

Systematic Review Article

## ***Ipomoea batatas* L. and Anti-Inflammation Effect: A Systematic Review Its Therapeutic Role in Rodent Models**

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### **ABSTRACT**

This systematic review aims to evaluate the health benefits of Purple Sweet Potato (PSP) contain anthocyanins, phenolic acids, and flavonoids in animal models, focusing on its antioxidant, anti-inflammatory, lipid peroxidation, and immunomodulatory properties. Owing to its increasing scientific significance, investigating its health effects in animal models offers important insights into its potential therapeutic applications for human health. Fourteen eligible *in vivo* studies were identified from 5.043 original research articles following predefined eligibility criteria based on population, intervention, comparison, outcome, and study design (PICOS). These studies employed various extracts (aqueous, ethanolic, methanolic, fermented) and animal models (Wistar rats, BALB/c mice, Kunming mice, Sprague-Dawley rats) to investigate the effects. The PSP significantly reduced oxidative stress markers such as Malondialdehyde (MDA) and enhancing endogenous antioxidant enzymes including Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), and Catalase (CAT). Anti-inflammatory effects were evident through downregulation of Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ), Interleukin-1 Beta (IL-1 $\beta$ ), Interleukin-6 (IL-6), Nitric Oxide (NO), and Matrix Metalloproteinase-3 (MMP-3), mediated via suppression of Nuclear Factor Kappa B (NF- $\kappa$ B) and Mitogen-Activated Protein Kinase (MAPK). Anti-inflammatory effects were observed in high-fat diet-induced obese rats, where PSP supplementation (5% weight/weight, w/w) markedly reduced TNF- $\alpha$ , IL-6, Monocyte Chemoattractant Protein-1 (MCP-1), and Interleukin-1 Beta (IL-1 $\beta$ ) in adipose tissue. Significant enhancement of endogenous antioxidants occurred in arthritic rats, with PSP extracts (300 mg/kg BW) increasing CAT, Peroxidase (POD), and SOD while lowering IL-1 $\beta$ , IL-6, and NO. The lipid peroxidation reduction was seen in Carbon Tetrachloride (CCl<sub>4</sub>)-induced liver injury, where anthocyanin-rich PSP extract (400 mg/kg BW) decreased MDA, increased SOD and Glutathione (GSH). Long-term intervention and aqueous-fermented extracts are particularly promising due to their safety profiles and suitability for functional food formulations, but heterogeneity in dosages and durations limits cross-study comparability. Future research should emphasize clinical trials to establish safety, efficacy, and translational relevance in human health.

### **INTRODUCTION**

Inflammation is a natural immune response to tissue damage, infection, or harmful stimuli (Medzhitov 2021; Meizlish *et al.* 2021). Acute

inflammation is rapid, lasting minutes to hours, but if unresolved, it can become chronic, contributing to diseases such as liver disease, cardiovascular disease, diabetes, and cancer (Wang *et al.* 2017b; Meizlish *et al.* 2021). Chronic inflammation

involves excessive proinflammatory mediators like Interleukin-6 (IL-6) and Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) which damage tissues and disrupt systemic homeostasis (Lee & Kim 2022; Dong *et al.* 2025). Effective and safe anti-inflammatory strategies are essential to control these pathological processes. While Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) remain the main treatment, emerging evidence shows that dietary, nutraceutical, and lifestyle interventions can complementarily modulate inflammation (Gouvarchinghaleh *et al.* 2023). This has driven interest in nature-based therapies, especially plants with high antioxidant content such as sweet potatoes (Samiappan & Chalakoth 2025).

Purple Sweet Potato (PSP) is a tuber rich in polysaccharides, anthocyanins, flavonoids, and phenolics and exhibits antioxidant and anti-inflammatory activities (Matsumoto *et al.* 2024). Its polysaccharides regulate macrophage polarization and suppress inflammasome activation, while anthocyanin-rich extracts reduce oxidative stress and inflammatory mediator expression (Sun *et al.* 2022; Wang *et al.* 2024). PSP anthocyanins increase blood and tissue anthocyanin levels, act as antioxidants, and reduce oxidative stress and inflammation (Jawi *et al.* 2024). Research shows that the anthocyanins in PSP may help prevent cardiovascular disease, support obesity management, and exhibit antitumor activity (Fauziyah *et al.* 2024). PSP contains anthocyanins such as cyanidin glucoside and peonidin-3-glucoside that are 2–8 times more total phenols and 3–15 times more flavonoids than other sweet potatoes, and 1.5–3.7 times stronger antioxidant activity than purple corn, red cabbage, elderberry, and grape skin. Highly active anthocyanins provide stronger, more stable oxidative and anti-inflammatory protection and potentially broader health benefits than ascorbic acid (Kurniasari *et al.* 2021).

