoniaceae/phytochemistry. Medicinal plants.

### INTRODUCTION

The Bignoniaceae family gathers 82 genus and 827 species (Lohmann, Ulloa, 2007), which are usually spontaneous tropical species in South America, including trees, vines, bushes and rarely herbs (Di Stasi, 2002).

Gentry (1980) was a pioneer in detailing the taxonomy of the family, later reviewed by Spangler and Olmstead (1999). In a more recent description by Fischer *et al.* (2004), there are seven of the eight clades, which

were proposed before: Bignoniaceae, Coleeae, Crescentieae, Eccremocarpeae, Oroxyleae, Tecomeae and Turretieae. Two clades, Bignoniaceae and Crescentiinae, represent more than 80% of the species from the family (Olmstead *et al.*, 2009). Lohmann (2006) organizes genus *Tynanthus* species within the Bignoniaceae tribe.

*Tynanthus* was originally described by Miers (1863) and later by Bureau (1868). The species from this genus are distributed throughout tropical America, mainly in rainforests, from Mexico to southern Brazil, and in several countries, including Costa Rica, Guatemala, Panama, Dominican Republic, French Guiana, Venezuela, Bolivia, Ecuador, Peru, Colombia, Argentina and Paraguay (Reitz, 1974; Lohmann, Ulloa, 2007).

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The species of this genus are vines, popularly known as clove vine (*cipó-cravo*), due to the strong smell of Indian clove that emanates when the stems or leaves are cut or macerated (Lopes *et al.*, 2008). Lohman (2006), in his description of the morphological synapomorphy of *Tynanthus*, noted that besides its smell, it shows bilabiate flowers with two upper lobes fused and fruits with raised margins, information that helped in the phylogeny reconstruction of these species.

In traditional medicine, *Tynanthus* species are used for several purposes, for example, for the treatment of rheumatism and diabetes, besides their application as a stimulant, aphrodisiac, carminative and anthelmintic. Most of these properties have been already verified by specialists (Vilegas *et al.*, 1993; Brack, 1999).

Because of their already known popular use, this review had the objective of gathering information from scientific studies related to the genus *Tynanthus*, aiming to improve the knowledge about their chemical constitution, biological activities and other issues related to these species. With this information, it will be possible to identify deficiencies in studies involving the members of this genus, and ultimately serve as a tool for research aiming to assess the unstudied properties of these plants.

## RESEARCH METHODOLOGY

The references were tracked based on a 20-year period, and were obtained from databases such as *Biological Abstract* and *Chemical Abstract*. In addition, references in the *Scientific Electronic Library Online* (SciELO), *Medline/Pubmed* and other internet sites were searched, without a time limitation.

### Recognized species from the genus *Tynanthus*

According to the *Missouri Botanical Garden*, *The New York Botanical Garden* and *The Board of Trustees of the Royal Botanic Gardens* (Lohmann, Ulloa, 2007), 15 recognized species in this genus are registered, and are listed in Table I.

### SPECIES WITHOUT STUDIES

When searching for studies related to the genus *Tynanthus*, no results were found for the following species: *Tynanthus croatianus* A.H. Gentry, *Tynanthus goudotianus* Bureau, *Tynanthus labiatus* (Cham.) Miers, *Tynanthus macranthus* L. O. Williams, *Tynanthus polyanthus*

**TABLE I** - Recognized species from the genus *Tynanthus*

#### Species

<i>Tynanthus cognatus</i> (Cham.) Miers
<i>Tynanthus croatianus</i> A.H. Gentry
<i>Tynanthus elegans</i> Miers
<i>Tynanthus fasciculatus</i> (Vell.) Miers
<i>Tynanthus goudotianus</i> Bureau
<i>Tynanthus guatemalensis</i> Donn. Sm
<i>Tynanthus labiatus</i> (Cham.) Miers
<i>Tynanthus macranthus</i> L. O. Williams
<i>Tynanthus micranthus</i> Mello ex K. Schum
<i>Tynanthus panurensis</i> (Bureau) Sandwith
<i>Tynanthus polyanthus</i> (Bureau ex Baill.) Sandwith
<i>Tynanthus pubescens</i> A.H. Gentry
<i>Tynanthus sastrei</i> A.H. Gentry
<i>Tynanthus schumannianus</i> (Kuntze) A.H. Gentry
<i>Tynanthus villosus</i> A.H. Gentry

Source: (Lohmann, Ulloa, 2007)

(Bureau ex Baill.) Sandwith, *Tynanthus pubescens* A.H. Gentry, *Tynanthus sastrei* A.H. Gentry and *Tynanthus villosus* A.H. Gentry.

