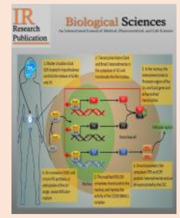
REVIEW ARTICLE

Biological Sciences

(An International Journal of Medical, Pharmaceutical, and Life Sciences)

Journal home: https://irrespub.com/biolsciences/index.php/1/index



Exploring the Ethnomedicinal Uses, Phytochemical Constituents and Biological Activities of Caladium Bicolor: A Review

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ARTICLE HISTORY

Received: 13-12-2025
Revised: 16-01-2025
Accepted: 04-05-2025
Online: 02-06-2025

KEYWORDS

Caladium bicolor
Biological activity
Traditional
Phytochemical

ABSTRACT

Caladium bicolor (Aiton) Vent is a genus of flowering plants in the family Araceae. The plant is occasionally gathered from the wild and used as a food source by local folks. It is often grown as an ornamental plant in tropical gardens, where it is valued particularly for its attractive foliage. Various parts of the plant have been used in traditional medicine to manage conditions such as convulsion in children, facial paralysis, tumours, sore throats, toothache, constipation, wounds, flu symptoms, as an antiseptic, emetic, laxative and insecticide. This is the first review that summarizes the botanical description, plant ecology, geographical distribution, traditional uses, phytochemical screening, biological activities and toxicity of *Caladium bicolor*. The information that are contained in this review article, being the first article that addresses this topic were gotten from online databases and published literatures on traditional uses and various research studies conducted on *Caladium bicolor* in various countries from 1985-2021.Phytochemical screening of extracts from different parts of *Caladium bicolor* showed the presence of tannins, flavonoids, alkaloids and saponins in its leaves, tubers, stem and roots, and cardiac glycosides in the leaves and tubers of the plant. Carbohydrates, lignin, starch, mucilage, cellulose, cutin and suberin were also found to be present in the methanolic extracts of its leaves with absence of calcium oxalate. Various studies have discovered its antimicrobial, antioxidant, antidiarrheal, antiproliferative, antiangiogenic, anti-inflammatory, mitogenic, cytotoxic and thrombolytic activities. This review therefore summarizes reports on *Caladium bicolor* plant in order to provide sufficient information for further and future research which are needed to complement these findings.

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Email: agoimary326@gmail.com
DOI: https://doi.org/10.55006/biolsciences.2025.5206
Published by IR Research Publication;

Introduction

Caladium bicolor (Aiton) Vent., often known as "The heart of Jesus," "Elephant ear," or "Angel wings," is a species of flowering plants in the family Araceae [1,2]. It is a perennial herbaceous plant with a tuberous root that sprouts a cluster of beautiful and multicolored leaves up to 80 cm tall. Occasionally, local people gather the plant from the wild and consume it as food. In tropical gardens, where it is

Abbreviations: *SRB assay: Sulforhodamine B Colorimetric assay; HCT-15: Human colon cancer cell line; MTT assay: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; HT-29: Human colorectal adenocarcinoma cell line; SW-620: Human Caucasian colon adenocarcinoma cell line; Colo-205: Human colon adenocarcinoma cell line; HOP-62: Human epithelial derived cancer cell line; MCF-7: Human breast cancer cell line; SK-OV-3: Human Ovarian cancer cell line; BALB/c: Albino laboratory-bred strain of the house mouse; DPPH: 1, 1, diphenyl-2-picrylhydrazyl.*

prized for its attractive leaf, they are frequently grown as an ornamental plant. The most distinctive features of the plant are its leaves, which come in a wide variety of sizes, shapes, and colors. It has a heart, lance, or arrowhead shape that defines it. The arrowhead-shaped leaves, often up to 50 cm long, have uniquely colored veins and come in a variety of shades of green that are mottled and blotched with pink, red, gray, white, or combinations of these colors [3]. Most members of the Araceae family have harmful properties; they contain water-insoluble calcium oxalate crystals and unidentified proteinaceous toxin constituents that, when they come into contact with them, [4, 5] cause painful burning of the lips, tongue, mouth, and throat and give the impression that hundreds of tiny needles are piercing them. Hoarseness, dysphonia, dysphagia, and an inflammatory reaction that frequently includes edema and blistering may also occur [6]. Overdosing may result in nausea, vomiting, diarrhea, eye, mouth and tongue edema, eye redness, and nausea [6]. The plant is safe to consume in either of these states since calcium oxalate is easily broken down by either thorough boiling or thorough drying.

