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Original Research Article

Effect of *Garcinia mangostana* Linn Extract on Systolic Blood Pressure and Inflammation in Hypertensives: A Systematic Review and Meta-Analysis

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ABSTRACT

The potential of *Garcinia mangostana* Linn Extract **(**GMLE) in managing hypertension has garnered increased interest, although its effects are not yet fully understood. This meta-analysis aimed to evaluate the efficacy of the GMLE in reducing systolic blood pressure (SBP) and inflammation. A systematic search of PubMed, Google Scholar, and Science Direct was conducted in April 2024, including randomized controlled trials (RCTs) and cohort studies that compared the GMLE to a placebo. The analysis included 299 participants from three RCTs and one cohort study. The results indicated that, compared with the placebo, the GMLE significantly reduced SBP (SMD = -1.25, p = 0.003, I^2 = 69%). Additionally, GMLE was associated with significant decreases in inflammatory markers, including high-sensitivity C-reactive protein (hs-CRP) (SMD = -5.09, p = 0.03), interleukin-1 (IL-1) (SMD = -1.04, p < 0.00001), and interleukin-6 (IL-6) (SMD = -1.05, p < 0.00001). In conclusion, GMLE appears to be an effective option for managing hypertension and may offer a safer, more economical alternative to conventional treatments.

Keywords: Garcinia mangostana Linn. Extract, Hypertension, Systolic blood pressure, Inflammation, Antihypertensive treatment.

Introduction

Garcinia mangostana is a popular tropical fruit, but its peel, which contains xanthones, including α-mangostin, procyanidins, and anthocyanidins, is often discarded as trash. [1] It has been identified as a potential natural remedy for managing various components of metabolic syndrome, including hypertension and related inflammatory processes. Recent studies have highlighted the pharmacological properties of mangosteen and its xanthones, which have shown promising antiobesity, antihyperglycemic, antidyslipidemic, antiatherosclerotic, antidiabetic, and anti-inflammatory effects in experimental settings [2 3] Research has shown that they have an anti-inflammatory impact by lowering IL-6, IL-1b, and TNFa production, which lowers systolic blood pressure.[4] These effects are particularly relevant for patients with hypertension, as metabolic syndrome components often coexist and contribute to cardiovascular risks. Additionally, the antioxidant activity of mangosteen has been evaluated in clinical trials and animal studies, and the results suggest that it plays a role in alleviating chronic diseases related to oxidative stress, which is a key factor in hypertension and cardiovascular diseases.[8]
Garcinia mangostana L. is a subtropical fruit commonly found in Indonesia and other Southeast Asian countries and is widely used as an ingredient in herbal medicine for various diseases. Xanthone, a compound found in *Garcinia mangostana L.* and known as α-mangostin, has beneficial therapeutic effects on diseases such as inflammation, hyperuricemia, tumors, and other metabolic disorders.

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In a recent study by Xu *et al*. (2024), the therapeutic effects and mechanisms of α-mangostin on hypertension and related kidney damage in spontaneously hypertensive rats were investigated. The authors divided the hypertension treatment groups into 3 groups: α-mangostin (0.5 mg/kg), α-mangostin (1 mg/kg), and losartan (20 mg/kg). Blood pressure was monitored at weeks 4, 5, and 6, at which points treatment with α-mangostin (1 mg/kg) effectively reduced systolic and diastolic blood pressure. In addition, the decrease in the serum Ang II concentration after treatment with losartan as well as with α-mangostin suggested that α-mangostin, an extract of the traditional medicinal plant *Garcinia mangostana L.*, may be a promising potential agent for hypertension treatment. [6] At a dose of 200 mg/kg per day, G. mangostana extract decreased cardiovascular remodeling, arterial wall thickness, and hypertension. By lowering plasma MDA levels, increasing plasma nitric oxide (NO) metabolites, and decreasing the expression of the iNOS protein and the p47phoxNADPH oxidase subunit in aortic tissue, therapy also attenuates the effects of oxidative stress. The addition of G. mangostana peel in powder form to the diet of obese rats (daily intake equivalent to an α-mangostin concentration of 168 mg/kg per day) improved the amount of fibrosis and collagen deposition and decreased the cardiovascular structure of the rats. In addition to decreasing blood pressure, therapy increases the function of aortic endothelial tissue. In a prospective cohort trial, individuals with a high risk Framingham score who received a daily dose of 2,520 mg of G. mangostana extract for 90 days demonstrated greater SOD and lower MDA levels than did the placebo group. [7] Charlie, Soetikno, Murwantara, Andini, Lazarus, and Louisa (2020) reported that in STZ-induced diabetic rats, treatment with α-mangostin (100 and 200 mg) reduced cardiac hypertrophy and fibrosis and inhibited immune cell infiltration of cardiac tissue, CK-MB, LDH, blood pressure, and proinflammatory cytokine levels (TNFα, MCP-1, IL-6, and IL-1β).[8]
A study investigated the effects of *Garcinia mangostana* on metabolic and cardiovascular parameters in rats with diet-induced metabolic syndrome. After 16 weeks of feeding a high-carbohydrate and high-fat diet, the systolic blood pressure increased continuously, and the systolic blood pressure decreased in the rats fed the same diet supplemented

