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Phytochemical constituents and pharmacological activities of *Enterolobium cyclocarpum* (Jacq.) Griseb. : An integrative review on its phytomedicinal potential

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Abstract

Enterolobium cyclocarpum (Jacq.) Griseb. (Elephant ear tree) is a tropical leguminous plant native to Central and South America and widely used ethnomedicinally in wound care, inflammation, gastrointestinal and respiratory diseases, parasite infection, and skin diseases. Recent studies have also pointed to its diverse and complex phytochemical composition in plant parts and geographic source, mostly comprising of phenolics and flavonoids, tannins, saponins, terpenoids, polysaccharides, proteins, minerals, and lipids. The antioxidant, antimicrobial, antiparasitic, anti-inflammatory, hepatoprotective, and cytotoxic properties of key bioactive compounds catechin, epicatechin, quercetin, rutin and p-coumaric acid have been demonstrated to play a role in experimental models. In addition to pharmacological potential, gum exudate of this species has become a possible effective natural pharmaceutical excipient in oral dissolving films and controlled drug release systems. This integrative review critically summarizes the existing literature in phytochemical composition, pharmacological activity, suggested mechanisms, safety, and formulation application, and shows significant gaps such as the use of crude extracts, lack of validations of mechanisms, and lack of clinical validation.

1. Introduction

Enterolobium cyclocarpum (Jacq.) Griseb. belongs to leguminous species, which belongs to the family Fabaceae, under subfamily of Mimosoideae. It is native to a significant tropical area evident in South America, North America, and Central America, introduced to Africa, Asia and the Pacific as one species that is multi-purpose and versatile in nature (CABI, 2019; Ekanem *et al*., 2022). It is a highly influential ecologically important object of agroforestry systems, soil fertility, and livestock production due to its coiled pods, which are unique and huge and can fix nitrogen (CABI, 2019). In Central and South America, it is used in the traditional medicinal systems to treat wounds, inflammation, pain, digestive, respiratory and parasitic infections using its trunk, leaf, pods, seeds and the gum (Sowemimo *et al*., 2015). It has also been reported that *E. cyclocarpum* contains high secondary metabolites, which include phenolics, flavonoids, tannins, saponins, terpenoids and polysaccharides and primary components, including proteins, minerals and lipids (Ekanem *et al*., 2022; Radillo *et al*., 2021). The content of seeds and pods amounts to large doses of amino acids, minerals, fatty, and phenolic compounds, which predetermine nutritional and therapeutic valuation summarized in Table 1 (Vargas Radillo *et al*., 2021). *E. cyclocarpum* has been reported to have a variety of biological activities recorded in pharmacological studies as antioxidant, antimicrobial, antiparasitic, anti-inflammatory, analgesic, hepatoprotective, and cytotoxic effects on plants (Sowemimo *et al*., 2015; Molina-Botero *et al*., 2019; Muro-Medina *et al*., 2024). Major contributors of these activities are polyphenols, flavonoid, tannin, and saponin, and they have been reported to regulate oxidative stress, microbial growth, inflammatory pathway, and cell growth (Sowemimo *et al*., 2015; Del Carmen Robles-Ramirez *et al*., 2025). Besides being relevant to human health, ruminal microbial communities and rumen methane emissions are also positively affected by some compounds indicating that this species can be applied to animal nutrition and sustainability (Molina-Botero *et al*., 2019; Rodriguez and Fondevila, 2012). The literature on *E. cyclocarpum* is disparate, regardless of growing interest among scientists. Recent studies use uncharacterized crude extract, do not standardize their extraction of phytochemical characterization practices, and do not carry out much mechanistic analysis or a safety assessment (Ekanem *et al*., 2022; Sowemimo *et al*., 2015). There is a absence of clinical evidence for this species, therefore, the comprehensive integrative review is needed to reflect on existing knowledge, evaluate rigorously the quality of the available evidence, as well as identify the priorities in research. The current review aims to consolidate all available information on phytochemical constituents, pharmacological, mechanism of action, safety, formulates, and translational perspectives of the plant *E. cyclocarpum* to explain why this plant content is rationally used as a phytomedicine and pharmaceutical resource.

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Table 1: Ethnobotanical and phytochemical features of Earpod tree

Feature	Details and activities	Citations
Plant parts used	Bark, leaves, pods, seeds, gum	Ekanem *et al.*, 2022; Sowemimo *et al.*, 2015
Traditional uses	Wound healing, inflammation, pain, gastrointestinal, respiratory	Sowemimo *et al.*, 2015
Main metabolites	Phenolics, flavonoids, tannins, saponins	Ekanem *et al.*, 2022; Sowemimo *et al.*, 2015
Biological activities	Antimicrobial, anti-inflammatory, antiparasitic	Ekanem *et al.*, 2022; Sowemimo *et al.*, 2015

