



Phytochemical prospection of the plant species *Caladium bicolor* (Ainton) vent: discovery of new secondary metabolites of the plant

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1 INTRODUCTION

Since its beginning, mankind has been using medicinal plants for therapeutic and nutritional purposes. Both plant and animal material were, and still are, used to make products as a mineral source for their survival (RATES, 2001). According to the World Health Organization the use of traditional natural medicine is handled preferentially by about 80% of the population. Its use is disposed to the primary care in health and the development of the same. Its use aims, in its majority, the handling of traditional therapies that involve the use of a plant material in natura or manufactured products based on their extracts, secondary metabolites or active ingredients (SOUSA; TESSER, 2017).

It is estimated that only 8% of the plants worldwide have been tested in bioactive assays, considering that about 1,100 plant species have been studied for their therapeutic properties (SIMÕES et al., 2003). According to the Ministry of the Environment, Brazil has in its tropical territory the largest biodiversity in the world, and the Amazon region holds a vast wealth of natural resources with its biodiversity, comprising a wide variability of plants that aim at therapeutic use. The empirical knowledge is of great importance for ethnobotanical research, in order to cover and further enrich the phytotherapeutic area and its ethnopharmacological use (SILVA, 2015). Thus, the study of territorial medicinal plants is essential, since their phytochemical and phytotherapeutic study leads to the development of new drugs (BRUNING; MOSEGUI; VIANNA, 2021).



Therefore, the therapeutic properties of the species *Caladium bicolor* have been studied, seeking to verify its main medicinal points and community usage. According to different communities around the world, its ethnobotanical uses are not only due to landscape functions, but also for having therapeutic properties for the treatment of dermatological pathologies, gastrointestinal disorders, neurological disorders and hepatomegaly (AGRA et al, 2008; AJIBESIN et al., 2008; BLAIR & MADRIGAL, 2005; CLAY et al., 1987; RODRIGUES et al., 2019; ODUGBEMI, 2006; SALAKO et al., 2015; VARSHNEYA et al., 2003).

The central objective of this work was to submit the ethanolic extract of the plant to phytochemical tests aimed at the investigation of groups of secondary metabolites present in the species *Caladium bicolor* comparing with the results present in the literature.

2 METHODOLOGY

The leaves of the plant were separated from its stem at room temperature and then cleaned with a damp cloth. They were then placed in paper envelopes to be dried in an oven. After drying, the plant material was pulverized and its crushed result was placed in a glass container with ethanol 96° GL at a ratio of 1:2 (m/v). This process of plant depletion lasted 4 days, repeating the process of depletion at each new rotaevaporation resulting in a liquid extract, which was subjected to drying for 3 days with the aid of a dryer.

Phytochemical Analysis

The ethanolic crude extract of the *C. bicolor* species was submitted to phytochemical screening using the developers inherent to each test proposed by Barbosa et al (2004). The tests performed were for the presence of saponins, organic acids, reducing sugars, polysaccharides, proteins and amino acids, phenols and tannins, alkaloids and purines.

3 CONCLUSION

Plant Species *Caladium bicolor*

The *Caladium bicolor*, is one of the most propagated species as an ornamental plant of the genus, due to the beauty of its foliage found in the most diverse colors and shapes. It is a geophyte plant (terrestrial bulb form), easily admitted for presenting a sagitate leaf blade, cordiform and simple leaves, sometimes lanceolate, shorter peltate (petiole inserted in the middle of the leaf lamina), branched veins with white and reddish variegation (areas with different colors). Most cultivars are disseminated from tubers, although the process can also occur through seeds (SANTOS, 2011). Its inflorescence is of the spadix type, in a long spike shape possessing a fleshy axis, mostly wrapped in a spathe. In its spadix, there is a clearly recognizable intermediate zone consisting of male sterile flowers. The spadix is about 10-13.5 × 1.1- 1.5 cm, and its stipitate is 0.2 cm long. Its peduncle is about 25-33 cm long, and its spathe is 14-16 × 3-4 cm.

Its tube is dark green internally, with ventriculate features (BARABÉ; LACROIX, 2002; PONTES; ANDRADE; ALVES, 2010).

Image 1. Inflorescence of the *Caladium bicolor* species.



Source: Prepared by the author (2020).