with *Garcinia Mangostana*. In the present study, we found less left ventricular diastolic stiffness in rats supplemented with *Garcinia mangostana*. Compared with rats treated with Garcinia mangostana, rats fed a high-carbohydrate and high-fat diet alone exhibited greater perivascular collagen deposition and inflammatory cell infiltration in the left ventricle. Endothelial dysfunction may arise from an imbalance of vasodilatory agents such as NO, prostacyclin and endothelial-derived hyperpolarizing factor and vasoconstrictive agents such as angiotensin-II, prostaglandins and endothelin-1. [9] The greater experimental relaxation and contraction responses of the aortic rings in treated rats could be explained by the decrease in inflammatory cell infiltration. Supplementation with *Garcinia mangostana* enhanced the noradrenaline-induced thoracic aortic contraction response and acetylcholine-induced relaxation in rats. This finding implies that endothelial changes caused by a high-fat and carbohydrate diet are limited by phytochemicals found in the rind of mangosteen. Additionally, a prospective cohort study demonstrated that supplementing diabetic patients with *G. Mangostana* extract improved endothelial dysfunction by increasing the number of endothelial progenitor cells and the level of the antioxidant enzyme superoxide dismutase (SOD) and decreasing the levels of oxidative stress and inflammatory markers. [10] Consuming mangosteen energy drinks for thirty days increased blood antioxidant capacity and decreased C-reactive protein concentration without affecting creatinine, alanine transaminase, or aspartate transaminase levels. In rats, an ethanol extract showed no toxicity or death, and up to 20 mg/kg/day for four weeks had no negative side effects. [11]

Hypertension is a prevalent disease [12] that affected 31.1% of the worldwide adult population (1.39 billion individuals) in 2010. [13] The JNC-8 guidelines update the classification of hypertension. At present, hypertension is categorized into two stages based on systolic and diastolic blood pressure: stage 1 hypertension is defined as a systolic BP between 130 and 139 mmHg or a diastolic BP between 80 and 89 mmHg, and stage 2 hypertension is defined as a systolic BP of 140 mmHg or higher or a diastolic BP of 90 mmHg or higher.[13,14]; however, hypertension is now classified into two (formerly three) stages. [14] Its diagnosis requires at least two blood pressure readings at two separate visits. [15] For many people, hypertension is a “silent illness” that can persist for several years. When symptoms do appear, there may be end-round damage. [16,17] There may be headaches, dizziness, insomnia, and palpitations, as well as less common signs such as nausea, anxiety, and epistaxis. Among these, headache is sometimes the most pervasive complaint. [16] Over half of people with hypertension also have other cardiovascular risk factors. The most prevalent further risk factors are metabolic syndrome (40%), overweight/obesity (40%), hyperuricemia (25%), diabetes (15–20%), and lipid disorders (30%). [17]

From 1990 to 2019, the number of individuals aged 30-79 years with hypertension doubled, from 331 million women and 317 million men in 1990 to 626 million women and 652 million men in 2019, despite the steady worldwide age-standardized incidence. [18] In 2015, men had a greater incidence of hypertension than women did, and the prevalence of hypertension has increased over time. However, there is a sharp increase in the incidence of hypertension in women relative to that in males following the start of menopause. [19] The therapeutic schedule must involve lifestyle modifications, consistent blood pressure monitoring, and successful treatment of other risk factors to lower residual cardiovascular risk. [17] Recently, traditional medicines have provided highly efficient approaches for reducing the prevalence of hypertension. According to previous studies, various techniques can be helpful for treating high blood pressure. These include diet, exercise, stress management, supplements, and herbs. [20] A randomized, double-blind, placebo-controlled clinical trial revealed that the extract of *Garcinia mangostana* has positive effects on several cardiovascular conditions, including hypertension. [4]

