

Antihyperuricemic Potential of *Syzygium polyanthum*: A Systematic Review

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Abstract

Hyperuricemia is a common metabolic disorder that increases the risk of gout and other chronic diseases. *Syzygium polyanthum* has long been used in traditional medicine to reduce uric acid levels, but the available evidence has not been systematically reviewed. This study aimed to summarize the current evidence on the antihyperuricemic activity of *S. polyanthum*. A systematic literature search was conducted in ScienceDirect, Google Scholar, Garuda, and the Directory of Open Access Journals (DOAJ) for articles published between 2010 and July 2026. Study selection followed the PRISMA 2020 guidelines. Fifteen studies met the inclusion criteria, consisting of eight *in vivo* studies, four clinical studies, two *in vitro* studies, and one *in silico* study. Most studies reported that *S. polyanthum* significantly reduced serum uric acid levels, and several experimental studies showed activity comparable to allopurinol. The *in vitro* studies also demonstrated xanthine oxidase inhibitory activity, suggesting that this enzyme is one of the main therapeutic targets. The antihyperuricemic effect was mainly associated with flavonoids and phenolic compounds present in the leaves. However, differences in extraction methods, dosages, and study design limited direct comparison between studies. Overall, the available evidence suggested that *S. polyanthum* may serve as a potential natural antihyperuricemic agent, although further well-designed clinical studies are still needed.

Keywords: *Syzygium Polyanthum*; Hyperuricemia; Gout; Xanthine Oxidase

INTRODUCTION

Hyperuricemia is a metabolic disorder characterized by elevated serum uric acid concentrations resulting from excessive uric acid production, impaired renal excretion, or a combination of both (Du et al., 2024; Yang et al., 2022a). Persistent hyperuricemia is the primary risk factor for gout, an inflammatory arthritis caused by the deposition of monosodium urate crystals in joints and surrounding tissues (Dalbeth et al., 2019). In addition to gout, accumulating evidence indicates that hyperuricemia is associated with chronic kidney disease, hypertension, cardiovascular disease, metabolic syndrome, and type 2 diabetes mellitus, highlighting its role as an important contributor to global morbidity (Borghini et al., 2020; Dehlin et al., 2020). The increasing prevalence of hyperuricemia worldwide has made it a growing public health concern, particularly in aging populations and individuals with unhealthy dietary and lifestyle habits (Chen-Xu et al., 2019; Li et al., 2025).

Hyperuricemia develops when the balance between uric acid production and its elimination is disrupted, resulting in elevated serum uric acid concentrations (Dalbeth et al., 2019). In humans, uric acid is the final product of purine metabolism and is produced through the sequential oxidation of hypoxanthine to xanthine and subsequently to uric acid, a process catalyzed by xanthine oxidase (Furuhashi, 2020; Liu et al., 2021). Under normal physiological conditions, approximately two-thirds of uric acid is excreted by the kidneys, while the remaining one-third is eliminated through the gastrointestinal tract. Hyperuricemia may therefore result from increased uric acid production, impaired renal urate excretion, or both, with reduced renal excretion accounting for most cases (Bobulescu & Moe, 2012). Persistent elevation of serum

uric acid promotes the formation and deposition of monosodium urate (MSU) crystals in joints and surrounding tissues, triggering inflammatory responses that ultimately lead to gout (Terkeltaub et al., 2006; Yang et al., 2022)

Current pharmacological management of hyperuricemia includes xanthine oxidase inhibitors, such as allopurinol and febuxostat, uricosuric agents that enhance renal urate excretion, and, in selected cases, recombinant uricase preparations. These therapies effectively lower serum uric acid concentrations and reduce the risk of gout flares and related complications (FitzGerald et al., 2020; George et al., 2023). However, their long-term use may be associated with adverse effects, including allopurinol hypersensitivity syndrome, hepatotoxicity, gastrointestinal disturbances, nephrolithiasis, and cardiovascular safety concerns associated with certain agents (Riegersperger et al., 2011; White et al., 2018; Xing et al., 2025). In addition, lifelong urate-lowering therapy and medication intolerance may negatively affect treatment adherence in some patients (White et al., 2018). Consequently, increasing attention has been directed toward identifying safer and more accessible therapeutic alternatives, particularly bioactive compounds derived from medicinal plants with a long history of traditional use (Lin et al., 2024).

