Traditional uses, phytochemistry and pharmacology of Commelina diffusa Burm: An updated systematic review

Md. Mizanur Rahman, Md. Abdul Mannan, Razia Sultana Nijhu and Ambia Khatun

Abstract
The goal of this research is to compile information on Commelina diffusa's traditional applications, phytochemistry, and pharmacological activity. Scientific databases such as PubMed, Google, Google Scholar, and Research gate were searched using certain keywords. It's been used for centuries to treat urinary tract infections, swellings, inflammation, diarrhoea, hemorrhoids, conjunctivitis, and ophthalma. Alkaloids, flavonoids, saponins, tannins, cardiac glycosides, terpenoids, and steroids were discovered by phytochemical analysis. The existence of 21 phytochemical components was confirmed by GC-MS spectrum profiles, the majority of which were sterols, terpenoids, and alkanes. Commelina diffusa contains anti-inflammatory, antioxidant, antibacterial, and anti-fungal, nephro-protective, hepatoprotective, diuretic and CNS depressant properties, according to scientific evidence. Toxicologically, there was no evidence of toxicity. More research is needed to determine the processes that mediate the plant's bioactivities in connection to therapeutic purposes, as well as to look into any potential toxicity in preparation for future clinical trials.

Keywords: Commelina diffusa, traditional uses, phytochemistry, pharmacology

1. Introduction
Due to the emergence of hazardous side effects of chemical pharmaceuticals and uncontrollable hazards of biological agents, tremendous efforts have been made to investigate reliable alternative therapies and medicinal natural products, especially those derived from plants, as public health awareness has increased. A botanical (plant-based) natural product is a substance made from a number of natural sources that might be a complicated mixture extracted from raw material or a single ingredient \[1\]. Medicinal plants have a significant role in primary health care and as a source of active principles in this regard. As a result, they are useful instruments for finding new medications that are well tolerated. Commelina diffusa, often known as a climbing or spreading dayflower, is a member of the Commelinaceae family. The Commelinaceae are a pantropical herbaceous plant family. There are 170 species of Commelina in the tropics and warm temperate parts of the world, and 50 species of Murdannia in the tropics and warm temperate parts of the world, with Tropical Asia having the most diversity \[2\]. It is found in Bangladesh in 10 taxa and 27 species \[3\]. Commelina diffusa (Bengali name: Manaina), a medicinal herb found in tropical and subtropical places around the world, belongs to the Commelinaceae family. This medicinal herb has long been used to treat a variety of ailments \[4\].

This review provided comprehensive and up-to-date information on Commelina diffusa's botanic characterization, distribution, traditional uses, phytochemistry, pharmacology and toxicological activities in order to investigate the medicinal plants' scientific ability and future potential applications.

2. Taxonomical Classification

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
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<tbody>
<tr>
<td>Phylum</td>
<td>Spermatophyta</td>
</tr>
<tr>
<td>Subphylum</td>
<td>Angiospermae</td>
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<tr>
<td>Class</td>
<td>Monocotyledona</td>
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<tr>
<td>Order</td>
<td>Commelinaceae</td>
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<tr>
<td>Family</td>
<td>Commelinaceae</td>
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<tr>
<td>Genus</td>
<td>Commelina</td>
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<tr>
<td>Species</td>
<td>Commelina diffusa Burm.</td>
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</tbody>
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Corresponding Author:
Md. Abdul Mannan
Department of Pharmacy,
Stamford University
Bangladesh, 51, Siddeswari
Road, Dhaka-1217, Bangladesh

4. Vernacular Names

English: Climbing dayflower, Creeping-spiderwort, Dayflower, Spreading dayflower, Wandering Jew, French weed, Pond grass, Water grass
Spanish: Babosilla, Canutillo, Tripa de pollo
French: Curage, Herbe de l’eau
Bangladesh: Manaina
Cuba: Canutillo
Indonesia: Brangbangan
Japan: Shimatsuyukusa
Philippines: Alibangon
Thailand: Phak-prap [5].

