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EXPLORING *MICROCOS PANICULATA*: PHYTOCHEMICALS, MEDICINAL VALUE, PHARMACOLOGICAL ACTIVITIES – A REVIEW ARTICLE

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ABSTRACT: *Microcos paniculata* (*Grewia Microcos*) is widely distributed throughout the India which belongs to the family Malvaceae. It is widely used for the treatment of various ailments including colds, diarrhoea, hepatitis, heat stroke, dyspepsia, wound healing, fever and as an insecticide. This review provides a comprehensive overview of *Microcos paniculata*'s phytoconstituents, traditional uses, and various activities present on the various parts of the plant. The primary photochemical evaluation of crude methanolic extract of stem bark of M. paniculata revealed the presence of flavonoids, diterpenes, alkaloids, saponin, tannin and phenols. This plant has anti diarrheal, analgesic, membrane stabilizing, cytotoxic, antioxidant, antimicrobial, antifungal and thrombolytic activities. Traditionally, *Microcos paniculata* has been used to treat heat stroke, hepatitis, diarrhoea, wounds, cold, and fever.

Keywords: *Microcos paniculata*, Phytoconstituents, Pharmacological activity, Pharmacognostical study.

I INTRODUCTION

Plants are integral to many traditional medicine systems and are a significant source of biologically active compounds. These compounds can lead to the development of innovative drugs. The Grewia genus, part of the Malvaceae family, is the most diverse and expansive flowering genus, predominantly consisting of shrubs and small trees. These plants are widespread across tropical and subtropical regions globally, particularly in Asia, Africa, Saudi Arabia, Yemen, and Australia. In Asia, they are found in countries such as India, Sri Lanka, and Pakistan, where they are commonly cultivated for their fruits and timber. Each species within this genus is utilized in traditional herbal medicine for treating various ailments[1].

Microcos paniculata is a herb or small tree belonging to Tiliaceae family. It is widely distributed in Bangladesh, India, Sri Lanka, China, Cambodia, Myanmar, Thailand, Vietnam, Indonesia and Malaysia. In the local area, different

portions of the plant are used to cure hepatitis, fever, diarrhoea, dyspepsia, heatstroke, colds, wound healing, and insects. Numerous activities of *Microcos paniculata* have been discovered, such as neuropharmacological, larvicidal, insecticidal, ability to scavenge free radicals, antimicrobial, brine shrimp lethality, antidiarrheal, analgesic, anti-inflammatory, antipyretic, inhibition of α-glucosidase, cytotoxic and nicotinic receptor antagonist activities as well as preventative effects in coronary heart disease and angina pectoris. Many phytochemical investigations on *Microcos paniculata* have been carried out, which reveal the presence of bioactive primary and secondary metabolites including flavonoids, alkaloids, triterpenoids and organic acids, phenol, carbohydrate, steroid, glycoside etc. These current research findings will be useful in comprehending the biological activities of this therapeutic plant and will also be relevant in the future developmen t of novel herbal products and functional foods.[1]

It is sometimes added to Chinese herbal tea,[3] having a mildly sour taste. In traditional Chinese medicine the plant is believed to help the digestive system, and it is also used for other health problems including colds, hepatitis, diarrhea, heat stroke, and dyspepsia.[4]

Fig 1 : *Microcos paniculata* plant with fruit

In this review, we aim to consolidate the conventional applications, botanical characteristics, phytochemical composition, pharmacological effects, quality assessment, and toxicity of extracts from the leaves, fruits, barks, and roots of *Microcos paniculata*, as documented over the years. These recent research findings will aid in comprehending the biological functions of this medicinal plant and can also be utilized in the creation of new herbal products and functional foods in the future.

PLANT DESCRIPTION

A small tree or shrub with branches, which are almost glabrous. The leaves are alternate, with petioles and stipules; the stipules are either falcate or linear to lanceolate, or deeply cut, measuring 0.5–0.8 cm long; the petiole ranges from 0.2–0.7 cm in length, is pulvinate, and has sparse puberulence, being stellately puberulous near the base of the lamina; the lamina is either ovate, oblong, or lanceolate, sized 5–25 × 2.5–7(–10) cm, with a rounded or heart-shaped base, faintly serrated or crinkled margins, and a long acuminate or caudate tip, having a leathery texture, with three

nerves originating from the base, five to six pairs of lateral nerves that are prominent on the underside, and exhibiting a transverse, parallel arrangement.