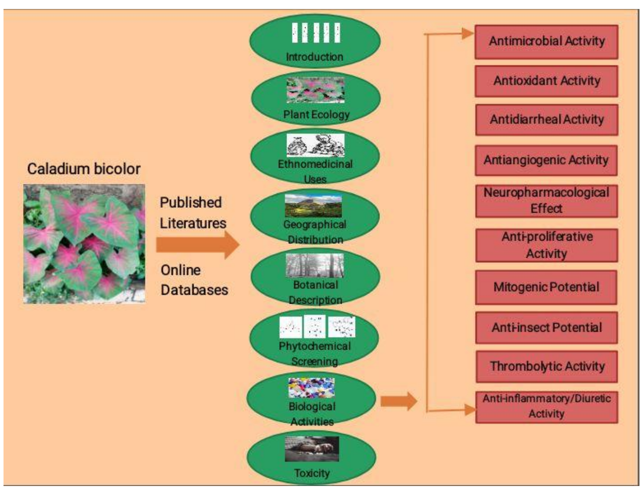

Figure 1. Workflow of the study.

Plant Ecology

C. bicolor is a plant that grows in damp tropical lowlands and at moderate elevations [3]. It prefers a wet, fertile, humus-rich, acidic soil in partly shady or filtered sunlight, grows well in sunny shade, but keeps away from direct sunlight because it will scorch the foliage [3]. Dry environments are undesirable to the plants during active growth, and needs to be grown in an area protected from severe winds. The plant can spread like a weed and is found on many Pacific Islands and wet, fertile soils in shady locations [3]. *C. bicolor* is currently classified as an invasive species in Trinidad and Tobago, Guam, Micronesia, Palau, Hawaii, and the Philippines, where it is thought to be a species that is displacing native species, disrupting community structures, and otherwise affecting native plant ecosystems [7-10].

Ethnomedicinal Uses

To treat a wide range of pediatric illnesses, the entire plant is macerated in fresh water. In veterinary treatment, crushed leaves are used to get rid of pests on cattle wounds [3]. Roundworms are expelled using the juice from the stems used as an enema [3]. The juice kills maggots when applied to the skin [3]. Angina is treated using an infusion of its fresh leaves. There is a dearth of knowledge regarding the therapeutic potential of the various varieties and species of Caladium that may be found in the wild in Nigeria on farmlands, on road sites, and in schools. Leaves are applied externally for furunculosis and used as a vermifuge and purgative. They can also be used to treat toothaches, sore throats, constipation, catarrh, wounds, and sores. They are also used as an antiseptic, anti-tumor, emetic, and laxative [4]. For facial paralysis, crushed bulbs are applied to the face. The Yoruba people of Nigeria utilize the plant's leaves and rhizome to heal boils, wounds, ulcers, purgatives, and convulsions. Although powdered leaves of *C. bicolor* are used as an insecticide [11] and an antidote for snake bites, [12] there have been no reports of folklore medical uses of the plant in the Philippines. Numerous C. bicolor components have been used in traditional medicine to treat a variety of diseases, including flu symptoms, tumors, sore throats, toothaches, facial paralysis, and convulsions in children.

Geographical Distribution

C. bicolor is a common ornamental plant that has naturalized in Pemba, Zanzibar, tropical and sub-tropical parts of Africa. Geographically, it is situated in South America, specifically in Brazil, Bolivia, and Peru, before heading north via Central America to Mexico [3]. The northwest regions of Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guyana, Honduras, Nicaragua, Panamá, Peru, Suriname, and Venezuela were also discovered to contain it [16].

Botanical Description

The habitat for the species of caladium is characterized as "typically an understory tuberous herb in open areas in the forest, on creek banks, common in the areas of semi deciduous forest." Caladium is adapted to disturbance and frequently grows in partially shaded regions alongside roadways, from sea level to at least 1,000 m [17]. The leaves of the wild plants are typically 6-18 inches (15-45 cm) long and broad, and they grow to a height of 15-35 inches (40-90 cm) [18]. C. bicolor is an erect, acaulescent herb with a fleshy corm at the base that is glabrous. Petioles erect, 35-55 cm long, sheathing, white at the very base, typically with purple stripes; blades pointing downward, 30 x 20 cm, chartaceous, usually with small, irregular whitish or pinkish spots, or variegated along secondary veins; less frequently completely green; glaucous beneath; apex acute or shortly acuminate; base peltate; cordate; margins more or less wavy. Flowers are unisexual; spathes are chartaceous, glaucous, to 14 cm long, the blade twice as long as the tube, withering, elliptic, and apiculate at the apex; spadix is shorter than the spathe, the staminate zone twice as long as the pistillate; peduncles are cylindrical, green, and usually have purple stripes [19]. Inflammatory sap is present [16].