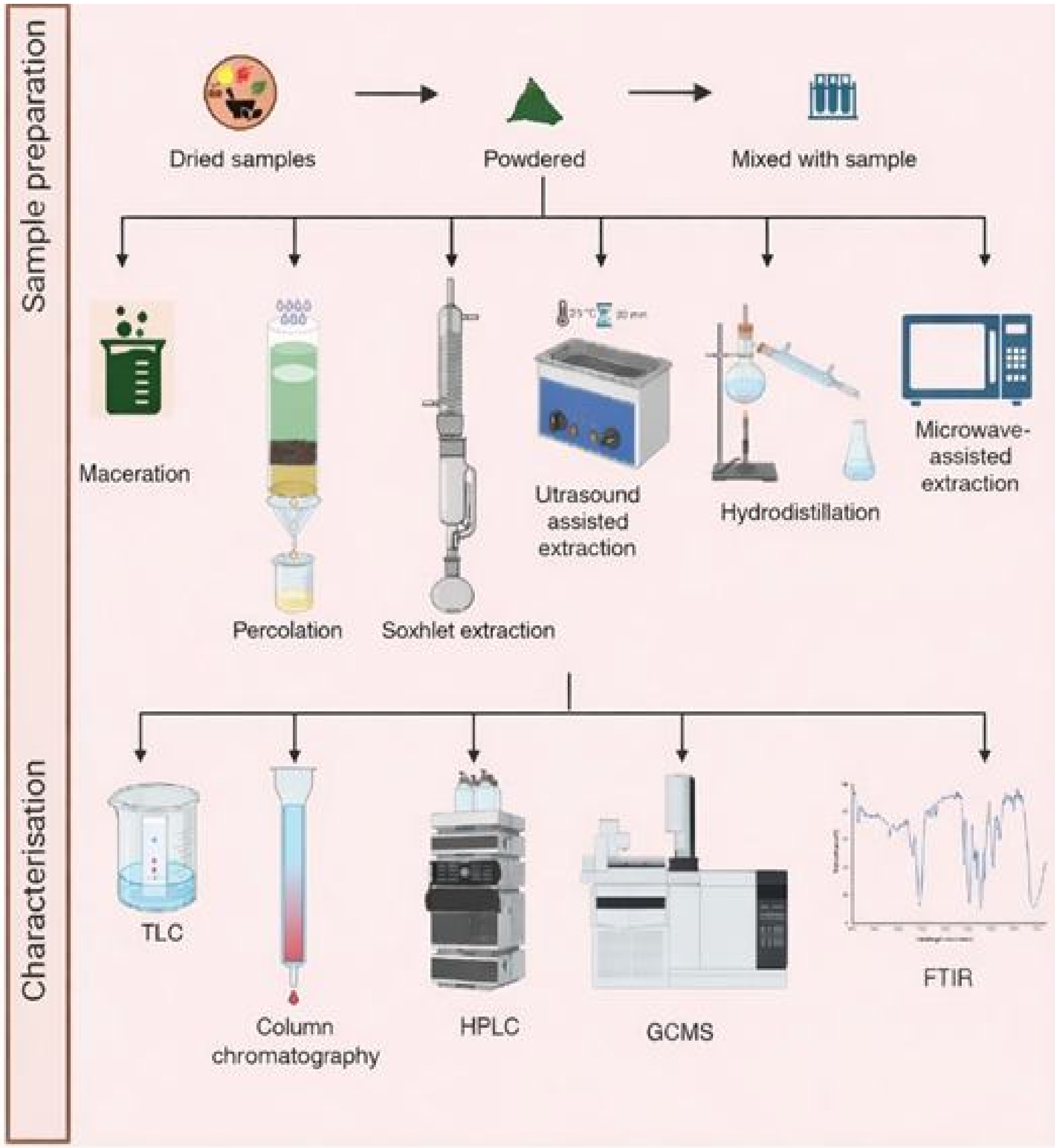

Figure 1: Flowchart showing the extraction, isolation, and characterization of natural products (Sanjai *et al.*, 2024).

2. Methods of extraction and isolation of phytochemical constituents

2.1 Identification of plant material

Dr. S. S. Hameed, Scientist 'F' and Head of Office, Ministry of Environment, Forest and Climate Change, Botanical Survey of India, Southern Regional Centre, TNAU Campus, Lawley Road, Coimbatore, Tamil Nadu, India, identified and verified, *Enterolobium cyclocarpum* (Jacq.) Griseb.-Fabaceae. The specimen is accessed to TNAU herbarium (TNAU Herbarium Accession Number 1069.

2.2 Sample collection and authentication: Critical considerations

The botanical identification and standard sampling are important in reliable pharmacological assessment of *E. cyclocarpum*. The species should be avoided by taxonomic validation by trained professionals and placement of voucher specimens in published herbaria, particularly within species with similar morphologies. Besides this, new authentication methods such as microscopic, chromatographic, spectroscopic and DNA-based methods can be used to enhance quality control and contribute to reproducibility. In general, it can be noted that best-practice advice underlines that transparent reporting of plant material, extraction procedures and chemical characterization are a minimum to ensure a quality interpretation of bioactivity and safety results (Heinrich *et al*., 2022; Mosic *et al*., 2020).

2.3 Extraction methods: Selectivity, methodological bias and efficiency

Phytochemical profile and biological activity of *E. cyclocarpum* extracts are highly dependent on extraction strategy. Solvents, including maceration and Soxhlet extraction are commonly used because of their simplicity (Lefebvre *et al*., 2021; Tzanova *et al*., 2020). They have however been related with excessive extraction time, high solvent usage and can degrade through a form of thermal degradation thus affecting recovery to stable and non-polar compounds which is biased. On the contrary, more recent methods like ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) enhance efficiency through the increased penetration of solvents and cellular disruption, often with higher yield of phenolics and flavonoids and bioactivity (Garcia-Vaquero *et al*., 2021; Quiterio *et al*., 2022). Supercritical fluids extraction is more environmentally friendly and especially in the case of the lipophilic compounds, but its use is more restricted due to the high cost and technical requirements. It has been predicted that compared to conventional methods, optimized UAE can yield better recovery of antioxidant containing fractions, whereas hybrid methods can potentially give better yields and selectivity, depending on the desired phytochemicals and final uses (Sun *et al*., 2025).

2.4 Fractionation and structural elucidation

Crude extracts are complex mixtures related to the phytochemicals and its biological activity, the process of fractionation and chemical profiling is necessary. Polar solvent partitioning is usually used to enrich groups of metabolites of interest, then chromatographic separation (*e.g.*, silica gel column chromatography) is used to isolate phenolics, flavonoids and terpenoids. Preparative TLC can be employed to carry out preliminary separation, while HPLC has a better resolution and compound purification while carrying out the isolation of compounds along with quantitative profiling, such as bioactivity-guided fractionation (Mondal *et al*., 2024). LC-MS and LC-MS/MS allow thoroughly profiling the metabolites, whereas NMR (1D and 2D) is the method to provide the unambiguous structural explanation. It is also complemented by complementary techniques like FTIR and high resolution mass spectrometry, which enhance the accuracy of the phytotransformed chemical determination and identification of all other functional groups, enhancing the confidence of phytochemical reports as shown in Figure 1 (Wolfender *et al*., 2001).

3. Phytochemical profile of *E. cyclocarpum*

3.1 Alkaloids and flavonoids

Based on the Drage Dorff and Mayer reagents, qualitative screening has shown that extracts of bark and leaves of *E. cyclocarpum* contain alkaloids, especially the methanolic and ethanol extracts. Nevertheless, certain alkaloids are yet to be separated and structurally identified, restricting the ability to interpret their pharmacological role and safety relevance. By contrast, phytochemical studies are in unison with the assertion that *E. cyclocarpum* is highly endowed with well characterized phenolic and flavonoid compounds. The diterpene manol, phenolic compounds were found in heartwood aqueous extracts, which are antimicrobial and antitumor compounds, suggesting that other classes of compounds contribute to bioactivity (Alonso-Hurtado *et al*., 2024).

