

The Effects of *Moringa oleifera* on Blood IL-6 Levels: A Scoping Review

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ABSTRACT

Interleukin-6 (IL-6) is widely used as an inflammatory biomarker and has also become a therapeutic target in several inflammatory and malignant diseases. *Moringa oleifera* (MO) has been reported to possess anti-inflammatory activity, yet evidence regarding its effect on blood IL-6 levels remains limited. This scoping review analyzed available evidence on the effect of MO on blood IL-6 levels. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). A PubMed search was conducted using the keywords ((*Moringa oleifera*) AND (Interleukin-6 OR IL-6)) AND (blood), covering publications from January 2006 to January 2026. Nine studies met the inclusion criteria. All studies used animal experimental models, measured IL-6 in serum using ELISA, and applied randomized placebo-controlled designs. Most studies reported a significant reduction in blood IL-6 levels after MO intervention. The preparations included aqueous extracts, ethanol extracts, polyphenol extracts, n-butanol fractions, seed powder, and beta-sitosterol isolated from n-butanol seed extract. Overall, MO may have prophylactic potential for chronic inflammatory conditions characterized by elevated blood IL-6 levels; however, standardized preparations and human studies are still needed.

Keywords: *Moringa Oleifera*, Blood IL-6, Anti-Inflammatory, Scoping Review, Animal Model

INTRODUCTION

The global trade of herbal medicines indicates that worldwide consumption of herbal-based products is increasing (Bilia et al., 2022). One herbal plant that has attracted growing interest is *Moringa oleifera* (MO) (Islam et al., 2021). MO is consumed not only for nutritional purposes but also for its potential medical benefits. This plant is native to the southern Himalayas in northern India and grows widely in tropical and subtropical regions, particularly in dry-to-humid climates (Kou et al., 2018; Leone et al., 2015). Its leaves, flowers, seeds, and other plant parts are edible and have been associated with therapeutic properties, including antidiabetic, anticancer, antiulcer, antimicrobial,

antioxidant, and anti-inflammatory effects (Kou et al., 2018). Studies on MO as an anti-inflammatory agent have increased, and several findings have reported anti-inflammatory activity in its leaves, seeds, and roots (Mittal et al., 2017; Yong-Bing et al., 2019).

Inflammation is an immune response to harmful stimuli, including pathogens, damaged cells, toxic compounds, or radiation (Maskrey et al., 2011). During an acute inflammatory response, cellular and molecular events help minimize injury or infection. However, when acute inflammation is not properly controlled, it can progress into chronic inflammation and contribute to chronic diseases such as cardiovascular disease, diabetes, arthritis, and cancer (Gonzalez-Jaramillo et al., 2019). Inflammatory markers are clinically useful for distinguishing normal and pathological biological processes and for evaluating responses to therapeutic interventions. Stimulation of inflammatory cells, including macrophages and adipocytes, can induce the production of pro-inflammatory cytokines such as IL-6. This cytokine has potential utility as a biomarker for diagnosis, prognosis, and therapeutic decision-making (Chen et al., 2018).

Given the development of IL-6 as a therapeutic target, previous reports linking MO administration with changes in blood IL-6 levels, and the limited number of studies on this specific topic, a scoping review was conducted to map the available evidence and identify concepts that require further investigation. A scoping review is appropriate for identifying research trends and summarizing the breadth of evidence in an emerging field (Tricco et al., 2018). Therefore, the purpose of this scoping review was to determine the available evidence regarding the effect of MO on lowering blood IL-6 levels in animal models.

IL-6 is produced by several cell types, including innate immune cells such as macrophages, dendritic cells, and mast cells; B cells; and several CD4 effector helper T-cell subsets. It is also secreted by non-leukocyte cells, including endothelial cells, fibroblasts, astrocytes, epithelial cells, and some malignant cells. IL-6 production can be triggered by tissue damage or stressors such as ultraviolet exposure, irradiation, reactive oxygen species, microbial products, viruses, or other pro-inflammatory cytokines. Its expression is largely regulated through nuclear factor-kappa B (NF- κ B) and CCAAT/enhancer-binding protein alpha (C/EBP α) pathways (Rincon, 2012).

The binding of IL-6 to the IL-6 receptor (IL-6R), followed by association with gp130, activates the Janus kinase (JAK) family of tyrosine kinases, specifically JAK1, JAK2, and Tyk2. Activated JAK phosphorylates and activates signal transducer and activator of transcription 3 (STAT3), an important transcriptional regulator of antiapoptotic genes and several cytokines. IL-6 can also regulate cells that do not express membrane-bound IL-6R through the trans-signaling pathway involving soluble IL-6R (sIL-6R). Because gp130 is broadly expressed, IL-6 can signal across a wide range of cell types (Rincon, 2012). This broad biological influence has made IL-6 not only a marker of inflammation or malignancy but also a therapeutic target for cancer and other inflammatory diseases (Unver & McAllister, 2018).