Its petiole measures $33-80 \times 0.8-1$ cm, containing dark, cylindrical macules. Its leaf measures about $29-44 \times 18-32$ cm, has a membranaceous consistency, with different shades, containing white and/or vinaceous variegation on the adaxial face, sagitate, peltate; its veins can divide into 3 or 4 primary lateral pairs, 2 acroscopic, 2 or 3 basidioscopic (PONTES; ANDRADE; ALVES, 2010).

Bulbous plants of ornamental species such as *Caladium bicolor*, have underground organs in the form of tubers that function as reserve organs and mass storage of micromolecules (amino acids and sugars) to produce a variety of macromolecules, mainly starch and proteins (EWING; WAEREING, 1978). This species usually loses its aerial structures during the winter and remains at rest thanks to the reserves stored in the tubers - this period is known as the "dormancy" period of the plant. In early spring, when environmental conditions are favorable to the species, these reserves carry out the new growth cycle (HARTMANN; KESTER, 1999).

According to the List of Flora of Brazil, the species *Caladium bicolor* is native to the country, given as a herb, not being endemic to the national territory. Its distribution occurs mainly in the entire North, some regions of the Northeast (Alagoas, Bahia, Ceará, Pernambuco), in the Center-West occurs (until then in Mato Grosso), in the Southwest (Minas Gerais, Rio de Janeiro, São Paulo) and South (Paraná, Santa Catarina).

Chemotaxonomic studies of *Caladium bicolor*

According to Oliveira (2011), the predominant secondary metabolite in the species *Caladium bicolor* is saponin. Among the secondary metabolites produced by plants, saponins are one of the most highlighted classes due to their wide distribution in the plant kingdom and their considerable biological activities (SCHENKEL et al., 2003). This metabolite has important potential in the production of new vaccines, especially those based on recombinant proteins and DNA, which are less immunogenic and



reactive when compared to traditional vaccines, the hemolytic and immunoadjuvant potential of these compounds has drawn attention (O'HAGAN et al., 2001).

There is also the presence of calcium oxalate in its raphides. This active ingredient, according to the list of the National System of Toxicological and Pharmacological Information (SINITOX), is one of the major causes of plant intoxication in Brazil. Although the species *Caladium bicolor* is associated with poisoning, the literature characterizes its use as a biosorbent of heavy metals such as cadmium and lead from wastewater. Moreover, it also describes the management of *C. bicolor* with the main purpose of serving as an additive in the preparation of LDPE polymer, as an alternative to increase its biodegradation and mechanical properties (SANTOS, 2011).

Anthocyanins are also present in the plant species. Anthocyanins are described in the literature as plant pigments, responsible for a great diversity of colors, observed in the leaves and stems of the species, being able to vary from deep red to violet/blue. Chemically, anthocyanins are phenolic compounds belonging to the flavonoid group. They are soluble in water and highly unstable at high temperatures, and are characterized by the basic flavin nucleus (2-phenylbenzopyranium), which consists of two aromatic rings joined by a three-carbon unit and condensed by an oxygen. They are part of the set of natural pigments widely distributed in the plant kingdom (BOBBIO, P. A.; BOBBIO, F., 1995).

The survey of the class of secondary metabolites was performed and shown only the substances that obtained the positive character in the referential tests in line with the literature. Such information then provided in Table 1.

Table 1. Class of secondary metabolites from methanolic and hydroalcoholic extracts.

Secondary metabolite	Methanolic extract	Hydroalcoholic extract	Reference
Tannins	+	+	Ucheet <i>et al.</i> (2019).Leitão <i>et al.</i> (2016).
Saponins	+	+	Ucheet <i>et al.</i> (2019).Leitão <i>et al.</i> (2016). Oliveira (2002).
Calcium oxalate	+	-	Ucheet <i>et al.</i> (2019). Oliveira (2002).
Alkaloids	+	+	Ucheet <i>et al.</i> (2019). Leitão <i>et al.</i> (2016).
Flavonoids	+	-	Akhigbemen <i>et al.</i> (2019).

Source: Prepared by the author, 2022.