Methanol or ethanol followed by recrystallization are common methods in detecting flavonoids and flavanols in leaf, bark, pod, and seed extracts and it is identified using aluminium chloride and Shinoda tests. HPLC analysis has established flavonoid analogues, including quercetin and kaempferol especially in pods and seeds and these agents are closely linked with antioxidant and anti-inflammatory actions. Besides, various other flavonoids have been commonly reported to be dominant in pods and seeds such as catechin, epicatechin, rutin and quercetin which have been reported to be associated with antioxidant and ovicidal effects against parasites. Notably, *E. cyclocarpum* flavonoids have similarly been shown in Figure 2 have insect growth regulatory effects yet have no acute mammalian toxicity and thus have potential usefulness both as a medical or applied resource (Del Carmen Robles-Ramirez *et al*., 2025; Olmedo-Juarez *et al*., 2025).

3.2 Phenolic acids and tannins

The extracts are phenolic and simple phenols which are typically extracted with aqueous or alcoholic solvents and measured by Folin-ciocalteu (expressed in gallic acid equivalents). These phenolic compounds have a significant contribution to antioxidant function to scavenge and reduce oxidative stress (Olmedo-Juarez *et al*., 2022). Phytochemical profiling also shows that pods and seeds carry significant phenolic and flavonoid indications of catechin, epicatechin, *p*-coumaric acid, rutin, and quercetin that is often linked to antioxidant and ovicidal capabilities on parasite.

Tannins are also found in abundance mainly in the form of condensed tannins in the bark and seeds. They are usually identified with the help of ferric chloride and gelatine precipitation tests and measured in terms of catechin equivalents. Condensed tannins have antimicrobial and wound-healing properties that are associated with the protein-binding capacity of tannins (Pizzi, 2021). This can however be offset by overconsumption of tannin which can lead to loss of nutrient absorption and hence the need to use tannin at controlled levels particularly where it is used along with nutrition or veterinary. Notably, preservation and processing technologies, such as ensiling, sun drying, boiling, toasting and others, decrease levels of tannins and other antinutritional agents (Falola *et al*., 2024). Moreover, condensed tannins have also been associated with lower rumen methane emissions by manipulating rumen microbial communities, which are also important in practice in livestock and environmental sustainability (Del Carmen Robles-Ramirez *et al*., 2025; Molina-Botero *et al*., 2019).

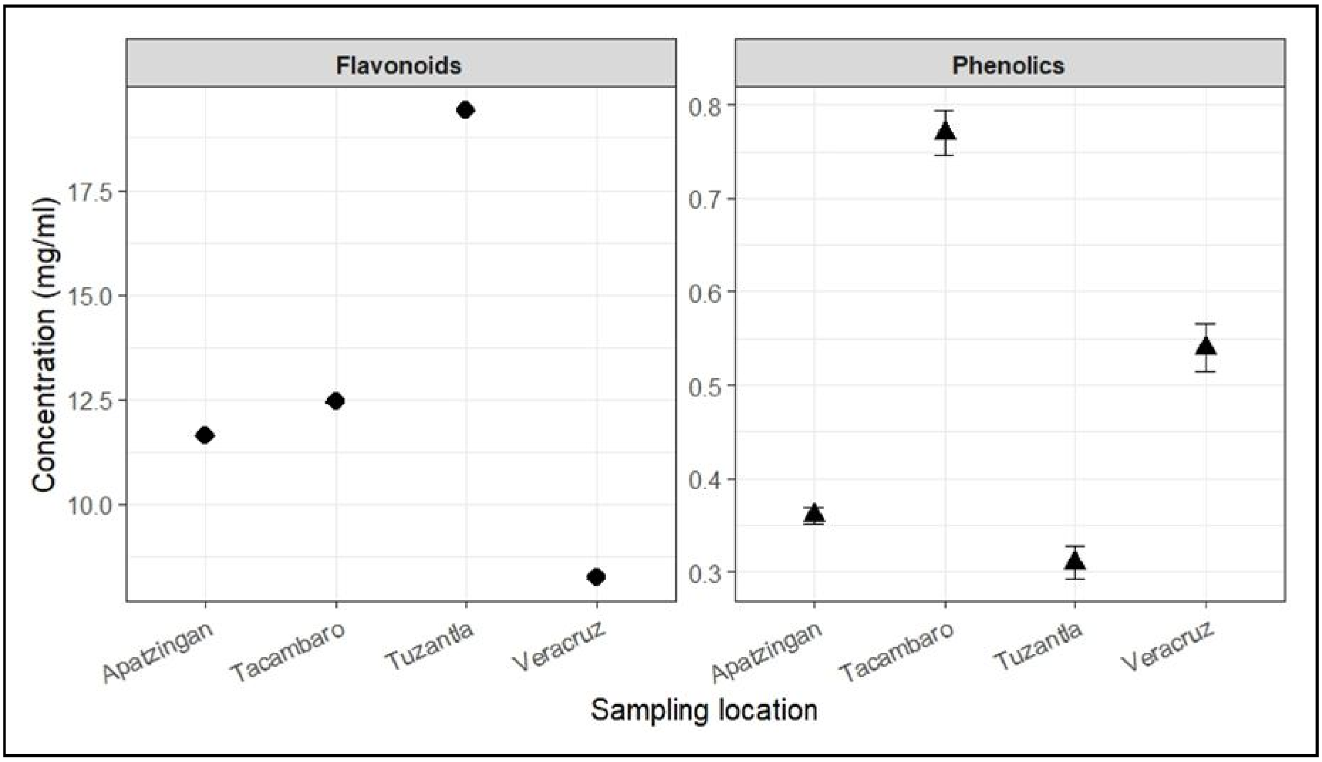

Figure 2: Natural variability in extractables, total phenolics and total flavonoids of aqueous heartwood extract *of E. cyclocarpum* across sampling locations (Raya Gonzlez *et al*., 2013).