Phytochemical screening

In the leaves and tubers of two different *Caladium bicolor* species—green background with white patches (GWS) and green background with pink veins (GPS)—Essien et al. (2015) screened for alkaloids, flavonoids, saponins, tannins, carbohydrates, sterols and triterpenes, phlobatannins, cardiac glycosides, anthraquinone, and deoxy sugar. Phlobatannins and anthraquinones were discovered to be absent. Alkaloids, saponins, tannins, terpenoids, and flavonoids were all detected in the ethanolic and methanolic extracts of the plant's leaves, stem, and roots by Ezebo et al. (2021) who also carried out phytochemical screening on them. In the whole leaf extract of C. bicolor, Akhigbemen et al. (2019) observed the presence of carbohydrates, proteins, alkaloids, and flavonoids but the absence of tannins, compounds with steroidal nuclei, cardiac glycosides, and phenolic compounds. Akindele et al. (2015) also identified the presence of phenolics and reducing sugars. Phytochemical analysis of extracts from Caladium bicolor's leaves, tubers, stem, and roots, reveals tannins, flavonoids, alkaloids, and saponins, as well as cardiac glycosides in the leaves and tubers of two different species variations of the plant [5, 20, 21]. The methanolic extracts of its leaves were discovered to contain carbohydrates, lignin, starch, mucilage, cellulose, cutin and suberin [22] with the presence of cardiac glycosides, which contrasts with the findings of Essien et al. (2015). Phlobatannins were also found by Akindele et al. (2015) in the aqueous leaf extract, which is also contrary to the results of Essien et al. (2015). This may be caused by variations in seasonal conditions, plant species, or inherent.

Figure 2. Caladium bicolor plant.

Biological Activities

Antimicrobial activity

Medicines known as antimicrobials are used to treat and prevent diseases in humans, animals, and plants. Antibiotics, antivirals, antifungals, and antiparasitics are some of them. Antimicrobial resistance is a growing threat to our ability to treat illnesses due to the creation and spread of drug-resistant bacteria that have developed new resistance mechanisms [24].

Staphylococcus aureus was the antimicrobial strain that *C. bicolor* was most effective against [25]. For testing purposes, pathogenic gram positive (Staphylococcus aureus and Streptococcus pyogenes) and negative (Pseudomonas aeruginosa, Kiebsiella pneumonia, and Proteus mirabilis) bacterial and fungal isolates (Candida albicans) were exposed to crude leaves and tuber extracts of two species of C. bicolor, green background with white patches (GWS) employing a modified discs diffusion assay (DDA) technique at various concentrations (0.1-0.4 g/ml) [26, 27]. Standard antibiotics included streptomycin (30 mg/ml) for use on bacterial isolates and nystatin (150 mg/ml) for use on fungus isolates. The studied extracts varied in their antibacterial activity (6–16 mm) against the test strains of bacteria. With respect to the extract and the organism under test, the zones of inhibition varied. As improved antibacterial action is concentration dependent, it was shown that the zones of inhibition grew as concentration rose. *S. aureus and P. mirabilis*, with the exception of bulb extracts of GPS and GWS, which had clear zones of 8 mm and 10 mm (400 mg/ml) respectively, demonstrated the greatest resistance to the test extracts. *S. pyogenes* was significantly suppressed by the tuber extracts compared to the leaves extracts, and *Pseudomonas aeruginosa* was more susceptible to the antimicrobial agents in the leaves extracts than the tuber extracts. Comparing GPS leaves extract to the gold standard medication, streptomycin (17 mm), the broadest zone of inhibition (16 mm) was seen against S. pyogenes. Significant inhibition of *Pseudomonas aeruginosa, K. pneumonia,* and *Candida albicans* was also achieved using GPS leaf extracts. Essien et al. (2015) [5] used the tube dilution method to estimate the minimum inhibitory concentration (M.I.C.), which is the lowest concentration of an extract that totally inhibits the growth of microorganisms in 24 hours. On examined bacteria and fungi, M.I.C ranged from 0.006 g/ml to 0.55 g/ml for different extracts. The lowest MIC value (0.006 g/ml) against S. pyogenes and *C. albican*s was demonstrated by GWS tuber extract, as well as by GPS leaves extract.