The inflorescences are terminal or consist of terminal and axillary panicles resembling triflorous cyme-like units, measuring 10–15 cm in length, and are minutely covered in stellate hairs; these cymes are surrounded by four to six deeply cut involucre bracts. The peduncle is approximately 0.5 cm long and has dense hairs; the bracts are also about 0.5 cm long and have sparse pubescent; the bracteoles are narrowly lanceolate and exceed the length of the peduncle, measuring around 0.7 cm long. The flowers are on minute pedicels, roughly 0.2 cm long, also puberulous. The sepals are spatulate, measuring about 0.8 × 0.3 cm, with a sinuate margin and an acute apex, sparsely covered in hairs on the outside, and glabrous on the inside, displaying a dull yellow color. The petals are ovate-oblong, around 0.3 × 0.1 cm, truncate at the base, sinuate at the apex, and are yellow–whitish with glandular and tomentose texture in the lower half. The androgynophore is turbinate, measuring approximately 0.1 cm long, with the upper part absent.

The stamens are numerous, with filaments of unequal lengths ranging from 0.2 to 0.4 cm, and the base has sparse hairiness; the anthers are yellow. The ovary is round, approximately 0.1 cm in diameter, smooth, containing three cells with 1 to 2 ovules in each; the style is about 0.4 cm long, tapering gradually towards the tip, and the stigma comprises three plano-convex arms. The fruits are either globose or obovoid, smooth, measuring between 0.8 and 1 cm in diameter, turning black when mature, with a fibrous endocarp; there are 3 to 6 pyrenes that are ovoid or trapezoidal and are separate. The periods of flowering and fruiting occur from May to February[1].

TAXONOMICAL CLASSIFICATION

Table 1: Taxonomical classification of *Microcos paniculata*

Kingdom:	Plantae
Phylum:	Streptophyta
Class:	Equisetopsida
Subclass:	Magnoliidae
Order:	Malvales
Family:	Tiliaceae
Genus:	Microcos
Species:	*Microcos paniculata*

VERNACULAR NAMES

Table 2: Vernacular names of *Microcos paniculata*

English	Elm-leaf grewia
Hindi	Shiral
Marathi	Shirali
Tamil:	Visalam
Kannada:	Biliyabhhrangu

2 METHODOLOGY

PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITY

Aziz MA (2015) carried out a study examining the methanolic extract of *Microcos paniculata* bark (BME) and fruit (FME), qualitatively analyzing the phytochemical constituents in the extracts, as well as assessing their anti-inflammatory, analgesic, and antipyretic effects. The extracts from *Microcos paniculata* were found to contain carbohydrates, alkaloids, saponins, tannins, flavonoids, and triterpenoids. All extracts showed significant proteinase-inhibitory activity ($P<0.05$ when compared to the aspirin group), with the BME extract exhibiting the most substantial effect, achieving a 75.94% proteinase inhibition and an IC50 of 61.31 µg/mL. Administered at doses of 200 and 400 mg/kg body weight, each extract significantly reduced ear edema and granuloma formation ($P<0.05$ in comparison to the control). These extracts also notably decreased paw licking and abdominal writhing in mice ($P<0.05$, when compared to the control). In addition, BME at 400 mg/kg and FME at both 200 and 400 mg/kg demonstrated significant analgesic effects ($P<0.05$, in comparison to the control) at 60 minutes in the tail immersion test. Moreover, BME at 200 and 400 mg/kg along with FME at 400 mg/kg displayed considerable antipyretic properties after treatment ($P<0.05$, relative to the control). The findings of their study suggested that M. paniculata might be a source of plant compounds possessing anti-inflammatory, analgesic, and antipyretic properties[2].

Fan H (2010) et al have investigated the free-radical-scavenging properties of different solvent extracts from *Microcos paniculata* using in vitro model systems, including 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulfonate) (ABTS), and Co (II) EDTA-induced luminol chemiluminescence via flow injection. The findings indicated that across all three systems, the ethyl acetate (EtOAc) extract exhibited the most significant free-radical-scavenging activity in comparison to the other three extracts (n-BuOH, water, and petroleum ether). The chromatographic separation of the EtOAc extract, guided by a free-radical-scavenging assay, employed both normal-phase and reverse-phase silica gel column chromatography, leading to the identification of five compounds: a novel triterpene named methyl 3β -O-p -hydroxy- E-cinnamoyloxy-2α,23- dihydroxyolean- 12-en- 28-oate (1), with its spectral data reported for the first time, alongside four previously known compounds: epicatechin (2), 3-trans-feruloyl maslinic acid (3), maslinic acid (4), and sucrose (5). All these compounds were isolated from *Microcos paniculata* for the first time. Identification of the compounds was achieved through spectroscopic methods.