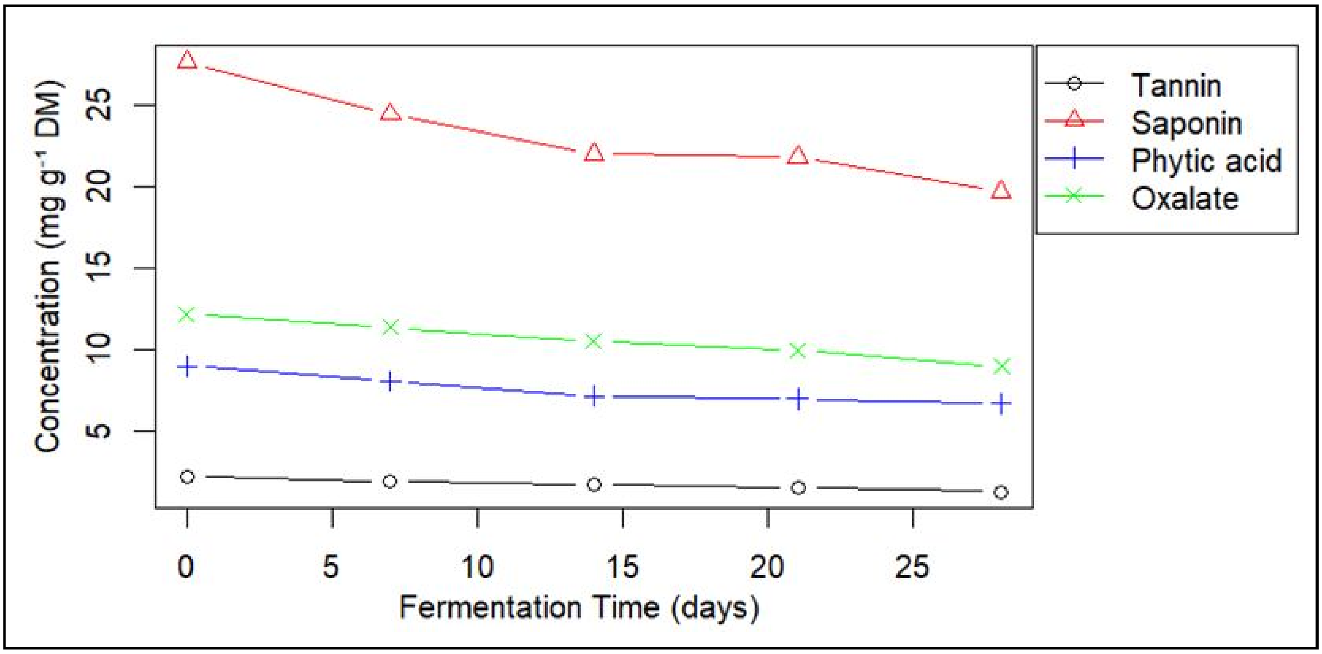

Figure 3: Changes in tannin, saponin, phytic acid and oxalate (mg /g DM) of *E. cyclocarpum* following solid substrate fermentation with *A. niger* (Ayuk *et al.,* 2014).

3.3 Saponins, terpenoids and essential oil

Hydroalcoholic extracts contain saponins in the bark and seeds, which are determined through the formation of foam and blood agar (Shen *et al*., 2023). These drugs are antimicrobial and immunomodulatory and are also haemolytic and this aspect should be evaluated with great caution in terms of toxicity. The saponins possess antifungal effects against pathogens such as *Colletotrichum gloeosporioides* thus making them control of plant diseases. Saponins interfere with rumen protozoa membrane causing decreased protozoa and megaphilic archaea community, a factor that does not adversely affect fecal intake or rumen microbial milieu (Patra and Saxena, 2009). Antimicrobial and anti-inflammatory activities and could be synergistic with other phytochemicals and terpenoids (mono and sesquiterpenes, primarily in non-polar seed and bark extract) add to *E. cyclocarpum* with essential oils provide terpenes (D-limonene and terpineol) that act as insect-repellent and slow-acting toxicants against termites as shown in Figures 2 and 3. Water extract of heartwood, as well as the essential oil fraction of *E. cyclocarpum*, contains monoterpenes, phenolics, especially D-limonene, terpineol, or eugenol, which function as slow-acting toxicants, repellents, in >60% of drywood termite mortality without affecting gut (Raya Gonzlez *et al*., 2013; Molina-Botero *et al*., 2019; Muro-Medina *et al*., 2024).

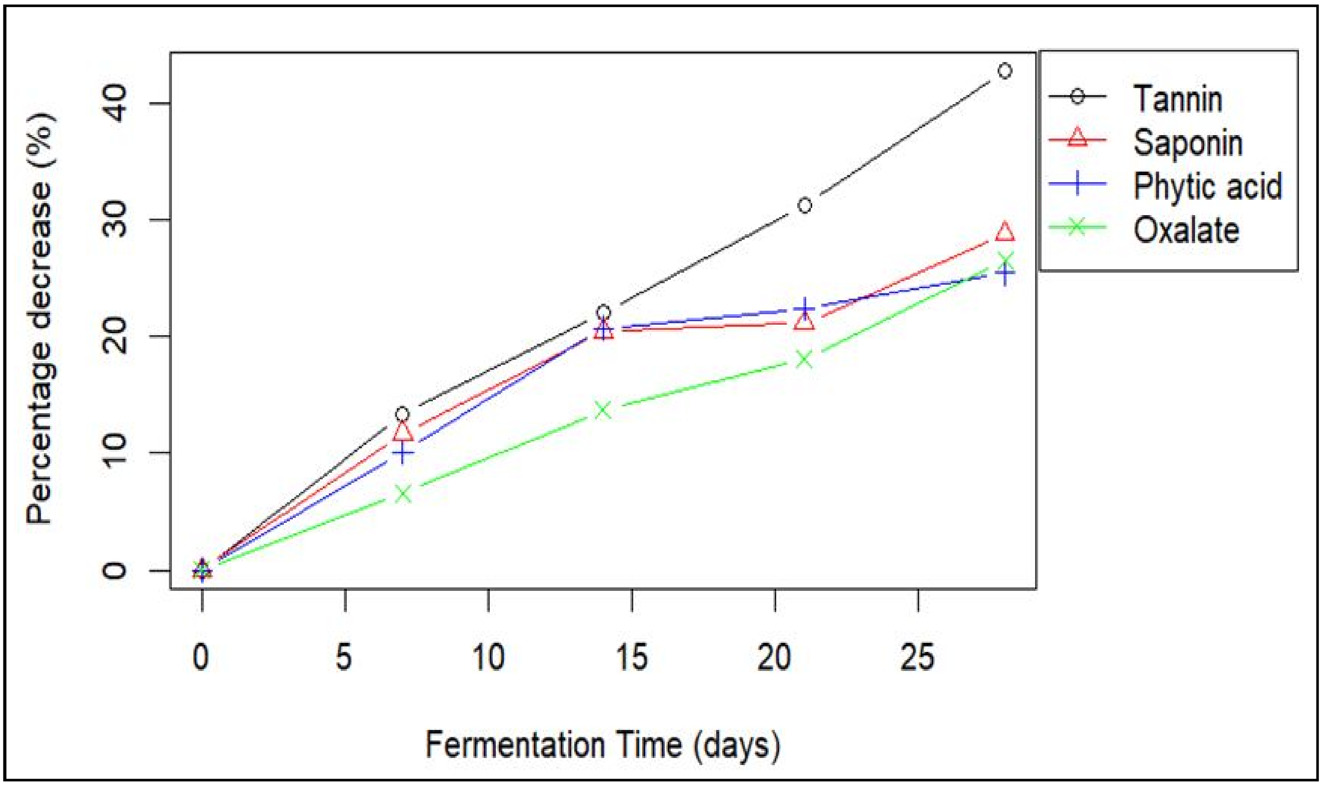

Figure 4: Percentage decrease in tannin, saponin, phytic acid and oxalate (mg /g DM) in *E. cyclocarpum* leaves by *A.niger* (Ayuk *et al*., 2014).