### *Tynanthus cognatus* (Cham.) Miers

This species is commonly found in Brazil, in the northeastern (Bahia), southeastern (Espírito Santo, Minas Gerais, Rio de Janeiro and São Paulo) and southern regions (Paraná, Rio Grande do Sul and Santa Catarina) (Lohmann, 2014a).

Lima, Pace and Angyalossy (2010), who studied issues concerning environmental and morphoanatomical aspects, especially those influencing vine growth, based their work on the characteristics of *T. cognatus*, and compared them to 31 other Bignoniaceae species. Thus, the stem anatomy, the seasonality of the formation and differentiation of secondary tissues and the influence on the change rate in xylem development were studied in this species in order to identify general growth standards in vines from this tribe. Some discoveries were made, among them the change activity during the end of the rainy season, in contrast to what is known about tropical trees and bushes. It was concluded that the change is a response to the environmental changes and that the growth rings are annual, happening in a period of roughly two months, which may explain the fact that the vines possess narrow rods.

### *Tynanthus elegans* Miers

*T. elegans* Miers is a native plant of Brazil, found in the southeastern (Espírito Santo, Minas Gerais, Rio de Janeiro and São Paulo) and southern (Paraná, Rio Grande do Sul and Santa Catarina) regions (Lohmann, 2014b).

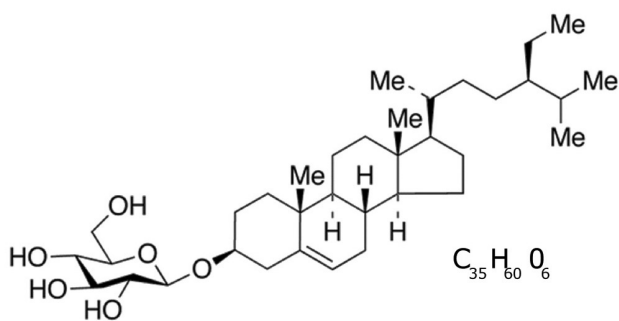
This species was highlighted in a phytosociological survey of a liana community in a seasonal semideciduous forest, located in São Carlos, São Paulo, Brazil, which showed a prevalence of species from the Bignoniaceae, Malpighiaceae, Sapindaceae and Apocynaceae families. The Bignoniaceae family comprised a major percentage in terms of species numbers, and *T. elegans* was had the third highest importance value (IV), a parameter which is directly related to the relative dominance (RD) in the studied region (Hora, Soares, 2002), which justifies, at least in part, its prevalence in the southeastern region of Brazil.

### *Tynanthus fasciculatus* (Vell.) Miers

*T. fasciculatus* shows a relatively restricted distribution, occurring in the Brazilian southeast, in Minas Gerais, São Paulo and Rio de Janeiro (Lohmann, 2014c).

The Brazilian Pharmacopoeia (Farmacopéia, 1929) describes *T. fasciculatus* and *T. elegans* as carminative plants, and Correa (1974) reports that the population uses these plants for aphrodisiac purposes, also citing their toxic effects.

Vilegas and colleagues (1993) showed in their studies the presence of coumarins, phenylpropanoids and steroids ( $\beta$ -sitosterol- $\beta$ -D-glucoside) (Figure 1) in the chemical constitution of *T. fasciculatus*, citing its use in traditional medicine as a stimulant, aphrodisiac, carminative and anthelmintic, the latter based on studies by Amorim *et al.* (1991), who demonstrated anthelmintic action in reducing the number of Oxyuridae in mice naturally infected by this parasite.



