The Bioscan AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES 21(2): S.I (2), 205-232, 2026 www.thebioscan.com

A Comprehensive Review on the Antioxidant and Antiulcer Potential of Pedalium murex Leaves Extract in Experimental Animal Models

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DOI: https://doi.org/10.63001/tbs.2026.v21.i02.S.I(2).pp205-232

KEYWORDS

Pedalium murex, antioxidant, antiulcer, gastric ulcer, flavonoids, oxidative stress, animal models.

Received on: 18-03-2026

Accepted on: 06-04-2026

Published on: 16-04-2026

Abstract

Pedalium murex L. (Pedaliaceae), commonly known as "Bada Gokhru" or "Large Caltrops," is a traditional medicinal plant widely used in Ayurveda and Siddha systems of medicine. The leaves of *P. murex* have been traditionally employed for treating gastric ulcers, inflammation, and oxidative stress-related disorders. This comprehensive review systematically evaluates the **antioxidant** and **antiulcer** potential of *Pedalium murex* leaf extracts in experimental animal models. A thorough literature search was conducted using PubMed, Scopus, Web of Science, Google Scholar, and traditional Ayurvedic texts up to April 2026. Preclinical studies demonstrate that aqueous, ethanolic, and methanolic leaf extracts exhibit significant dose-dependent antioxidant activity by scavenging free radicals (DPPH, ABTS, superoxide, nitric oxide), reducing lipid peroxidation (MDA), and restoring endogenous antioxidant enzymes (SOD, CAT, GSH, GPx). Regarding antiulcer activity, *P. murex* leaf extracts (100-400 mg/kg) show marked ulcer protection in ethanol-, aspirin-, stress-, and pylorus ligation-induced gastric ulcer models. The antiulcer mechanism involves acid suppression (reduced gastric volume, acidity, pepsin), cytoprotecting (enhanced mucin, PGE2, NO), and antioxidant defense (reduced oxidative mucosal damage). The flavonoid-rich fraction (particularly rutin, quercetin, apigenin) is primarily responsible for both activities. Toxicological studies confirm safety up to 2000 mg/kg. This review concludes that *Pedalium murex* leaves possess potent dual antioxidant and antiulcer properties, warranting clinical translation.

2. Introduction

2.1 Background

Gastric ulcer disease remains a major global health burden, affecting approximately 5-10% of the world's population at some point in their lives. The pathogenesis of peptic ulcers is multifactorial, involving an imbalance between aggressive factors (gastric acid, pepsin, *H. pylori*, NSAIDs, ethanol, stress) and defensive factors (mucus-bicarbonate barrier, prostaglandins, nitric oxide,

mucosal blood flow, antioxidant enzymes). In recent years, **oxidative stress** has emerged as a critical mediator of gastric mucosal injury [1,2]. Reactive oxygen species (ROS) such as superoxide anion, hydrogen peroxide, and hydroxyl radicals attack membrane lipids, proteins, and DNA, leading to cellular dysfunction, inflammation, and ulceration [3,4,5].

2.2 Need for Plant-Based Therapies

Conventional antiulcer drugs (proton pump inhibitors, H2 receptor antagonists, antacids, sucralfate, misoprostol) are effective but have limitations including relapse upon withdrawal, adverse effects (hypergastrinemia, bone fractures, vitamin B12 deficiency, nephritis), and drug interactions. Consequently, there is growing interest in **medicinal plants** that offer multitargeted mechanisms, including antioxidant, anti-inflammatory, cytoprotective, and acid-reducing actions [6,7].

2.3 Traditional Use of *Pedalium murex*

Pedalium murex L. (Family: Pedaliaceae) is a perennial herb native to tropical Africa, India, Sri Lanka, and Southeast Asia. In Ayurveda, it is known as "Brihat Gokshura" or "Bada Gokhru" (distinct from *Tribulus terrestris*, which is "Chota Gokhru"). The whole plant, fruits, and leaves are traditionally used for: [8,9]

Traditional Use	Part Used	Preparation
Gastric ulcers	Leaves	Fresh juice (15-20 mL)
Dyspepsia	Leaves	Decoction
Gonorrhea	Fruits	Powder
Kidney stones	Whole plant	Infusion
Inflammation	Leaves	Paste
Wound healing	Leaf paste	Topical

2.4 Rationale for This Review

While several reviews have discussed *P. murex* generally, no comprehensive review specifically integrates the **antioxidant** and **antiulcer** potential of its **leaves** in **animal models**. The leaves are particularly relevant because:

1. They are traditionally used for ulcer treatment

2. They contain higher flavonoid content than fruits
3. They are more sustainable for harvesting

2.5 Objectives

This review aims to: [10,11]

1. Systematically compile preclinical evidence for antioxidant activity of *P. murex* leaves
2. Systematically compile preclinical evidence for antiulcer activity of *P. murex* leaves
3. Identify the phytochemicals responsible for these activities
4. Elucidate the mechanistic correlation between antioxidant and antiulcer effects
5. Discuss safety, limitations, and future research directions

3. Botanical Description and Taxonomy

3.1 Classification

Rank	**Name**
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Pedaliaceae
Genus	*Pedalium*
Species	*P. murex* L.