3.4 Polysaccharides, protein and minerals

E. cyclocarpum has a complex polysaccharide in their gum exudate which is traditionally used in soothing and wound healing, has shown immunomodulatory and antioxidant activity, although structural studies of the polysaccharide are only limited. It has proteins and peptides, but these proteins have not been fully studied in this species because of the presence of lectins and inhibitions of enzymes which are common in legumes and the need of more proteomic studies. The essential minerals, including calcium, potassium, magnesium, iron, or zinc, found abundantly in the seeds and pods help in the metabolism and immune system, and are different depending on the environment. Boiling and roasting are some of the methods used in food processing to increase the protein content and lower anti-nutritional components such as tannins, saponin, oxalates and phytates, maximizing nutritional value summarised in Tables 2, 3. Seeds have high protein content (H-19-35 g/100 g) and an amino acid profile comparable to common edible legumes, with good levels of essential amino acids mentioned in Table 4 (Moo-Huchin *et al*., 2025). Thermal and hydration processing (boiling, soaking, roasting, ensiling, sun drying) increase apparent protein availability and reduce tannins, saponins, oxalates, phytates and other anti nutrients, while modestly lowering mineral levels (Kamalasundari *et al*., 2019). Legume contains the enzyme inhibitors and other anti nutritional proteins (*e.g*., trypsin inhibitors are well defined in the congener *E. contortisiliquum* (Batista *et al*., 1996). The lipids and fatty acids also exhibit nutritional values and anti-inflammatory properties and the starch of *E. cyclocarpum* exhibits promising physicochemical properties in the application of food industry. The sulphated polysaccharides have cancer chemo preventive effects were reported in *E. cyclocarpum* can be used in health other than nutrition through modulation of carcinogen metabolism and immune responses (Ekanem *et al*., 2022; Falola, 2020; Gamal-Eldeen *et al*., 2021).

Table 2: Antinutritional factors (mg/100 g) of fresh and treated *E. cyclocarpum* leaves (Ekanem *et al.*, 2020)

Parameters	FENT	ENENT	DENT	ENENT 75	ENENT 50	ENENT 25	SEM
Tannins	93.40[c]	74.41[e]	75.97[d]	158.11[a]	74.59[e]	130.73[b]	7.81
Saponin	3.92c	4.30e	3.18d	3.80d	4.49a	3.64b	0.10
Oxalate	450.21d	315.14c	288.13bd	276.12ab	234.10a	253.30ab	17.76
Phytate	3.60e	2.51f	3.96d	89.90a	81.48b	80.84c	9.81
HCN	6.10e	4.50f	11.70c	15.90b	10.27d	19.96a	1.29

a-f Means on the same row with different superscripts are significantly different (p<0.05).

FENT = Fresh *E. cyclocarpum* leaf sample (unprocessed)

ENENT = Ensiled *E. cyclocarpum* leaf sample

DENT = Sun dried *E. cyclocarpum* leaf sample

ENENT 75 = Ensiled leaf sample with 75% *E. cyclocarpum* inclusion level

ENENT 50 = Ensiled leaf sample with 50% *E. cyclocarpum* inclusion level

ENENT 25 = Ensiled leaf sample with 25% *E. cyclocarpum* inclusion level

SEM = Standard error of mean

HCN = Hydrocyanic acid

Table 3: Proximal chemical analysis of different locations of *E. cyclocarpum* (Vargas Radilla *et al.*, 2021)

Proximal chemical analysis	Autlan (Mean ± SD)	Tequila (Mean ± SD)
Moisture	10.00 ± 1.46	11.35 ± 0.64
Crude protein	30.34 ± 1.10	19.56 ± 2.15
Ether extract	03.22 ± 0.15	01.98 ± 0.25
Crude fiber	20.38 ± 4.61	08.14 ± 3.16
Ash content	04.00 ± 0.36	04.61 ± 0.24
Carbohydrates	43.35 ± 6.45	66.22 ± 8.54

Table 4: Composition of amino acids in the seed *of E. cyclocarpum* at different locations (Vargas Radilla *et al.*, 2021)

Amino acids	Autlan (mg/g protein)	Tequila (mg/g protein)
Essential amino acids		
Aromatic amino acids (phenylalanine + tyrosine)	47.9 ± 0.45	40.5 ± 0.24
L-Isoleucine	46.1 ± 0.52	35.3 ± 0.31
L-Leucine	80.5 ± 0.43	68.3 ± 0.72
Lysine	70.2 ± 0.70	59.0 ± 0.81
Sulphured amino acids (methionine + cysteine)	18.5 ± 0.57	41.8 ± 0.98
Threonine	31.5 ± 0.23	39.3 ± 1.32
L-Valine	47.2 ± 0.37	38.2 ± 0.44
L-Histidine	45.4 ± 0.47	33.2 ± 0.23
Non-essential amino acids		
Aspartic acid	100.5 ± 1.33	88.6 ± 1.22
Alanine	45.7 ± 2.97	43.1 ± 1.08
Arginine	77.6 ± 0.15	61.7 ± 1.51
Glycine	41.7 ± 0.69	45.1 ± 0.84
L-Serine	49.3 ± 0.82	59.4 ± 0.51
Total	**702.1**	**653.5**

4. Pharmacological activities of Earpod tree

Pharmacological activity is majorly due to its phenolics, flavonoids, tannin, saponins and terpenoids were present in the *E. cyclocarpum*. The antioxidant effect is always practiced *in vitro* with the help of free radical scavenging tests: DPPH, ABTS and FRAP, and it is closely associated with the polyphenolic fraction (Samarakoon Dnaw, 2023). Flavonoids and phenolic acid, such as catechin, epicatechin, rutin, quercetin and p-coumaric acid, are viewed to be major recent contributors since they have been established to have radical scavenging as well as redox modulating effects. *E. cyclocarpum* has nutritional and pharmaceutical values, with the reported nutritional contents of the leaves, pods, seeds and fruits being rich in essential vitamins like A, C, D and E and significant content of protein, fibre and mineral components. Besides these bioactive phytochemicals, this nutritive composition highly contributes to the nutraceutical and therapeutic potential of the species mentioned in Table 5 (Ekanem *et al*., 2022).