Notably, compound 2 exhibited a significant free-radical-scavenging activity comparable to that of the standard antioxidant ascorbic acid (VC), suggesting it may serve as a valuable natural antioxidant[3].

Sarker MA et al., 2016 conducted the phytochemical screening on the methanolic extract of steam bark of *M. paniculata* revealed the presence of flavonoids, diterpenes, alkaloids, saponin, tannin and phenols. [1] They have also investigated the in-vitro thrombolytic and membrane stabilizing activity of the methanolic extract. The in-vivo antidiarrheal and analgesic activities were also studied according to the method of castor oil and acetic acid induce writhing respectively. Phytochemical study revealed the presence of flavonoids, diterpenes, alkaloids, saponin, tannin and phenols. During the estimation of anti-diarrheal activity of *Microcos paniculata*, the selected plant extract showed most significant inhibition of 63.30% and 56.70% diarrhoea at 400 mg/kg and 200 mg/kg, respectively. Analgesic activity studies showed pain inhibition of 41.36% and 32.0% at 500 mg/kg and 250 mg/kg, respectively in contrast to standard drug (Ibuprofen) showed 46.64% inhibition of pain. The membrane stabilizing study revealed that the inhibition of haemolysis increases respectively when the dose increased. Similar result was found in thrombolytic activity which means that when the dose increased, the thrombolytic activity of the plant extract got increased[4].

Rahman MA (2011) investigated the possible analgesic and cytotoxic activities in animal models using the ethanolic extract of dried leaves of *Microcos paniculata* L. Their study revealed that the extract has significant writhing inhibition in acetic acid induced writhing in mice at the oral dose of 250 and 500 mg/kg of body weight comparable to the standard drug diclofenac sodium at the dose of 25 mg/kg of body weight. The crude ethanolic extract of the selected plant also produced the most prominent cytotoxic activity against brine shrimp (LC50 = 60 µg/ml and LC90 = 120 µg/ml)[5].

Li K et al (2018) used the experimental model of lipopolysaccharide (LPS)-induced ALI in BALB/c mice inorder to evaluate the therapeutic potential of purified apigenin C-glycosides (ACGs). The results of their study showed that M. paniculata ACGs (apigenin C-glycosides) inhibited lung inflammation in animals undergoing ALI. The protective effects of ACGs were assessed by the determination of cytokine levels and in situ analysis of lung inflammation. ACGs were found to reduce the pulmonary edema and microvascular permeability, demonstrating a dose-dependent down-regulation of LPS-induced TNF-α, IL-6 and IL-1β expression in lung tissue and bronchoalveolar lavage fluid, along with reduced apoptosis. Furthermore, the metabolic profiling of mice serum, along with subsequent Ingenuity Pathway Analysis, indicated that ACGs stimulated protective protein networks and pathways involving inflammatory regulators and factors related to apoptosis, such as JNK, ERK1/2, and caspase-3/7. This suggested that the effects mediated by ACGs are linked to MAPKs and mitochondrial apoptosis pathways. These findings were further corroborated by assessing protein expression, which revealed that ACGs inhibited the LPS-induced phosphorylation of p38, ERK1/2, and JNK within the MAPK signaling pathway, while significantly increasing Bcl-2 expression and decreasing the levels of Bax and cleaved caspase-3. Notably, ACGs also suppressed the LPS-induced upregulation of TLR4 and TRPC6 observed during acute lung injury (ALI). Their investigation showed for the first time that ACGs inhibit acute inflammation and apoptosis by suppressing activation of TLR4/TRPC6 signalling pathway in a murine model of ALI[6].

Aziz MA (2014) examined the antibacterial properties, toxicity levels, and larvicidal activities against 4th instar Culex quinquefasciatus mosquito larvae of M. paniculata fruit extracts utilizing various organic and inorganic solvents (methanol, chloroform, and water). The antibacterial, toxicity, and larvicidal effects were assessed through agar disc diffusion, brine shrimp lethality bioassay (BSLB), and a slightly modified standard WHO protocol. The susceptibility of the microorganisms to the plant extracts was evaluated in comparison to the standard antibiotic flucloxacillin. The methanol extract of the fruit (FME) displayed a broad range of antibacterial effectiveness, notably more than the other extracts (Fruit chloroform extract - FCE and Fruit water extract - FWE), especially against gram-negative bacteria, with Proteus mirabilis exhibiting the highest susceptibility (zone of inhibition 28 mm). Additionally, the FME demonstrated the highest toxicity to brine shrimp nauplii, showing an LC50 value of 52.7 µg/ml, which suggests that there may be harmful compounds present in this plant. The mortality of 4th instar Culex quinquefasciatus larvae was noted following a 24-hour exposure period. Both FME and FCE displayed significant larvicidal properties, with LC50 values of 342.1 µg/ml and 441.7 µg/ml, respectively. Overall, these findings indicate that the organic fractions, FME and FCE, could serve as potential sources of antibacterial agents due to their toxic and larvicidal capabilities[7].