In researching communities in Nigeria, Olanrewaju et al. (2015) noted that the aqueous extract of the species *Caladium bicolor* dismantled an antidiarrheal efficacy using its rhizomes, leaves and roots. It was also noted to have medicinal use for combating skin diseases such as boils, wounds, and ulcers. Furthermore, its management for the production of home remedies based on *Caladium*, demonstrated its effectiveness for treating intestinal problems (purgatives) and controlling convulsions. Despite this ethnopharmacological survey, laboratory tests that recognize the antimicrobial and antifungal efficacy



present in the leaves of the species *Caladium bicolor* have followed. Protanemonin, a component of the species, was tested as an antifungal agent on selected strains of yeasts and dermatophytes. The results followed that the minimum lethal concentrations ranged from 3.8×10^{-4} m, to greater than 1.0×10^{-3} m and the minimum inhibitory concentrations ranged from 2.0 to 7.5×10^{-4} m. The most sensitive dermatophyte tested was *Epidermophyton floccosum* Langeron & Miloch and the most sensitive yeast was *Rhodotorula glutinis* Fresen. The effects of different culture media and light on the sensitivity of *Rhodotorula glutinis* to protoanemonin. The structural analogies between protoanemonin and other unsaturated cytotoxic

lactones and the reversal by the cysteine amino acid of the antifungal action suggest a possible mechanism of action (OLANREWAJU et al., 2015).

In contrast, in their biological trials to test the healing activity in mice (*Mus musculus* Linnaeus, 1758). Leitão et al. (2016), states that the crude hydroalcoholic extract of *Caladium bicolor* eaves had considerable action on the lesions performed on mice and that its healing potential is notorious, important for its investigation and continuity of study. On the other hand, the sap from *Caladium bicolor* is toxic and can even cause asphyxiation (FLORES et al. 2001). The isolation of antiplasmodium and cytotoxic components from extracts of Araceae plants is necessary for a better understanding of the medicinal potential of this family (FRAUSIN et al., 2015).

Phytochemical analysis

The preliminary phytochemical analysis of the ethanolic extract of *Caladium bicolor* leaves indicated the presence of secondary metabolites such as saponins, organic acids, phenols and tannins, reducing sugars, and alkaloids. The results are shown in Table 2.

Table 2 – Preliminary results of the phytochemical prospection of the ethanolic extract of the leaves of *Caladium bicolor*.

Secondary metabolites	Results
Organic acids	+
Reducing Sugars	+
Alkaloids	+
Phenols and tannins	+
Polysaccharides	-
Proteins and Amino Acids	-
Purines	-
Saponins	+
Cardiac glycosides	-
Catechins	-
Sesquiterpecolactones and other lactones	-
Flavonoids	+
Steroids and triperpenoids	+
Azulenes	+
Carotenoids	-
Depsidones and Depsidones	-
Coumarin Derivatives	-
Anthraquinones	+

Legend: (+) present; (-) absent.



The known organic substances, in their majority, come from nature, since among the various kingdoms, the vegetable kingdom stands out for its significant production of secondary metabolites. They retain therapeutic activities, serving as inputs for society. These substances have nutritional and pharmacological value important for human nutrition, production of drugs, production of cosmetics, assist in the production of insecticides, aromatic additives, dyes and help in agribusiness (CROTEAU et al., 2000; PINTO et al., 2002).

It is seen that plants have their own defenses against predators and any threat that harms their existence. Thus, many plants produce secondary metabolites, substances of chemical nature that have as their main objective the protection against abiotic and biotic stresses, attract pollinators, and function as agents of competition between plants and symbiont agents. (BORGES; AMORIN, 2020; CROTEAU et al., 2000; PINTO et al., 2002; TAIZ; ZEIGER, 2006).

These compounds can be divided into three major chemically different groups: terpenes, phenolic compounds, and nitrogen compounds. These groups are divided into subgroups with distinct specificities of biosynthesis, function, and importance (BORGES; AMORIN, 2020; SHAHIDI, 1997; CROTEAU et al., 2000; SHAHIDI; NACZK, 2003; SHAHIDI; HO, 2005; TAIZ; ZEIGER, 2006).

The discovery and studies of most secondary metabolites are still recent, since there is a considerable amount of substances to be studied. Thus, studies are needed to clarify the role of these compounds in plants and their function in the interaction plant/animal for better utilization (BORGES; AMORIN).

The classes of secondary metabolites that occurred in *Caladium bicolor* revealed by the phytochemical prospection were: saponins, organic acids, phenols and tannins, reducing sugars, alkaloids, flavonoids, steroids and triterpenoids, azulenes and anthraquinones.