It has also been reported to have antimicrobial, antifungal activity with gram positive and gram negative in fungal pathogens such as Candida and *Colletotrichum gloeosporioides*. The presence of antimicrobial functions either via protein binding or membrane-disturbing functions. Moreover, antiproliferative effects towards cancer cell lines have also been reported with crude extracts causing a cell cycle arrest and apoptosis, which supports ethnomedicinal anticancer properties. Most studies are extract-based and do not always determine and measure the active components of the extracts that are cytotoxic. *In vitro* results appear promising but there is little *in vivo* validation. In animal research, anti-inflammatory and analgesic properties, inhibition of inflammatory mediators, and the carrageenan-induced and pain behaviour have been reported in rodents (Kulshreshtha *et al*., 2025). These actions are related to flavonoids and phenolics through the alteration of cyclooxygenase and lipoxygenase pathways and inhibition of pro-inflammatory cytokines. Most of the studies are performed by using crude extracts and do not offer enough mechanistic validation, standard dosing or dose-response relations. *In vitro* antiparasitic, and anthelmintic activity has also been proposed, where condensed tannins and saponins have been proposed to destabilise parasite metabolism and disrupt membrane homeostasis. Nevertheless, confirmatory *in vivo* investigations are few. On the same note, antidiabetic potential is also modest: An *in vitro* α-amylase and α-glucosidase inhibition show that glucose absorption may reduce, although *in vivo* studies reveal that extracts have minimal effects on blood glucose reduction, and do not normalize hyperglycaemia in diabetic rat models, nevertheless, there are slight changes in lipid profiles. Moreover, phenolic compounds produced by fruits demonstrate ovicidal activity against parasite eggs, which is why they may play an antiparasitic role, but this activity has not been fully proven in practice (Gamal El-Din *et al*., 2017; Olmedo-Juarez *et al*., 2025; Urtecho-Novelo *et al*., 2024).

The application in humans, *E. cyclocarpum* possesses applied bioactivity in the rumen and livestock systems as shown in Figure 5. Saponins have been reported to decrease the levels of methane emission and alter rumen fermentation, which may lead to improved protein flow and protein digestibility in microbes without a drastic effect in microbial population (Albores-Moreno *et al*., 2017; Lopez-Garrido *et al*., 2020). These results indicate nonclinical pharmacology (agricultural and environmental). The biological processes and dose optimization can still use more elucidation, and research should distinctly disconnect rumen modulating effects and human therapeutic assertions (Muro-Medina *et al*., 2024; Rodriguez and Fondevila, 2012; Sowemimo *et al*., 2015).

Table 5: Vitamin contents (mg/100 g) of fresh and treated *E. cyclocarpum* leaves (Ekanem *et al*., 2020)

Parameters	FENT	ENENT	DENT	ENENT 75	ENENT 50	ENENT 25	SEM
Vitamin A	1.44e	1.02f	2.39a	1.82c	2.09b	1.61d	0.11
Vitamin C	308.79f	489.40d	613.40c	657.60a	626.33b	444.21e	29.74
Vitamin D	57.96c	58.85a	55.67d	58.72b	55.48e	53.96f	0.45
Vitamin E	22.18a	17.33c	13.10e	11.28f	13.78e	20.10b	0.95

a-f Means on the same row with different superscripts are significantly different ($p < 0.05$).

FENT = 100% Fresh *E. cyclocarpum* leaves

ENENT = 100% Ensiled *E. cyclocarpum* leaves

DENT = 100% Sundried *E. cyclocarpum* leaves

ENENT 75 = 75% Ensiled + 25% Sundried *E. cyclocarpum* leaves

ENENT 50 = 50% Ensiled + 50% Sundried *E. cyclocarpum* leaves

ENENT 25 = 25% Ensiled + 75% Sundried *E. cyclocarpum* leaves

SEM = Standard error of mean

The study demonstrates immunomodulatory and antiparasitic potential, supporting the pharmacological relevance of *E. cyclocarpum* in veterinary applications and aligning with its broader phototherapeutic value

5. Hepatoprotective, cardiovascular and cytotoxicity effects

The hepatoprotective effects in experimental models of chemically induced liver injury *e.g*., carbon tetrachloride and paracetamol toxicity where extracts lower serum liver enzymes (ALT, AST) and ameliorate liver histology, presumably due to the antioxidant effect and hepatocyte membrane stabilisation (Pandey *et al*., 2024; Yan *et al*., 2024). Nevertheless, they are small studies, which are not compared with conventional hepatoprotective drugs. The cardiovascular effects are not well investigated and preliminary hints of hypotensive and lipid modulating effects are made through traditional use, but no strong *in vivo* and other mechanistic evidence. The plant has a moderate cytotoxic and anticancer effect in vitro, especially with cervical (HeLa) and breast (MCF7) cancer cell lines as shown in Figure 6, which is manifested by cell cycle arrest and apoptosis, but does not select between cancer cells and normal cells and shows no data on preference in tumour models *in vivo*. Sulfated polysaccharide extracts are also reported to have chemo preventive effects due to the regulation of carcinogen metabolism enzyme and suppression of tumour initiation markers in liver cancer models. All in all, hepatoprotective and anticancer capabilities should be validated in more studies, but experimental evidence confirms such efficacy and safety (Gamal-Eldeen *et al*., 2021; Sowemimo *et al*., 2012).