Aziz MA et al (2018) conducted a study on the antioxidant and antidiarrheal properties of the methanolic extract from the roots of M. paniculata (RME). They assessed the antioxidant and antidiarrheal effects of RME through various methods, including total antioxidant capacity (TAC), DPPH free radical scavenging assay (DPPHFRSA), nitric oxide scavenging capacity assay (NOSCA), lipid peroxidation measured by the thiobarbituric acid assay (LPTAA), reducing capacity evaluation (RCA), and cupric reducing antioxidant capacity (CRAC), alongside castor oil and $MgSO_4$ induced diarrheal tests. The concentrations of total phenols and flavonoids along with TAC were determined to be 182.78 ± 0.12 mg/g RME (expressed as gallic acid equivalent), 43.5 ± 0.32 mg/g RME (as quercetin equivalent), and 40.83 ± 0.69 mg/g RME (as ascorbic acid equivalent), respectively. The IC_{50} values for RME in DPPHFRSA, NOSCA, and LPTAA were recorded as 158.47 ± 2.66 µg/mL, 157.91 ± 4.56 µg/mL, and 148.29 ± 6.48 µg/mL, respectively. A concentration-dependent increase in reducing power was observed in both RCA and CRAC. In addition, RME 400 mg/kg resulted in 68.10±16.99 % and 55.83±21.95 % suppression of diarrhoea in the antidiarrheal tests. The findings suggest that M. paniculata may be a valuable source of plant-based compounds exhibiting antioxidant and antidiarrheal effects[8].

Aziz MA et al (2018) conducted another study to assess the antimicrobial properties of methanol, chloroform, and aqueous extracts from the leaves of *Microcos paniculata* against various gram-positive and gram-negative bacteria, including B. subtilis, B. cereus, S. typhi, V. cholerae, P. mirabilis, E. coli, S. aureus, Serratia spp., Erwinia spp., Pseudomonas spp., Salmonella spp., Shigella boydii, and B. megaterium. The in vitro antimicrobial efficacy was evaluated using the agar disc diffusion method. Notably, the plant extracts exhibited the strongest antimicrobial activity against gram-negative bacteria. Among the different extracts, the methanolic extract of *Microcos paniculata* leaves demonstrated the greatest zone of inhibition (27mm) against Salmonella spp[9].

Bandara KP et al (2000) have studied the dichloromethane and methanol extracts of M. paniculata stem bark and showed moribund/toxic and growth-inhibitory effects on the second instar larvae of the mosquito Aedes aegypti.

They have isolated a new alkaloid, N-Methyl-6β-(deca-l′,3′,5′-trienyl)-3β-methoxy-2β-methylpiperidine, from the stem bark of *Microcos paniculata* contained which showed good insecticidal activity against Aedes aegypti second instar larvae[10].

Al-Amin Sarker M et al (2016) conducted a study aimed at assessing the anti-diarrheal, analgesic, membrane stabilizing, and thrombolytic properties of the methanolic extract derived from the stem bark of M. paniculata. The methanolic extract of this part of the plant was prepared and the concentrated extracts were utilized for phytochemical screening through appropriate methods to identify the phytoconstituents. This extract was subsequently employed to explore its in-vitro thrombolytic and membrane stabilizing activities. The antidiarrheal and analgesic effects in vivo were assessed using methodologies involving castor oil and acetic acid-induced writhing, respectively. Results from the phytochemical analysis indicated the presence of flavonoids, diterpenes, alkaloids, saponin, tannin, and phenols. The evaluation of anti-diarrheal activity revealed that the plant extract significantly inhibited diarrhoea by 63.30% and 56.70% at doses of 400 mg/kg and 200 mg/kg, respectively. In pain relief tests, the analgesic effects showed an inhibition of pain at 41.36% and 32.0% for doses of 500 mg/kg and 250 mg/kg, respectively, whereas the standard drug (Ibuprofen) achieved a 46.64% reduction in pain. The study on membrane stabilization demonstrated that hemolysis inhibition progressively increased with higher doses. A similar pattern was observed in the thrombolytic activity, indicating that an increase in dosage corresponded with greater thrombolytic effects of the plant extract [11].
Yuan M et al (2019), in their research examined the anti-inflammatory properties and chemical composition of the total flavone glycosides (MpTFG) fraction. MpTFG (10, 15, 20 μg/mL) was administered to 1 μg/mL LPS-induced RAW 264.7 macrophages in vitro, while MpTFG (10, 20, 40 mg/kg body weight) was used in the xylene-induced ear edema test. The findings indicated that 20 μg/mL of MpTFG significantly reduced pro-inflammatory cytokine levels of IL-6, IL-1β, and TNF-α in the supernatant of LPS-stimulated RAW 264.7 cells, and that 40 mg/kg of MpTFG effectively reduced ear swelling in mice induced by xylene. These results suggest that MpTFG possesses notable anti-inflammatory properties. Furthermore, ten compounds were isolated using macro-porous resin, sephadex LH-20 gel column chromatography, and semi-preparative HPLC in succession. These compounds were identified as vicenin-2 (i), isoschaftoside (ii), schaftoside (iii), vitexin (iv), vicenin-1 (v), isovitexin (vi), isoviolanthin (vii), nicotiflorin (viii), astragalin (ix), and narcissoside (x) through 1H-NMR, 13C-NMR, and HRMS spectral analysis[12].