Syzygium polyanthum (Wight.) Walp., commonly known as Indonesian bay leaf, is a medicinal plant widely distributed in Southeast Asia and traditionally used to manage various diseases, including diabetes, hypertension, hyperlipidemia, and gout (Ismail et al., 2019; Julizan et al., 2023). Phytochemical investigations have demonstrated that its leaves contain diverse bioactive constituents, including flavonoids, phenolic acids, tannins, alkaloids, saponins, and essential oils (Abd Wahab & Aqilah Ja'afar, 2021; Widyawaty et al., 2021). Among these compounds, flavonoids and phenolic constituents have attracted considerable attention because of their antioxidant properties and their ability to inhibit xanthine oxidase, the key enzyme responsible for the conversion of hypoxanthine and xanthine into uric acid (Cos et al., 1998; Nagao et al., 1999). In addition, these phytochemicals may alleviate oxidative stress and inflammatory responses associated with hyperuricemia, suggesting multiple mechanisms that could contribute to their therapeutic effects (Sabandar et al., 2022).

Over the past decade, numerous experimental studies have investigated the antihyperuricemic potential of *S. polyanthum* using *in vitro* xanthine oxidase inhibition assays, animal models of hyperuricemia, and phytochemical analyses (Aryosyaputra & ., 2025; Sabandar et al., 2022). These studies generally report promising findings, including reductions in serum uric acid levels, inhibition of xanthine oxidase activity, and identification of bioactive compounds potentially responsible for these effects. However, the available evidence remains fragmented because of variations in extraction methods, plant parts, experimental models, dosages, outcome measures, and study quality. Consequently, it remains difficult to draw comprehensive conclusions regarding the efficacy and mechanisms of *S. polyanthum* as an antihyperuricemic agent.

To date, no systematic review has comprehensively synthesized the available preclinical evidence regarding the antihyperuricemic activity of *S. polyanthum*. Therefore, this study aimed to systematically review and critically evaluate experimental studies investigating the antihyperuricemic potential of *S. polyanthum*. Specifically, this review summarizes the phytochemical constituents associated with antihyperuricemic activity, evaluates evidence from *in vitro* and *in vivo* studies, discusses the proposed mechanisms of action, and identifies current research gaps to support future pharmacological investigations and the development of *S. polyanthum* as a potential natural therapeutic agent for hyperuricemia.

METHODS

This study employed a systematic literature review to identify, evaluate, and synthesize scientific evidence regarding the potential of *Syzygium polyanthum* as an antihyperuricemic agent. A comprehensive literature search was conducted using four electronic databases: ScienceDirect, Google Scholar, Garuda, and the Directory of Open Access Journals (DOAJ). Articles published between January 2010 and July 2026 were considered eligible for inclusion. The search strategy was adapted to each database using combinations of keywords related

to the research topic, including "*Syzygium polyanthum*", "bay leaf", "hyperuricemia", "uric acid", "gout", and "antihyperuricemic".

The retrieved articles were screened according to predefined inclusion and exclusion criteria. Eligible studies were original research articles investigating the antihyperuricemic activity of *Syzygium polyanthum*, its xanthine oxidase inhibitory mechanism, or bioactive compounds associated with antihyperuricemic effects. Only full-text articles published in English or Indonesian between 2010 and 2026 were included. Review articles, conference abstracts, editorials, letters, theses, dissertations, duplicate records, articles unrelated to the research objective, studies lacking full-text availability, and studies that did not investigate the antihyperuricemic activity or xanthine oxidase inhibitory mechanism of *Syzygium polyanthum* were excluded.

The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A total of 369 records were identified from the database search. After duplicate removal and screening based on titles, abstracts, and full-text eligibility, 15 studies met the predefined inclusion criteria and were included in the final qualitative synthesis. The detailed study selection process is presented in **Figure 1**.