Ezebo et al. (2021)[20] also investigated the antibacterial effects of ethanol and methanol leaf, stem, and root extracts of *Caladium bicolor* (Aiton) Vent against two clinical pathogens, Aspergillus flavus and Candida albican. Depending on the extract concentration, all of the plant extracts inhibited the test fungus to varied degrees. The lowest inhibitory effect (slightly effective) was seen on *C. albican* at 10% extract concentration, while the ethanol leaf extract at 40% extract concentration had the highest inhibitory effect (moderately effective) on *A. flavus*, which was significantly higher than other interactions. The lowest inhibitory impact (somewhat effective) was seen on *A. flavus* at 10% extract concentration, while the methanol leaf extract at 40% extract concentration demonstrated the highest inhibitory effect (moderately effective) on *C. albican*. The largest inhibitory impact of the ethanol stem extract (somewhat effective) was observed on *A. flavus* at a 40% extract concentration, while the lowest inhibitory effect (slightly effective) was observed on *C. albican* at a 10% extract concentration. The lowest inhibitory impact (somewhat effective) was seen on *A. flavus* at 10% extract concentration, while the methanol stem extract at 40% extract concentration displayed the highest inhibitory effect (moderately effective) on *C. albican*. The lowest inhibitory impact (somewhat effective) was seen on *A. flavus* at 10% extract concentration, while the methanol stem extract at 40% extract concentration displayed the highest inhibitory effect (moderately effective) on *C. albican*.

Table 1. Ethnomedicinal Uses of different parts of C. bicolor and their method of use

S/N	Country	Diseases	Plant parts/ method of use	References
1.	Brazil	Tumor Emetic and purgative	Heated bulbs are covered with olive oil and applied to tumors.Tubers	[4]
2.	French Guiana	Infected sores, Facial Skin Blemishes.	Powdered dried leaf is used to treat infected sores. Powdered tuber employed to treat facial skin blemishes.	[13]
3.	Cameroon	Vaginal Inflammation	Decoction of some tubers and leaves are used for vaginal inflammation.	[4]
4.	India	Cattle festers caused by worms.	Decoction of leaves are also used for external cattle festers caused by worms.	[4]
5.	Nigeria(Southwestern Region)	Boils, Wounds, Ulcer, Purgative and Convulsion.	The leaves and rhizome of the plant is used to treat boils, wounds, ulcer, purgative and convulsion.	[14, 15]
6.	Phillipine	Insect Invasion, Snake bites.	Powdered leaves are used as insecticide.It is also used as antidote for snake bites	[11, 12]

The test organisms were therefore reported to be inhibited in vitro by the ethanol and methanol extracts of the leaf, stem, and root of C. bicolor at all doses, with the ethanol extract being the most effective.

The antibacterial activity of *C. bicolor* leaf extract was examined by Uche et al. (2019) [22] using the agar well diffusion method against a number of clinical isolates, including Staphylococcus aureus, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, Aspergillus fumigatus, and Candida albicans. In contrast to P. mirabilis and Candida albicans, Aspergillus fumigatus showed greater susceptibility to the test extracts. It is possible that the origin of the organisms and the area of the plant under research are to blame for P. mirabilis and *C. albicans*' resistance in the study, which is inconsistent with other studies [5]. According to a previous publication [28] resistances, whether acquired or innate, can spread from one organism to another through the vertical or horizontal exchange of genetic material. According to Mesak et al. (2008), past exposure to sub-inhibitory antibiotic doses may have caused the transcriptional alterations [29]. Additionally, it has been demonstrated that some species of organisms have different cell walls from others, making them more susceptible to chemical compounds [5] properties of the constituents.

