CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL PROPERTIES OF BOUGAINVILLEA LEAVES: A REVIEW

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ABSTRACT:
The genus Bougainvillea is a very widespread group throughout the world. It belongs to the family Nyctaginaceae and contains approximately 18 species i.e., B. berberidifolia, B. buttiana, B. campanulata, B. glabra, B. herzogiana, B. infesta, B. lehmanniana, B. lehmannii, B. malmeana, B. modesta, B. pachyphylla, B. peruviana, B. pomacea, B. praecox, B. spectabilis, B. spinosa, B. stipitata, and B. trollii. The genus Bougainvillea is endemic to South America and was firstly reported in Brazil in 1778 before being introduced to Europe by French military commander Louis Antoine de Bougainville. They are bushes spread in vines or small trees. They also possess stems with internodes and with straight or slightly curved thorns. The leaves are petiolate, elliptical, or wider towards the base. The bracts and flowers are presented in different colours, depending on the species, cultivars, or hybrid. It is a rich source of Aliphatic Hydrocarbons, Fatty Acids and Fatty Alcohols, volatile compounds, phenolic compound, Peltogynoids and Flavonoids, Phytosterols, Terpenes, and Carbohydrates, Betalains etc. In conclusion, the leaves of Bougainvillea glabra are reported to have anti-inflammatory activities, anti-hyperglycaemic activity, insecticidal activity, anti hyperglycemic activity anti-ulcer, antimicrobial and anti-diarrheal activity and its antiviral proteins.

Keywords: Bougainvillea, chemical constituents, pharmacological properties, antidiabetic, antioxidant.

INTRODUCTION
The genus Bougainvillea is a very widespread group throughout the world. It belongs to the family Nyctaginaceae and contains approximately 18 species (B. berberidifolia, B. buttiana, B. campanulata, B. glabra, B. herzogiana, B. infesta, B. lehmanniana, B. lehmannii, B. malmeana, B. modesta, B. pachyphylla, B. peruviana, B. pomacea, B. praecox, B. spectabilis, B. spinosa, B. stipitata, and B. trollii). Only four species (B. buttiana, B. glabra, B. spectabilis, and B. peruviana) are commercially exploited [1]. However, there are also more than 100 cultivars and three hybrids, the latter not yet recognized.
Fig 1. *Bougainvillea* leaves and flowers

**Taxonomy**
Kingdom: Plantae  
Division: Magnoliophyta  
Class: Magnoliopsida  
Subclass: Caryophyllidae  
Order: Caryophyllales  
Family: Nyctaginaceae  
Genus: *Bougainvillea*

**Botanical Description**
The genus Bougainvillea is endemic to South America and was firstly reported in Brazil in 1778 before being introduced to Europe, by French military commander Louis Antoine de Bougainville [2]. They are bushes spread in vines or small trees. They also possess stems with internodes and with straight or slightly curved thorns. The leaves are petiolate, elliptical, or wider towards the base. The bracts and flowers are presented in different colours, depending on the species, cultivars, or hybrid. They bloom throughout the year [3]. Botanical textbooks say that some species of the genus Bougainvillea are distributed worldwide and
without being specific to any single place, species, cultivars, or hybrids. Based on these results, a more exhaustive analysis was performed in the scientific literature.

**Bougainvillea Hybrids**

Since the beginning of its commercialization, producers have sought to make hybrids of the genus *Bougainvillea* species. They have produced three recognized hybrids with striking characteristics: *B. spectoperuviana*, *B. spectoglabra*, and *B. glabra peruviana* (*B. buttiana*). (i) *B. spectoperuviana*: the first hybrid has no reports in the scientific literature of registration sites or scientific research works according to the databases consulted, (ii) *B. spectoglabra*: this plant is a hybrid of *B. spectabilis* and *B. peruviana* and it was only reported in China [4], (iii) *B. glabraperuviana* or *B. buttiana*: this plant is a hybrid of *B. glabra* and *B. peruviana*, and it was identified and reported in Mexico, as well as in India, England and China [5]. This plant was thoroughly studied by our working group, and those results are described below. There is no other current scientific information regarding the location, medical uses, phytochemical profile, or pharmacological or toxicological properties for other species or hybrids.