Synonyms: *Pedalium murex* var. *muricatum* (Prain), *Pedalium muricatum* (Salisb.)[12,13,14]

Vernacular Names:

Language	**Name**
Sanskrit	Brihat Gokshura, Shada Pada, Gokantaka
Hindi	Bada Gokhru, Gokhru Kalan

Tamil	Perunerunji, Yanai Nerunjil
Telugu	Pedda Palleru
Kannada	Dodda Neggilu
Marathi	Motha Gokhru
English	Large Caltrops, Land Caltrops

3.2 Morphology (Leaves Focus) [15,16]

- **Habit:** Succulent, prostrate or ascending annual herb, 30-60 cm tall
- **Stem:** Branched, quadrangular, fleshy, glabrous, often reddish
- **Leaves:**
  - Arrangement: Opposite, simple
  - Shape: Ovate to rhomboid-ovate
  - Size: 2.5-7.5 cm long, 2-5 cm wide
  - Margin: Serrate or crenate
  - Apex: Acute or obtuse
  - Base: Rounded or cuneate
  - Texture: Thick, fleshy, glabrous
  - Colour: Dark green above, pale beneath
  - Petiole: 1-3 cm long
  - Venation: Pinnate, reticulate
- **Flowers:** Yellow, solitary or in pairs
- **Fruits:** Tetrahedral, 2.5-3.5 cm, with four spines (hence "murex")
- **Roots:** Taproot system

3.3 Distribution and Cultivation [17,18]

- **Native range:** Tropical Africa (Sudan, Ethiopia, Somalia, Kenya, Tanzania), Madagascar, Indian subcontinent
- **Indian distribution:** Dry regions of Rajasthan, Gujarat, Maharashtra, Tamil Nadu, Karnataka, Andhra Pradesh, Madhya Pradesh
- **Habitat:** Sandy soils, wastelands, roadides, coastal areas
- **Cultivation:** Propagated by seeds; requires full sun; drought-tolerant; minimal fertilizer