Table 2. Phytochemicals from different plant parts and species of C. bicolor

Plant Part	Plant Species	Plant Extract	Phytochemicals present	References
Leaves	Green background with white patches		Alkaloids, flavonoids, saponins, tannins, carbohydrates, sterols and triterpenes, cardiac glycosides and deoxy sugar.	[5]
Leaves	Green background with pink veins		Alkaloids, flavonoids, saponins, tannins, carbohydrates, sterols and triterpenes, cardiac glycosides and deoxy sugar.	[5]
Tuber	Green background with white patches		Alkaloids, flavonoids, saponins, tannins, carbohydrates, sterols and triterpenes, cardiac glycosides and deoxy sugar.	[5]
Tuber	Green background with pink veins		Alkaloids, flavonoids, saponins, tannins, carbohydrates, sterols and triterpenes, cardiac glycosides and deoxy sugar.	[5]
Leaves		Ethanolic and Methanolic extracts	Alkaloids, saponins, tannins, terpenoids, and flavonoids.	[17]
Stem		Ethanolic and Methanolic extracts	Alkaloids, saponins, tannins, terpenoids, and flavonoids.	[17]
Roots		Ethanolic and Methanolic extracts	Alkaloids, saponins, tannins, terpenoids, and flavonoids.	[17]
Leaves		Whole leaf extract	Carbohydrates, proteins, alkaloids, and flavonoids	[15]
Leaves		Aqueous leaf extract	Phlobatannins, phenolics and reducing sugars.	[18]
Leaves		Methanolic leaf extract	Carbohydrates, lignin, starch, mucilage, cellulose, cuti, suberin and cardiac glycosides	[19]

Antioxidant activity

Damage to cells and tissues can result from oxidative stress, which is caused by an imbalance of free radicals and antioxidants in the body. Free radicals are created by the body's cells during routine metabolic processes. Antioxidants, however, which counteract these free radicals, are also produced by cells. Oxidative stress is caused by an excessive generation of free radicals and a biological system's incapacity to detoxify these reactive species [30]. The aging process is influenced by oxidative stress. A substantial body of research implies that persistent oxidative stress has a role in the emergence of a number of chronic diseases, such as cancer, diabetes, and heart disease [30].

In distilled water, *C. bicolor* methanolic extracts at different concentrations (100%, 75%, 50%, and 25%) were tested for their capacity to scavenge hydrogen peroxide [4]. Tannic acid (control) and the scavenging percentage activities were compared. The methanolic extract test results revealed that all concentrations are positive for antioxidant properties, though qualitative analysis revealed that three concentrations (25–75%) have lower antioxidant activities when compared to 100%, which is even higher than the antioxidant properties of tannic acid; the differences between concentrations, however, were not statistically significant.

Using the methods of Blois [31] and Meda et al. [32], Essien et al. [5] also measured the DPPH scavenging activity and quantity of total phenols in the methanol extracts of the leaves and tuber of two *C. bicolor* species, green background with white patches (GWS) and green background with pink veins (GPS). Content of polyphenols exhibited concentration dependency. From 6.423 mg GAE/g (GPS leaves) to 10.192 mg GAE/g (GWS leaves) at 2.0 mg/ml, the total phenolic content varied. The chemical make-up of the endogenous extractable chemicals as well as the plant portion under study may both contribute to variations in the phenolic content of extracts. In close agreement with this study, Mirdha et al. [33] also discovered polyphenols content (1.27-12.35 mg GAE/g). In a concentration-dependent manner, *C. bicolor* extracts (0.25–2.0 mg/ml) significantly scavenged the DPPH radical. When compared to the conventional medication BHA, the GWS leaves extract reduced DPPH radicals by 64.7% at a concentration of 2.0 mg/ml. More antioxidant activity was present in GWS leaves extract than GWS tuber extract. According to Mridha et al. [33], DPPH activity was slightly higher (124.21-211.48 g/ml) for various organic fractions of the entire *C. bicolor* plant.

Antidiarrheal activity

As the second most common cause of mortality in children under the age of five, diarrheal illness claimed the lives of 370,000 kids in 2019 [34]. Dehydration is the most serious danger that diarrhea presents. Water and electrolytes such as sodium, chloride, potassium, and bicarbonate are lost during a bout of diarrhoea through watery stools, vomit, sweat, urine, and respiration [34].