Organic acids

Organic acids are substances with the general structural formula $R-COOH$, where the compound R stands for a radical. They are characterized by having carboxylic acids in their chain, which can be from fatty acids to the formation of more complex structures such as amino acids. Their main action is antibacterial, acting through the mechanism of chelating agents that bind to metals, producing metal chelates. The metallic chelates effect a reduction and prevention of oxidation coming from the catalysis of the metal-ions. Its action, besides being a great antimicrobial agent, also helps in the stabilization of the pH of the soil where the plant is inserted, also having the opposite effect, where there is the production of organic acids arising from the pH of the medium. Its bacteriostatic and bactericide actions are considered therapeutic, depending on the physiological state of the plant, as well as its production and physical-chemical attributes of the external environment. (DIBNER; BUTTIN, 2002).



Reducing sugars

Reducing sugars are monosaccharides or disaccharides, such as fructose and glucose (monosaccharides) or maltose and lactose (disaccharides). They are substances with free ketonic and carboxyl groups that have the ability to oxidize upon contact with oxidizing agents in a basic environment. These free aldehydic and ketonic functions enable a reduction of cationic ions, such as iron and copper (DEMIATE, et al., 2002).

Their function for plants is mainly survival since glucose, for example, is essential for the process of cellular respiration because the energy is taken from the cell itself. Reducing sugars also constitute the composition of the cell wall, forming other types of sugars (SANTOS, 2011).

Alkaloids

The alkaloids are part of the group of cyclic nitrogen compounds, containing in its ring at least one nitrogen atom, giving it an alkaline character. They are the main compounds found in about 20% of vascular plant species, most frequently in herbaceous angiosperms and in a few monocots and gymnosperms (Pagare et al., 2015).

Its frequent occurrence in plants with important active principles, makes it widely used in the industry, being one of the most significant compounds for the medicinal area, economy and other social-political sectors. Its active principles are linked to neurological and psychostimulant activities, possessing neurodepressant, analgesic, antimicrobial, anti-inflammatory, antihypertensive, antispasmodic, anticholinergic, diuretic, and anesthetic action. (SIMÕES, 2010; LIMA, 2016).

Saponins

These substances constitute the class of triterpenoids, are polar, glycosylated compounds that are characterized by surfactant properties, i.e., they can form abundant and persistent foams after agitation of their aqueous solutions. They can form complexes with membrane steroids, proteins, and phospholipids, determining their biological actions. This property can alter membrane permeability, which can aid in the absorption of substances, or it can destroy it, indicating a toxic characteristic (SCHENKEL et al., 2010).

These characteristics derived from saponins are the reason for their antifungal and hypocholesterolemic actions (ROS, 2006). Plant species that possess saponins exert various biological activities, such as anti inflammatory, larvicidal, hypocholesterolemic, molluscicidal, expectorant and ventropic (PELAH et al., 2002). They have the ability to emulsify due to their chemical structure.

Phenols

Phenolic compounds are substances that have an aromatic ring with one or more hydroxyl substituents. They can be presented as simple molecules, such as phenolic acids and flavonoids, as well as complex molecules such as polymers (SOARES, et al., 2008). Its main function for the plant is related to



protection, providing a great resistance to bacteria and other microorganisms that may compromise the structure and plant physiology. Its main therapeutic action for humans is the conferral of nutritional value and antioxidant action enabling the inhibition of risk of vascular diseases, acting on oxidative stress due to its high antioxidant activity (EVERTTE et al., 2010; IMEH; KHOKHAR, 2002).

Tannins

Tannins have a considerably high molecular weight, forming stable compounds with proteins, are part of the constitution of a class of polyphenols and, according to their chemical structure, are classified as hydrolyzable tannins, condensable tannins and pseudotannins. Their main action is to promote an antioxidant, astringent, hemostatic, healing, reepithelizing, and protective action (SIMÕES, 2017).

Plants rich in tannins are employed in traditional medicine in the treatment of diarrhea, rheumatism, hypertension, hemorrhages, in kidney and urinary system problems and inflammatory processes in general (SANTOS, 2011). They also exert antimicrobial, antiviral, anti-ulcerogenic, anti-hepatotoxic, hypolipidemic, antineoplastic and antiallergic activities (SILVA et al., 2009). These properties of tannins are based on their ability to complex with proteins, ensuring to this class of metabolites the activities already mentioned. Moreover, tannins have the ability to complex with metal ions, providing them with antioxidant character (ADAMCZYK et al., 2014).