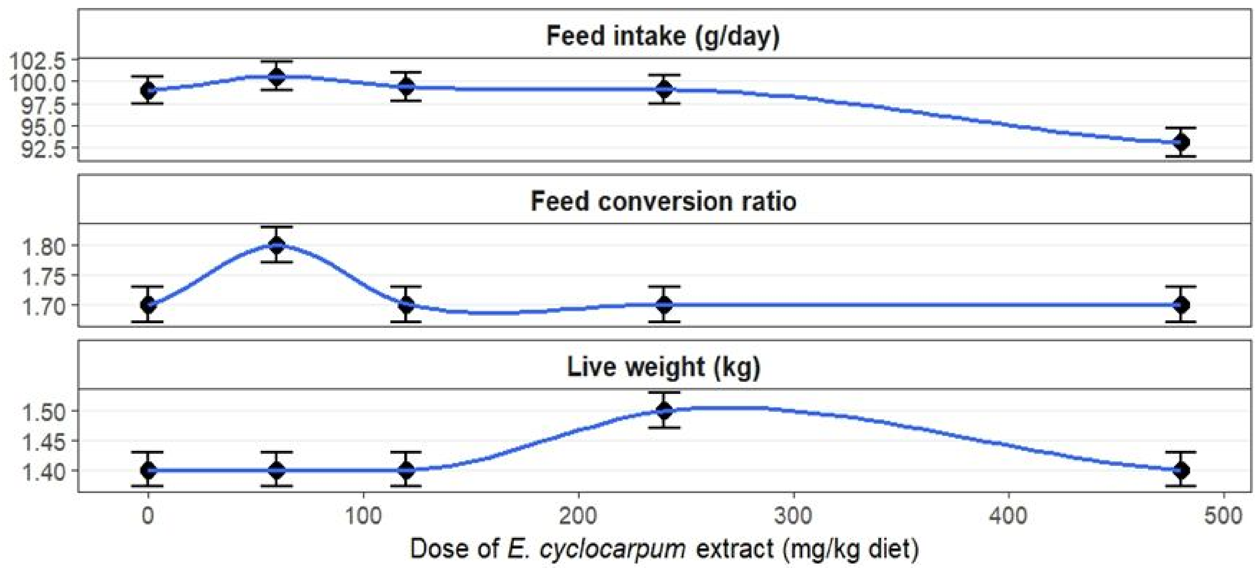

Figure 5: Dose-response effects of ethanolic *E. cyclocarpum* fruit extract on laying hen performance traits (Urtecha-Novelo *et al.*, 2024).

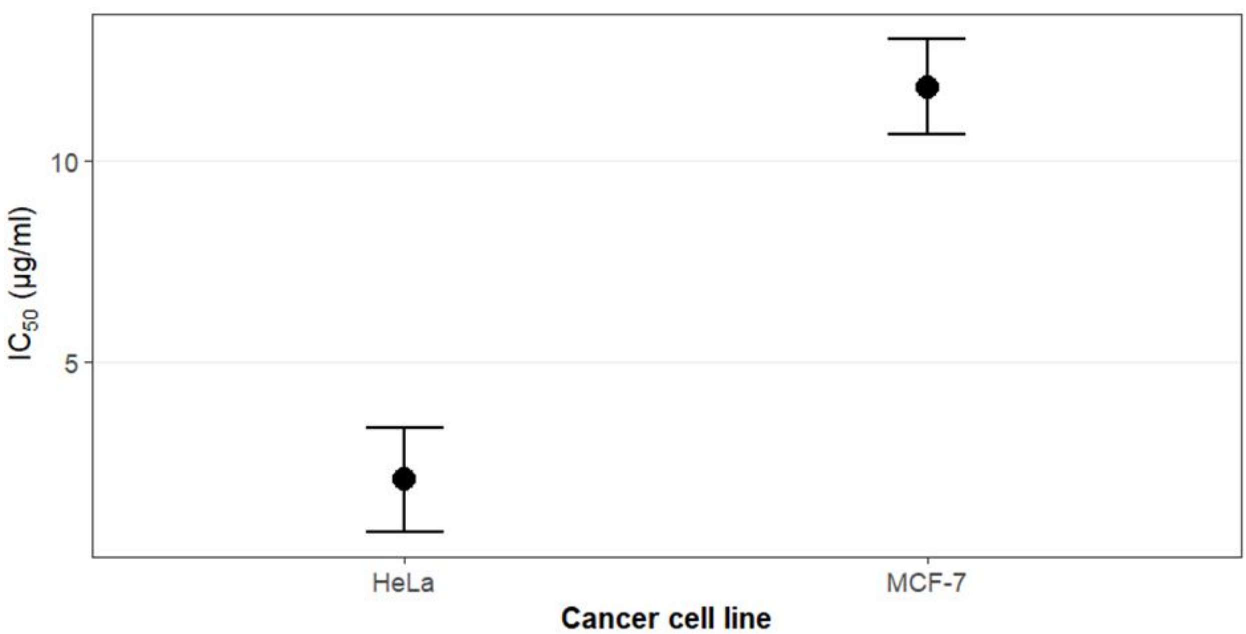

Figure 6: *In vitro* cytotoxic activity of *E. cyclocarpum* extract against HeLa and MCF-7 cancer cell lines (IC_{50}, mean ± SEM) (Sowemimo *et al.*, 2015).

The Figure 6 summarizes the inhibitory concentration (IC_{50}) values of the methanolic extract of *E. cyclocarpum* against human cervical carcinoma (HeLa) and breast adenocarcinoma (MCF-7) cell lines. Lower IC_{50} values indicate stronger cytotoxic activity. Error bars represent mean ± SEM. The extract showed stronger cytotoxicity against HeLa cells compared with MCF-7 cells, supporting its antiproliferative potential *in vitro*.

6. Neuroprotective immunomodulatory and antiallergic effects

Several pharmacological effects with potential preclinical results in *E. cyclocarpum*. It has cancer chemo preventive activities demonstrated by its sulphated polysaccharide extract preventing carcinogen metabolism enzymes and regulating the anti-inflammatory activity of macrophages, as well as by cytotoxic activity on liver cancer cells by arresting their cell cycles and inducing necrosis (Gamal-Eldeen *et al*., 2021). The antiproliferative effect of the methanolic leaf extract against cervical and breast cancer cell lines is achieved by causing apoptosis and a cell cycle arrest, which give credence to the old anticancer assertions (Sowemimo *et al*., 2012). There is evidence of antioxidant and acetylcholinesterase inhibitory action which may confer neuroprotective activity, but there are no CNS experiments. Topical extracts improve wound healing by supporting tissue repair by antimicrobial and antioxidant activities primarily through the action of tannins and flavonoids. *In vitro* immune cell proliferation and cytokine regulation are shown to have immunomodulatory effects, presumably because of saponins and polysaccharides, but these effects need to be confirmed. To date, there are no clinical trials, and toxicological data is mainly based on acute studies that demonstrate its safety at moderate doses (Gamal El-Din *et al*., 2017; Muro-Medina *et al*., 2024; S. Sun *et al*., 2025).

7. Molecular targets and intracellular pathways

The pharmacological actions of *E. cyclocarpum* are mediated by its phytochemicals mainly polyphenols, saponins and sulfated polysaccharides. Its antiproliferative activity against human cancer cells that is mediated through apoptotic induction and arrest at G1/G0 or G2/M phase of the cell cycle, established in hormone driven human cervical and breast cancer cell lines treated with methanolic leaf extracts (Sowemimo *et al*., 2015). The sulfated polysaccharide extract influences carcinogen metabolism by downregulating cytochrome P450-1A and upregulating glutathione-S-transferase, and this is responsible for chemo preventive and anti-inflammatory effects, such as macrophage activation and nitric oxide suppression (Gamal-Eldeen *et al*., 2021; Olmedo-Juarez *et al*., 2025). In ruminants, *E. cyclocarpum* saponins temporarily decrease protozoal populations, modify rumen fermentation by increasing propionate and decreasing methane synthesis, and enhance microbial protein outflow, although they might compromise total fiber digestion (Koenig *et al*., 2007; Rodriguez and Fondevila, 2012). All mechanisms suggest antioxidant, anti-inflammatory, antimicrobial, antiproliferative, and modulation of the rumen microbiome actions, but receptor specific and ion-channel interactions remain to be studied.

