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Effect of Crude Ethanolic Extract of Mangosteen Pericarp (Garcinia mangostana Linn.): A Comprehensive Narrative Review

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ABSTRACT

Objective: This comprehensive narrative review aims to consolidate and critically evaluate the existing scientific literature on the biological effects and pharmacological potential of the crude ethanolic extract of mangosteen pericarp (CEMP). Methods: A systematic literature search was conducted in PubMed, Scopus, and Google Scholar for articles published from database inception to March 31, 2024. Search terms included "Garcinia mangostana", mangosteen, pericarp, "crude extract", "ethanolic extract", and key pharmacological activities. Results: The findings reveal that CEMP is rich in bioactive xanthones, particularly α-mangostin, and exhibits a wide spectrum of potent pharmacological activities. These include antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, and neuroprotective effects, primarily demonstrated in *in vitro* and *in vivo* studies. The mechanisms are largely attributed to the modulation of key signaling pathways, such as NF-κB and MAPK. Conclusion: Preclinical evidence strongly supports the multifaceted bioactivity of CEMP. However, clinical research is scarce. Translation to human therapeutics requires standardized extracts, detailed pharmacokinetic and drug interaction studies, and robust clinical trials to establish safety and efficacy.

Keywords: *Garcinia mangostana*, Xanthones, alpha-mangostin, Ethnopharmacology, Biological Activities, Natural Products.

1. Introduction

The search for novel therapeutic agents from natural products has gained immense momentum in recent decades, driven by their historical efficacy, structural diversity, and often favorable toxicity profiles compared to synthetic drugs [1]. Among these, *Garcinia mangostana* Linn. (Family Clusiaceae), commonly referred to as the mangosteen, has emerged as a subject of significant scientific interest. Traditionally dubbed the "queen of fruits," its dark purple pericarp (rind) has been a cornerstone in Southeast Asian folk medicine for centuries, used to treat skin infections, wounds, diarrhea, and various inflammatory conditions [2]. The crude ethanolic extract of mangosteen pericarp (CEMP) is particularly valued as it effectively solubilizes a wide range of both polar and non-polar bioactive compounds, primarily xanthones. α -Mangostin, a prenylated xanthone, is the most abundant and studied compound within CEMP, often serving as a marker for standardization





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[3]. Modern pharmacological investigations have unveiled a plethora of biological activities associated with CEMP, positioning it as a promising candidate for drug development. However, the existing literature is vast yet fragmented. Therefore, this comprehensive narrative review aims to systematically compile, summarize, and critically appraise the current knowledge on the extraction, phytochemistry, pharmacological effects, and toxicological profile of CEMP, thereby identifying research gaps and future directions for its potential application in modern medicine.

2. Review Methodology

This review was conducted as a comprehensive narrative synthesis. A systematic literature search was performed to identify all relevant English-language studies on the biological effects of CEMP. Electronic databases, including PubMed, Scopus, and Google Scholar, were searched from their inception until March 31, 2024.

The search strategy utilized a combination of keywords and Boolean operators: ("Garcinia mangostana" OR mangosteen) AND (pericarp OR rind) AND ("crude extract" OR "ethanolic extract") AND (pharmacology OR "biological activity" OR antioxidant OR anti-inflammatory OR antimicrobial OR anticancer OR antidiabetic OR neuroprotective).

Articles were included if they were original research studies or reviews published in English that focused on the crude or ethanolic extract of mangosteen pericarp. Studies focusing solely on isolated compounds (e.g., pure α -mangostin) without reference to the crude extract, or those not available in English, were excluded. The reference lists of retrieved articles were also screened for additional relevant publications. The data from selected studies were extracted and synthesized thematically to provide a comprehensive overview of CEMP's pharmacological profile.

Limitations of the methodology: This review may be subject to publication bias, as it relied primarily on published literature in English. Grey literature and non-English publications were not systematically searched.

3. Phytochemistry and Extraction

3.1. Bioactive Compounds

The mangosteen pericarp is a rich reservoir of secondary metabolites. The most therapeutically relevant compounds are xanthones, with over 50 different types identified. The crude extract predominantly contains α -mangostin, γ -mangostin, garcinone C, garcinone D, and gartanin [4]. Besides xanthones, CEMP also contains other beneficial compounds like flavonoids, tannins, anthocyanins, and phenolic acids, which contribute synergistically to its overall antioxidant capacity [5].

3.2. Extraction Efficiency

The ethanolic extraction method is preferred for preparing CEMP due to ethanol's efficiency in extracting a broad spectrum of xanthones and its status as a generally recognized as safe (GRAS) solvent. Studies have optimized extraction variables—including ethanol concentration, extraction time, temperature, and solvent-to-material ratio—to maximize the yield of total phenolics, flavonoids, and specifically α-mangostin [6]. Maceration and Soxhlet extraction are commonly used, though advanced techniques like ultrasound-assisted extraction have been shown to improve yield and reduce extraction time significantly.

3. Pharmacological Activities

Table 1 summarizes Key Pharmacological Activities of Crude Ethanolic Mangosteen Pericarp Extract (CEMP).