Mice and rats share genetic, physiological, and biochemical similarities with humans, including conserved inflammatory pathways, cytokine responses, and immune cell functions (Lemos *et al.* 2025). Rodent inflammation models, such as LPS-induced systemic inflammation and Collagen-Induced Arthritis (CIA), are widely used to study inflammatory responses (Lemos *et al.* 2025). Administration of 40 mg/kg PSP anthocyanins for 14 days in female Wistar rats with CIA significantly reduced TNF- $\alpha$ , Interleukin-1

Beta (IL-1 $\beta$ ), rheumatoid factor, Interleukin-1 Alpha (IL-1 $\alpha$ ), IL-6, and Interleukin-18 (IL-18) in MH7A cells, while inhibiting cell proliferation and promoting apoptosis (Dong *et al.* 2025). PSP polysaccharides also showed effects: 50  $\mu$ g/ml administered for 28 days in male BALB/c mice with liver injury significantly decreased TNF- $\alpha$  and Interferon-Gamma (IFN- $\gamma$ ) (Ding & Fan 2024).

Findings are fragmented due to variations in study design, animal models, dosages, and outcome measures. To date, no systematic review has synthesized or critically analyzed this evidence, leaving a gap in understanding PSP's therapeutic potential in inflammation. This systematic review therefore aims to identify, compile, and evaluate preclinical studies on PSP's anti-inflammatory effects in rodent models, focusing on inflammatory markers, experimental designs, dosages, and mechanisms of action.

## METHODS

### Design, location, and time

This study employed a Systematic Literature Review (SLR) about *Ipomoea batatas* L. and its anti-inflammatory effect approach following PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines. The review was based on secondary data and comprised Randomized Controlled Trials (RCTs). Research locations were predominantly conducted in Indonesia, China, Pakistan, and Taiwan with the highest proportion from Indonesia. Publication years ranged from 2016 to 2025, indicating research interest in this topic in recent years.

### Sampling

A comprehensive search was carried out to identify original studies that met specific inclusion criteria: RCTs involving rats and/or mice experiencing inflammation, interventions using anthocyanins derived from PSP, and written in either English or Indonesian. Articles were sourced from major academic databases including Google Scholar, PubMed, ResearchGate, and ScienceDirect. The search used the following keywords: *Ipomoea batatas* L. OR purple sweet potato AND anti-inflammatory response on rats OR mice. The primary variables extracted from the selected studies were inflammatory

indicators, particularly cytokines like TNF- $\alpha$ , IL-6, and other related markers of inflammation.

### Data collection

Three reviewers (FU, IKR, and DA) independently conducted a systematic exploration of four journal databases using Rayyan.ai. They performed the initial search, screening process, and downloaded all potentially relevant full-text articles. In cases where there were differences in judgment, three reviewers held discussions to reach an agreement. Meanwhile, another author (YP and YN) contributed to data interpretation and discussion, providing critical insights for analysis and contextualization of the findings.

The selection of articles was based on the PICOS framework, and most of the included studies were published in the English language from China, Pakistan, and Taiwan while Indonesian studies were published in *Bahasa Indonesia*. The intervention focused on anthocyanins derived specifically from PSP and studies combining anthocyanins with other plant compounds were excluded. Studies published before 2016 or without accessible full texts were also excluded, as insufficient information prevented evaluation of methods, outcomes, and risk of bias.

### Data analysis

The quality appraisal of the included full-text studies was performed using the SYRCLE's risk of bias tool, which comprises 10 evaluation Domains (D1–D10). Each selected study was then systematically analyzed by comparing key characteristics, including the names of the authors, year of publication, country of origin, experimental subjects, control groups, interventions applied, and the main outcomes reported in the findings.