**FIGURE 1** - Chemical and structural formula of  $\beta$ -sitosterol- $\beta$ -D-glucoside (Vilegas *et al.*, 1993).

A report from Vilegas *et al.* (1994) reinforced the presence of coumarins in all parts of the plant. Besides coumarin, melilotic acid and its derivatives were identified, as well as the phytosteroid stigmasterol, in the hexanic extract from roots. According to Carvalho *et al.* (2009), *T. fasciculatus* also contains flavonoids, cardiotoxic heterosides and tannins. This same study showed high toxicity of the stem's aqueous extract to the microcrustacean *Artemia salina*.

The growth of *T. fasciculatus* seedlings was evaluated with the purpose of showing the location and characteristics of the forest where this plant develops best. It was verified that the forest edge was the location where the seedlings developed best, showing 100% survival and the greatest lengths and numbers of leaves. Only in this treatment was there development of tendrils in seedlings, which exceeded 80 cm in length (Lopes *et al.*, 2008).

Because of the traditional application of this plant as an aphrodisiac, Melo *et al.* (2010) proposed in their study to evaluate the morphometry of male reproductive organs in adult male Wistar rats after treatment with an infusion of *T. fasciculatus* stems. In dose of 200 mg/animal/day, a significant increase in testicular parenchyma weight was observed, as well as an increase in the volume and total length of the seminiferous tubules and, as a consequence of this, an increase in sperm production.

### *Tynanthus guatemalensis* Donn. Sm

*T. guatemalensis* is distributed from Mexico to Guatemala (Tropicos, 2014a). It presents in its chemical constitution saponins, anthocyanins and flavonoids in the stem, as demonstrated in a study by Miranda-Cruz *et al.* (2012), which also showed the antimicrobial activity of a hexane extract of its leaves against *Bacillus cereus* ATCC 11778.

Besides the antimicrobial activity of *T. guatemalensis*, Ferrier and colleagues (2013) reported its efficacy for the treatment of diabetes, based on ethnobotanical information from Mayan healers in the Mesoamerica region. Such activity was confirmed by *in vitro* tests which evaluated the inhibition of the formation of advanced glycation end-products (AGE), substances which are considered to be important pathogenic mediators of diabetic complications. Extractions of milled *T. guatemalensis* wood were made with solvents of increasing polarity (hexane, ethyl acetate, and methanol). The extracts were assayed, and activity was found mainly in the ethyl acetate fraction, in a comparable way to the positive control, quercetin, known to possess activity as an AGE inhibitor.

UPLC-MS-QToF analysis of the crude extract of *T.*

*guatemalensis* confirmed the presence of katchimoside analogs, 4-hydroxybenzoate and salicylic acid. In addition, verbascoside was identified by HPLC-MS-QTRAP in the ethyl-acetate extract and eugenol was detected by GC-MS in the essential oil (Ferrier, 2014).

### *Tynanthus micranthus* Mello ex K. Schum

This plant is commonly found in Brazil, in the state of Paraná, as well as in the southeastern (São Paulo) and midwestern (Mato Grosso do Sul) regions (Lohmann, 2014d).

The study from Souza, Santos and Moscheta (2010) reported the morphoanatomical flower characteristics of three Bignoniaceae family species, including *T. micranthus* in the comparative study. They concluded that, although the flowers are structurally similar, there are significant differences in some characters, which allow their identification, for example the color and shape of the corolla, the number of cell layers in the perianth, and the types of trichomes in the perianth, among other characteristics.

The substances  $\beta$ -sitosterol and apigenin were isolated from *T. micranthus*, as well as chemical groups such as flavonoids (dihydroflavonoids and leucoanthocyanidins), steroids and/or triterpenoids, heterosidic anthraquinones (Cansian *et al.*, 2012) and eugenol in the essential oil (Custódio *et al.*, 2010).