The clinical relevance of IL-6 is reflected in the development of IL-6R-blocking therapies. Tadami Kishimoto and colleagues pioneered the development of tocilizumab, a humanized anti-IL-6R antibody that binds cell-surface IL-6R and sIL-6R to block interaction with IL-6 (Mihara et al., 2011). During the COVID-19 pandemic, IL-6 inhibitors were also considered for patients with severe symptoms. A systematic review reported that tocilizumab reduced all-cause mortality at day 28 compared with standard care or placebo (Ghosn et al., 2021).

RESEARCH METHODS

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR), with predetermined inclusion criteria (Tricco et al., 2018). An electronic search was performed in PubMed to identify literature related to MO and its ability to influence blood IL-6 levels. The search keywords were: ((*Moringa oleifera*) AND (Interleukin-6 OR IL-6)) AND (blood). The search covered worldwide publications between 1 January 2006 and 1 January 2026. The inclusion criteria were peer-reviewed studies published in English, studies conducted on experimental animals and humans, and studies in which serum IL-6 was examined using the ELISA technique. The first screening focused on title and abstract eligibility. The second screening applied the same criteria to full texts. Articles that passed both screening stages were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal tool to control potential bias and assess publication quality.

Two reviewers independently extracted data from all literature that met the inclusion criteria using Microsoft Excel, and the extracted data were checked by a third reviewer. The extracted information included first author, year of publication, country, study objective, type of MO preparation, induction model, species, study design, material methods, dose and duration of MO therapy, blood IL-6 values, level of significance, and main findings. Any uncertainty about study inclusion was resolved through discussion among the reviewers until consensus was reached. After the eligible studies were determined, trends and similarities across the studies were examined.

RESULTS AND DISCUSSION

A. Study Selection

A total of 33 potential articles were collected from the electronic database. These articles were evaluated against the inclusion criteria and filtered based on topic relevance. After screening, nine articles met the inclusion criteria and were retained for this scoping review. The identification and selection process is presented in Figure 1.

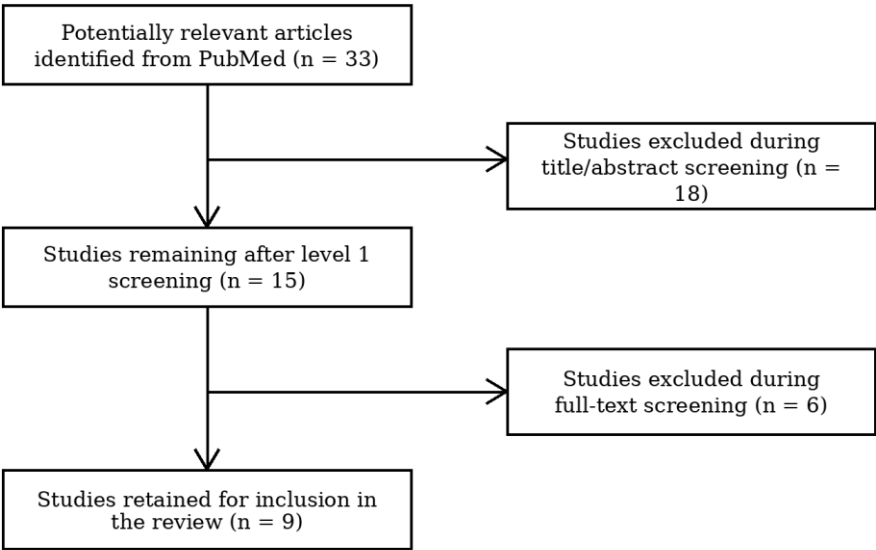


Figure 1. Identification and selection of studies for inclusion in the review.

B. Study Characteristics

The included studies were conducted in four countries. Most studies were published in India (n = 5) (Mahajan et al., 2007a, 2007b, 2009; Mahajan & Mehta, 2008, 2011), followed by China (n = 2) (Wen et al., 2022; Zhang et al., 2020), Brazil (n = 1), and Saudi Arabia (n = 1) (Al-malki & El Rabey, 2015; Azevedo et al., 2018). Publication years ranged from 2007 to 2022, and the highest number of included publications appeared in 2007 (n = 2). All studies were randomized placebo-controlled animal studies. All studies measured blood IL-6 in serum using ELISA. Overall, the included studies showed that experimental animals experienced lower IL-6 levels after receiving MO intervention. Detailed characteristics and findings are summarized in Table 1.