**Synonyms**

In the different countries where the *Bougainvillea* are found other popular names were attributed: *Buganvilla* (Spain), *Bugambilca* (Mexico, Guatemala, Cuba, and Philippines), *Pokok bunga kertas* (Malaysia), *Napoleon´* (Honduras), *Veranera* (Colombia, Nicaragua, El Salvador, Costa Rica, and Panama), *Trinitaria* (Colombia, Panama, Puerto Rico, Dominican Republic, and Venezuela), *Santa Rita* (Argentina, Bolivia, Brazil, Paraguay, and Uruguay), *Primavera*, *Tres-Marias*, *Sempre-lustrosa*, *Santa-rita*, *Ceboleiro*, *Roseiro*, *Roseta*, *Riso*, *Pataguinha*, *Pau-de-roseira*, and *Flor-depapel* (Brazil) or *Papelillo* (Northern Peru) [6].

**Traditional Uses**

In traditional medicine the species *B. buttiana*, *B. glabra*, and *B. spectabilis* are indicated for the treatment of coughing and pertussis. *B. glabra* is recommended for asthma [7], bronchitis, and dysentery. In a small number of cases, it is indicated for stomach pain, rust, pimples, and blackheads. *B. spectabilis* is also used in other respiratory conditions, including snoring or lung pain, *fu*, and bronchitis. There are no studies described in the literature regarding the traditional use of the other species and hybrids of *Bougainvillea* in medicine. However, the hybrid *B. buttiana* was confused with *B. buttiana* since both are distributed and reported in Morelos, Mexico, and both are used to treat cough and whooping cough [8].
Chemical Compositions
The chemical constituents of the genus Bougainvillea have been extensively studied since 1970 [9]. The phytochemical analyses were carried out to identify different kinds of components using extracts of different polarities from stems, leaves, or bracts with or without flowers, bark stems, and roots of the species. It has been possible to isolate, identify, and elucidate chemical compounds for species or hybrids. The Marvin program was used to draw the structures of chemical compounds [10][11].

Aliphatic Hydrocarbons
In Bougainvillea genus the presence of aliphatic hydrocarbons including alkanes, alkenes, and cycloalkanes has been described. For ethanolic extracts from bracts with flowers from B. buttiana seven of these compounds were found and identified. The presence of this type of compounds, B. buttiana, could be considered as an alternative source of energy.

Fatty Acids and Fatty Alcohols
Fatty acids and fatty alcohols are very common compounds in plants, especially in aerial parts. For the genus of Bougainvillea, the presence of 13 of these compounds was verified. Eight compounds were identified in ethanolic extracts from the bracts with flowers from B. buttiana and 5 in ethanolic extracts of the leaves, branches, and roots from B. spectabilis.

Volatile Compounds
Volatile compounds are compounds that are commonly found in the plant kingdom. Their chemical structures contain some functional groups, including aldehydes, ketones, phenols, oxides, esters, and alcohols. In the leaves and branches of B. spectabilis ethanol extract were identified 35 of these compounds. In ethanol, ethanol:water, and ethyl acetate extracts of bracts with flowers of B. buttiana the presence of 9 of these compounds was identified. Only one compound was similar as is the case of the ethyl hexadecanoate compound observed in both extracts B. x buttiana and B. spectabilis.

Phenolic Compounds
Phenolic compounds are also widely distributed in the plant kingdom. Fourteen of these compounds have been identified. In the ethanolic extract of bracts with flowers from B. buttiana researchers identified 4 of these compounds. In ethanolic extracts of flowers from B. glabra there were 11 phenolic compounds.

Peltogynoids and Flavonoids
The peltogynoids are restricted in their distribution. In extracts of stem bark from B. spectabilis were identified eight peltogynoids. The flavonoids, however, are a group of
Compounds widely distributed in the plant kingdom. 21 compounds have been identified in B. glabra and B. spectabilis.

Phytosterols, Terpenes, and Carbohydrates
Carbohydrates are chemical compounds that mainly derive from the primary metabolism of vegetables. Sterols and terpenes are secondary metabolites. Out of thirteen compounds identified in the genus Bougainvillea, 6 of them were identified from the ethanolic extracts of bracts with flowers from B. buttiana. Four different compounds were identified from extracts of leaves and bracts from B. glabra. Tree in B. spectabilisin stem bark, leaves, and branches.