## RESULTS AND DISCUSSION

From 5,043 articles in Figure 1, we identified 14 studies that investigated the health effects of PSP, particularly focusing on its antioxidant, anti-inflammatory, lipid peroxidation and immunomodulatory effects. A total of 5,043 articles were identified from ResearchGate, PubMed, ScienceDirect, and Google Scholar. After removing 351 duplicates, 4,692 articles were screened by title and abstract, excluding 4,667 for being off-topic or review papers. The remaining 25 full-text articles were assessed, with

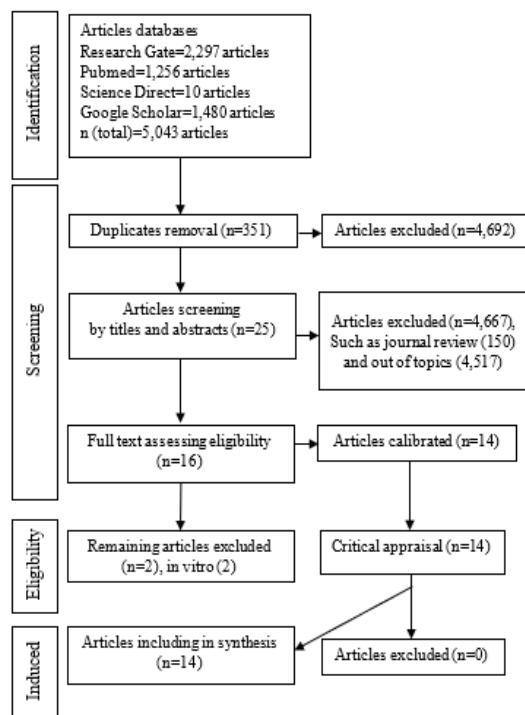
11 excluded for insufficient data or being in vitro studies. Ultimately, 14 articles met the inclusion and exclusion criteria for further evaluation.

The SYRCLE's Risk of Bias tool was used to assess methodological quality (Table 1), with overall study quality ranging from low to moderate risk. Six studies were rated low risk of bias (Wang *et al.* 2017a; Dwi *et al.* 2020; Dewangga *et al.* 2022; Rahman *et al.* 2023; Ding & Fan 2024; Dong *et al.* 2025) for fulfilling most criteria, including random allocation, complete outcome data, and low selective reporting. The studies varied in research setting, animal models, dietary interventions, extraction methods, dosage, duration, and outcome measures. Conducted in Indonesia, China, Iran, and Pakistan, they used male Wistar rats, Sprague-Dawley rats, BALB/c mice, and C57BL/6 mice, with disease models including High Carbohydrate Diet (HCD), High Fat Diet (HFD)-induced obesity, High-Fat, High-Fructose Diet (HFFD), Monosodium Urate MSU (gout arthritis), Complete Freund's Adjuvant (CFA) or Collagen-Induced Arthritis (CIA) (rheumatoid arthritis), restraint stress, cigarette smoke, and CCl<sub>4</sub>-induced liver injury. Intervention durations ranged from 9–14 days (acute) to 8–12 weeks (chronic).

Seven studies such as Majid *et al.* (2018), Yen *et al.* (2025), Kurnianingsih *et al.* (2023), Jawi *et al.* (2024), Elvana *et al.* (2016), Setiawan and Nadhil (2019), and Yasa *et al.* (2024) showed unclear risks in both domains, potentially affecting internal validity. Heterogeneity in animal models, intervention duration, dosage, and extraction methods also limit PSP anthocyanins' effectiveness. PSP's anti-inflammatory effects are most pronounced in metabolic or obesity-related inflammation, endogenous antioxidant enhancements are strongest in arthritis models, and lipid peroxidation reduction is most evident in hepatotoxicity models. The differences across experimental conditions and outcome indicators are summarized in Table 2.