The pericarp of *Garcinia mangostana Linn* or its extract possesses a broad spectrum of biological properties and has been adequately studied in humans. For example, the efficacy of a mangosteen dietary supplement was proven in a study on the human immune response. It can be emphasized that *Garcinia mangostana* extracts contain prenylated xanthones, including α-, β-, and γ-mangostin, which exhibit diverse pharmacological activities. [21] These properties include anticancer, anti-inflammatory, antiproliferative, antioxidant, and proapoptotic activities. The extensive study of α-, β-, and γ-mangostin has led to its application in nutritional supplements, herbal cosmetics, and pharmaceutical preparations, underscoring the significant impact of *Garcinia mangostana* extracts on human health. [22,23] The potential of antioxidants in GEL also plays a key role in reducing systolic blood pressure and inflammation. This effect of mangosteen extract is attributed to its chemical composition, which includes a variety of bioactive compounds. Specifically, the ethyl acetate fraction (EAF) of mangosteen has been shown to exhibit strong antioxidant activity. [24]

Moreover, a systematic review of the anti-inflammatory potency of mangosteen indicated its effectiveness in various inflammatory conditions, highlighting its therapeutic potential in mitigating the upregulated inflammatory response in hypertension. [25] These findings collectively suggest that GEL could be a valuable addition to hypertension management strategies, as it can target both blood pressure reduction and the mitigation of inflammation, thereby addressing two critical aspects of cardiovascular health. In conclusion, further clinical research investigating the efficacy of *Garcinia mangostana Linn* extract in reducing systolic blood pressure and inflammation in hypertension patients is warranted. Given the promising results from preliminary studies, the GMLE could represent a novel therapeutic avenue, offering a natural, multifaceted approach to hypertension management.

Materials and Methods

This systematic review was conducted in accordance with the guidelines outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). [26] Furthermore, the protocol for this review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO), with registration number CRD42024522742.

Eligibility criteria

Studies were included if they met the following criteria were met: (1) they reported intervention associations between the GMLE and placebo; (2) they reported populations based on people with hypertension; (3) they utilized randomized controlled trial and cohort study designs; (4) they reported the data standard mean difference and standard deviation of systolic blood pressure, IL-1, IL-6, and hsCRP; and (5) they were written in English. Selection, quality assessment, and data extraction were independently conducted by three reviewers, with discrepancies resolved by consensus among a fourth reviewer. The study adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.

Search strategy and selection of studies

A search protocol was implemented across several databases, including PubMed, ScienceDirect, and Google Scholar, covering articles up to February 2024 ~~(Table S2)~~. The search employed Boolean operators "AND" or "OR" with keywords such as "*Garcinia mangostana Linn Extract*," (GMLE), "interleukin-1," (IL-1), "interleukin-6," (IL-6), "high sensitivity c-reactive protein," (hsCRP), "placebo," "randomized controlled trial," and "effect."

Data Extraction

The reviewers independently collected baseline characteristics, exposures, and outcomes from the included studies, encompassing author names, publication years, study designs, mean ages, study periods, and participant numbers (GMLE vs placebo and total population).

Quality Assessment

All the included studies underwent further assessment using the JBI (Joanna Briggs Institute) risk-of-bias tool, which was also used to assess the risk of bias in randomized controlled trials (RCTs) with 13 questions ~~(Table S5)~~, and cohort studies using 11 questions. All calculations and assessments based on five major domains were carried out

automatically using the JBI tool.[27] Two investigators (A.S.A. and A.B.) performed the quality assessment. If any discrepancies arose during this evaluation phase, the investigators collaboratively resolved them.

Outcome Measure
The primary outcomes of interest included the effect of GMLE vs. placebo on systolic blood pressure (SBP); inflammatory factors, such as interleukin-1 (IL-1) and interleukin-6 (IL-6); and high-sensitivity c-reactive protein (hsCRP), expressed as the standard mean difference (SMD) with 95% confidence intervals (CIs).

Statistical analysis
Adjusted risk estimates were calculated using the best-adjusted SMD with 95% CIs, with significance determined at $p < 0.05$. Heterogeneity was assessed using the Q test, with significance set at $p < 0.05$

Results and Discussion

Study selection process and quality assessment
This review initially started with 8,579 studies gathered from online sources such as PubMed, ScienceDirect, and Google Scholar. A duplication check removed 512 entries, reducing the pool to 8,067 studies. After further screening, 7,950 articles were excluded due to their nature as book chapters, guidelines, study protocols, editorials, observational studies, or reviews. We subsequently attempted to retrieve 117 studies but failed to access 5 of them. After the remaining 112 reports were evaluated for relevance and accessibility, 108 were dismissed. Only 4 studies fully met the inclusion criteria and were selected for the review (Figure 1).