The same study by Cansian *et al.* (2012) showed that some fractions are toxic against *Artemia salina* in a number of concentrations, suggesting care in the administration of the extracts of this plant. These preparations were also tested against some bacterial strains, and the results showed activity of the crude extract from the root against *E. coli*, whereas the crude extract from the stem was effective against *S. aureus*, *P. aeruginosa* and *E. coli* and the crude extract from the leaves was effective against *S. aureus* and *P. aeruginosa*, all of them with a minimal inhibitory concentration of 1000  $\mu\text{g/mL}$ . Custódio *et al.*, 2010 had previously evaluated the antimicrobial activity of the essential oil of *T. micranthus*, whose bioautography indicated eugenol as the substance responsible for its activity against *Cladosporium herbarum*.

Cansian *et al.* (2013) confirmed the influence of the chloroform fraction of the stem of *T. micranthus* on *Lactuca sativa* seeds hypocotyl germination and growth, indicating its allelopathic potential. More recently, another research group, also led by Cansian, showed that the residual hydroalcoholic fraction from *T. micranthus* protects erythrocytes against oxidative damage, using an enzymatic *in vitro* assay to evaluate the action of

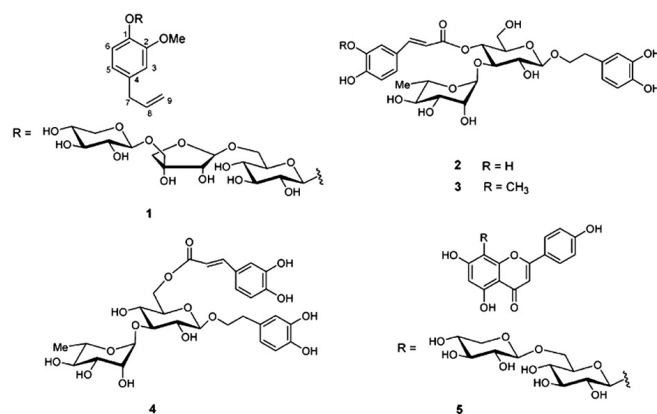
the enzyme tyrosinase, suggesting its application in hypopigmentation disorders (Cansian *et al.*, 2014a).

More recently, Cansian *et al.*, (2014b) showed that mice treated with the extract presented a significant reduction in the latency time for mounts and an increased frequency of mounts, especially after three hours of treatment, in a dose-related manner, as compared to the control group. These results demonstrate the influence of *T. micranthus* on the sexual behavior of mice and allow the inclusion of this species in the list of aphrodisiac plants of the genus.

### *Tynanthus panurensis* (Bureau) Sandwith

In the Peruvian Amazon, *T. panurensis* has been traditionally used as an aphrodisiac, energizing tonic and analgesic, as well as for the treatment of rheumatism and diabetes (Brack, 1999). In Brazil, this species is found in the northern region (Amazonas and Pará) (Lohmann, 2014e).

Studies by Plaza and colleagues (2005) have revealed, by LC-MS of the methanolic extract, the presence of the phenylpropanoid glycosides eugenol- $O$ -[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 5)- $O$ - $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)- $O$ - $\beta$ -D-glucopyranoside]verbascoside, leucosceptoside, isoverbascoside and the flavonoid katchimoside, apigenin-8-C-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranoside] (Figure 2).



**FIGURE 2** - Compounds isolated from the bark of *Tynanthus panurensis*. (1) Eugenol- $O$ -[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 5)- $O$ - $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)- $O$ - $\beta$ -D-glucopyranoside], (2) verbascoside, (3) leucosceptoside, (4) isoverbascoside and (5) katchimoside (apigenin 8-C-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranoside]) (Plaza *et al.*, 2005).

Based on reports about the use of *T. panurensis* for the treatment of rheumatism, Morales *et al.* (2011)

performed a study that aimed to demonstrate the anti-inflammatory and antioxidant activity of the extract from the bark of this plant. *In vitro* assays showed that the extract possessed antioxidant properties and reduced microsomal lipid peroxidation, as well as uric acid and tumor necrosis factor (TNF) synthesis. Its powerful anti-inflammatory property was confirmed by the *in vivo* carrageenan-induced paw edema tests in rats, indicating that the bark extracts of *T. panurensis* actually have a beneficial effect in the treatment of inflammation, in accordance with the main traditional uses of this plant.