5. Description

Commelina diffusa is an annual or perennial herb with creeping stems climbing above and branching below that is smooth and sparingly hairy. It quickly establishes roots at nodes and reproduces both vegetatively and by seeds. In temperate climates, the weed is always an annual, whereas in tropical and subtropical climates, it is either an annual or a perennial, depending on moisture availability [5]. The long, open spathe with a sharp apex, the lanceolate to broadly lanceolate leaves, and seeds that are coarsely reticulated and ridged on one side distinguish it from other species; it is not geocarpic. The stem can reach a length of up to 100 cm. The leaves are 4-6 cm long, lanceolate to broadly lanceolate, and eventually become acute to acuminate. The flower (spathe) is surrounded by bracts that are broad, rounded, or shallow heart-shaped at the base and gradually taper above to a relatively acute apex 2-3 cm long, 1.5-2 cm wide when opened. The margins of the leaves have hairs on them. Flowers are actinomorphic, with three fertile stamens and two (sometimes three) sterile stamens that open only in the morning (staminodes). There are three petals that are unattached. The fruit is a three-celled capsule that is 4-5 mm long and contains five seeds. Seeds are 2-3 mm long, dark brown, reticulate-ribbed, ridged on one side, and delicately reticulated [5].

Table 1: Plant description of Commelina diffusa Burm.

<table>
<thead>
<tr>
<th>Part of plant</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stem</td>
<td>Stems are up to 1 meter long, thick, cylindrical, and glabrous.</td>
</tr>
<tr>
<td>Leaves</td>
<td>The leaves are glabrous, oblong to lanceolate in shape, bright green in color, and 2 to 5 cm long and 0.5 to 2 cm wide.</td>
</tr>
<tr>
<td>Fruits</td>
<td>A three-celled capsule-like structure measuring 4 to 5 mm in length.</td>
</tr>
</tbody>
</table>
6. Geographic Range

6.1. Distribution: Commelina diffusa can be found in the tropics of America, Africa, Asia, and the Pacific, as well as in the subtropics of the United States, South America, Australia, and the South Asian Islands [5].

6.2. Habitat

Commelina diffusa is a pantropical (a lesser degree subtropical) weed that thrives in open, damp environments, such as rice fields. It can resist wet circumstances and flooding for a short period of time. Commelina diffusa is a weed that can be found on cultivated land, field boundaries, moist grazing lands, roadside ditches, gardens, and waste areas [5].

6.3. Growth Stages

Seedling stage, Vegetative growing stage [5].

6.4. Biology and Ecology

Commelina diffusa is an annual plant in temperate areas and a perennial plant in tropical and subtropical lowlands [5]. The weed may be practically subaquatic when growing on rice and other lowland crops. Commelina diffusa thrives on cultivated regions, roadside ditches, pastures, and wastelands, and can endure flooding. Commelina diffusa is mostly an issue in immature crops during the first 2-5 weeks, but because of its sprawling behavior, it may even be a problem in older crops [6]. Seedlings of Commelina diffusa began to emerge at temperatures below 10 °C and attained a peak emergence temperature of 10-15 °C. When it infests crops, the weed's pace of growth and sprawling leads to quick establishment. In general, the species is tenacious [7].

6.5. Natural Enemies

Natural enemies of Commelina diffusa have been discovered to be Puccinia spp. and Kordyana celebensis [5].

6.6. Impact

In Mexico and Hawaii, Commelina diffusa is a major weed of bananas; in Mexico, it is a weed of beans, oranges, lemons, grapes, apricots, coffee, and cotton; in Hawaii, it is a weed of papaya; in Puerto Rico, it is a weed of sugarcane; and in Thailand, it is a weed of sorghum. Maize and vegetables in Mexico; bananas, papayas, and pineapples in the Philippines; rice in Colombia; sugarcane in Mexico and Trinidad; taro and pastures in Hawaii and coffee in Costa Rica [5]. Commelina diffusa is a major weed of soyabeans in various states in the United States [8-10]. In Central America, Commelina diffusa is also found in maize, rice in Mexico, wheat in Costa Rica and potatoes in Guatemala [11]. Commelina diffusa is a weed that has been noted as a problem in Japanese forest nurseries and citrus plantations [12, 13]. In Russia, Commelina diffusa is a significant weed of wheat, oats, barley, and soyabeans. In Cameroon's cocoa farms, Commelina diffusa is tough to manage [14]. Commelina diffusa is considered one of the most important weeds in rice production in Texas, where it fights fiercely for nutrients and light [15]. Commelina diffusa was discovered to be infesting 55 percent of Texas' rice fields and growing at a rate of 10% each year. Cuscuta filiformis and Commelina sandwichiana, as well as the root-knot nematode Meloidogyne incognita, have alternate hosts in Commelina diffusa [16]. In Brazil, a link was discovered between Commelina diffusa development and four different fungal species [17].