Study characteristics
This review included a total of 4 studies comprising 299 patients on the impact of administering GMLE (*Garcinia mangostana Linn Extract*) at a dosage of 25 mmg/day over a period of 90 days to hypertension patients. The participants varied in age and body mass index (BMI).

Risk of Bias Assessment
The four included studies were classified as having a different risk of bias according to the method used (Table 2). All studies were assessed by the JBI (Joanna Briggs Institute), and all of the studies were classified as having a low risk of bias, which indicates that the studies included are of high quality.
Answer categorized: Y: Yes; N: No; Unclear; NA: Not applicable
The grading scores were as follows: low risk/high quality (scores 70%), medium quality/moderate risk (50%-69%), and low quality/high risk (scores <50%).

Outcome Results
We pooled approximately 299 patients in four studies, including 3 RCTs and 1 cohort. The effect of GMLE versus placebo was significantly good in hypertension patients. Our exploration showed a large decrease in all the results compared with those of the placebo group. As shown in Figure 2, compared with the placebo, the GMLE had a significant effect on reducing systolic blood pressure (SMD = -1.25 [-1.93; -0.57], p=0.003, I^2 = 69%). Our secondary outcome was inflammatory factor, which significantly reduced hsCRP levels (SMD = -5.09 [-9.67; -0.51], p=0.03, I^2 = 98%), and interleukin-1 (IL-1) significantly decreased (SMD = -1.04 [-1.30; -0.79], p<0.00001, I^2 = 0%), as did interleukin-6 (SMD = -1.05 [-1.30; -0.79], p<0.00001, I^2 = 0%).

The anti-inflammatory properties of GMLE (Fig. 3) mediate its ability to lower systolic blood pressure. Xanthones in the GMLE reduce oxidative stress by neutralizing ROS, which can cause elevated blood pressure and cardiovascular remodeling, aggravating the risk of hypertension. Xanthones may inhibit NF-κB signaling, leading to decreased cytokine production. By acting at the transcriptional level or interfering with signaling pathways leading to cytokine expression, GMLE significantly decreases the secretion of IL-1, IL-6, and hsCRP and decreases the expression of proinflammatory indicators. A significant reduction in these inflammatory mediators results in decreased systolic blood pressure.

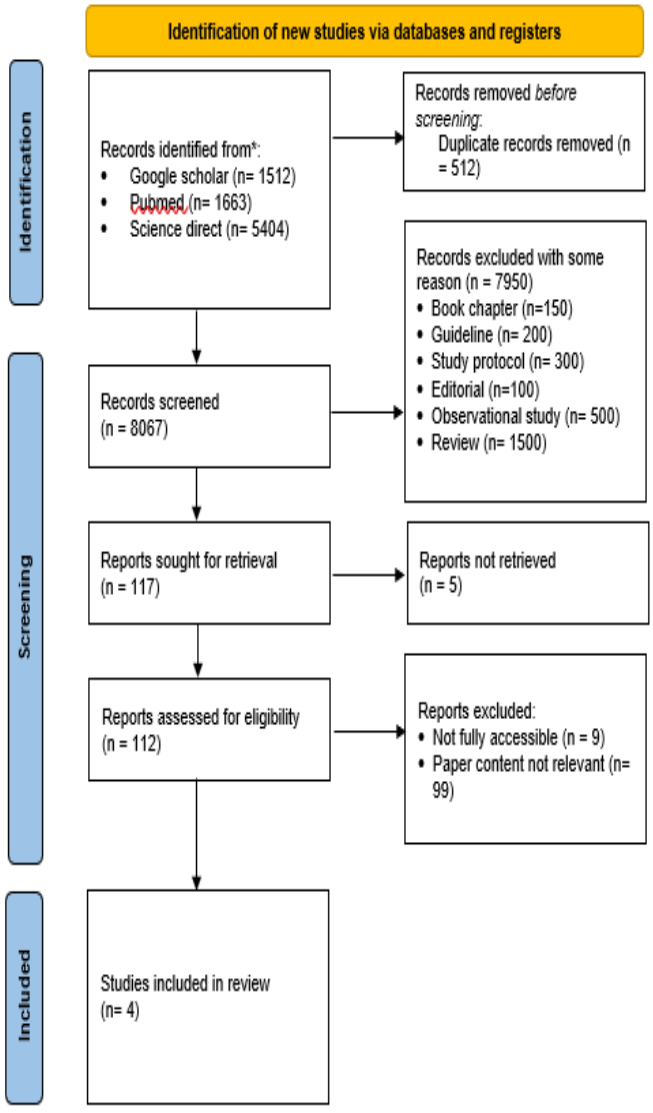

Figure 1: PRISMA flow diagram of the study selection process.