Akindele et al. [21] examined the antidiarrheal properties of *Caladium bicolor* aqueous leaf extract in a mouse model of Caster oil-induced diarrhea. One hour prior to the administration of castor oil (0.2 ml/mouse), five groups of mice were pre-treated orally with the extract (1, 5, 10 and 50 mg/kg) and loperamide hydrochloride (5 mg/kg). Distilled water (10 ml/kg) was administered orally to the control group. The onset of diarrhoea, the total amount of hard, semi-solid, and watery stools, the weight of watery stools (which includes semi-solid and watery stools), and the total weight of all stools (which includes hard, semi-solid, and watery stools) were all tracked for 4 hours for each group. The consistency of the stools was then graded numerically. When compared to the control, *C. bicolor* aqueous extract 1 mg/kg and loperamide 5 mg/kg significantly delayed the beginning of diarrhoea, but there was no difference ($p > 0.05$) between the effects of the extract and the standard medication. The quantity of wet stools, overall stools, wet stools weight, and total stools weight did not vary significantly ($p > 0.05$) with the extract at any of the doses employed and in loperamide. Based on the diarrhea score, the extract at doses of 1 and 50 mg/kg and loperamide at doses of 5 mg/kg had inhibition values of 47.53, 43.83, and 54.94%, respectively. The in vivo antidiarrheal index was calculated to be 50.07 and 42.81%, respectively, at doses of 1 and 50 mg/kg, which were lower but comparable to the figure for loperamide (58.15%).

Antiangiogenic activity

The creation of new blood vessels is known as angiogenesis. Endothelial cells, which line the interior wall of blood arteries, migrate, proliferate, and differentiate during this process [35]. The implication of angiogenesis in cancer has been reported [36]. Tumour cells are covered, causing platelets to protect tumour emboli from immune surveillance and thereby promoting their lodging at distant metastatic sites. Novel strategies of anticancer therapy targeting tumor vessels are therefore needed.

Tosoc et al. [4] tested the antiangiogenic activity of *C. bicolor*'s methanol extract using a duck embryo experiment at various concentrations (25%, 50%, 75%, and 100%). Thirty pieces of three-day-old fertilized duck eggs were used as part of a modified windowing approach. By comparing the rate of proliferation of the extra-embryonic blood vessels between the treatment groups and the controls, the antiangiogenic activity of the extracts was determined. The optimal concentration of the *C. bicolor* methanolic extract to produce antiangionetic effects is at 50%, according to a comparison of the antiangiogenetic effects of the various concentrations.

Neuropharmacological Effect

Around 70 million people globally, 80% of whom reside in developing nations, suffer from epilepsy, the second most prevalent neurological illness [37]. According to studies, up to 50% of epilepsy patients experience the onset of psychiatric illnesses, the most prevalent of which are sadness, anxiety, and psychotic disorders [38]. Antiepileptic medication (AED) side effects may lead to patient noncompliance and decreased therapeutic efficacy. Although the previous generation of AEDs may have had a worse adverse effect profile, the newer ones still have significant CNS-related side effects including diminished cognitive function and mental issues [39]. This implies the demand for safer yet effective medications.

The neuropharmacological effects of the whole extract, hexane extract, ethyl acetate extract, and methanol extract of *C. bicolor* leaf were studied by Akhigbemen et al. [15]. When compared to the control in strychnine-induced convulsion, the entire extract provided 20% protection at a dose of 100 mg/kg with no appreciable change in latency to tonic convulsion. Whole plant produced 100% protection against strychnine-induced convulsion at dosages of 200 and 400 mg/kg. At dosages of 100, 200, and 400 mg/kg, hexane, ethyl acetate, and methanol extract did not offer any protection against strychnine-induced convulsion. When compared to the control, doses of 200 and 400 mg/kg hexane extract significantly reduced the latency to tonic convulsion ($P < 0.05$ and $P < 0.01$ respectively) which, at 100 and 400 mg/kg, was significant ($P < 0.01$ and $P < 0.05$ respectively). Hexane extract improved the latency to tonic convulsion for pentylenetetrazole-induced convulsion at doses of 100 mg/kg ($P < 0.0001$), 200 mg/kg ($P < 0.001$), and 400 mg/kg ($P < 0.001$). When compared to the control, the latency to tonic convulsion was further lengthened by methanol and ethyl acetate extract at doses of 200 mg/kg ($P < 0.001$) and 400 mg/kg ($P < 0.01$), respectively. At dosages of 100, 200, and 400 mg/kg of whole extract, there was no protection against hind limb extension seizure (HLES) in maximal electroshock-induced convulsions. However, hexane extract demonstrated 100% protection against HLES at 200 and 400 mg/kg, respectively, and 60% protection against HLES at 100 mg/kg. All mice were protected by ethyl acetate extract at doses of 100 and 400 mg/kg, while at 200 mg/kg, protection was only 60%. At 100 and 400 mg/kg, methanol extract provided 40% protection, while at 200 mg/kg, 20% protection.