### *Tynanthus schumannianus* (Kuntze) A.H. Gentry

This species is found in Bolivia, in the La Paz and Santa Cruz regions (Tropicos, 2014b) and in Brazil, in the northern (Acre, Amazonas, Pará and Rondônia) and northeastern (Maranhão) regions (Lohmann, 2014f).

In the Covendo region of Bolivia, the population uses this plant for the treatment of diarrhea, by drinking a tea which is made with pieces of stem and some fruits

(Quintana, Vargas, 1995). This traditional use indication motivated Muñoz *et al.* (2000) to include this species in their research, which evaluated the anti-malarial activity of some Bolivian plants used by the Mosetene Indians for the cure of several diseases. The residue from the fruit extract of *T. schumannianus*, obtained from maceration with ethanol-water, showed moderate activity *in vivo* (49% with 510 mg/kg) in rodents with malaria caused by *Plasmodium vinckei petteri*, and excellent *in vitro* activity (98% with 10 mg/mL) against *Plasmodium falciparum*, comparable to the standard drug, chloroquine.

### DISCUSSION

Of the 15 recognized species, only *T. fasciculatus*, *T. guatemalensis*, *T. micranthus* and *T. panurensis* have information about their chemical characteristics, allowing the detection of some common chemical groups, such as flavonoids, phenylpropanoids and steroids (Table II).

Eugenol and its derivatives are found in the majority of species with a delineated phytochemical profile. Studies

**TABLE II** - Chemical groups and isolated substances of species from the genus *Tynanthus*

Species	Chemical groups	Identified substances	References
<i>T. fasciculatus</i> (Vell.) Miers	Tannins, flavonoids and cardiogenic heterosides, coumarins, phenylpropanoids and steroids	$\beta$ -sitosterol- $\beta$ -D-glucoside, coumarin, stigmasterol, melilotic acid ethyl ester, melilotic acid, melilotic acid-O- $\beta$ -D-glucopyranoside (melilotoside)	Carvalho <i>et al.</i> , 2009; Vilegas <i>et al.</i> , 1993; Vilegas <i>et al.</i> , 1994
<i>T. guatemalensis</i> Donn. Sm	Saponins, anthocyanins and flavonoids, in the stem; benzoic acid derivatives, C-glycosyl flavonoids and phenylpropenes	katchimoside analogs, 4-hydroxybenzoate, salicylic acid and eugenol	Miranda-Cruz, <i>et al.</i> , 2012; Ferrier, 2014
<i>T. micranthus</i> Mello ex K. Schum	Flavonoids (dihydroflavonoids and leucoanthocyanins), steroids and/ or triterpenes, anthraquinones heterosides, eugenol	$\beta$ -sitosterol, apigenin	Cansian <i>et al.</i> , 2012; Custódio <i>et al.</i> , 2010
<i>T. panurensis</i> (Bureau) Sandwith	Phenylpropanoid glycoside and flavonoid	Eugenol-O- $[\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 5)-O- $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)-O- $\beta$ -D-glucopyranoside, verbascoside, leucosceptoside, isoverbascoside and katchimoside (apigenin 8-C- $[\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranoside)	Plaza <i>et al.</i> , 2005

have shown aphrodisiac activity in some plants such as cloves (*Syzygium aromaticum*) and nutmeg (*Myristica fragrans*). These plants have eugenol-rich essential oils, as do some species of the genus *Tynanthus*. Despite this evidence, no study has related the aphrodisiac activity of these species with the eugenol content.

In addition, *T. guatemalensis* and *T. panurenses* have both exhibited verbascoside and katchimoside in their chemical composition; the latter is an apigenin-derived flavonoid, a substance which is present on *T. micranthus*. *T. guatemalensis* and *T. panurenses* have traditional uses for the treatment of diabetes; however, there have been no studies relating this activity to compounds common to these species.

The chemical constitution of the genus *Tynanthus* follows the same pattern described for the Bignoniaceae family, as shown by Cipriani *et al.* (2012), who performed data collection on the chemical profile of this family. This study lists the most predominant metabolites in the studied species, starting with terpenoids, followed by special aromatic derivatives, quinones and flavonoids.