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Table 1: Patient characteristics

No.	Author, year	Study design	Location (country)	GMLE group					Control group					Study Quality
				Number	Age (yr)	Male (n)	BMI (kg/m^2)	Methods	Number	Age (yr)	Male (n)	BMI (kg/m^2)	Methods	
1	Fadlan, 2018	RCT	Indonesia	33	66	12	24.15	GMLE 2520 mg/day for 90 days	33	66	9	24.10	Placebo	Low Risk
2	Fadlan, 2019	RCT	Indonesia	33	60	16	25.12	GMLE 2520 mg/day for 90 days	33	60	14	25.31	Placebo	Low Risk
3	Handayani, 2020	Cohort	Indonesia	37	64.08	6	24.75	GMLE 2520 mg/day for 90 days	40	64.08	5	26.95	Placebo	Low Risk
4	Sargowo, 2018	RCT	Indonesia	45	60	12	26.51	GMLE 2520 mg/day for 90 days	45	60	15	25.32	Placebo	Low Risk

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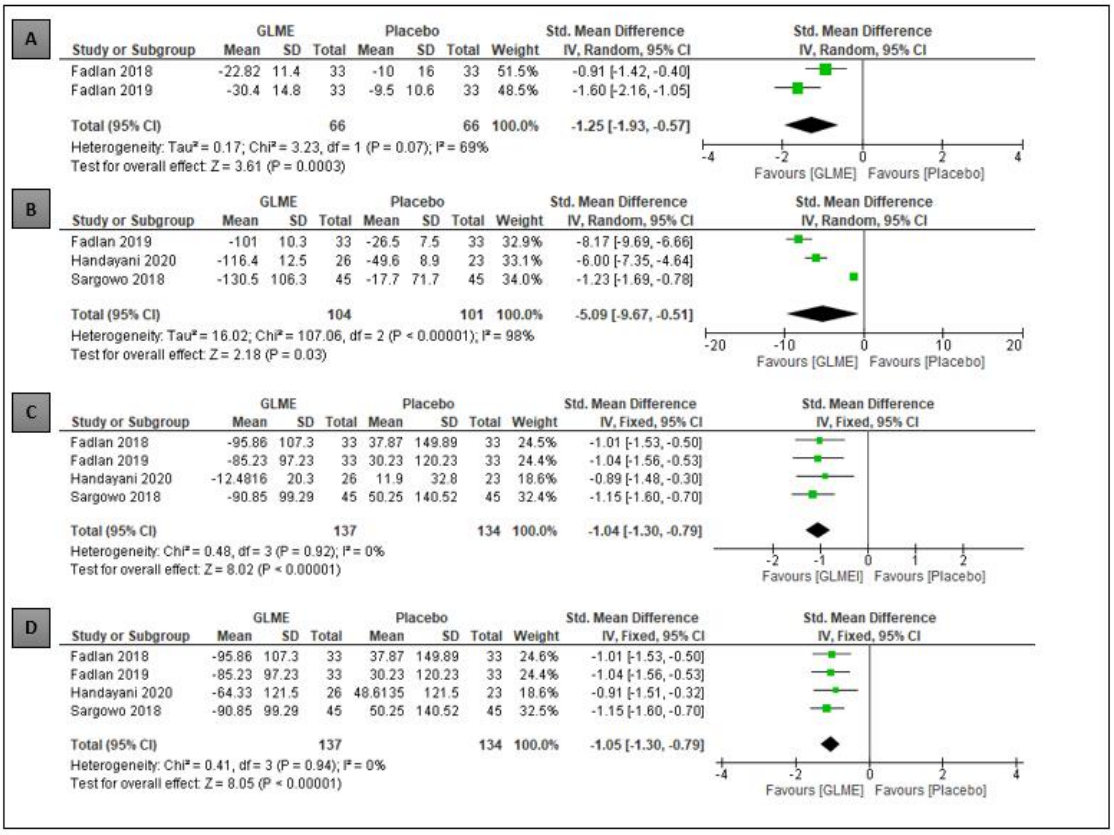

Figure 2: Results of the meta-analysis of *Garcinia mangostana Linn extract* compared with placebo; (a) systolic blood pressure (mmHg), (b) high-sensitivity c-reactive protein (pg/ml), (c) interleukin-1 (pg/ml), and (d) interleukin-6 (pg/ml) levels

Table 2: Assessment of risk of bias in the included studies (RCTs and cohort studies)