6.7. Similarities to Other Species

There are several other weedy Commelina species that can be confused with Commelina diffusa, but the following characteristics can be used to distinguish it from the majority of them: all three petals are blue, leaves are narrowly elliptical (length 3-4 times width), spathe is elongated and open, seeds are shallowly reticulated, and there are no stolons. Commelina benghalensis, the most frequent other species, has a triangular pocket formed by the spathe being shut along two corners; it also has wider leaves (length 2-3 times width), stolons with subterranean flowers, and leaf sheaths with reddish-brown-tipped hairs. Commelina forskalaei possesses stolons, rough seeds, a sealed spathe, and wavy-edged leaves [18, 5, 19]. Commelina sikkimensis and Commelina caroliniana, two additional South Asian species, are quite similar to Commelina diffusa, with the exception of the seeds, which are severely pitted in Commelina sikkimensis and smooth in Commelina caroliniana. Commelina communis, which is widely distributed in North America and other parts of the world, and Commelina latifolia, which is prevalent in Ethiopia, each have the lower petal white or very pale, not blue [20].

7. Traditional Uses

For millennia, Commelina diffusa has been applied as a medicinal herb. The use of Commelina diffusa leaves to cure edema was a common medical practice in ancient China.
Urinary tract infections, swellings, inflammation, diarrhoea, hemorrhoids, enteritis, eye irritation, conjunctivitis, and ophthalmia are all common uses. The stem juice is used to treat laryngitis and sore throats acute tonsillitis, pharyngitis, otitis media, and nose bleeding. Abscess, boils, fever, malaria, insect, snake, bug bites, rheumatoid arthritises, mumps, gonorrhea, common cold, cough, coughing up blood, influenza, bladder infection, and edema are among conditions that the herb is used for topically or orally. The plant components are utilized in dermatitis and burns all across Latin America [23]. Hemorrhoids, an irritated uterus, laryngitis, leprosy, malaria, mumps, otitis media, painful menses, pharyngitis, rheumatoid arthritises, sore throats, snake bites, tonsillitis, and tumors are all treated with it in Nepal. The plant is used as a refrigerant and tonic in Egypt to heal stomach and groin ailments [22]. The herb is used as a tea to prevent influenza and in therapeutic baths by Caribbean Indians. It is used to treat conjunctivitis, dermatitis, and dysmenorrhea in Mexico. It's used to treat enteritis, gonorrhea, and infertility in Paraguay. It's utilized for renal problems, leucorrhrea, malaria, neurological illnesses, postpartum pain, TB, tumors, and venereal disorders in the Dominican Republic, Haiti, and South America. In Ecuador and Peru, the small blue blooms are cooked to form a headache-relieving tea [23]. It's used as a de purative, bladder infection treatment, and cooling medicinal infusions in Trinidad. It is used to treat jaundice in young children in the Windward Islands and Cuba [24]. Previous research has shown that Commelina diffusa has antibacterial action against a variety of Gram positive and Gram-negative bacteria, as well as fungi [25]. The extract's anti-inflammatory properties were investigated utilizing a chick carrageenainduced foot oedema model [26]. It also showed that MRC-5 cells are protected from reactive oxygen species oxidation [27]. According to another study, the extract is useful in the treatment of cancer [28], antidiabetes [29], leprosy, and nervous system related disorders [30].

8. Phytochemical Constituents
8.1. Chemistry of Commelina diffusa
Chemical constituents: anthocyanins, dammaranetriterpenes, stigmasterol, n-octacosanol, n-triacontanol, β-sitosterol, alkanols, n-dotriacontanol, sterols, campesterol. Alkaloids, flavonoids, saponins, tannins, cardiac glycosides, terpenoids, and steroids were found in the methanolic extract of Commelina diffusa, according to phytochemical analysis [31]. Commelina diffusa extracts exposed the presence of various phytochemical element such as alkaloids, phenolic compounds, tannins, steroids, flavonoids, proteins and physteroi ds. Methanol extracts demonstrated the presence of these substances with varied degrees of alkaloids, phenolic compounds, tannins, saponins, and proteins across the three extracts. The other two extracts, chloroform and acetone, have the greatest levels of flavonoids, alkaloids, and phenolic chemicals [32, 33].