### Variations by animal conditions and outcomes

Several studies (Majid *et al.* 2018; Yen *et al.* 2025; Kurnianingsih *et al.* 2023) used HFD-induced obese models to assess metabolic and inflammatory effects of PSP anthocyanins, while others (Jawi *et al.* 2024; Elvana *et al.* 2016) applied CCl<sub>4</sub> or LPS to induce oxidative stress. Therefore, these findings should be interpreted with caution as the physiological responses



**Figure 1. PRISMA-based flowchart illustrating the identification and inclusion of eligible research articles**

induced by dietary models and chemical agents may differ in mechanisms and severity. The studies used various animal models (Wistar,

BALB/c, Kunming, and Sprague-Dawley rats) and PSP extracts (aqueous, ethanolic, methanolic, and polysaccharide). In addition, A few studies (Setiawan & Nadhil 2019; Yasa *et al.* 2024) examined effects under aging or normal conditions using outbred strains to assess the antioxidant potential of PSP extract. Animal age, strain characteristics, and breeding type (inbred vs. outbred) can influence physiological baselines and treatment responsiveness. Most showed reduced MDA and increased antioxidant enzymes (SOD, GPx, GSH) (Wang *et al.* 2017a; Majid *et al.* 2018; Dewangga *et al.* 2022; Jawi *et al.* 2024). PSP also decreased pro-inflammatory cytokines (TNF- $\alpha$ , IL-6, IL-1 $\beta$ ) (Rahman *et al.* 2023; Ding & Fan 2024; Yasa *et al.* 2024; Dong *et al.* 2025; Yen *et al.* 2025) and improved ovarian function in smoke-exposed rats, suggesting additional immunoprotected effects (Dwi *et al.* 2020; Rahman *et al.* 2023).

Through 14 studies on anti-inflammatory effects, PSP-anthocyanins consistently reduced TNF- $\alpha$ , IL-6, IL-1 $\beta$ , and NF- $\kappa$ B, with six high-quality and eight moderate-quality studies. Ten studies showed increased SOD, CAT, and GPx activity, while all study decreased MDA levels. Despite methodological variations, evidence confirms the strong antioxidant and anti-inflammatory potential of PSP anthocyanins. Table 3 summarizes study number and quality,

**Table 1. Evaluation of study quality and risk of bias in fourteen selected articles based on the SYRCLE's tools**

Authors	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10
Subawa <i>et al.</i> (2023)	UC	UC	L	UC	UC	L	UC	L	L	L
Majid <i>et al.</i> (2018)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Dong <i>et al.</i> (2025)	L	UC	L	UC	L	L	L	L	L	L
Yen <i>et al.</i> (2025)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Wang <i>et al.</i> (2017a)	L	UC	L	L	L	L	L	L	L	L
Kurnianingsih <i>et al.</i> (2023)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Jawi <i>et al.</i> (2024)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Dewangga <i>et al.</i> (2022)	L	L	L	L	L	L	L	L	L	L
Elvana <i>et al.</i> (2016)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Ding & Fan (2024)	L	L	L	L	L	L	L	L	L	L
Setiawan & Nadhil (2019)	UC	UC	L	UC	UC	UC	UC	L	UC	L
Yasa <i>et al.</i> (2024)	UC	UC	L	UC	UC	UC	UC	L	UC	UC
Rahman <i>et al.</i> (2023)	L	L	L	L	L	L	L	L	L	L
Dwi <i>et al.</i> (2020)	L	L	L	L	L	L	L	L	L	L

D1–D10: Domain 1–10; L: Low; UC: Unclear; H: High; SYRCLES: Systematic Review Centre for Laboratory Animal Experimentation; Tool for assessing risk of bias D1–D10

**Table 2. The anti-inflammatory effects of *Ipomoea batatas L.* (Purple sweet potato) on tissue inflammation in rat and mice models**