RCT Study	**Fadlan et al., 2018**	**Fadlan et al., 2019**	**Sargowo et al., 2018**
1. Was true randomization used for assignment of participants to treatment groups?	Yes	Yes	Yes
2. Was allocation to treatment groups concealed?	Yes	Yes	Yes
3. Were treatment groups similar at the baseline?	Yes	Yes	Yes
4. Were participants blind to treatment assignment?	Yes	Yes	Yes
5. Were those delivering treatment blind to treatment assignment?	Yes	Unclear	Yes
6. Were outcomes assessors blind to treatment assignment?	Yes	No	Yes
7. Were treatment groups treated identically other than the intervention of interest?	No	No	No
8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Yes	Yes	Yes
9. Were participants analyzed in the groups to which they were randomized?	Yes	Yes	Yes
10. Were participants analyzed in the groups to which they were randomized?	Yes	Yes	Yes
11. Were outcomes measured in a reliable way?	Yes	Yes	Yes
12. Was appropriate statistical analysis used?	Yes	Yes	Yes
13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	Yes	Yes	Yes
Grading	92.3%	76.9%	87.5%
Risk of bias	Low Risk	Low Risk	Low
Cohort Study		**Handayani et al., 2020**	
1.Were the two groups similar and recruited from the same population?	Yes		
2.Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Yes		
3.Was the exposure measured in a valid and reliable way?	Unclear		

4.Were confounding factors identified?	No
5.Were strategies to deal with confounding factors stated?	Yes
6.Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Yes
7.Were the outcomes measured in a valid and reliable way?	Yes
8.Was the follow-up time reported and sufficient to be long enough for outcomes to occur?	Yes
9.Was follow-up complete, and if not, were the reasons for loss to follow-up described and explored?	Yes
10.Were strategies to address incomplete follow-up utilized?	Yes
11.Was appropriate statistical analysis used?	Yes
Grading	81.8%
Risk of bias	Low risk

Answer categorized: Y: Yes; N: No; Unclear; NA: Not applicable
The grading scores were as follows: low risk/high quality (scores 70%), medium quality/moderate risk (50%-69%), and low quality/high risk (scores <50%).

This meta-analysis assessed the effectiveness of *Garcinia mangostana Linn extract* (GMLE) as a natural antihypertensive treatment on the basis of data from 3 randomized controlled trials and 1 cohort study involving a total of 299 participants (Table 3). Our research showed that GMLE significantly reduced systolic blood pressure (SBP) and the expression of inflammatory markers in patients with hypertension. One study demonstrated that the consumption of GELEs significantly lowered SBP and inflammatory processes in hypertensive patients with high-risk Framingham scores. This reduction in SBP was accompanied by significant decreases in inflammatory markers, such as the interleukins IL-1 and IL-6, suggesting that the antihypertensive effects of GMLE might be mediated through its anti-inflammatory effects. Additionally, while nitric oxide (NO) plays a crucial role in vasodilation and blood pressure regulation, its increased production under certain conditions may contribute to oxidative stress and inflammation. This mechanism could involve the modulation of endothelial function and the reduction of oxidative stress, both of which are key factors in the pathophysiology of hypertension. [28] Another study reinforced these findings, showing similar reductions in SBP and improvements in inflammatory markers, thereby supporting the potential therapeutic role of GMLE in managing hypertension and its associated inflammatory processes. [28] Research by Boonprom P, Boonla O, Chayaburakul K, Welbat JU, Pannangpetch, and Kukongviriyapan (2017) on the pericarp extract of *Garcinia mangostana* highlighted its protective effects against oxidative stress and cardiovascular remodeling in nitric oxide-deficient rats, a condition that underscores the essential role of NO in maintaining cardiovascular function and mitigating hypertension-related damage. This study underscores the antioxidant properties of the GMLE and its role in enhancing nitric oxide bioavailability, which leads to improved vascular function. [29] Similarly, Abdallah, El-Bassossy, Mohamed, El-halawany, and Alshali, and Banjar (2016) found that phenolics from *Garcinia mangostana* could alleviate exaggerated vasoconstriction in metabolic syndrome through direct vasodilation and nitric oxide generation, crucial mechanisms for lowering SBP as enhanced vasodilation promotes blood flow and reduces vascular resistance.[30]

Table 3: Summary of Results for GMLE (*Garcinia mangostana Linn Extract*) in Hypertensive Patients

End Point	**GMLE (*Garcinia mangostana Linn Extract*) in Patient with Hypertension**	
	SMD (95% CI)	**p value**
Efficacy		
Systolic Blood Pressure (SBP)	-1.25 (-1.93; -0.57)	0.0003*
High Sensitivity C Reactive Protein (hsCRP)	-5.09 (-9.67; -0.51)	0.003*
Interleukin-1 (IL-1)	-1.04 (-1.30; -0.79)	<0.00001*
Interleukin-6 (IL-6)	-1.05 (-1.30; -0.79)	<0.00001*