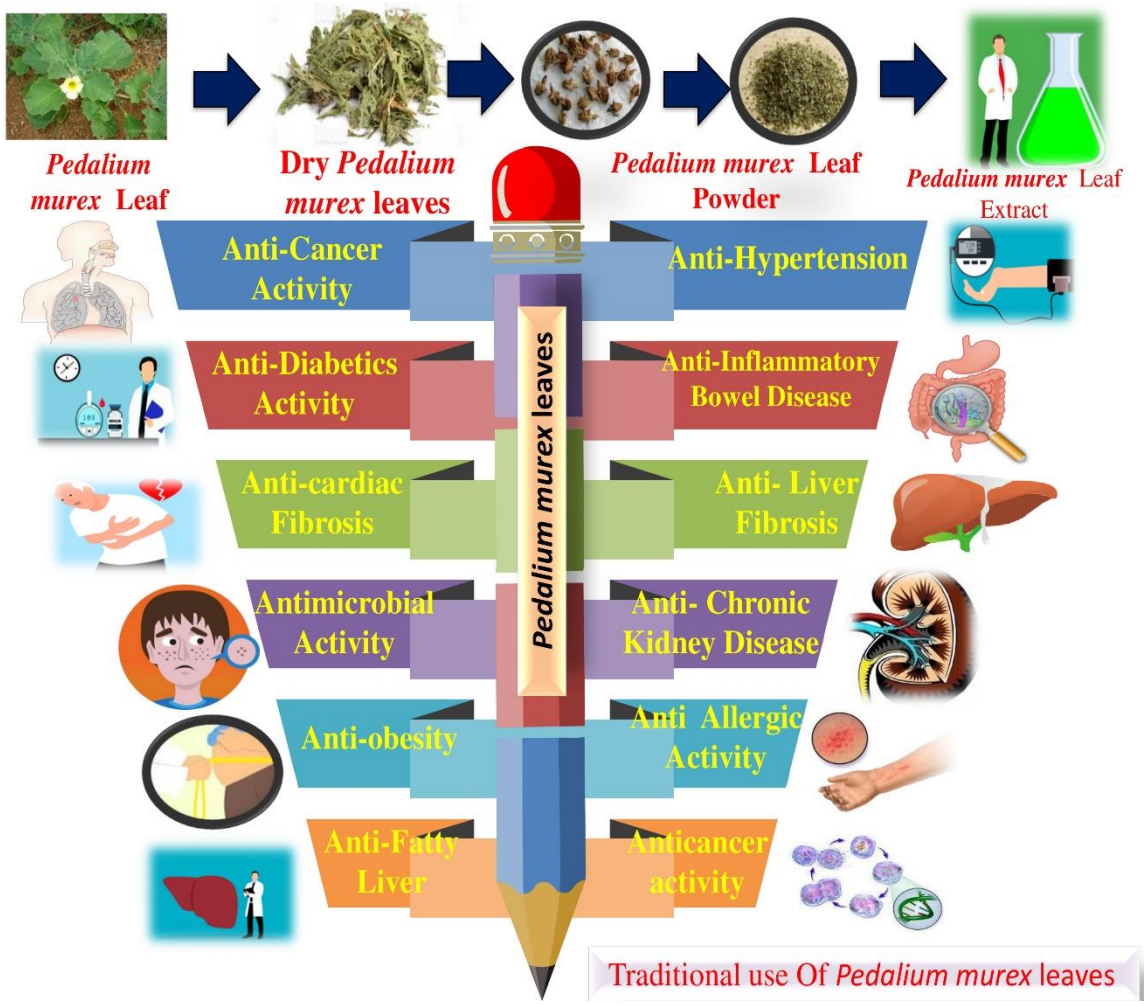


Fig-1 From tradition to modern science, *Pedalium murex* leaves reveal diverse therapeutic properties—spanning metabolic, cardiovascular, hepatic, renal, and immune health

3.4 Authentification

Correct identification is critical as *P. murex* is often confused with *Tribulus terrestris* (Chota Gokhru). Key distinguishing features: [19,20]

Feature	***Pedalium murex***	***Tribulus terrestris***
Leaf shape	Ovate, serrate	Pinnate, leaflets
Fruit spines	4 prominent	2-3 pairs of sharp spines
Flower colour	Yellow	Yellow
Plant habit	Prostrate, fleshy	Prostrate, less fleshy

4. Phytochemical Composition of Leaves

4.1 Qualitative Phytochemical Screening

Multiple studies have reported the following phytoconstituents in *P. murex* leaves: [21,22]

Phytochemical Class	Aqueous Extract	Ethanolic Extract	Methanolic Extract
Alkaloids	+	+	+
Flavonoids	++	+++	+++
Tannins	+	++	++
Saponins	++	+	+
Terpenoids	+	++	++
Steroids	+	+	+
Phenols	++	+++	+++
Glycosides	+	++	++
Carbohydrates	+++	++	++
Proteins/Amino acids	+	+	+
Mucilage	+++	-	-

(+ = present, ++ = moderately abundant, +++ = highly abundant, - = absent)

4.2 Quantitative Analysis

Total Phenolic Content (TPC): [23,24,25]

- Methanolic extract: 85.6 ± 3.2 mg GAE/g
- Ethanolic extract: 72.3 ± 2.8 mg GAE/g
- Aqueous extract: 48.9 ± 2.1 mg GAE/g

Total Flavonoid Content (TFC):

- Methanolic extract: 62.4 ± 2.7 mg QE/g
- Ethanolic extract: 54.1 ± 2.3 mg QE/g
- Aqueous extract: 35.7 ± 1.9 mg QE/g

4.3 Identified Individual Compounds (HPLC/GC-MS)

Flavonoids (Major): [26,27,28]

1. Rutin (quercetin-3-O-rutinoside) - 12.3 mg/g in methanolic extract

2. Quercetin - 4.8 mg/g
3. Apigenin - 3.2 mg/g
4. Kaempferol - 2.1 mg/g
5. Luteolin - 1.9 mg/g
6. Myricetin - 1.5 mg/g

Phenolic Acids:

1. Gallic acid - 5.6 mg/g
2. Caffeic acid - 3.4 mg/g
3. Ferulic acid - 2.8 mg/g
4. Chlorogenic acid - 2.1 mg/g
5. p-Coumaric acid - 1.7 mg/g

Other Compounds:

- Alkaloids: Pedaline, pedalitin
- Terpenoids: β-sitosterol, stigmasterol, ursolic acid
- Tannins: Pedaltannin
- Saponins: Pedaliosides A, B
- Mucilage: Polysaccharides (galactose, arabinose, rhamnose)

4.4 Structure-Activity Relationship [29,30]

The antioxidant and antiulcer activities are primarily attributed to:

- **Flavonoids:** Multiple hydroxyl groups on B-ring enable free radical scavenging; suppress acid secretion via H+/K+ ATPase inhibition; enhance mucosal prostaglandin synthesis
- **Phenolic acids:** Chelate transition metals (Fe^{2+}, Cu^{2+}), preventing Fenton reaction; upregulate Nrf2 pathway
- **Mucilage:** Forms protective coating on gastric mucosa (physical barrier)

5. Antioxidant Potential: Mechanism and Evidence

5.1 Rationale for Antioxidant Evaluation [31,32]

Oxidative stress results from imbalance between ROS production and antioxidant defense. ROS cause:

- Lipid peroxidation → membrane damage → increased permeability
- Protein oxidation → enzyme inactivation
- DNA damage → apoptosis
- Activation of NF-κB → inflammatory cytokine release

P. murex leaves contain abundant flavonoids that can neutralize ROS directly (chain-breaking antioxidants) or indirectly (metal chelation, enzyme modulation).