Author (Year), Country	Sample	Control groups	Intervention groups	Study design	Key findings
Subawa <i>et al.</i> (2023), Indonesia	16 <i>Rattus norvegicus</i> (Strain Wistar) with MSU induced gout	<b>Negative control:</b> MSU-induced rats received 0.9% saline orally for 9 days and intra-articular MSU injection (0.1 mL, 30 mg/mL) on day 6.	PSP extract (400 mg/kg BW) was given orally for 9 days; on day 6, MSU was injected 30 min before PSP treatment.	RCT-Posttest-Only	PSP extract (400 mg/kg BW/day) ↓IL-1 $\beta$ (-1.26 ng/mL), ↓MDA (-2.77 ng/mL), ↓MMP-3 (-1.82 ng/mL), and ↑chondrocytes (+13.39) (p<0.05).
Majid <i>et al.</i> (2018), Pakistan	30 male <i>Rattus norvegicus</i> (Strain Sprague Dawley) with CFA-induced arthritis	<b>Positive control:</b> Ibuprofen 10 mg/kg BW. <b>Negative control:</b> Inflammation induction only. <b>Normal control:</b> No induction or treatment.	PSP extract 300 mg/kg BW, administered as either ethanolic or methanolic extract.	RCT-Posttest-Only	PSP extract in arthritic rats ↑CAT (+16.32%), ↑POD (+18.11%), ↑SOD (+16.85%) (p<0.05), and ↓IL-1 $\beta$ (4.28 pg/mL), ↓IL-6 (21.28 pg/mL), ↓NO (38.73 $\mu$ M/mL).
Dong <i>et al.</i> (2025), China	30 female <i>Rattus norvegicus</i> (Strain Wistar) with CIA	<b>Normal control:</b> Healthy rats receive physiological saline. <b>Negative control:</b> CIA rats receive physiological saline.	PSP anthocyanins 10, 20 and 40 mg/kg: CIA rats treated for 14 days.	RCT-Posttest-Only	PSP anthocyanins (hot ethanolic-citric acid extract) ↓TNF- $\alpha$ , IL-1 $\beta$ , RF, IL-1 $\alpha$ , IL-6, IL-18; inhibited MH7A proliferation; induced apoptosis (↑Bax, Caspase-3/9; ↓Bcl-2); restored PI3K/AKT in CIA rats. PSP-exosomes (40 mg/kg) showed strongest effect: TNF- $\alpha$ 309.65±1.34, IL-1 $\beta$ 30.88±0.46, RF 42.13±0.35 ng/L (p<0.05–0.01).
Kurnianingsih <i>et al.</i> (2023), Indonesia	25 adult male BALB/c mice (5 groups)	<b>Negative control:</b> STR 2h/day for 14 days.	Anthocyanin from PSP (10, 20, 40 mg/kg BW orally) + restraint stress 2h/day for 14 days.	RCT-Posttest-Only	ANC from PSP ↓IL-6 in visceral fat of stressed rats (p=0.0066 vs control; p=0.0271, 0.0136 vs STR+ANC20/40), ↑IL-10 (ns), and ↓IL-6/IL-10 ratio (p=0.0229, 0.0409 vs STR); STR+ANC20 showed strongest anti-inflammatory effect (p=0.0448 vs STR+ANC60).
Yen <i>et al.</i> (2025), Taiwan	20 male <i>Rattus norvegicus</i> (Strain Sprague Dawley) with HFD-induced obese rats	<b>Normal control:</b> Normal diet. <b>Negative control:</b> HFD.	HFD mixed with 5% w/w PSP powder, daily feeding for 19 weeks.	RCT-Posttest-Only	PSP supplementation ↓TNF- $\alpha$ (-109%), IL-6 (-104.1%), MCP-1 (-110.1%) in subcutaneous fat and ↓TNF- $\alpha$ (-81.4%), IL-6 (-178.3%), MCP-1 (-65.4%) in visceral fat of HFD-fed mice; also ↓IL-1 $\beta$ (-75.8% subcutaneous, -1 08.4% visceral) via inflammasome downregulation.