The GC-MS study of the methanolic extract of Commelina diffusa resulted in the discovery of a number of chemicals. These chemicals were detected using mass spectrometry in conjunction with gas chromatography. The existence of 21 phytochemical components from Commelina diffusa was confirmed by the GC-MS spectrum profile. The results revealed that 1-Phenyl-2-butane (1.62%), Phenol, 4-ethyl, acetate (17.90%), 2-Methoxy-4-vinylphenol (0.26%). Piperidine-1-yl-acetic acid, hydrazide (0.33%), 2,6-Difluorobenzoic acid, 3,5-difluorophenyl ester (0.71%), 2-Cyclopenten-1-one, 4-hydroxy-3-methyl-2-(2-propenyl)- (1.12%), Cyclopentaneundecanoic acid (2.60%), 1-{2-[3-(2-Acetylloxiran-2-yl)-1,1-dimethylproply]cycloprop-2 en (0.77%), Cyclopentaneundecanoic acid (0.99%), Di-nocetylphthalate (1.37%), 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (1.31%), Cyclopropaneundecanoic acid, 2-octyl-, methyl ester (1.40%), n-Hexadecanoic acid (1.93%), 9,12-Octadecadienoic acid, methyl ester (10.67%), Phytol (0.91%), Methyl stearate (1.00%), 9,12,15-Octadecatrienoic acid, (Z.Z.Z)- (9.59%), Octadecanoic acid (41.49%), Hexadecanoic acid, 15-methyl-, methyl ester (0.02%), Carbonic acid, 2-dimethylaminoethyl propyl ester (0.15%), 9-(2’-2’ Dimethylpropanoiloxydrazono)-3,6-dichloro-2,7-bis- [2-d (0.61%), 9,12,15-Octadecatrienoic acid, 2,3-dihydroxypropyl ester, (Z.Z.Z.) (1.00%). The other ingredients were present in trace amounts. The most prevailing major components were Phenol, 4-ethenyl-, acetate (17.90%), n-Hexadecanoic acid (1.93%), 9,12-Octadecadienoic acid, methyl ester (10.67%), Phytol (0.91%), Methyl stearate (1.00%), 9,12,15-Octadecatrienoic acid, (Z.Z.Z)- (9.59%), Octadecanoic acid (41.49%) etc., other major and minor compounds were also present. The GC-MS approach has been used to analyze many phytoconstituents in various regions of the world. Among the 21 phytochemicals studied, 10 have been found to have biological action [34].

9. Pharmacological Activities
9.1. Anti-inflammatory Activity
For many years, the leaves of Commelina diffusa have been used to treat inflammatory illnesses. It's also been used to treat wounds as a healing agent [35]. This plant has an anti-inflammatory impact that is 1.1 times lower than dicolofenac and dexamethasone, according to a research [36]. In vitro research done before to this study revealed that the plant's leaves are unable to suppress NF. -Kb. This study was proved otherwise by another in-vivo study done later [37].

9.2. Antioxidant Activity
The antioxidant activities of an extract from the leaves of the plant Commelina diffusa were investigated. Because the antioxidant effects of medicinal plants must be investigated using many methods, numerous investigations were conducted before a result could be reached [38]. This plant's leaf extract has a high phenolic content of 193.7 mg/g of tannic acid per mg of extract, which might be related to the high phenolic content. Secondary metabolites such as reducing sugar, alkaloids, phytostersols, flavonoids, and terpenoids are also responsible for the antioxidant and anti-inflammatory activities of the plant [36]. This plant's anti-inflammatory benefits are aided by its antioxidant properties [39].