Antiproliferative Activity

In almost all tissues, cell division known as proliferation takes place physiologically, increasing the total number of cells. From the period of embryogenesis to the development of the entire organism from single- or double-cell embryos, the process of cell proliferation plays a crucial function. It also continues to play a crucial part in the maintenance of adult tissue homeostasis by recycling the old cells with new cells [40]. Any sort of cell's uncontrolled multiplication can lead to cancer. The understanding of the mechanisms of malignant tumors, which can invade healthy tissues and spread throughout the body, and search for phytocompounds with antiproliferative activity, is crucial for proper diagnosis and treatment approach [41].

Using the approach developed by Monks et al. [42], Singh et al. [43] assessed the inhibitory ability of *C. bicolor* Lectin (CBL) against various human cancer cell lines. From the tubers of C bicolor Vent, a novel lectin with in vitro anti-proliferative activity was discovered [44]. 13 human cancer cell lines from various organs and tissues were used to test the *C. bicolor* lectin's in vitro anti-cancer efficacy. Out of the four colon cancer cell lines used in the SRB assay, CBL reduced the proliferation of HCT-15 and HT-29 by 80% while only inhibiting the growth of SW-620 and Colo-205 by about 50% at 100 g ml-1 of CBL. Additionally, 82% of the liver cancer cell line HOP-62 was suppressed. MCF-7 and SKOV-3, two of the four cancer cell lines of the reproductive system used, demonstrated 31% and 55% inhibition, respectively, while the other cell lines tested exhibited almost no inhibition. This implies that CBL's anti-proliferative activity is selective for particular tumor cell lines. According to Brooks et al. [45], the presence of glycoconjugates with somewhat varied levels of activity may be the cause of the variance in the inhibition of proliferation on different cell lines. This will result in different lectin signaling actions. Although several theories have been put forth that suggest this effect is linked to lectins' capacity to modulate the growth, differentiation, proliferation, and apoptosis of premature cells in vivo and in vitro [46], the precise molecular mechanism(s) of plant lectins' anti-proliferative effect is currently unclear.

Mitogenic potential

Inbred female BALB/c mice splenocytes and human peripheral blood mononuclear cells (PBMC) that were isolated from BALB/c mice spleen and human blood, respectively, under sterile conditions, were used to test the mitogenic potential of affinity-purified *C. bicolor* lectin [45]. Their mitogenic ability was examined using the MTT assay [47] and the methyl-3 H thymidine uptake assay [48]. Both human peripheral blood mononuclear cells (PBMC) and BALB/c splenocytes responded mitogenically strongly to *C. bicolor* lectin. Compared to Con A, a well-known standard plant mitogen, *C. bicolor* lectin has approximately twice the relative mitogenic stimulation of human lymphocytes. In the case of BALB/c and human lymphocytes, the optimal dose of *C. bicolor* lectin was 1.25 and 5 g/ml, respectively. The better understanding of the connection between chromosomal abnormalities and human diseases made possible by the use of mitogenic lectins can greatly aid in diagnosis. In addition to other cells, lymphocytes have traditionally been the focus of mitogenic assays, and research on the relationship between lectins and lymphocytes, and can significantly advance our understanding of how cells grow and develop by illuminating the mechanism of lymphocyte activation and its regulation.

Anti-inflammatory/Diuretic Activity

In albino rats, the anti-inflammatory and diuretic effects of a cold ethanol extract from *C. bicolor* leaves were examined and compared to those of the conventional medications aspirin (300 mg/kg) and furosemide (100 mg/kg), respectively [46]. The dosages for the extract were 1000 mg, 500 mg, 250 mg, 125 mg, 62 mg, and 31 mg. The anti-inflammatory effect of the *C. bicolor* leaf extract was demonstrated by the dose-dependent reduction of acid-induced rat paw oedema. High concentrations of the extracts were observed to inhibit diuretic action while also causing inflammation over time. The extract with the highest inhibitions in diuresis showed a minor reduction at high concentrations of 1000 mg and 500 mg, respectively [46].