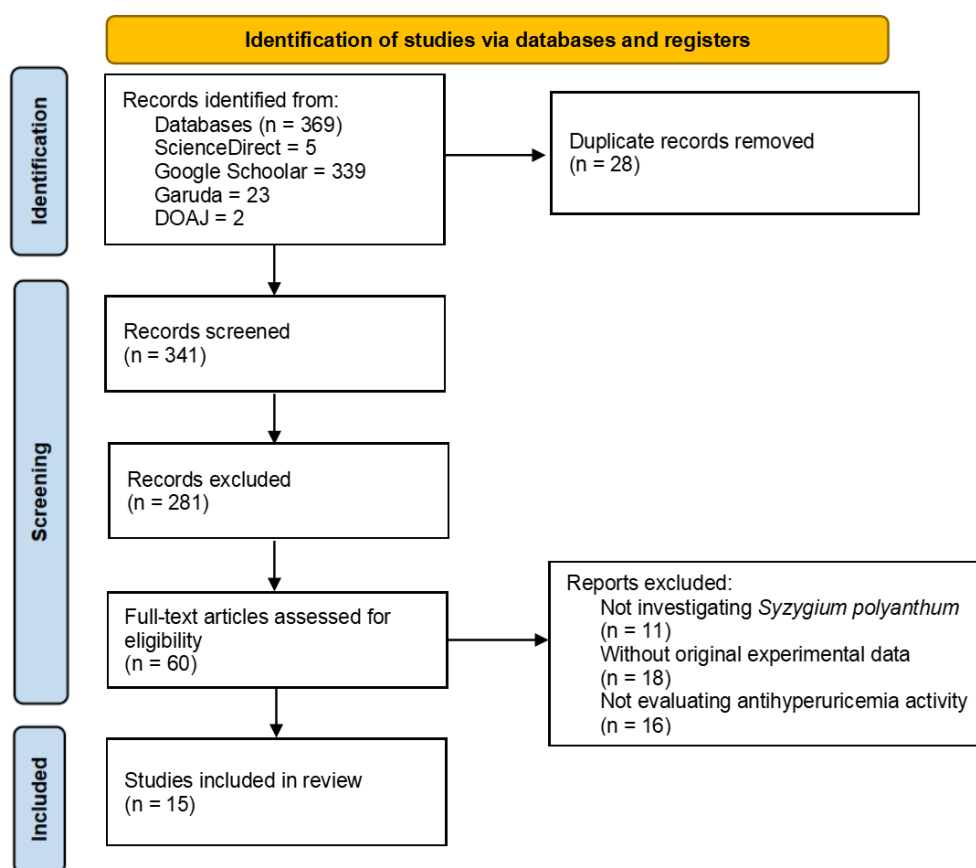


Figure 1. PRISMA 2020 flow diagram illustrating the study selection process for the systematic literature review.

RESULT AND DISCUSSION

A total of 15 studies met the inclusion criteria and were included in this systematic review. The included studies comprised eight *in vivo* studies, four clinical studies, two *in vitro* studies, and one *in silico* study. The studies varied in experimental models, extract preparations, dosages, comparators, and outcome measures. The main characteristics and findings of the included studies are summarized in **Table 1**.

Table 1. Summary of studies evaluating the antihyperuricemic activity of *Syzygium polyanthum*.

Author (Year)	Study Design	Experimental Model	Extract	Dose/ Conc	Comparator	Outcome Measured	Main Finding
(Sari & Sinaga, 2025)	<i>In vivo</i>	Male white mice (<i>Mus musculus</i>) induced with alloxan	Ethanolic leaf extract	70, 140, and 280 mg	Control group	Blood uric acid level	Ethanolic leaf extract significantly reduced uric acid levels, with the 280 mg dose showing the highest efficacy.
(Hilda S. et al., 2025)	<i>In vivo</i>	Hyperuricemic male mice induced with 1% chicken liver juice and potassium oxonate	Ethanolic leaf extract	100, 200, and 400 mg/kg BW	Induction group and allopurinol (10 mg/kg BW)	Blood uric acid level	Bay leaf ethanol extract significantly reduced blood uric acid levels at all doses, with 100 mg/kg BW showing the greatest antihyperuricemic effect, comparable to allopurinol.
(Pratama et al., 2024)	<i>In vivo</i>	Caffeine-induced male mice (<i>Mus musculus</i>)	Ethanolic leaf extract	20, 40, and 80 mg/kg BW	Allopurinol; Na-CMC 1%	Blood uric acid level	The 80 mg/kg BW extract produced the greatest reduction in serum uric acid levels.
(Nasrullah et al., 2024)	<i>In vivo</i>	Hyperuricemic male Wistar rats induced with chicken liver juice	70% Ethanolic leaf extract	150, 200, and 250 mg/kg BW	Allopurinol; negative control	Plasma uric acid level	The 250 mg/kg BW extract significantly reduced plasma uric acid levels and showed efficacy comparable to allopurinol.