*= Significant ($p<0.05$)

In addition to its antihypertensive properties, GMLE has significant antioxidant effects, primarily due to its high content of xanthones. These compounds are effective at scavenging reactive oxygen species (ROS), thereby mitigating oxidative stress, a critical driver of inflammation. By neutralizing ROS, GMLE prevents the activation of signaling pathways that lead to the production and release of proinflammatory cytokines. While specific studies on the effect of GMLE on reducing IL-1, IL-6, and hsCRP levels on ROS are limited, the antioxidant activity of mangosteen extracts has been well documented. For instance, a study highlighted the potent antioxidant capacity of mangosteen, suggesting its potential in combating oxidative stress-related pathologies.[31] The antioxidant action of GMLE, which is rich in xanthones, helps mitigate the upstream triggers of inflammation. Additionally, the influence of the extract on cytokines such as IL-1, IL-6, and hsCRP was emphasized, revealing its potential for modulating inflammatory responses. These processes are linked to cardiovascular remodeling, suggesting that GELEs may play a beneficial role in mitigating the effects of oxidative stress and inflammation, ultimately improving cardiovascular health. Nitric oxide (NO) is also a contributing factor to the reduction in inflammation, further supporting the potential therapeutic effects of GMLE in hypertensive individuals (Figure 1). 3). Ismail, Sargowo, Tjahjono, Widito, Rizal, Rahimah, and Sargowo (2021) demonstrated that *Garcinia mangostana* pericarp extract significantly reduced the expression of oxidative stress markers, such as malondialdehyde (MDA), while increasing the expression of antioxidative enzymes, such as superoxide dismutase (SOD), indicating that this fungus has a strong antioxidative effect that could contribute to the reduction of inflammation.[31]

Furthermore, the NF-κB pathway plays a central role in mediating inflammatory responses, including the transcription of inflammatory cytokines such as IL-1 and IL-6, as well as hsCRP. GMLE inhibits the activation of NF-κB, thus downregulating the expression of these inflammatory markers. The inhibition of NF-κB by GMLE can be attributed to the ability of xanthones to interfere with the transcription of NF-κB, leading to reduced NF-κB activity and subsequent decreases in cytokine production. Sargowo (2018) demonstrated that GMLE significantly decreased the levels of IL-1, IL-6, and hsCRP in patients, implicating the inhibition of NF-κB as a possible mechanism.[32] In the NF-κB pathway, GMLE inhibits the TNF-α/NF-κB axis, contributing to its potent anti-inflammatory, antioxidant, and antiapoptotic activities.[32]

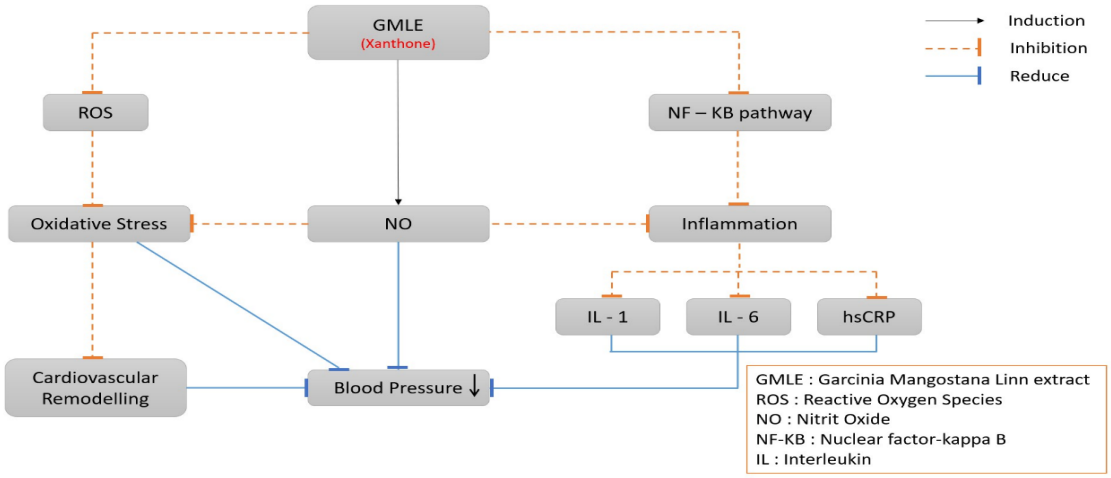

Figure 3: Schematic Diagram of *Garcinia mangostana Linn Extract*-mediated Reduction in Systolic Blood Pressure and Inflammation