Moushome RA et (2016) explored the qualitative phytochemical components of hydromethanol (HMPB) and petroleum benzene extracts of *Microcos paniculata* bark (PBMPB), as well as to assess their antinociceptive and antidiarrheal properties. The phytochemical components were identified and the antinociceptive and antidiarrheal effects were assessed using various tests, including Molisch's, Fehling's, Mayer's, Wagner's, Dragendorff's, frothing, FeCl3, alkali, Pew's, and Salkowski's tests, alongside glycoside general tests, Baljet and NH4OH tests, formalin-induced paw licking, acetic acid-induced writhing, tail immersion, hot plate tests, and castor oil and MgSO4 induced diarrhea testing. Findings. The analyses indicated the presence of saponins, flavonoids, and triterpenoids, which significantly ($*P < 0.05$, compared to control) decreased paw licking and abdominal writhing in mice. Thirty minutes post-administration, PBMPB showed a notable increase in latency ($*P < 0.05$, compared to control) in the tail immersion test. In the hot plate test, both HMPB and PBMPB at a dosage of 200 mg/kg exhibited a significant

increase in response latency ($*P < 0.05$, compared to control) 30 minutes after administration. Additionally, both extracts significantly ($*P < 0.05$, compared to control) reduced the percentage of diarrhea in antidiarrheal assessments[13].

Haque MA et al (2017) assessed the potential central nervous system (CNS) depressant and antinociceptive effects of various extracts from *Microcos paniculata* (M. paniculata), namely methanol (MMPS), petroleum ether (PMPS), chloroform (CMPS), dichloromethane (DMPS), and aqueous (AMPS) extracts. The CNS-depressant effects of the different extracts from the M. paniculata stem were evaluated in Swiss albino mice through open field, hole cross, and head dipping tests at doses of 100 and 200 mg/kg. The analgesic properties were measured using acetic acid-induced writhing and hot plate assays at the same dosages. Each extract demonstrated significant CNS depressant and analgesic effects in a dose-dependent manner ($Pb < 0.01$, $Pa < 0.001$). Among the extracts, MMPS exhibited the most substantial CNS depressant effect, with a 93.39% reduction in movement in the open field test, a 78.92% decrease in hole cross activity, and an 86.90% reduction in head dipping at a 200 mg/kg dose. Additionally, DMPS displayed the strongest analgesic effect, achieving a 75.52% reduction in abdominal writhing and a 65.55% increase in paw licking duration at the 200 mg/kg dosage[14].

Aziz MA et al (2018) aimed to explore the lipid peroxidation (LPO) and the protective effects of the methanolic extract of *Microcos paniculata* fruits (FME) against hepatotoxicity induced by CCl4 in rats. The extent of lipid peroxidation in FME was assessed by measuring the levels of thiobarbituric acid reactive substances (TBARS). Subsequently, the hepatoprotective potential of FME was assessed by analyzing changes in serum biochemical markers (SGPT, SGOT, ALP, TP, and TB) and examining the histopathological features in Sprague Dawley rats[15].