(Manopo et al., 2020)	<i>In vivo</i>	Hyperuricemic male white rats (<i>Rattus norvegicus</i>) induced with potassium oxonate	Combination of ethanolic extracts of <i>Syzygium polyanthum</i> leaves and <i>Peperomia pellucida</i>	50, 100, and 200 mg	Negative control (1% CMC) and positive control (allopurinol)	Blood uric acid level	The combined extracts significantly reduced blood uric acid levels, with the highest dose (200 mg) showing the greatest antihyperuricemic activity, comparable to allopurinol.
(Djohar & Paramitha, 2015)	<i>In vivo</i>	Hyperuricemic male white mice (<i>Mus musculus</i>)	Bay leaf decoction	50% (3.9 g); 100% (7.8 g)	Negative control (distilled water)	Serum/blood uric acid level	Significantly reduced blood uric acid levels in hyperuricemic mice, with the 100% decoction showing the greatest antihyperuricemic effect.
(Sinaga, 2014)	<i>In vivo</i>	Potassium oxonate-induced male Wistar rats (<i>Rattus norvegicus</i>)	96% Ethanolic leaf extract	6,413 g/Kg dan 12,826 g/Kg BW	Allopurinol; negative control	Blood uric acid level	The 12.826 g/kg BW ethanolic leaf extract produced the greatest reduction in serum uric acid levels, with efficacy comparable to allopurinol.
(Andi Asda Astiah et al., 2026)	Quasi-experimental	Adults with hyperuricemia	Standardized <i>Syzygium polyanthum</i> tea infusion	2 g tea bag, twice daily for 7 days	Dietary control group	Serum uric acid level	Standardized bay leaf tea significantly reduced serum uric acid from 8.1 to 6.9 mg/dL (p=0.034) with no adverse effects reported.

(Hartanti et al., 2026)	Experimental (pre-post control group)	Hyperuricemic male Swiss Webster mice induced with potassium oxonate	Ethanolic leaf extract	200, 300, 400 mg/kg BW/day	Distilled water and allopurinol (10 mg/kg BW)	Serum uric acid level	Bay leaf extract significantly reduced serum uric acid at all doses, with 400 mg/kg BW producing the greatest reduction (5.2 mg/dL) and showing efficacy comparable to allopurinol.
(Maryam et al., 2025)	Quasi-experimental	Elderly patients with hyperuricemia	Bay leaf decoction	Repeated decoction intervention (dose not specified)	Pre-intervention values	Serum uric acid level	Bay leaf decoction significantly reduced mean serum uric acid levels from 8.0 to 7.0 mg/dL ($p < 0.001$).
(Febriyanti et al., 2018)	Pre-experimental (one-group pretest–posttest)	Elderly patients with hyperuricemia	Bay leaf decoction	10 leaves decoction (400→200 mL), twice daily for 7 days	Pre-intervention values	Serum uric acid level	Bay leaf decoction significantly reduced mean serum uric acid levels from 8.14 ± 0.78 to 4.24 ± 0.72 mg/dL ($p < 0.001$).
(Darussalam et al., 2016)	Quasi-experimental	Patients with hyperuricemia	Bay leaf decoction	0.36 g/kg BW/day (100 mL once daily for 14 days)	Pre-intervention values	Blood uric acid level	Bay leaf decoction significantly reduced blood uric acid levels after 14 days (7.28 to 6.76 mg/dL; $p = 0.009$).

(Sakti et al., 2020)	<i>In vitro</i>	Xanthine oxidase inhibition assay	Ethyl acetate fraction of 80% methanolic leaf extract	IC ₅₀ = 18.43 µg/mL (ethyl acetate fraction)	Allopurinol (IC ₅₀ = 0.067 µg/mL)	Percentage inhibition and IC ₅₀ against xanthine oxidase	The ethyl acetate fraction showed the highest xanthine oxidase inhibitory activity among all fractions tested.
(Candra et al., 2018)	<i>In vitro</i>	Xanthine oxidase inhibition assay	70% Ethanolic leaf extract	5, 10, 20, 50, 100 ppm	Allopurinol	Xanthine oxidase inhibition (%)	The 70% ethanolic leaf extract exhibited xanthine oxidase inhibitory activity, with complete inhibition observed at 5, 20, and 50 ppm, although the effect was not dose-dependent.
(Watung et al., 2023)	<i>In silico</i>	CDK2 protein molecular docking	Phloretin (compound identified from <i>S. polyanthum</i>)	Binding affinity -6.0 kcal/mol	Allopurinol (-5.7 kcal/mol)	Binding affinity and ligand-protein interactions	Phloretin showed stronger CDK2 binding than allopurinol, suggesting potential anti-inflammatory activity against gout.