Table 1. Characteristics and Findings of Included Studies

Study	Model and induction	MO intervention	Main IL-6 finding
Wen et al. (2022), China	C57BL/6 mice; non-induced model	MO leaf polysaccharide extract; 20, 40, and 60 mg/kg BW/day for 28 days	The 40 mg/kg BW/day dose significantly reduced IL-6, while 20 and 60 mg/kg BW/day were not significant ($p < 0.05$).
Azevedo et al. (2018), Brazil	Wistar rats; diabetic wound model with skin excision and STZ 45 mg/kg BW in diabetic groups	MO leaf aqueous extract; 100 mg/kg BW/day for 10 days	MO significantly reduced IL-6 in non-induced and STZ-induced groups ($p < 0.05$).
Zhang et al. (2020), China	C57BL/6 mice; colitis model induced by 3% dextran sulfate sodium (DSS)	MO leaf polyphenol extract; 50 and 200 mg/kg BW/day for 14 days	Both doses significantly reduced IL-6 compared with positive control ($p < 0.05$).
Al-malki & El Rabey (2015), Saudi Arabia	Male albino rats; diabetes model induced by STZ 60 mg/kg BW	MO seed powder; 50 and 100 mg/kg BW/day for 28 days	Both doses significantly reduced serum IL-6; 100 mg/kg BW/day was more effective ($p < 0.001$).
Mahajan et al. (2007a), India	Wistar rats; asthma model induced by toluene diisocyanate (TDI)	Ethanol extract of MO seeds; 100 and 200 mg/kg BW/day for 28 days	Both doses reduced IL-6, but only 200 mg/kg BW/day was statistically significant ($p < 0.05$).
Mahajan & Mehta (2011), India	Dunkin-Hartley guinea pigs; ovalbumin-induced asthma model	Beta-sitosterol isolated from n-butanol seed extract; 2.5 mg/kg BW/day for 12 days	Beta-sitosterol significantly decreased IL-6 levels ($p < 0.05$).
Mahajan & Mehta (2008), India	Dunkin-Hartley guinea pigs; ovalbumin-induced asthma model	Ethanol extract of MO seeds; 200 mg/kg BW/day for 12 days	MO extract significantly decreased IL-6 levels ($p < 0.05$).
Mahajan et al. (2009), India	Dunkin-Hartley guinea pigs; ovalbumin-induced asthma model	n-butanol extract of MO seeds; 100 mg/kg BW/day for 12 days	n-butanol fraction significantly decreased IL-6 levels ($p < 0.05$).
Mahajan et al. (2007b), India	Female Wistar rats; arthritis model induced by Complete Freund's Adjuvant (CFA)	Ethanol extract of MO seeds; 100 and 200 mg/kg BW/day for 21 days	Only 200 mg/kg BW/day significantly decreased IL-6 levels ($p < 0.05$).

Source: Extracted and optimized from the reviewed studies.

C. Results of Animal Studies

Of the nine studies, four used *Rattus norvegicus* (Al-malki & El Rabey, 2015; Azevedo et al., 2018; Mahajan et al., 2007a, 2007b), three used Dunkin-Hartley guinea pigs (Mahajan et al., 2009; Mahajan & Mehta, 2008, 2011), and two used C57BL/6 mice (Wen et al., 2022; Zhang et al., 2020). All

studies reported a statistically significant decrease in animal blood IL-6 levels following MO administration. Eight studies reported $p < 0.05$, while one study reported $p < 0.001$ (Al-malki & El Rabey, 2015). The longest MO intervention duration was 28 days (Al-malki & El Rabey, 2015; Wen et al., 2022), while the shortest was 10 days (Azevedo et al., 2018). Eight studies used induction models, whereas one study did not induce experimental animals (Wen et al., 2022).

Four studies used asthma induction models. Three studies used ovalbumin, while one study used toluene diisocyanate (TDI) (Mahajan et al., 2007a, 2009; Mahajan & Mehta, 2008, 2011). The ovalbumin model was applied to Dunkin-Hartley guinea pigs, whereas TDI was applied to *Rattus norvegicus*. These studies used MO seed preparations, including ethanolic extract, n-butanol extract, and beta-sitosterol isolated from n-butanol extract. In the ethanolic seed extract group, 200 mg/kg BW/day significantly reduced blood IL-6 levels, while 100 mg/kg BW/day reduced IL-6 without statistical significance. The n-butanol extract at 100 mg/kg BW/day and beta-sitosterol at 2.5 mg/kg BW/day also significantly reduced IL-6 levels.

Two studies induced diabetes mellitus using streptozotocin (STZ) at different doses. One study used STZ at 45 mg/kg BW, while another used STZ at 60 mg/kg BW. Both studies used *Rattus norvegicus* but applied different MO preparations: aqueous leaf extract and seed powder (Al-malki & El Rabey, 2015; Azevedo et al., 2018). Aqueous leaf extract at 100 mg/kg BW/day for 10 days significantly reduced blood IL-6 in both induced and non-induced groups (Azevedo et al., 2018). Seed powder at 50 mg/kg BW/day and 100 mg/kg BW/day also significantly decreased blood IL-6 levels (Al-malki & El Rabey, 2015).