Garcinia mangostana reduces inflammation through multiple mechanisms, including the direct suppression of cytokine production, which plays a critical role in its anti-inflammatory effects. This suppression helps modulate immune responses, thereby alleviating the inflammatory process. Such mechanisms are integral to the overall therapeutic potential of GMLE in managing inflammation-related conditions. By acting at the transcriptional level or interfering with the signaling pathways that lead to cytokine synthesis, GMLE effectively reduces the secretion of IL-1, IL-6, and hsCRP. This effect not only diminishes local inflammation but also has systemic implications, potentially reducing the risk of diseases associated with chronic inflammation. The evidence for the role of GMLE in suppressing cytokine production was further supported by Fadlan, Rizal, and Sargowo (2018), who reported significant reductions in systolic blood pressure and in the levels of IL-1 and IL-6 following GMLE treatment, indicating its broad anti-inflammatory effects.[28] In vitro *and* in vivo studies have demonstrated that GMLE significantly inhibits the production of proinflammatory cytokines, such as TNF-α and IL-6, at concentrations of 8 and 14 µg/ml. This suppression of cytokine production is part of the broader anti-inflammatory effects of α-mangostin (aMN), which also includes the inhibition of nitric oxide production, iNOS protein expression, and the selective inhibition of COX-2 enzymes without affecting COX-1. These findings suggest that α-mangostin (aMN) from *Garcinia mangostana Linn* can effectively suppress cytokine production as part of its anti-inflammatory action.[33–36]

Our analysis demonstrated a clear and significant reduction in systolic blood pressure in patients treated with the GMLE, with a standardized mean difference (SMD) of -1.25 (95% CI: -1.93; -0.57) and a p value of 0.0003. Additionally, GMLE administration resulted in significant reductions in inflammatory marker levels, with hsCRP, IL-1, and IL-6 showing SMDs of -5.09 (-9.67; -0.51), -1.04 (-1.30; -0.79), and -1.05 (-1.30; -0.79), respectively, all with p values less than 0.00001. These findings align with previous research that has highlighted the antihypertensive and anti-inflammatory potential of plant extracts. Similar effects have been reported for other natural compounds, such as curcumin and resveratrol, both of which have shown efficacy in reducing inflammatory cytokines and lowering blood pressure in hypertensive individuals. [37–39] Additionally, similar reductions in cytokine levels have been observed with other plant extracts, such as ginger and garlic, further reinforcing the notion that the effect of GMLE on inflammation may play a crucial role in its blood pressure-lowering effects. [40–42] These results suggest that GMLE could be a promising therapeutic option for managing hypertension and inflammation in hypertensive patients.

The global consumption of herbal medicines, especially in Indonesia, China, and India, is increasing due to their pharmacological effects and few side effects. However, issues such as low bioavailability, solubility, and stability persist. For example, mangosteen inhibits cytokine release, reducing inflammation. This medicine is often considered a complementary or alternative form of therapeutic management that is associated with low costs and minimal adverse effects. [43] This growing popularity has also led to an increased focus on integrating herbal remedies into mainstream healthcare practices, particularly for chronic conditions such as hypertension, diabetes, and inflammatory diseases. Despite the challenges associated with bioavailability and stability, advancements in formulation techniques, such as nanoencapsulation and phytosome technology, have improved the efficacy and delivery of herbal compounds such as mangosteen. These innovations enhance the therapeutic potential of these agents, making them viable candidates for addressing the global burden of noncommunicable diseases.

Conclusion

The findings of this study indicate that GMLE (*Garcinia mangostana Linn Extract*) has significant efficacy in reducing systolic blood pressure and inflammatory marker levels in patients with hypertension. Specifically, GMLE effectively lowers systolic blood pressure and high-sensitivity C-reactive protein (hsCRP), interleukin-1 (IL-1), and interleukin-6 (IL-6) levels. These findings suggest that GMLE can be beneficial as an herbal remedy for managing hypertension and associated inflammation. Importantly, compared with conventional drugs, GMLE appears to offer these benefits with fewer side effects, making it a more efficient and economical option. Further studies should explore the optimal dosage, mechanism of action, and safety profile of GMLE in diverse patient populations, particularly those with comorbidities. Additionally, comparisons between GMLE and conventional antihypertensive treatments in terms of efficacy, cost-effectiveness, and quality of life are necessary to establish its place in the clinical management of hypertension. Finally, investigating potential interactions between GMLE and other medications will be crucial for ensuring its safe use in combination therapies.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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