Anti-insect potential

Plants that are excellent sources of food and plant-based treatments have consistently faced serious threats from insect pests. Along with posing a major threat to other plants, the melon fruit fly is a serious pest of the Cucurbitaceae family worldwide. The majority of traditional control techniques have thus far failed to stop the bug. By using an artificial diet bioassay [50] to measure the development of the second instar of the melon fruit fly, *B. cucurbitae*, Singh et al. [43] evaluated the effect of *C. bicolor* lectin, and the activity of enzymes (esterases, acid phosphatases, and alkaline phosphatases) involved in metamorphosis, hydrolysis, and detoxification in melon fruit fly using the methods of Katzenellenbogen and Kafatos [47] and McIntyre [51]. The development was significantly affected by *C. bicolor* lectin. The inclusion of *C. bicolor* lectin in the food resulted in a significant ($P < 0.01$) extension of the larval duration, which increased from 6.14±0.13 days in the control to 10.97±0.29 days, or 4.83 days at the highest concentration examined, whereas the pupal period exhibited an increase but was not statistically significant. At 160 gml-1, the whole development time was greatly delayed, taking 5.93 days. Compared to larvae raised on a control diet, the percentages of pupation and emergence at 160 gml-1 were only 33 and 36%, respectively. Insecticidal lectins were found to be linked to midgut epithelial cells in a variety of insect pests by ultrastructural studies [52]. When compared to the corresponding controls, the larvae raised on lectin-containing diets showed a significant ($P < 0.01$) increase in esterase activity, which was almost three times higher i.e larvae raised on a diet containing *C. bicolor* lectin showed an increase in activity that was almost three times that of the control, but there was no discernible alteration in acid phosphatase activity. In the normal course of development, alkaline phosphatase (AkP) activity increases up to 96 hours of age and then considerably declines as the age increases to 144 hours. Esterases may be important in the detoxification of these lectins, as evidenced by the increase in the plateau of esterase activity in the lectin-treated larvae [53, 54]. The increase in activity may be explained by a positive feedback reaction. Because both acid and alkaline phosphatases were suppressed, it was clear that phosphatases were not involved in the detoxification of these lectins in *B. cucurbitae* and that lectin may be interfering with these enzymes' synthesis-related feedback mechanisms.

Thrombolytic activity

Using the technique created by Prasad et al. [55] and streptokinase as a positive control, Sharmin et al. [56] assessed the thrombolytic activity of *C. bicolor*. *C. bicolor*'s chloroform-soluble fraction demonstrated 37.93±0.91% clot lysis compared to conventional streptokinase's 66.77% clot lysis. Therefore, this portion of *C. bicolor* had mild thrombolytic activity.

Toxicity

The use of herbal medicinal plants for therapeutic purposes has been widespread since antiquity and they are a vital part of plant biodiversity. Studies were done to determine any potential pathogenic consequences of sub-acute exposure to the methanol extract of *C. bicolor* on the experimental Wistar rats' hepatic histomorphology [57]. The results showed that experimental rats' body and hepatic tissue weights were significantly ($p<0.05$) reduced when exposed to a methanol extract of *C. bicolor*. The hepatic parenchyma of experimental rats exposed to the methanol extract of *C. bicolor* also showed additional notable histological alterations. Therefore, sub-acute exposure to *C. bicolor* methanol extract results in dose-independent hepatopathy in experimental mice as shown by substantial histological alterations in the animals' hepatic parenchyma.

Based on the deadly reactions of the lymphocytes that were initially cultured, Tosoc et al. also assessed the cytotoxic effects of the *C. bicolor* leaf extracts (100%, 75%, 50%, and 25%) for a period of 24 hours of exposure time. The methanolic extracts of *C. bicolor* showed notable cytotoxic effects, but only at concentrations of 75 and 100%. This indicates that the extract's constituents can only potentially cause cytotoxicity at higher doses. In order to prevent its associated hepatic tissue diseases, there is therefore need for its therapeutic use at low doses.

Conclusion

Caladium bicolor has been used for many years in traditional medicine to treat wounds. Numerous biological activities that are also consistent with their ethnomedicinal usage have been uncovered by studies. These several studies on *Caladium bicolor* paint a picture of a plant with many intriguing potentials. There has been extensive research on the antimicrobial and antioxidant activity, but there are other less putative effects, particularly in the treatment of wounds and inflammation as well as its vermifugal and purgatorial use, that have not been investigated. As a result, more studies are required in order to uncover its therapeutic benefits.

Contribution of authors

Not Applicable

Acknowledgments

We are grateful to Dr. (Mrs.) Toyin Saliu of the Department of Chemical Sciences, Adekunle Ajasin University, Akungba-akoko, Ondo State, Nigeria, for her contributions in terms of guidance and instructions.

Conflict of Interest

We confirm that there are no conflicts of interest associated with this publication and there have been no significant financial support for this work that could have influenced its outcome.

Funding

This work did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

Data availability

The original data presented in this study are included in the article. Further inquiries can be directed to the corresponding author(s).

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