Bulbul L et al (2023) assessed the impact of various extracts from M. paniculata (MP) on convulsions and antioxidant activities in mice. Six polyphenolic compounds were detected, with the highest concentrations of epicatechin and quercetin found in MP leaf and stem extracts, quantified at 23.01 and 32.23 mg/100 g of dry MP extract, respectively, through Ultra Performance Liquid Chromatography. Oral administration of MP for seven days at doses of 100, 200, and 400 mg/kg body weight (BW) notably decreased convulsions and lowered mortality rates when compared to the seizure inducer groups. The antioxidant capacities were evaluated using measurements of superoxide dismutase (SOD), catalase (CAT), thiobarbituric acid reactive substances (TBARS), and reduced glutathione (GSH) levels in whole-brain homogenates. The levels of gamma-aminobutyric acid (GABA) significantly increased in the groups treated with leaves and stems, indicating that MP leaves and stems possess strong antioxidant capabilities that may alleviate convulsions by influencing the GABAergic system and enhancing antioxidant activities[16].

Aziz MA et al (2016) assessed the safety of the methanolic extract from the roots of *Microcos paniculata* (RME) as well as the neuropharmacological effects of the methanolic)extracts from M. paniculata fruits (FME), RME, and the whole plant of Richardia scabra (MRS) following OECD guidelines, including tests such as the Y-maze and Elevated plus-maze. No fatalities, signs of toxicity, or noticeable behavioral alterations were observed even at doses up to 4000 mg/kg. The Y-maze test indicated both anti-depressant and depressive effects at doses of FME 200 mg/kg and 400

mg/kg, RME 200 mg/kg and 400 mg/kg, MRS 200 mg/kg and 400 mg/kg. Additionally, results from the Elevated plus-maze test showed that all extracts, including those at doses of 200 mg/kg and 400 mg/kg, exhibited both anxiolytic and depressive effects[17].

Aziz MA et al (2016) investigated the safety profile of water extract of *Microcos paniculata* leaves (LWE) as well as neuropharmacological activity of both LWE and methanolic extract of *Microcos paniculata* fruits (FME) by following OECD guidelines and open field test respectively. In acute oral toxicity study, mortality, sign of any toxicity or behavioural changes were not noticed as the doses increased up to 4000 mg/kg. In open field test, gradual decrease of movement was found by LWE 200 mg/kg. Again, LWE 400 mg/kg exhibited both depressive and antidepressive activities. In addition to, FME 200 mg/kg and 400 mg/kg exhibited fluctuating effects of movement at various observations [18].

Saha S et al (2017) evaluated the phytochemical composition and the oral acute toxicity of the leaves from *Microcos paniculata*. Soxhlet extraction and established methods were employed for the extraction and phytochemical evaluation. The substance was administered orally, with animals monitored through cage-side observations, and their average body weight measured over a period of 14 days. Phytochemical analysis of the ethanolic extract of the leaves identified the presence of alkaloids, carbohydrates, glycosides, tannins, phytosterols, saponins, and flavonoids. The oral acute toxicity test exhibited no significant clinical signs of toxicity or death throughout the 14-day study duration. There were no statistically significant changes in body weights when compared to the control group. The ethanolic extract was determined to be non-toxic up to a dosage of 5000 mg/kg body weight, indicating that the LD50 is above 5000 mg/kg body weight [19].

Haque MA et al (2016) assessed the potential analgesic and central nervous system (CNS) depressant effects of methanol (MMPL), petroleum ether (PMPL), chloroform (CMPL), dichloromethane (DMPL), and aqueous (AMPL) extracts from M. paniculata leaves. The analgesic effect was measured using the acetic acid-induced writhing and hot plate methods at doses of 50 and 100 mg/kg. The CNS depressant effect was evaluated through open field, hole cross, and head deep tests at doses of 100 and 200 mg/kg. All extracts demonstrated significant effects ($Pb < 0.01$, $Pa < 0.001$) on analgesia and CNS depression in a dose-dependent manner. AMPL exhibited the greatest analgesic effect, showing 72.92% inhibition of abdominal writhing and a 33.03% maximal possible effect (MPE) on paw licking time at a dose of 100 mg/kg. In contrast, CMPL displayed the highest CNS depressant effect with 93.80% inhibition in the open field test, 84.63% inhibition in the hole cross test, and 81.54% inhibition (head dipping) in the head deep test at a 200 mg/kg dose. Among the five extracts, AMPL proves to be a strong analgesic, while CMPL acts as a potent CNS depressant [20].