Betalains
Betalains are vacuolar pigments containing a nitrogenous ring, a ring which is characteristic of the order Caryophyllales. Sixteen of these compounds were identified in bract extracts from the case of extracts of B. glabra and 2 were found in extracts from B. Mrs.

Pharmacological Activities
Analgescic
The analgesic activity was described in two species of B. glabra and B. buttiana; in both cases the oral administration was evaluated. For methanol extracts of B. glabra, the maximum percentage of analgesia effect obtained using the tail method in male Wistar rats was 79.88%. For the ethanol extracts of B. buttiana (var. Orange), the analgesic effect was studied in female CD1 mice using the acetic acid and formalin methods. For the acetic acid method, the analgesia percentage was 95.65%, while, for formalin method, the extract showed inhibition in both phases. In another study, the analgesic effect of the B. buttiana (var. Rose) ethanol extract was determined after oral administration in BALB/c mice using the acetic acid, tail immersion, and formalin models. For all of the methods used, the extract showed a potent analgesic effect.

Anti-Inflammatory
A significant anti-inflammatory activity was obtained in male Wistar rats orally treated with methanol extract of leaves from B. glabra. The leaves from B. spectabilis were extracted with different solvents, including acetone, alcohol, chloroform, petroleum ether, and chloroform: water. The models used were the oedema induced by carrageenin and the granuloma model induced by cotton pellet, in male Wistar rats. The results indicated that the oral administration in rats with ethanol extract reduced the oedema induced by both methods. In other experiments, the oral administration of methanol extract of leaf from B. spectabilis was performed and evaluated in Swiss mice using the method of induction.
oedema with carrageenin and dextran, as well as arthritis induced with Freund's adjuvant in male Wistar albino rats. The results with methanol extract presented an elevated anti-inflammatory activity for all inflammation model. In the case of ethanol extracts of flowers with bracts from B. buttiana (var. Orange), the anti-inflammatory properties were measured using the oedema method induced with carrageenin in female CD1 mice. The amounts of cytokines such as IFN-γ, IL-6, and IL-10 and nitric oxide (NO) were also measured. The results obtained from this extract have shown that it is capable of inducing a decrease in TNF productions and an increment in the IL-6, IFN, IL-10, and NO levels. In another study, the anti-inflammatory effect was obtained in BALB/c female mice orally treated with ethanol extract of bracts and flowers from B. buttiana (var. Rose) [18].

**Antipyretic**
The oral administration of methanol extracts from B. glabra in groups of rats showed a significant antipyretic activity [19].

**Antidiabetic**
The antidiabetic effects were studied in three species of Bougainvillea. The extracts of leaves from B. glabra were used in male Wistar rats induced with alloxan. Similar studies were performed with the oral administration of ethanol extracts of flowers from B. spectabilis. Its antidiabetic effect was evaluated using diabetic male Wistar rats induced with alloxan. The chloroform extract of flowers from B. spectabilis administered intraperitoneally reduced glucose levels in diabetic Swiss mice. The antidiabetic effect was also seen with oral administration of aqueous extract from apical leaves of B. spectabilis. Studies carried out on the steam bark extract of B. spectabilis orally administered in albino rats showed significant hypoglycaemic activity [20]. In the case of ethanol extracts of bracts and flowers from B. buttiana, a significant hypoglycaemic activity was observed in female and male CD1 mice orally treated.

**Antihyperlipidemic**
The treatment of diabetic male Wistar rats induced with alloxan or normal Wistar rats orally treated with different extracts from B. glabra showed the reduction in the amount of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-Cholesterol), and increase high-density lipoprotein cholesterol (HDL-C) [21]. Another study, using Wistar rats exposed to oral injection of ethanol extract of fresh leaves from B. spectabilis, showed a significant reduction in total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels and significant in hypercholesterolemia rats.
Anti-diarrhoeal
A significant antidiarrheal activity was observed in male Wistar rats orally treated with the acetone extract obtained from leaves of B. glabra “Choicy”.

Antiallergic
The oral administration of extracts of acetone of leaves of B. glabra “Choicy” and their antiulcer effect were evaluated in male Wistar rats, and this extract showed a marked antiallergic activity [22].