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Table 1: Summary of Key Pharmacological Activities of Crude Ethanolic Mangosteen Pericarp Extract (CEMP)

Activity	Key Findings	Proposed Mechanisms	References
Antioxidant	Potent free radical scavenging in DPPH, ABTS, and FRAP assays.	High phenolic/xanthone content donates hydrogen atoms to neutralize free radicals.	[5, 7]
Anti-Inflammatory	Inhibits production of NO, PGE2, TNF-α, IL-6, and COX-2.	Suppression of NF-κB and MAPK signaling pathways.	[8]
Antimicrobial	Effective against Gram-positive and Gram- negative bacteria, fungi, and viruses.	Disruption of microbial cell membranes; inhibition of energy metabolism.	[9]
Anticancer	Induces apoptosis and cell cycle arrest; inhibits proliferation and metastasis in various cancer cell lines.	Modulation of apoptosis-related proteins (e.g., Bcl-2, Bax, caspases).	[11]
Antidiabetic	Reduces blood glucose; enhances insulin sensitivity in diabetic rat models.	Inhibition of α-glucosidase enzyme; improvement of insulin signaling.	[12]
Neuroprotective	Demonstrates protective effects in models of neuronal damage.	Antioxidant and anti-inflammatory actions; reduction of oxidative stress in neural tissues.	[13]

4.1. Antioxidant Activity

CEMP demonstrates potent free radical scavenging activity in various assays (e.g., DPPH, ABTS, FRAP). This activity is directly correlated with its high phenolic and xanthone content, which donate hydrogen atoms to stabilize free radicals, thereby mitigating oxidative stress, a key contributor to chronic diseases and aging [5, 7].

4.2. Anti-Inflammatory Effects

The anti-inflammatory properties of CEMP are among its most well-documented effects. In vitro and in vivo studies show that CEMP, primarily through α -mangostin, inhibits the production of pro-inflammatory mediators such as nitric oxide (NO), prostaglandin E2 (PGE2), tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and cyclooxygenase-2 (COX-2) [8]. This suppression is mediated via the inhibition of the NF- κ B and MAPK signaling pathways.

4.3. Antimicrobial and Antiparasitic Properties

CEMP exhibits broad-spectrum antimicrobial activity against Gram-positive bacteria (e.g., *Staphylococcus aureus*, *Bacillus subtilis*), Gramnegative bacteria (e.g., *Salmonella* Typhimurium, *Escherichia coli*), fungi, and viruses [9]. Its mechanism involves disrupting microbial cell membranes and inhibiting energy metabolism. It also shows efficacy against parasites like *Plasmodium falciparum* and *Leishmania* species [10].

4.4. Anticancer Potential

Numerous studies have investigated the anticancer potential of CEMP against various cancer cell lines, including breast, colon, and liver cancer. It induces apoptosis (programmed cell death) and cell cycle arrest, inhibits cancer cell proliferation, and suppresses metastasis [11]. These effects are mediated through the modulation of multiple apoptosis-related proteins and signaling pathways.



LEBDA MEDICAL JOURNAL, Vol. 10. No. 2. Pages 95-99



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4.5. Other Activities

Research also supports other beneficial effects of CEMP, such as antidiabetic (by enhancing insulin sensitivity and inhibiting α -glucosidase), anti-obesity, cardioprotective, and neuroprotective activities, primarily in animal models [12, 13].

4.6 Toxicological and Safety Profile

CEMP demonstrates high efficacy, but its safety profile is crucial for therapeutic use. Acute and sub-chronic toxicity studies conducted on rodents show that CEMP has a relatively high safety margin, with no observed adverse effect levels (NOAEL) reported in multiple studies[14]. However, high doses may cause mild lethargy or gastrointestinal discomfort. Additionally, certain xanthones have been found to inhibit cytochrome P450 enzymes, indicating a potential for herb-drug interactions that require further investigation before CEMP can be widely used in clinical settings [15].

5. Conclusion and Future Perspectives

This review confirms that the crude ethanolic extract of mangosteen pericarp (CEMP) is a pharmacologically rich natural product with multifaceted therapeutic benefits, as demonstrated consistently in preclinical studies. The primary advantage of CEMP lies in its multi-target mechanism of action, driven by a complex mixture of bioactive xanthones.

However, significant limitations exist. The lack of standardized extracts with defined xanthone content and the scarcity of well-designed human clinical trials represent the major hurdles for its translation into evidence-based medicine. Preclinical evidence indicates that crude ethanolic mangosteen pericarp extract exhibits multiple promising biological activities, but translation to clinical use requires standardization of extracts, detailed pharmacokinetic and interaction studies, early-phase human safety trials, and robust randomized controlled trials before therapeutic recommendations can be made.

Future research should focus on:

- 1. Standardizing extraction protocols to ensure batch-to-batch consistency.
- 2. Conducting detailed pharmacokinetic and pharmacodynamic studies in humans.
- 3. Rigorously investigating potential drug interactions in clinical settings.
- 4. Designing robust randomized controlled trials to validate efficacy for specific human health conditions.

With concerted and rigorous research efforts, CEMP holds potential for development as an adjunct therapy or a preventive nutraceutical, but its journey to the clinic is still at an early stage.

ETHICAL STATEMENTS

Not Applicable.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR S' CONTRIBUTIONS:

Adell Abubakeer: Conceptualization, Writing - Original Draft, Writing - Review & Editing.

Asam M. A. Abudalazez: Writing - Review & Editing, Investigation.

Fouz Abdul Aziz: Writing - Review & Editing, Investigation.

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