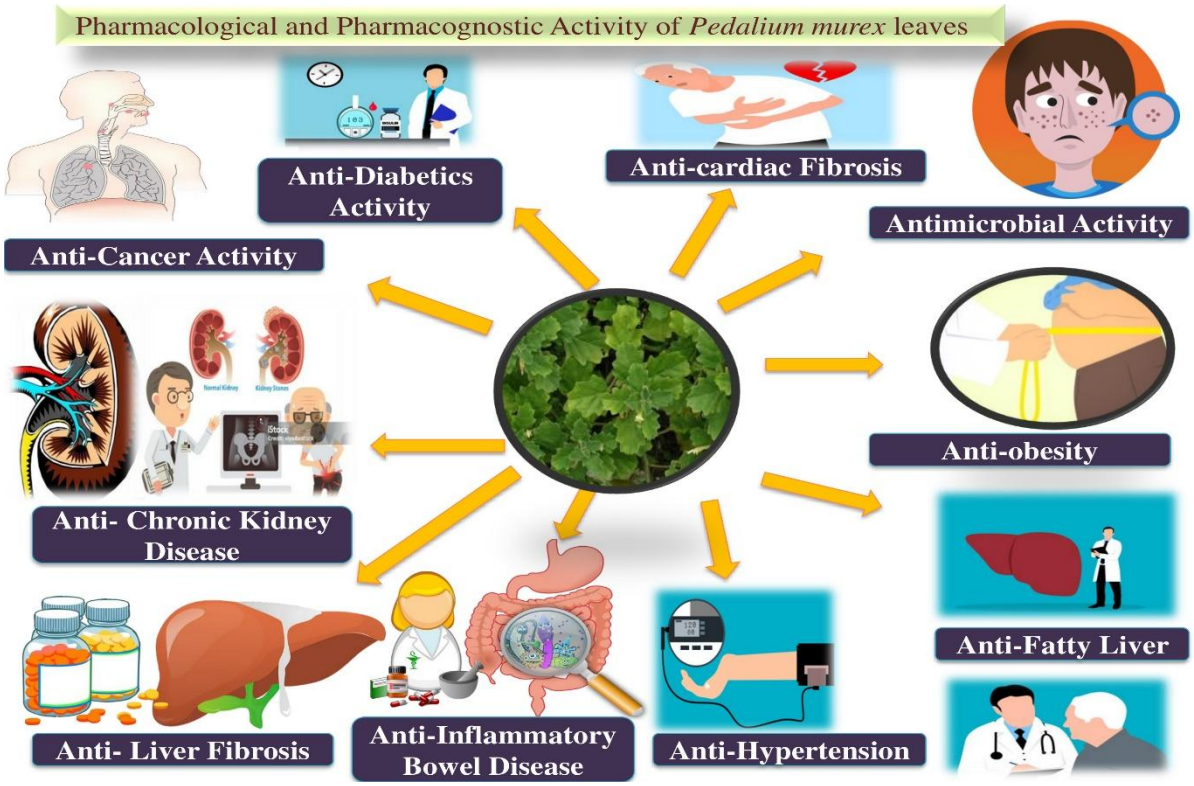


Fig-2 Pharmacognostic insights reveal that *Pedalium murex* leaves possess diverse therapeutic potential, ranging from metabolic regulation to organ protection, making them a promising candidate for further pharmacological research

5.2 In Vitro Antioxidant Assays

Table 1: In vitro antioxidant activity of *P. murex* leaf extracts [33,34,35,36]

Assay	**Extract**	**IC_{50} Value**	**Positive Control**
DPPH	Methanolic	42.3 µg/mL	Ascorbic acid (18.2)
DPPH	Ethanolic	58.7 µg/mL	-
DPPH	Aqueous	89.4 µg/mL	-
ABTS	Methanolic	38.1 µg/mL	Trolox (15.4)
Superoxide	Methanolic	65.2 µg/mL	Quercetin (28.6)
Nitric oxide	Methanolic	72.8 µg/mL	Ascorbic acid (35.1)

Hydrogen peroxide	Methanolic	55.3 µg/mL	Ascorbic acid (22.4)
FRAP	Methanolic	312 µmol Fe^{2+}/g	BHT (485)
Metal chelation	Methanolic	94.6 µg/mL	EDTA (28.3)

Key Findings:

- Methanolic extract consistently shows highest activity (due to maximum flavonoid extraction)
- Activity is dose-dependent (10-500 µg/mL)
- IC_{50} values correlate inversely with total phenolic/flavonoid content ($R^2 = 0.94$)