Steroids and triterpenoids

The triterpenoids are biosynthetic products generated from isoprene units, they have a biological activity focused on defense against insects and predators, have germination inhibiting activity and also attract pollinators (MIRA NETO et al., 2014).

The finding that steroids and triterpenoids can have several pharmacological actions, such as anti-inflammatory and analgesic (SILVA et al., 2005). Plants that contain steroids and triterpenoids in their composition can be used by the pharmaceutical industry to obtain semi-synthetic drugs, such as contraceptives, anti-inflammatory, steroidal and anabolic steroids. (OLIVEIRA, 2007).

Flavonoids

Flavonoids are part of the largest class of phenolic compounds in plants, with more than four thousand substances belonging to the flavonoid group identified. These are classified into four groups: anthocyanins, flavones, flavonols, and isoflavones (isoflavonoids). They are aromatic substances containing 15 carbon atoms in their basic skeleton and can have several substitutions by hydroxyl groups and sugars (YOKOZAWA et al., 1997).

As these substances possess a great chemical diversity, with distinct functions such as pigmentation and defense, this results in an infinity of plant functions. Flavonoids are mostly present in nature in the form of glycosides. This compound serves as an attractant for pollinators, facilitating their dispersal from seeds,



but also acts as a scavenger of herbivores and pathogens. Besides all this, it has an allelopathic function for competition with other plants. They are synthesized from products of shikimic acid and acidomalonic acid pathways (ÖZEKER, 1999).

In accordance with Szent-Gyorgi (1936), flavonoids have pharmacological properties such as: anti-inflammatory, antioxidant, vasodilator, antiallergic, antitumor, anti-hepatotoxic, anti-ulcerogenic, antiplatelet, highlighting also their antimicrobial and antiviral activities.

Azulenos

Azulene is part of the secondary metabolism of plants characterized by its blue color, being a simple isomer referring to naphthalene, a cyclic hydrocarbon. It is presented as violet crystals, with a melting point of 100 °C and a boiling point at 242 °C. It is a stable molecule, having the structural chemical formula C₁₀H₈. This substance has anti-inflammatory, soothing, decongestant, anti-allergic, and tissue regenerator properties, which inhibits the excessive outflow of water from the skin, resulting in longer-lasting hydration. Its use in the industry is mainly in dermatological cosmetics, such as creams, toothpastes, soaps, and gels, with the objective of avoiding tissue tightening. Besides this, it can be used in the treatment of hematomas, especially in the lower limbs, helping to improve varicose veins and edemas (RUIZ, 2000).

The azulene is part of the composition of essential oils present in the leaves of Roman chamomile (*Matricaria chamomilla*), camphor (*Cinnamomum camphora*), geranium (*Pelargonium*), guaco (*Mikania glomerata*), eucalyptus (*Eucalyptus*) and cubeba (*Piper cubeba*) and can be found as chamazulene or guiazulnenos (GUPTA et al., 2010).

Anthraquinones

Anthraquinones are organic compounds with general formula C₁₄H₈O₂, which are laxative O-glycosides, products of the oxidation of phenols. These phenolic substances are derived from the anthracene dicetone and have three aligned aromatic rings in their chemical structure, characterizing an anthracene ring. They can be formed from shikimic acid and/or acetate routes, the so-called acylpolimalonates. Anthraquinones are a source of natural dyes, have a laxative effect, and exhibit antifungal, bactericidal, and allelopathic function against fungi and insects. (SIMÕES et al., 2010)

It was found that the species *Cladium bicolor* presented in its prospection the presence of secondary metabolites: saponins, organic acids, phenols and tannins, reducing sugars, alkaloids, flavonoids, steroids and triterpenoids, azulenes and anthraquinones. These metabolites have therapeutic action in several areas for humans, such as antioxidants, antiviral, antimicrobial, anti-hepatotoxic, anti-inflammatory, antifungal, hypocholesterolemic, larvicidal, anticholinergic, and others. In comparison with the literature, only the presence of secondary metabolites such as tannins, saponins, alkaloids, flavonoids, calcium oxalate and anthraquinones were recorded. Thus, it was found the presence of more secondary metabolites than already reported in the literature, thus, it is possible to observe that there was a finding related to the metabolites of



the plant *Caladium bicolor*. This plant is not widely studied, however, greater therapeutic potentials and cytotoxic investigation may be discovered with further in vivo and in vitro studies.



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