8. Standardization, quality control, and formulation

Total phenolic and flavonoid contents (expressed as gallic acid and quercetin equivalents) are widely used, pharmacologically relevant markers for *E. cyclocarpum,* with HPLC confirming the presence of catechin, epicatechin, *p*-coumaric acid, rutin, and quercetin in pods and seeds (Del Carmen Robles-Ramirez *et al*., 2025; Olmedo-Juarez *et al*., 2025). Condensed tannins and saponins also serve as functional markers, especially for bark and seed extracts, and their levels can be influenced by preservation methods (Ekanem *et al*., 2022).**.** Analytical methods for quality control uses chromatographic techniques (HPLC, TLC) that are essential for fingerprinting and batch to batch consistency, enabling identification and quantification of key phytochemicals (Lourenco De Souza *et al*., 2018; Olmedo-Juarez *et al*., 2025). Spectrophotometric assays for total phenolics and flavonoids are routine, rapid, and cost effective for quality assessment (Del Carmen Robles-Ramirez *et al*., 2025; Sun and Shahrajabian, 2023). Phenolic compounds are sensitive to light, temperature, and oxygen, leading to oxidative degradation; thus, controlled storage and packaging are vital (Ekanem *et al*., 2022). *E. cyclocarpum* gum has been successfully used as a natural polymer in oral dissolving films, with chemical modification improving mechanical and drug release properties. The manufacturing process must adhere to Good Manufacturing Practice (GMP) standards, which encompass the cultivation of raw materials, extraction, formulation, and final product testing, ensuring that all components meet defined quality criteria and that the finished product is safe and effective for use (Ramos Barbosa *et al*., 2012; Yau *et al*., 2015)

9. Critical appraisal and limitations

Although there is a growing scientific interest, the existing evidence base on *E. cyclocarpum* is yet to be finalized. To begin with, pharmacological studies are predominantly based on crude extracts or semi characterized fractions, which prevents assigning observed activities to any active principles (Sowemimo *et al*., 2015; Muro-Medina *et al*., 2024). This problem is magnified by the methodological inconsistency in the selection of plant parts, the geographical origin, and processing conditions affecting phytochemical profiles significantly and making cross studies comparison challenging (Ekanem *et al*., 2022; Vargas Radillo *et al*., 2021; Ekanem *et al*., 2022). Second, numerous studies do not have significant standardization in extraction and phytochemical characterization and lack effective use of validated analysis workflows and transparency of reporting, weakening the reproducibility and confidence in translational interpretation (Heinrich *et al*., 2022; Mosic *et al*., 2020).

Third, there exists the constrained mechanistic knowledge of some of the reported activities. As an example, the antioxidant effects are better studied *in vitro*, although validation *in vivo* is underdeveloped and mechanical connection to specific compounds is inadequate (Samarakoon Dnaw, 2023). Likewise, the anti-inflammatory, antimicrobial, antiparasitic, and antiproliferative effects are commonly reported without a solid dose response support, molecular verification of targets or compound specific mechanistic data (Sowemimo *et al*., 2015; Kulshreshtha *et al*., 2025). Fourth, there is ineffective safety assessment. Although the traditional use indicates possible tolerability, the plant also has antinutritional components including tannins, oxalates, hydrocyanic acid, phytases and trypsin inhibitors, which still need proper processing and safety considerations especially in nutritional or veterinary application (Ekanem *et al*., 2022). Moreover, saponins can also play a role in the development of biological activity, although they also have poisonous implications with haemolytic properties, and the systematic toxicological profiling has not been carried out (Shen *et al*., 2023).

The last weakness is the lack of properly structured clinical studies. Efficacy and safety in humans are thus yet to be proved and most of the present-day claims can be deemed as preclinical (Sowemimo *et al*., 2015; Ekanem *et al*., 2022). Generally, these drawbacks remark the necessity of standard phytochemical characterization, bioactivity driven fractionation, mechanism-based pharmacology, and holistic toxicology and clinical validation to facilitate evidence based phytomedicinal and pharmaceutical translation of *E. cyclocarpum* (Heinrich *et al*., 2022).

10. Conclusion

This integrative review focuses on *E. cyclocarpum* as a botanically and pharmacologically viable tropical legume whose phytomedicinal potential is promising. The plant has varying phytochemical classes, especially phenolic acids, flavonoids, condensed tannins, saponins, terpenoids and polysaccharides and proteins and essential minerals. These constituents are different in plant parts, processing identities and geographical source, and serve to add to a diverse diversity of reported biological activities, including antioxidant, antimicrobial, antiparasitic, anti-inflammatory, hepatoprotective, cytotoxic, immunomodulatory and rumen modulating .The most plausible therapeutic opportunities of *E. cyclocarpum,* according to the power of the existing evidence, are the ones based on antioxidant, antimicrobial, anti-inflammatory, wound healing and antiproliferative uses, which are mostly backed with *in vitro* experimentation and little *in vivo* confirmation. Simultaneously, the gum exudate and polysaccharide fractions are a significant translational prospective in terms of natural pharmaceutical excipients and functional biomaterials, especially in drug delivery systems and controlled release formulations. Nevertheless, existing evidence base is not sufficient to support clinical translation because of excessive use of crude extracts, methodological heterogeneity, absence of extract standardization, poor mechanistic understanding and inadequate toxicological and pharmacokinetic analysis The issue of safety should be given more attention, owing to the availability of the antinutritional factors (tannins, phytates, oxalates, cyanogenic components) and to the probability of the hemolytic toxicity of saponins at extreme concentrations. These concerns underscore the phenomenon of dose optimization, the validation of processing and stringent safety profiling prior to any development of a nutraceutical or a therapeutic. Future studies aiming at bioactivity directed fractionation to discover and verify active principles. Uniform phytochemical characterization that has a reproducible marker based quality control. Strong dose response and mechanism driven studies in validated *in vivo* models, systemic toxicological and PK studies should receive priority. Lastly, clinical studies that are well designed are necessary to support efficacy and safety in humans and facilitate acceptance of regulations. In general, *E. cyclocarpum* is an untapped but promising phytotherapy and pharmaceutical technology source if future efforts are based on the screening of crude extracts with standardized and mechanistically justified and valid clinical evidence.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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