9.3. Antibacterial Activity
The antibacterial testing was carried out using the crude extract of the plant Commelina diffusa. When compared to water, the aqueous methanolic crude extract of the plant's leaves is a superior extraction solvent [40]. The extract was dried in the oven at 40 °C. It inhibited Staphylococcus aureus with a zone of inhibition of 13 mm, which is better than other antibiotics employed as positive controls in the study [41].

9.4. Anti-Fungal Activity
The anti-fungal test was carried out using a methanol extract of the leaves of the medicinal plant Commelina diffusa. Dry methods, such as oven drying at 40 °C or drying in the shade, ...
are preferable drying procedures because they exhibit a defined zone of inhibition. The leaves of this plant have antifungal action, according to the study, and can be utilized to treat a variety of skin conditions.

9.5. Nephro-Protective Activity
An experiment was conducted using ethanolic leaf extract of Commelina diffusa at 200 and 400 mg/kg, which was given to albino rats for 20 days while they were also given doxorubicin. In the study, the rats that were pretreated with the extract had normal kidney stroma with Bowman's capsule, glomerulus, and renal tubules, indicating that the extract had a beneficial nephroprotective activity of the plant.

9.6. Hepato-Protective Activity
Hepatoprotective properties have been identified for Commelina diffusa. The liver secretions of albino rats treated with doxorubicin were shown to exhibit neutrophil infiltration and patchy inflammation, according to studies. Rats pretreated with 200 and 400 mg/kg of the plant's leaf extract exhibited better cell integrity, as seen by normal hepatic stroma with hepatocytes, sinusoid and central vein.

9.7. Diuretic Activity
This work provides a mathematical foundation to explain the traditional folkloric usage of Commelina diffusa as a diuretic, which may function by lowering sodium ion reabsorption in the kidneys, in addition to its potassium sparing function and low toxicity. This effective diuretic feature supports its use among Cameroonians and central vein.

9.8. Central Nervous System (CNS) Depressant Activity
The methanolic extract of Commelina diffusa was tested in mouse models using standard depression models to identify the plant's CNS depressive effects. The mice models were given 50, 100, and 200 mg/kg plant extracts orally, as well as distilled water (0.1 mL/mouse, p.o.). Diazepam (1 mg/kg) was regarded as a typical medication. In comparison to the control group, the plant extract reduced locomotor activity in the open field and hole-cross tests, but increased immobility time in forced swimming and tail suspension tests. In addition, compared to the control group, it increased the amount of time spent sleeping. In mouse models, the study demonstrates the possibilities of CNS depressants.

9.9. Food value
The food value of Commelina diffusa aqueous leaf extracts was investigated. The results reveal that moisture (83.36 percent), carbohydrate (63.2 percent), vitamin C (44.8 mg/100g dry weight), vitamin B3 (63.18 mg/100g), and vitamin B2 (8.30 mg/100g) were the primary components of Commelina diffusa's proximate and vitamin compositions, respectively. The mineral contents of the defatted leaf extracts were found to be Na (69.32mg/100g), Ca (232.00mg/100g) and Mg (84.28mg/100g). The leaf's proximate, vitamin, and mineral compositions imply that the leaves can be included into human and animal diets to satisfy their required daily intakes of vitamins C, B3, and B2, as well as other macro- and micronutrients. The presence of flavonoids and vitamin C in leaf extracts indicate that these leafy vegetables may have anti-oxidant properties.

10. Acute toxicity
The brine shrimp lethality bioassay has been demonstrated to be a safe, practical, and cost-effective approach for determining the bioactivities of synthetic and plant compounds. This approach was used to verify the ethnomedical claim that Commelina diffusa can help with cancer therapy. The crude extract has an LC50 value of 3.79 g/mL, as determined by regression analysis after 24 hours. When compared to the conventional vincristine sulfate (0.81 g/ml), the crude extract was shown to be fatal, indicating its potential therapeutic value against tumor cells, as well as insecticides and herbicides.

11. Conclusions
Despite the fact that Commelina diffusa plants have a long history of use, pharmacological research has been lacking. As a result, additional secondary metabolites must be investigated in order to conduct more in-depth pharmacological research. More research is needed to determine the processes that mediate the plant's bioactivities in connection to therapeutic purposes, as well as to look into any potential toxicity in preparation for future clinical trials.

12. Conflict of interest statement
We declare that we have no conflict of interest.

13. Acknowledgements
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14. References