Continue from Table 2

Author (Year), Country	Sample	Control groups	Intervention groups	Study design	Key findings
<i>(continued)</i>					
<b>Positive control:</b>					
Wang <i>et al.</i> (2017a), China	60 male <i>Mus musculus</i> Kunming	<b>Normal control:</b> HFD + atorvastatin 10 mg/kg BW, gavage 3×/ week.  <b>Negative control:</b> CCl <sub>4</sub> only.	Anthocyanin-rich PSP extract 100, 200, 400 mg/kg BW orally for 10 days; CCl <sub>4</sub> IP injection to induce liver injury.	RCT-Posttest-Only	Anthocyanin-rich PSP extract alleviated CCl <sub>4</sub> -induced liver oxidative stress dose-dependently, ↑GSH & SOD, ↓MDA; 400 mg/kg showed strongest effect (MDA 5.15±0.48; SOD 330±7.53; GSH 2.06±0.12), comparable to silymarin.
Jawi <i>et al.</i> (2024), Indonesia	32 male Wistar rats	<b>Positive control:</b> Silymarin 50 mg/kg.  <b>Negative control:</b> HCD only.	HCD + 200 mg/mL Aqueous extract of PSP tuber for 3 months.	RCT-Posttest-Only	Aqueous PSP extract ↓MDA (0.6 mmol/mL) and IL-1 (0.063±0.002 pg/mL), ↑SOD (5.22 U/mL) in hypercholesterolemic vs high-cholesterol group ( $p<0.05$ ).
Dewangga <i>et al.</i> (2022), Indonesia	24 male Wistar rats	<b>Normal control:</b> Standard feed only.  <b>Negative control:</b> Exercise + standard feed.	Exercise + feed + PSP 2.6 mg/day.  Exercise + feed + PSP 5.2 mg/day.	RCT-Posttest-Only	PSP supplementation (2.6–5.2 mg/day) ↑SOD and ↓MDA post-high-intensity exercise ( $p<0.05$ ); 5.2 mg/day → SOD 75.2 U/mL (vs 29.4) and MDA 1.9 nmol/mL.
Elvana <i>et al.</i> (2016), Indonesia	24 male <i>Mus musculus</i> mice (strain DD Webster)	<b>Negative control:</b> MPE only.	Various doses of PSP extract + maximal exercise.	RCT-Posttest-Only	PSP extract ↑GPx activity in liver ( $p=0.024$ ); highest in P5 (19.39±7.06 mU/mL) vs MPE-only (P2: 1.84±0.92 mU/mL).
Ding & Fan <i>et al.</i> (2024), China	48 male BALB/c mouse	<b>Normal control:</b> No treatment, saline injection.  <b>Negative control:</b> PSPP-1, 400 mg/kg without Con-A.  <b>Positive control:</b> Con-A induced liver injury.	PSPP 200 mg/kg, 400 mg/kg, and bifendate 200 mg/kg for 28 days in liver-injured rats.	RCT-Posttest-Only	PSPP ↓TNF- $\alpha$ , IFN- $\gamma$ , IL-1 $\beta$ , IL-18 in immune-mediated liver injury. Con A ↑these cytokines ( $p<0.001$ ), while PSPP-1 (200–400 $\mu$ g/mL) dose-dependently ↓IL-1 $\beta$ and IL-18 ( $p<0.01$ – $0.001$ ).

Continue from Table 2

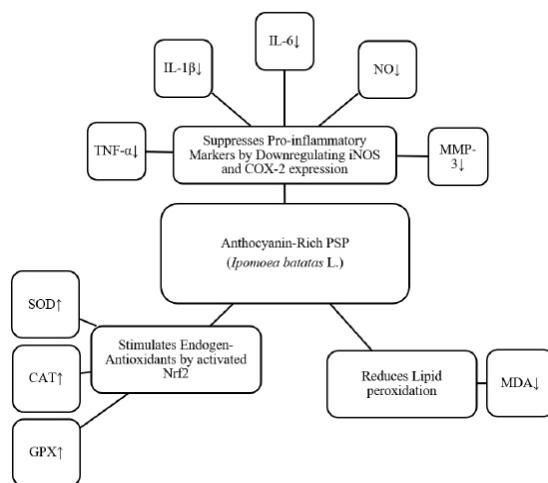
Author (Year), Country	Sample	Control groups	Intervention groups	Study design	Key findings
Setiawan & Nadhil (2019), Indonesia	25 male <i>Rattus norvegicus</i> (Strain Wistar)	<b>Normal control:</b> Standard diet, no treatment.  <b>Negative control:</b> Atherogenic diet, no treatment.	PSP extract in 3 dose variations (120, 240, and 480 mg/kgBW) on rats with induced a HCD for 2 months.	RCT-Posttest-Only	PSP extract ↓MDA dose-dependently ( $p=0.00$ ). $K^+ >400$ , while treatments I-III ↓toward $K^+ <300$ . Regression ( $R^2=0.71$ ) showed 71% of MDA reduction due to the extract.
Yasa <i>et al.</i> (2024), Indonesia	27 male <i>Rattus norvegicus</i> (Strain Wistar)	<b>Normal control:</b> Standard diet, no treatment.	PSP tuber extract 200 mg/day for 14 days.  Sembung extract 200 mg/day for 14 days.	RCT-Posttest-Only	PSP extract ( $3.86 \pm 1.28 \rightarrow 2.82 \pm 0.17$ , $p=0.008$ ) and ↓TNF- $\alpha$ ( $14.15 \pm 2.60 \rightarrow 7.61 \pm 0.95$ , $p=0.000$ ).
Rahman <i>et al.</i> (2023), Indonesia	30 female male <i>Rattus norvegicus</i> (Strain Wistar)	<b>Normal control:</b> Standard diet, no treatment.  <b>Negative control:</b> Standard diet and cigarette smoke.	PSP extract 20, 40, and 80 mg/kgBW/day orally by gavage for eight weeks.	RCT-Posttest-Only	In systemic circulation, PSP ↓MDA ( $3.86 \pm 1.28 \rightarrow 2.82 \pm 0.17 \mu M$ , $p=0.008$ ) and ↓TNF- $\alpha$ ( $14.15 \pm 2.60 \rightarrow 7.61 \pm 0.95 \text{ pg/mL}$ , $p=0.001$ ). In mammary tissue of smoke-exposed rats, anthocyanins ↓MDA ( $1.64 \pm 0.21 \rightarrow 1.08 \pm 1.03 \mu M$ , $p=0.002$ ).
Dwi <i>et al.</i> (2020), Indonesia	30 female Wistar rats (5 groups)	<b>Normal control:</b> Standard diet, no treatment.  <b>Negative control:</b> Standard diet and cigarette smoke.	Anthocyanins from PSP at 40 mg and 80 mg doses; 2 cig/day for 8 weeks.	RCT-Posttest-Only	PSP anthocyanins ↓ovarian MDA in smoke-exposed rats ( $p<0.001$ ); 80 mg/kg BW group= $0.41 \pm 0.06 \mu M$ vs positive= $0.77 \pm 0.09 \mu M$ , approaching negative control= $0.34 \pm 0.07 \mu M$ .