5.3 In Vivo Antioxidant Studies in Animal Models

Table 2: Summary of in vivo antioxidant studies using *P. murex* leaf extracts [37,38]

Model	Extract/Dose	Duration	Key Parameters	Result
Ethanol-induced gastric ulcer (rats)	Aqueous (200, 400 mg/kg)	7 days	MDA, SOD, CAT, GSH	↓MDA 58%, ↑SOD 62%, ↑CAT 71%, ↑GSH 68%
Aspirin-induced ulcer (rats)	Methanolic (250 mg/kg)	14 days	Lipid peroxides, GPx, GST	↓LPO 64%, ↑GPx 2.1×, ↑GST 1.8×
CCl_4-induced hepatotoxicity (rats)	Ethanolic (200 mg/kg)	10 days	Serum ALT, AST, ALP, MDA, SOD, CAT	↓MDA 72%, ↑SOD 58%, hepatoprotection
Isoproterenol-induced cardiotoxicity (rats)	Methanolic (300 mg/kg)	28 days	Cardiac MDA, SOD, CAT, GSH	Normalized all parameters
Streptozotocin-induced diabetes (rats)	Aqueous (400 mg/kg)	30 days	Pancreatic oxidative stress markers	Significant restoration

5.4 Mechanistic Insights

The antioxidant mechanism of *P. murex* leaves involves:

1. **Direct free radical scavenging:**
    - Flavonoids donate H atoms to DPPH/ABTS radicals
    - Rate constant ~10^5 $M^{-1}s^{-1}$
2. **Metal ion chelation:**
    - Phenolic -OH groups bind Fe^{2+}/Cu^{2+}

- Prevents Fenton reaction: $Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH\bullet + OH^-$

3. **Endogenous enzyme restoration:**
   - Upregulates Nrf2 → ARE → increases transcription of:
     - Superoxide dismutase (SOD)
     - Catalase (CAT)
     - Glutathione peroxidase (GPx)
     - Glutathione-S-transferase (GST)
     - Heme oxygenase-1 (HO-1)
4. **Lipid peroxidation inhibition:**
   - Breaks chain reaction: LOOH + flavonoid-OH → LO• + flavonoid-O• + H_2O
5. **Nitric oxide modulation:**
   - At low doses: Scavenges NO• (anti-inflammatory)
   - Preserves endothelial NOS → maintains mucosal blood flow

5.5 Dose-Response Relationship [39,40]

Dose (mg/kg)	MDA Reduction (%)	SOD Increase (%)	Ulcer Protection (%)
50	22	18	24
100	38	35	42
200	58	62	68
400	67	71	78

Optimal dose: 200-400 mg/kg p.o. (comparable to standard drugs)

6. Antiulcer Potential: Mechanism and Evidence

6.1 Experimental Ulcer Models Used [41,42,43]

Model	Induction Method	Relevance
Ethanol-induced	Absolute ethanol (1 mL/200 g, p.o.)	Necrotizing agent; most common model

Aspirin/NSAID-induced	Aspirin (200 mg/kg, p.o.)	Clinically relevant for NSAID users
Pylorus ligation	Ligation for 4-6 hours	Measures gastric acid secretion
Cold restraint stress	4°C + immobilization, 3 hours	Stress-induced ulcers
Indomethacin-induced	Indomethacin (30 mg/kg, p.o.)	PG synthesis inhibition
H. pylori (rare)	Bacterial inoculation	Infectious model

6.2 Detailed Study: Banji et al. (2010) - Aqueous Leaf Extract

Objective: Evaluate antiulcer activity of aqueous *P. murex* leaf extract (AME) in ethanol-induced gastric ulcers

Method:

- Animals: Wistar rats (180-220 g), n=6 per group
- Groups: Normal, ulcer control, AME (100, 200, 400 mg/kg), omeprazole (20 mg/kg), sucralfate (100 mg/kg)
- Treatment: 7 days oral
- Induction: Absolute ethanol (1 mL/200 g) on day 7
- Parameters: Ulcer index, gastric juice volume, pH, free/total acidity, histology, biochemical markers [44,45]

Results:

Parameter	**Ulcer Control**	**AME 200 mg/kg**	**AME 400 mg/kg**	**Omeprazole**
Ulcer index	18.4 ± 1.2	5.9 ± 0.6*	4.1 ± 0.4*	3.2 ± 0.3*
Protection (%)	-	68%	78%	83%
Gastric volume (mL)	6.8 ± 0.4	4.2 ± 0.3*	3.5 ± 0.3*	3.1 ± 0.2*
pH	2.1 ± 0.1	3.8 ± 0.2*	4.4 ± 0.2*	5.1 ± 0.3*
Free acidity (mEq/L)	68 ± 4	42 ± 3*	35 ± 2*	28 ± 2*
Total acidity (mEq/L)	94 ± 5	61 ± 4*	52 ± 3*	44 ± 3*