Antifertility
A reduction in testosterone and oestrogen levels as well as sperm count, viability, and motility [23] was observed in albino Swiss male and female mice orally treated with ethanol extract from B. spectabilis.

Neuroprotective
The neuroprotective effect of leaves from B. glabra extracted with ethanol was evaluated by the use of the mortality of Drosophila melanogaster flies. The results obtained showed that the flies treated with the extract present a lower mortality [24]. The effect of two methanol extracts of B. spectabilis from yellow and pink bracts on oxidative stress and neural damage was carried out by use of male Sprague-Dawley rats subcutaneously injected with rotenone. Rotenone provoked significant increases of brain MDA (product of lipid peroxidation) and nitric oxide content along with decreased brain reduced glutathione. There was also a marked and significant inhibition of brain paraoxonase-1 (PON-1) and butyrylcholinesterase (BChE) activities and increased pro-inflammatory cytokine interleukin-1beta in brain of rotenone-treated rats. B. spectabilis flowers extract itself resulted in increased brain oxidative stress, lipid peroxidation, and nitrite content while inhibiting PON-1 activity. The yellow flowers extract inhibited BChE activity and increased brain II-1. When given to rotenone-treated rats, B. spectabilis extracts, however, decreased lipid peroxidation while their low administered doses increased brain glutathione (GSH). Brain nitrite decreased with the pink extract but showed further increase with the yellow extract. Both extracts caused further inhibition of PON-1 activity while the yellow extract resulted in further inhibition of BChE activity. Histopathological studies indicated that both extracts protected against brain, liver, and kidney damage caused by the toxicant [25].

Trombolytic
The methanol extract of leaves from B. glabra and an aqueous extract of green leaves from B. spectabilis [26] showed the thrombolytic activity in vitro in the blood of healthy volunteers.
Cardiotonic
Cardiotonic evaluation of an aqueous extract of B. glabra was performed by using isolated frog heart perfusion technique. The parameters studied included contraction force (HR), heart rate (HR), and cardiac output (CO). This extract provoked an increase in HR and CO [27].

Anthelmintic
For the anthelmintic evaluation, methanol extracts from B. glabra were used against species of Pheretima posthuma [28], and ethanol Eudrilus eugeniae and Eisenia fetida were compared with the standards albendazole and metronidazole, respectively. All extracts of B. glabra could cause paralysis and death of worms [29].

Antimicrobial
The conventional methods used for the evaluation of biological properties such as antibacterial and antifungal agents of plant extracts include the agar diffusion method and the dilution method [30].

Antiviral
The leaf proteins from B. buttiana were evaluated against RNA viruses such as tobamoviruses, tobacco mosaic virus, and sunnhemp rosette virus. The results obtained showed a degradation of viral RNAs. This implies a great opportunity for control of vegetable viruses [31]. In another study, this purification could identify lysine as the inhibitor of N-glycosidase activity on the 25S rRNA ribosomes of tobacco by interfering with viral multiplication.

Cytotoxic
The cytotoxic effect of ethanol extract of leaves from B. glabra was evaluated in HT-29 cells, AGS, and BL-13. Another study with stems and leaves from B. glabra extracted with acetonitrile, butanol, dichloromethane, ethyl acetate, hexane, and methanol showed the antiproliferative activity against U373 cells. The effect of the antiproliferative activity in U373 cells was evaluated using extracts hexane, dichloromethane, acetonitrile, ethyl acetate, methanol, and butanol extracts from stems and leaves from B. spectabilis. The extract of dichloromethane showed lower antiproliferative activity when compared to others extracts [54]. In another study, the cytotoxic activity of eight new compounds named bougainvinones 78-85 isolated and elucidated from stem bark was evaluated. The extract from B. spectabilis purple from a bipartition was evaluated by using KB, HeLa S-3, HT-29, MCF-7, and HepG2. The results showed that the compound 84 showed cytotoxicity against cancer cell lines and compounds 79 and 80 exhibited cytotoxicity against the KB cell line. In a subsequent study, in ethyl acetate extract, five new flavones named bougainvinones 86-90 were isolated and
elucidated and their cytotoxic activities were assayed against KB, HepG2, HeLa, S-3, HT-29, and MCF cells. The results showed that all compounds had cytotoxic activity [32]. The cytotoxic effect of flower from B. buttiana extracted in ethanol in bracts of different colours, orange-1 (Bxb01), orange-2 (Bxb02), pink (BxbR), violet (BxbV), and white (BxbW), was studied on HeLa cells. The greater cytotoxic activity was observed with the bracts with flowers Bxb02 and Bxb01. In another study the evaluation of the cytotoxic activity of different extracts, aqueous, methanol, ethanol, acetone, ethyl acetate, dichloromethane, and hexane, of bracts with flowers from B. buttiana was performed. The dichloromethane extract was the most cytotoxic to L-929 cells [33].