Of the fifteen studies incorporated into this systematic review, eight adopted an *in vivo* experimental design using mice or rats as the animal model (Sari & Sinaga, 2025; Hilda S. et al., 2025; Pratama et al., 2024; Nasrullah et al., 2024; Manopo et al., 2020; Djohar & Paramitha, 2015; Sinaga, 2014; Hartanti et al., 2026), four were conducted in human subjects using quasi-experimental or pre-experimental designs (Andi Asda Astiah et al., 2026; Maryam et al., 2025; Febriyanti et al., 2018; Darussalam et al., 2016), two evaluated xanthine oxidase inhibitory activity through *in vitro* enzymatic assays (Sakti et al., 2020; Candra et al., 2018), and one applied an *in silico* molecular docking approach (Watung et al., 2023). This distribution indicates that current evidence regarding the antihyperuricemic potential of *Syzygium polyanthum* is predominantly derived from preclinical pharmacological studies, whereas clinical evidence in human populations remains comparatively limited in both quantity and methodological rigor.

With respect to the tested preparations, ethanolic leaf extract was the most frequently investigated form, employed in six of the eight *in vivo* studies at concentrations ranging from 20 mg/kg BW to 12.826 g/kg BW, reflecting substantial variation in extraction concentration and dosing units across laboratories. Aqueous decoction of the leaves was evaluated in one *in vivo* study (Djohar & Paramitha, 2015) and in three of the four clinical studies (Maryam et al., 2025; Febriyanti et al., 2018; Darussalam et al., 2016), while a standardized tea infusion was tested in the remaining clinical trial (Andi Asda Astiah et al., 2026). Allopurinol served as the active comparator in the majority of *in vivo* and clinical studies, allowing a preliminary assessment of the relative efficacy of *S. polyanthum* against a recognized xanthine oxidase inhibitor.

***In vitro* Evidence of Xanthine Oxidase Inhibition**

Two studies directly assessed the xanthine oxidase inhibitory capacity of *S. polyanthum* extracts using enzymatic assays. Sakti et al. (2020) reported that the ethyl acetate fraction of an 80% methanolic leaf extract exhibited the strongest inhibitory activity among the fractions tested, with a half-maximal inhibitory concentration (IC₅₀) of 18.43 µg/mL, compared with 0.067 µg/mL for allopurinol. Candra et al. (2018) similarly demonstrated that a 70% ethanolic leaf extract inhibited xanthine oxidase activity, achieving complete inhibition at concentrations of 5, 20, and 50 ppm, although the inhibitory effect did not follow a clear dose dependent pattern, as no inhibition was observed at 10 and 100 ppm. This non-monotonic response may reflect assay-specific factors such as extract solubility, matrix interference, or variability in enzyme preparation, and it highlights the need for standardized *in vitro* protocols before firm conclusions regarding potency can be drawn.

***In vivo* Evidence in Animal Models of Hyperuricemia**

The eight *in vivo* studies consistently reported that administration of *S. polyanthum* extract or decoction significantly reduced serum or blood uric acid levels compared with untreated hyperuricemic control groups. Sari and Sinaga (2025) observed the greatest reduction at the highest tested dose of 280 mg, whereas Hilda S. et al. (2025) reported that the lowest dose of 100 mg/kg BW produced the greatest antihyperuricemic effect among the doses examined, a pattern that departs from a simple linear dose-response relationship.

Pratama et al. (2024), Nasrullah et al. (2024), Manopo et al. (2020), Sinaga (2014), and Hartanti et al. (2026) each identified their respective highest tested dose (80 mg/kg BW, 250 mg/kg BW, 200 mg, 12.826 g/kg BW, and 400 mg/kg BW) as producing the most pronounced reduction in uric acid levels, which is more consistent with a conventional dose dependent effect. Djohar and Paramitha (2015) found that a 100% bay leaf decoction produced a greater reduction than a 50% decoction, further supporting a concentration-related response for the decoction preparation.

Notably, several studies reported that the antihyperuricemic effect of the optimal extract dose was statistically comparable to that of allopurinol (Hilda S. et al., 2025; Nasrullah et al., 2024; Manopo et al., 2020; Sinaga, 2014; Hartanti et al., 2026), suggesting that *S. polyanthum* extract may achieve efficacy similar to a standard xanthine oxidase inhibitor under experimental conditions. This convergence of findings across independent research groups, using different induction models such as potassium oxonate and chicken liver juice administration, strengthens the plausibility of a genuine pharmacological effect rather than a chance finding confined to a single laboratory.