Some plant groups show a variety of chemical components, which can be used as taxonomic markers, since common characteristics in secondary metabolism can indicate kinship among species, beyond morphological similarities (Hegnauer, 1986). Although the number of publications is continually increasing, only a small proportion of plants have been chemically investigated, such as the genus studied in this review, rendering the available information insufficient. Hence, this study

contributes to future investigations on the chemical taxonomic aspects of species of the genus *Tynanthus*.

The species *T. fasciculatus*, *T. guatemalensis*, *T. micranthus* and *T. panurenses*, besides having their phytochemical profile delineated, have been studied regarding their biological and pharmacological activities. Most of these studies were based on their traditional uses; for example, *T. fasciculatus* is an aphrodisiac plant whose application promoted studies that evaluated the influence of its extracts on the male reproductive organs of adult Wistar rats (Melo *et al.* 2010). Besides *T. fasciculatus*, *T. micranthus* and *T. panurenses* are also traditionally used for aphrodisiac purposes, although no study has demonstrated the chemical component and the mechanism responsible for this activity.

Table III shows a list of species, which have biological and pharmacological studies and their relationship between traditional and scientific uses.

Among all studied species, *T. cognatus* (Cham.) Miers and *T. elegans* Miers have related studies, although they do not mention their chemical composition, and only refer to morphological and phytosociological aspects.

This analysis allowed us to appreciate the deficiency of studies involving the toxicity of plants of the genus *Tynanthus*, a very important parameter when the subjects are plants which are routinely used by the population. Only *T. fasciculatus* and *T. micranthus* have been evaluated and showed a certain degree of toxicity against the microcrustacean *Artemia salina*, which may argue against the indiscriminate use of these plants.

**TABLE III** - List of species from the genus *Tynanthus* with traditional use indications, as well as studies related to biological and pharmacological activities

Species	Traditional Use	Biological and pharmacological studied activities	References
<i>Tynanthus fasciculatus</i> (Vell.) Miers	Carminative, anthelmintic, stimulant and aphrodisiac	Male reproductive organs morphometry anthelmintic activity	Farmacopéia, 1929; Correa, 1974; Vilegas <i>et al.</i> , 1993; Melo <i>et al.</i> , 2010; Amorim <i>et al.</i> , 1991
<i>Tynanthus guatemalensis</i> Donn. Sm	Diabetes	Antimicrobial activity and diabetes	Ferrier, 2013; Miranda-Cruz <i>et al.</i> , 2012
<i>Tynanthus micranthus</i> Mello ex K. Schum	Aphrodisiac	Antimicrobial, allelopathic and antioxidant activity, tyrosinase stimulant and aphrodisiac activity	Custódio <i>et al.</i> , 2010; Cansian <i>et al.</i> , 2012; Cansian, <i>et al.</i> , 2013; Cansian <i>et al.</i> , 2014a; Cansian <i>et al.</i> , 2014b
<i>Tynanthus panurensis</i> (Bureau) Sandwith	Aphrodisiac, energizing tonic, analgesic, for the treatment of rheumatism and diabetes	Antioxidant and anti-inflammatory activity	Brack, 1999; Morales <i>et al.</i> , 2011
<i>Tynanthus schumannianus</i> (Kuntze) A.H. Gentry	Anti-diarrheal	Anti-malarial activity	Quintana, Vargas, 1995; Muñoz <i>et al.</i> , 2000

## CONCLUSION

During the assessment of all the data incorporated into this review, it became possible to verify the deficiency of studies involving the majority of species of the genus *Tynanthus*. Also, it was observed that some members have potential for their use, because they are already known and traditionally used, but need to be better evaluated with respect to their toxicity.

Hence, this work contributes significantly to research fields which aim to identify potential plants which are insufficiently explored, in order to delineate their chemical profile and possible biological activities and thus contribute to the discovery of natural substances which may serve as the basis for the development of new drugs and cosmetics, among other beneficial products for the population.

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## CONFLICTS OF INTEREST

There have been no conflicts of interest in carrying out this work.

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