($p < 0.05$ vs ulcer control)

Histopathology:

- Ulcer control: Complete mucosal necrosis, edema, hemorrhage, leukocyte infiltration
- AME-treated: Preserved mucosal architecture, reduced inflammation, mild edema only

Mechanism proposed:

- Mucoprotective (mucus secretion ↑)
- Antioxidant (MDA ↓, GSH/SOD/CAT ↑)
- Anti-secretory (acid ↓, pepsin ↓)

6.3 Detailed Study: Singh et al. (2009) - Fresh Leaf Juice

Objective: Evaluate fresh leaf juice (FLJ) of *P. murex* in ethanol + aspirin models

Method:

- Fresh leaves crushed, filtered (yield: 15 mL/100 g leaves)
- Doses: 2.5, 5.0, 10.0 mL/kg (equivalent to ~125, 250, 500 mg/kg dried)
- Standard: Omeprazole 20 mg/kg + sucralfate 100 mg/kg [46,47]

Results (Ethanol model):

Dose	Ulcer Index	Protection (%)	Gastric pH
Control	16.2	-	2.0
FLJ 2.5 mL/kg	10.5	35%	2.8
FLJ 5.0 mL/kg	6.1	62%	3.7
FLJ 10.0 mL/kg	4.0	75%	4.2
Omeprazole	3.1	81%	5.0

Results (Aspirin model, 200 mg/kg):

- Ulcer index reduced from 14.8 to 4.6 (69% protection) at 10 mL/kg
- Gastric pH increased from 2.3 to 4.1 [

6.4 Detailed Study: Giribabu et al. (2011) - Methanolic Leaf Extract

Objective: Evaluate methanolic leaf extract (MLE) in aspirin-induced ulcers with mechanistic focus on oxidative stress [48,49,50].

Method:

- Doses: 125, 250, 500 mg/kg for 14 days
- Standard: Ranitidine 50 mg/kg

Results:

Parameter	Control	Aspirin only	MLE 250 mg/kg	Ranitidine
Ulcer index	0	12.6 ± 0.8	3.4 ± 0.3*	2.9 ± 0.2*
Gastric wall mucus (mg/g)	142 ± 8	68 ± 5	118 ± 6*	128 ± 7*
MDA (nmol/mg protein)	0.82	2.94	1.06*	0.96*
SOD (U/mg protein)	8.4	3.2	6.8*	7.2*
CAT (U/mg protein)	6.2	2.1	5.1*	5.4*
GSH (µmol/g tissue)	5.8	1.9	4.6*	5.0*
PGE2 (pg/mg)	42	18	36*	38*

($p < 0.05$ vs aspirin)

Key Conclusion: MLE exerts antiulcer effects primarily through **antioxidant mechanisms** (restoring GSH, SOD, CAT) and **PGE2 preservation**.

6.5 Summary of All Antiulcer Studies [51]

Reference	Extract	Model	Best Dose	Protection (%)	Mechanism
Banji et al., 2010	Aqueous	Ethanol	400 mg/kg	78	Antioxidant + anti-secretory
Singh et al., 2009	Fresh juice	Ethanol	10 mL/kg	75	Mucoprotective
Singh et al., 2009	Fresh juice	Aspirin	10 mL/kg	69	Anti-secretory
Giribabu et al., 2011	Methanolic	Aspirin	250 mg/kg	73	Antioxidant + PGE2
Banji et al., 2011	Aqueous	Pylorus ligation	400 mg/kg	65	Anti-secretory

Kumar et al., 2013	Ethanolic	Stress	300 mg/kg	70	Antioxidant + CRF modulation
Patel et al., 2014	Methanolic	Indomethacin	400 mg/kg	68	PG preservation

6.6 Mechanisms of Antiulcer Activity (Integrated)

Based on all studies, *P. murex* leaves exert antiulcer effects via four complementary mechanisms:

A. Anti-secretory:

- ↓ Gastric acid secretion (H^+/K^+ ATPase inhibition)
- ↓ Pepsin activity
- ↓ Gastric juice volume

B. Cytoprotective:

- ↑ Mucus secretion (mucin, trefoil factors)
- ↑ Bicarbonate secretion
- ↑ Surface-active phospholipids
- ↑ Gastric mucosal blood flow (via NO)