Aziz MA et al (2016) evaluated the safety profile and neuropharmacological effects of the chloroform extract from the barks of *Microcos paniculata* (BCE) was conducted, adhering to OECD guidelines, utilizing the elevated plus-maze and hole cross tests for assessment. No mortality, signs of toxicity, or behavioural changes were observed even at increasing doses up to 4000 mg/kg. In the elevated plus-maze assessment, both depressive and anxiolytic effects

were noted at the dose of BCE 200 mg/kg. Furthermore, the dose of BCE 400 mg/kg demonstrated both depressive and anti-depressive effects. Additionally, both BCE 200 mg/kg and 400 mg/kg led to a gradual reduction in movement; however, BCE 200 mg/kg displayed a significant ($p < 0.05$, vs. control) increase in movement over 180 minutes in the hole cross test. The findings of this study suggest that BCE has the potential to serve as sources of CNS depressant, anti-depressant, and anxiolytic compounds, although further research is necessary to confirm these effects[21].

Wu ZL et al (2022) isolated eight new 2,6-disubstituted piperidin-3-ol alkaloids (**1**–**8**), featuring a C_{10} unsaturated alkyl side chain and the isolated compounds were assessed for their effects on preventing angiogenesis in human umbilical vein endothelial cells (HUVECs). Compound 2 showed a concentration-dependent inhibition of tube formation in HUVECs[22].

Aziz MA et al (2018) assessed the anti-inflammatory and antipyretic properties of the barks of *Microcos paniculata*, both hydro-methanol extract (HMBE) and petroleum-benzene extract (PBBE). The extracts' anti-inflammatory and antipyretic effects were measured using the xylene-induced ear edema test, the cotton pellet-induced granuloma formation test in mice, and the pyrexia induced by Brewer's yeast in mice. In the xylene-induced ear edema test, we found that HMBE at 400 mg/kg body weight demonstrated the highest inhibition of ear edema at 86.07±0.57%, which was statistically significant (*P<0.05 compared to control). Meanwhile, in the cotton pellet-induced granuloma formation test, PBBE at 400 mg/kg body weight exhibited the greatest inhibition of granuloma formation at 40.84±2.23%, which was also significant (*P<0.05 compared to control) [23].

Aziz MA et al (2015) assessed the aqueous extract of *Microcos paniculata* fruits (FAE) for its anti-inflammatory, anthelmintic, and antidiabetic properties using a proteinase inhibitory assay, a Pheretima posthuma model, and an α-amylase inhibitory assay. In the proteinase inhibitory assay, FAE exhibited considerable (P<0.05) antiproteinase activity, showing 41.05% proteinase inhibition at a concentration of 250 µg/mL with an IC50 of 285.47 µg/mL. Furthermore, FAE administered at a dose of 50 mg/mL resulted in the paralysis and subsequent death of *Pheretima posthuma* at 34.24 minutes and 55.25 minutes, respectively. Additionally, the extract showed significant (P<0.05) inhibition of α-amylase with an IC50 value of 1367.56 µg/mL[24].

CHEN YF (2013) investigated the protective effects of total flavones derived from *Microcos paniculata* (TFMP) against acute myocardial ischemia (AMI) induced by isoprenaline (ISO) and its underlying mechanisms. The rats received TFMP (8, 4, and 2 mg/kg) via oral administration once daily for five consecutive days, and an AMI model was created using subcutaneous injection of ISO (2 mg/kg) one hour after the final dosage. The impacts of TFMP on electrocardiogram (ECG) readings at various time points and the pathological histomorphology of myocardial tissue stained with hematoxylin were examined; biochemical methods were used to measure the superoxide dismutase (SOD) and malondialdehyde (MDA) levels in myocardial tissue, along with assessing glutathione peroxidase (GSH-Px), lactate dehydrogenase (LDH), and creatine kinase (CK) activities in serum. In comparison to the model group, the high- and medium-dose groups (8 and 4 mg/kg) of TFMP significantly mitigated the downward J point on the

ECG during myocardial ischemia ($P < 0.05$), particularly notable 10 minutes after the ISO injection. Additionally, the myocardial damage caused by ISO in these two groups was alleviated, indicated by the reduced levels of LDH and CK in serum ($P < 0.05$) and a decrease in MDA content in myocardial homogenate ($P < 0.01$), while SOD ($P < 0.01$) and GSH-Px ($P < 0.05, 0.001$) activities in the myocardial homogenate were increased [25].

Mei Q et al (2010) examined the anti-inflammatory properties of the water extract from *Microcos paniculata* and to offer scientific experimental evidence for its clinical use. To investigate the anti-inflammatory effects, various inflammatory models were utilized, including xylene-induced ear swelling and acetic acid-induced capillary permeability enhancement in mice. The findings revealed that both high and medium doses of *Microcos paniculata* significantly reduced ear edema, while all three doses notably decreased the increase in capillary permeability. The water extract of *Microcos paniculata* demonstrates a significant anti-inflammatory effect[26].