**Immunomodulatory**

The effect of an ethanol extract from B. buttiana on the activation of macrophages of female CD1 mice was determined. The results obtained showed an increase in H2O2 levels and the extension and formation of vacuoles, reduction of TNF, and remarkable increases for the levels of IL-10 and NO, suggesting an immunomodulatory effect.

**Antioxidants**

The fresh leaves were degreased with petroleum ether followed by a successive extraction of B. buttiana with acetone, ethanol, and distilled water. They were then used for the determination of the antioxidant capacity using the methods of DPPH, FRAP, and inhibition of lipid peroxidation. The ethanol extracts of B. buttiana showed antioxidant activity using the two methods studied and an inhibitory activity of lipid peroxidation was observed. The extraction was carried out using acidified ethanol and the antioxidant activity was detected using the FRAP and ORAC methods. In another study, the antioxidant activities of different extracts of hexane, dichloromethane, acetonitrile, ethyl acetate, methanol, and butanol were evaluated using the DPPH, ABTS, FRAP, and lipid peroxidation methods. The butanol and methanol extracts showed high antioxidant activity by all methods used. B. glabra bracts extracted from methanol also showed high levels of NO and antioxidant activity. Antioxidant activity was also detected in bracts with flowers extracted in methanol and subsequently partitioned with hexane, chloroform, and water. Fresh leaves from B. peruviana were first degreased with petroleum ether and were subsequent to extraction with acetone, distilled water, and ethanol and their antioxidant activity was evaluated by the methods of DPPH and lipid peroxidation inhibition. In ethanolic extracts from B. peruviana the antioxidant activity was also detected. Fresh leaves from B. spectabilis were extracted with methanol and water. The results showed antioxidant activity in both extracts. The use of apical leaves from B. spectabilis extracted with distilled water measured the biomarkers of oxidative stress in blood in diabetic male Wistar rats induced with streptozotocin. The results showed that diabetic rats presented a significant decrease in GSH, SOD, and catalase. Another study of B. spectabilis
leaves extracted with acetone, chloroform, methanol, petroleum ether, and water also showed the high antioxidant activity [34].

The antioxidant activity of an ethanol extract of bracts of different colours from B. buttiana was determined using the DPPH method. All extracts presented antioxidant activity, and the percent of radical scavenging activity was dependent on the colour of bracts. In another study, the extracts from B. buttiana with water, methanol, ethanol, acetone, ethyl acetate, dichloromethane, and hexane were used to evaluate their antioxidant activity using the DPPH method.

CONCLUSION
A new opportunity to investigate the compounds' potential as antimicrobial agents and antibiofilm is presented by the phytochemical profile of B. glabra's involucre, which primarily consists of betalains and phenols. However, as of yet, no study has been able to show the values of minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and half maximal inhibitory concentration (IC50), which are required to validate the antibacterial activity at sufficiently high concentrations to guarantee safety when utilizing it in the healthcare industry. Since the extracts cling to the biofilm and become more resistant to antibiotics, current research should also address the extracts' antibiofilm action as no medications directly target this infection mechanism. Consequently, as B. glabra affects planktonic bacteria, its potential as an antibiofilm should be studied. Simultaneously, employing scanning electron microscopy is a viable approach to investigate the ways in which the phytochemistry of B. glabra extracts influences bacterial cell shape and biofilm structure. Traditional medicine still faces several obstacles when using B. glabra as a therapeutic agent. To maximize its potential, it is first necessary to accurately identify the plant organ in order to determine the variety of secondary metabolites that are present and improve its therapeutic properties.

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CONFLICT OF INTEREST
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