Clinical Evidence in Human Subjects

Four studies evaluated the antihyperuricemic effect of *S. polyanthum* in human populations, predominantly among elderly individuals with hyperuricemia. Andi Asda Astiah et al. (2026) conducted a pilot trial in which a standardized tea infusion administered twice daily for seven days reduced serum uric acid from 8.1 to 6.9 mg/dL ($p=0.034$), with no adverse effects reported. Maryam et al. (2025) reported a reduction in mean serum uric acid from 8.0 to 7.0 mg/dL ($p<0.001$) following bay leaf decoction, while Febriyanti et al. (2018) documented a markedly larger reduction from 8.14 ± 0.78 to 4.24 ± 0.72 mg/dL ($p<0.001$) after seven days of decoction administration. Darussalam et al. (2016) similarly reported a significant reduction from 7.28 to 6.76 mg/dL ($p=0.009$) following fourteen days of decoction intake at a dose of 0.36 g/kg BW per day. Although all four studies reported statistically significant reductions in uric acid levels, the magnitude of reduction varied considerably, which may be attributable to differences in study population, decoction concentration, treatment duration, and baseline severity of hyperuricemia rather than to a single unifying dose-response relationship.

In silico Evidence and Proposed Mechanism of Action

Watung et al. (2023) provided molecular-level insight through an *in silico* screening study, demonstrating that phloretin, a compound identified from *S. polyanthum*, exhibited a stronger binding affinity toward cyclin-dependent kinase 2 (CDK2) than allopurinol (-6.0 kcal/mol compared with -5.7 kcal/mol). Because CDK2 is implicated in inflammatory signaling pathways relevant to gouty arthritis, this finding suggests that phloretin may confer anti-inflammatory benefit independent of xanthine oxidase inhibition, thereby offering a complementary mechanism to the uric acid lowering effect observed in the *in vitro* and *in vivo* studies.

Taken together, the collective evidence points toward two converging mechanisms underlying the antihyperuricemic activity of *S. polyanthum*. First, flavonoid and phenolic constituents present in the leaves appear to inhibit xanthine oxidase activity directly, thereby

limiting the conversion of hypoxanthine and xanthine into uric acid, as demonstrated by the *in vitro* inhibition assays and supported by the consistent reduction in uric acid levels observed in animal models. Second, the antioxidant properties of these phytochemicals may mitigate the oxidative stress generated by xanthine oxidase activity, while compounds such as phloretin may additionally suppress inflammatory signaling associated with monosodium urate deposition, addressing both the biochemical and inflammatory dimensions of hyperuricemia and gout.

Study Limitations

Despite the generally consistent direction of findings across the included studies, considerable methodological heterogeneity limits the strength of conclusions that can be drawn regarding the optimal preparation and dose of *S. polyanthum* for antihyperuricemic use. Extraction methods varied widely, encompassing ethanolic extracts at concentrations ranging from 70% to 96%, an 80% methanolic extract, and simple aqueous decoction, while reported doses were expressed inconsistently across studies using milligrams, grams per kilogram body weight, and parts per million, precluding direct cross-study comparison of potency. Furthermore, only one study (Watung et al., 2023) identified a specific bioactive compound responsible for the observed activity, whereas the majority of *in vivo* and clinical studies attributed the antihyperuricemic effect broadly to flavonoid or phenolic content without isolating or quantifying the active constituents. Clinical evidence remains particularly limited, being confined to small sample sizes, short intervention periods of seven to fourteen days, and quasi-experimental or pre-experimental designs lacking randomization and blinding. No study reported data on long-term safety, chronic toxicity, pharmacokinetic behavior, or a standardized therapeutic dose suitable for human use. Addressing these gaps through randomized controlled trials, standardized extraction protocols, and bioactivity-guided isolation of the responsible compounds will be essential to establish *S. polyanthum* as a validated antihyperuricemic phytotherapeutic agent.

CONCLUSION

This systematic review showed that *Syzygium polyanthum* has antihyperuricemic activity supported by evidence from *in vitro*, *in vivo*, and limited clinical studies. The available findings suggest that its uric acid-lowering effect is mainly related to xanthine oxidase inhibition and the presence of flavonoids and other phenolic compounds. However, variations in extract preparation, dosage, and study design, together with the limited number of clinical studies, make it difficult to determine the optimal therapeutic use. Further randomized clinical trials using standardized extracts are needed to confirm the efficacy and safety of *S. polyanthum* for the management of hyperuricemia.

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