Wu H et al (2017) studied Folium Microcos (FM), which is derived from the leaves of *Microcos paniculata* L., exhibits a range of biological properties, including antioxidant capabilities and inhibition of α-glucosidase. Despite this, its potential for treating acute liver injury has not been explored. This research aimed to evaluate the hepatoprotective effects and the mechanisms involved in the polyphenol-rich fraction (FMF) obtained from Folium Microcos. FMF demonstrated significant free radical scavenging activities and protected HepG2/Hepa1–6 cells from hydrogen peroxide- (H_2O_2-) induced reactive oxygen species (ROS) production and apoptosis in vitro. The antioxidant effects and protective properties were further confirmed by reducing APAP-induced liver damage in mice. Western blot analysis showed that pretreatment with FMF markedly reduced APAP-induced phosphorylation of MAPKs, activation of the pro-apoptotic proteins caspase-3/9 and Bax, and restored levels of the anti-apoptotic protein Bcl2. Mice that were subjected to APAP toxicity and pretreated with FMF displayed increased nuclear accumulation of nuclear factor erythroid 2-related factor (Nrf2), along with heightened hepatic expression of its target genes, NAD(P)H:quinone oxidoreductase 1 (NQO1) and heme oxygenase-1 (HO-1). HPLC analysis identified the four main phenolic compounds present in FMF: narcissin, isorhamnetin-3-O-β-D-glucoside, isovitexin, and vitexin. Therefore, these results suggest that FMF has a protective effect on the liver against APAP-induced toxicity, primarily through the dual regulation of the ROS/MAPKs/apoptosis pathway and the Nrf2-mediated antioxidant response, which can be attributed to the robust antioxidant properties of its phenolic constituents.[27]

Li KP (2014) has studied the chemical components from the effective fraction of *Microcos paniculata* leaves for their ability to protect against acute myocardial ischemia injury caused by isoprenaline. The isolation and purification of these chemical constituents were accomplished through a combination of chromatography on silica gel, Sephadex LH-20 column, and preparative HPLC. The structures of the isolated compounds were determined using NMR and MS spectral analysis. A total of eleven compounds were extracted from the effective protective fraction, all of which demonstrated protective effects against acute myocardial ischemia injury, and were identified as vitexin (1), isovitexin (2), isorhamnetin (3), kaempferol (4), quercetin (5), 5, 6, 7, 8, 4'-pentamethoxyflavone (6), nobiletin (7), vanillic acid (8), caffeic acid (9), ferulic acid (10), and erucicamide [28].

Bi HePing BH et al have extracted essential oil from the leaves of *Microcos paniculata* L. using steam distillation. The chemical components were isolated and recognized through GC-MS analysis. The relative proportions of the volatile oil were assessed using peak area normalization. The oil yield from steam distillation was 0.63%, and a total of 15 compounds from the volatile oil were isolated and identified, representing 99.99% of the overall volatile oils. The main chemical constituents were 2-methoxy-4-vinylphenol (18.12%), octacosane (11.77%), *n*-hexadecanoic acid (11.29%), pentacosane (10.32%), heptacosane (8.61%), 2,3-dihydro-benzofuran (6.29%), tetratetracontane (5.99%) and hexatriacontane (5.51%).[29]

Lu Peng LP et al (2012) set the quality criteria for *Microcos paniculata* L. The identification of M. Paniculata was performed using thin-layer chromatography (TLC), while high-performance liquid chromatography (HPLC) was utilized to quantify the levels of vitexin and narcissin. The identification of M. Paniculata through TLC was successfully established. The calibration curve for vitexin was linear between 0.1-4 µg (r=0.9996), with an average recovery of 96.44% and a relative standard deviation (RSD) of 1.68%. Similarly, the calibration curve for narcissin showed a linear response in the range of 0.1-4 µg (r=0.9996), and the average recovery for narcissin was found to be 97.16% with an RSD of 1.85%. They concluded that the methods of TLC and the quantification of the active compounds from M. Paniculata are both simple and precise, making them suitable for quality control purposes[30].

Feng ShiXiu FS et al (2018) have isolated ten compounds isolated for the first time from the leaves of *Microcos paniculata*. On the basis of spectral data, they were identified as friedelin (1), arjunghicoside II (2), kaempferol-3-*O*-β-D-[3,6-di-(*p*-hydroxycinnamoyl)]-ghicopyranoside (3), kaempferol-3-*O*-β-D-glucopyranoside (4), isorhamnetin-3-*O*-β-D-glucopyranoside (5), narcissin (6), vitexin (7), violanthin (8), isoviolanthin (9) and isovitexin (10).[31]

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