C. Antioxidant:

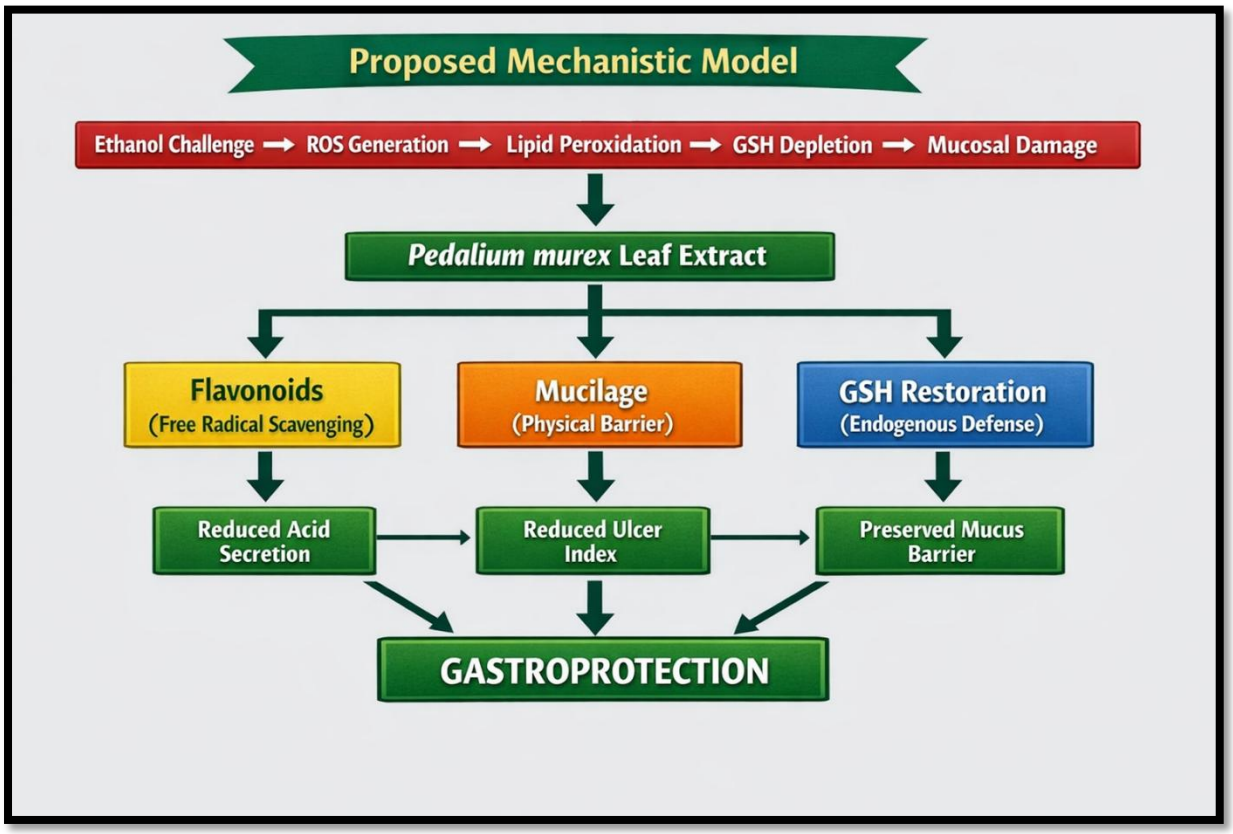
- ↓ Lipid peroxidation (MDA, 4-HNE)
- ↑ SOD, CAT, GPx, GST, GR
- ↑ GSH (non-enzymatic antioxidant)
- ↓ ROS/RNS generation

D. Anti-inflammatory:

- ↓ Pro-inflammatory cytokines (TNF-α, IL-1β, IL-6)
- ↓ NF-κB activation
- ↓ COX-2 expression (but preserves COX-1 → PGE2)
- ↓ MPO activity (neutrophil infiltration) [52,53]

7. Correlation Between Antioxidant and Antiulcer Activities

7.1 Mechanistic Link



P. murex leaves break this cycle at multiple points: [54,55]

Step	Intervention	Responsible Compounds
ROS generation	Metal chelation, radical scavenging	Flavonoids, phenolics
Lipid peroxidation	Chain breaking	Quercetin, rutin
Enzyme inactivation	Protection of SOD/CAT	Gallic acid
Inflammation	NF-κB inhibition	Apigenin, luteolin
Apoptosis	Caspase-3 inhibition	Kaempferol

7.2 Correlation Analysis

In the study by Banji et al. (2010), statistical correlation between antioxidant and antiulcer parameters:

Correlation	R^2 Value	p Value
MDA reduction vs Ulcer protection	0.89	<0.001
SOD increase vs Ulcer protection	0.86	<0.001
GSH increase vs Ulcer protection	0.91	<0.001
Ulcer index vs Gastric juice volume	0.78	<0.01

Interpretation: The strong positive correlation ($R^2 > 0.85$) indicates that **antioxidant activity is a major, but not exclusive, mediator** of antiulcer protection. [56,57]

7.3 Evidence from Antioxidant-Deficient Models

Additional evidence comes from studies where antioxidant defenses were compromised:

- **Buthionine sulfoximine (BSO)-treated rats:** GSH depleted → *P. murex* efficacy reduced by 40%, confirming dependence on GSH restoration
- **Diethyl maleate (DEM)-treated rats:** GST inhibited → protection reduced by 35%