One study induced colitis in C57BL/6 mice using dextran sulfate sodium (DSS). Polyphenol extract from MO leaves was administered at 50 mg/kg/day and 200 mg/kg/day for 14 days, and both doses significantly reduced blood IL-6 levels (Zhang et al., 2020). One study induced arthritis in *Rattus norvegicus* using Complete Freund's Adjuvant (CFA). Ethanolic extract from MO seeds was administered at 100 mg/kg BW and 200 mg/kg BW for 21 days. Only the 200 mg/kg BW dose significantly decreased blood IL-6 levels (Mahajan et al., 2007b). In the non-induced C57BL/6 mouse study, polysaccharide extract from MO leaves was administered at 20, 40, and 60 mg/kg/day for 28 days. Based on the extracted table, the 40 mg/kg/day dose significantly reduced IL-6 levels, while 20 and 60 mg/kg/day did not reach significance (Wen et al., 2022).

D. Discussion

This scoping review found that *Rattus norvegicus* was the most frequently used experimental animal (Al-malki & El Rabey, 2015; Azevedo et al., 2018; Mahajan et al., 2007a, 2007b). This species is widely used in laboratory research because of its relatively small size, known genetic background, short generation time, similarity to human disease conditions, and manageable microbial status. Its docile nature also makes it easier to handle than many other rodents in laboratory settings (Hickman et al., 2017).

Most studies used aqueous extracts, ethanol extracts, polyphenol extracts, n-butanol fractions, beta-sitosterol isolated from n-butanol seed extract, or MO seed powder (Al-malki & El Rabey, 2015; Mahajan et al., 2007a, 2007b, 2009; Mahajan & Mehta, 2008, 2011). Both MO seeds and leaves have been reported to have anti-inflammatory activity (Yong-Bing et al., 2019). Interestingly, ethanolic extract from MO seeds at 100 mg/kg BW/day, given for either 21 or 28 days, did not significantly reduce blood IL-6 levels (Mahajan et al., 2007a, 2007b). By contrast, aqueous leaf extract at 100 mg/kg BW/day for only 10 days significantly reduced IL-6 levels (Azevedo et al., 2018).

Previous evidence also suggested that the anti-inflammatory activity of MO leaves may be stronger than that of MO seeds and may even be stronger than aspirin (Yong-Bing et al., 2019).

This review identified nine studies that met the inclusion criteria, and all were conducted in animal models. This indicates that human studies examining the effect of MO on blood IL-6 levels remain scarce. At least four inflammatory pathology models were represented: asthma, diabetes mellitus, colitis, and arthritis. Overall, various forms of MO, including seed extracts, aqueous leaf extracts, polyphenol leaf extracts, n-butanol fractions, and isolated compounds, reduced blood IL-6 levels. These findings support the potential role of MO in regulating inflammatory processes, especially those involving IL-6.

Mechanistically, MO leaf extract has been reported to inhibit inflammation through NF- κ B pathway inactivation, blocking I κ B- α degradation and nuclear translocation of p65. Inhibition of NF- κ B binding to target DNA may downregulate pro-inflammatory mediators such as IL-6 (Luetragoon et al., 2020). The findings of this scoping review are consistent with previous reviews indicating that MO has anti-inflammatory properties (Ray et al., 2017) and may have beneficial anti-inflammatory effects in diabetes-related inflammation (Mthiyane et al., 2022). However, the present review differs from previous reviews because it specifically focuses on the effect of MO on blood IL-6 levels in animal models, rather than covering broader anti-inflammatory, antioxidant, or antidiabetic endpoints.

This scoping review has several limitations. First, only studies published in English were included. Second, all included studies used animal models, so direct clinical application to humans remains limited. Third, the included studies used different approaches to prepare and administer MO, which may have produced different ratios of bioactive components. Differences in induction models, extract types, treatment doses, treatment durations, and experimental animal species also made direct comparisons difficult. Future studies should standardize MO preparations, clarify optimal dose and duration, compare MO with established anti-inflammatory drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), and conduct well-designed human studies.

CONCLUSION

This scoping review supports the potential beneficial effect of *Moringa oleifera* in reducing blood IL-6 levels in animal models. Nevertheless, differences in preparation, dose, treatment duration, and induction models indicate that the current evidence should be interpreted cautiously. Standardized MO preparations, human trials, and comparative studies with established anti-inflammatory drugs are needed before MO can be recommended for clinical application. Overall, MO appears to be a promising prophylactic candidate for chronic inflammatory conditions characterized by elevated blood IL-6 levels.

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