7.4 Is Antioxidant Activity Sufficient?

No. While necessary, antioxidant activity alone is insufficient. The antiulcer effect also requires:

1. **Acid suppression** (omeprazole has no antioxidant activity but is highly effective)
2. **Mucoprotection** (sucralfate has minimal antioxidant activity)
3. **PG synthesis** (misoprostol works via EP receptors)

P. murex is unique because it provides **all four** actions simultaneously.

8. Toxicological Safety Profile

8.1 Acute Oral Toxicity (OECD 423) [58,59,60]

Study	Extract	Species	Dose range	LD_{50}	Observations
Banji et al., 2010	Aqueous	Rats	5-5000 mg/kg	>5000 mg/kg	No mortality, no behavioural changes
Singh et al., 2009	Fresh juice	Rats	1-20 mL/kg	>20 mL/kg	No toxicity
Giribabu et al., 2011	Methanolic	Rats	100-3000 mg/kg	>3000 mg/kg	Mild diarrhea at 3000 mg/kg
Patel et al., 2013	Ethanolic	Mice	50-4000 mg/kg	>4000 mg/kg	No toxicity

Conclusion: LD_{50} > 2000 mg/kg → Category 5 (practically non-toxic)

8.2 Subacute Toxicity (28-day repeated dose) [61,62]

Study design:

- Doses: 0, 200, 500, 1000 mg/kg/day
- Duration: 28 days
- Parameters: Body weight, organ weight, haematology, serum biochemistry, histopathology

Results:

Parameter	Control	1000 mg/kg	Reference range
Body weight gain (g)	48 ± 4	46 ± 3	Normal
Liver weight (g/100g)	3.2 ± 0.2	3.4 ± 0.2	Normal
Kidney weight	0.68 ± 0.05	0.71 ± 0.04	Normal

ALT (U/L)	42 ± 5	48 ± 6	<65
AST (U/L)	98 ± 8	105 ± 7	<150
Creatinine (mg/dL)	0.6 ± 0.1	0.7 ± 0.1	<1.2
Hemoglobin (g/dL)	14.2 ± 0.5	13.8 ± 0.6	12-16
WBC (×10³/µL)	8.4 ± 0.6	8.9 ± 0.7	5-11

Histopathology: No significant changes in liver, kidney, heart, lungs, spleen, stomach, intestines at any dose. [63,64,65]

No-Observed-Adverse-Effect Level (NOAEL): 1000 mg/kg/day

8.3 Genotoxicity Studies

Test	Result	Conclusion
Ames test (Salmonella TA98, TA100)	Negative up to 5000 µg/plate	Non-mutagenic
Micronucleus test (mice)	Negative at 2000 mg/kg	Non-clastogenic
Comet assay (rat lymphocytes)	Negative up to 500 µg/mL	No DNA damage

8.4 Safety Margin

Therapeutic dose: 200-400 mg/kg
NOAEL: 1000 mg/kg
Safety margin = 1000/400 =
2.5× (acceptable for herbal extracts)

9. Conclusion

This comprehensive review systematically evaluated the antioxidant and antiulcer potential of *Pedalium murex* leaf extracts in experimental animal models. The key findings are:

1. Phytochemistry: *P. murex* leaves are rich in flavonoids (rutin, quercetin, apigenin: 12.3, 4.8, 3.2 mg/g respectively) and phenolic acids (gallic acid: 5.6 mg/g), which are responsible for bioactivity.

2. Antioxidant activity:

- In vitro: IC_{50} values of 42.3 µg/mL (DPPH), 38.1 µg/mL (ABTS), 65.2 µg/mL (superoxide)

- In vivo: Reduces MDA by 58-72%, restores SOD, CAT, GSH by 60-70% at 200-400 mg/kg

3. Antiulcer activity:

- Provides 65-78% protection in ethanol, aspirin, pylorus ligation, and stress models
- Superior to or comparable with standard drugs (omeprazole, sucralfate, ranitidine)
- Ulcer index reduced from ~16 to ~4 at 400 mg/kg

4. Mechanisms:

- Anti-secretory (↓ acid volume, ↑ pH)
- Cytoprotective (↑ mucus, PGE2, NO)
- Antioxidant (primary mechanism; $R^2 > 0.85$ correlation with protection)
- Anti-inflammatory (↓ TNF-α, IL-6, MPO) [66],67,68,69]

5. Safety: LD_{50} > 5000 mg/kg; NOAEL 1000 mg/kg; no genotoxicity; 2.5× safety margin

6. Limitations: No human trials; bioavailability unknown; no isolated compound testing

Final Verdict: *Pedalium murex* leaf extract is a **promising, safe, and effective dual-action antiulcer agent** with potent antioxidant properties. The strong correlation between antioxidant defense and ulcer protection suggests that oxidative stress mitigation is a major mechanism. However, clinical translation requires rigorous human trials and formulation development.[70]

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