ANC: Anthocyanin; ANC20: Anthocyanin 20 mg/kg; ANC40: Anthocyanin 40 mg/kg; BW: Body Weight; CAT: Catalase; CCl<sub>4</sub>: Carbon Tetrachloride Intraperitoneal Injection; CCl<sub>4</sub>: Carbon Tetrachloride; CIA: Collagen-Induced Arthritis; CFA: Complete Freund's Adjuvant; Con-A: Concanavalin A; GPx: Glutathione Peroxidase; GSH: Glutathione; HCD: High Carbohydrate Diet; HFD: High Fat Diet; IL-18: Interleukin-18; IL-1 $\alpha$ : Interleukin-1 Alpha; IL-1 $\beta$ : Interleukin-1 Beta; IL-6: Interleukin-6; MCP-1: Monocyte Chemoattractant Protein-1; MDA: Malondialdehyde; MMP-3: Matrix Metalloproteinase-3; MSU: Monosodium Urate Crystals; NO: Nitric Oxide; PI3K/AKT: Phosphatidylinositol 3-Kinase/Protein Kinase B; POD: Peroxidase; PSP: Purple Sweet Potato; PSPP: Purple Sweet Potato Polysaccharides; RCT: Randomized Controlled Trials; RF: Rheumatoid Factor; SOD: Superoxide Dismutase; STR: Stress; TNF- $\alpha$ : Tumor Necrosis Factor-Alpha

highlighting PSP's promise as a functional food for managing chronic diseases related to oxidative stress, inflammation, and immune modulation (Figure 2). However, most evidence comes from animal studies, which may not fully reflect human physiological complexity. Variations in dosage,

extraction methods, and intervention duration further limit result generalizability.

PSP anthocyanins that are rich in acylated cyanidin and peonidin with triple sugars, are more stable than those from grapes or black soybeans, with only 25% degradation during intestinal



**Figure 2. Bioactive mechanisms of purple sweet potato (*Ipomoea batatas* L.) distinctive features of PSP-derived anthocyanins**

digestion (Ryu & Koh 2022). Acylation with caffeic and ferulic acids enhances their antioxidant activity and stability under pH or heat stress (Wu *et al.* 2024; Feng *et al.* 2024). Furthermore, PSP has also been applied in smart packaging due to strong antioxidant capacity and pH-sensitive color changes (Wu *et al.* 2024). These findings indicate that PSP anthocyanins offer superior chemical stability and more sustained antioxidant effects than other anthocyanin-rich sources.

#### Anthocyanin-rich PSP suppresses pro-inflammatory markers

The reviewed studies used various rodent models across chronic inflammation models such as HFD-induced obesity, LPS-induced systemic

inflammation, and CCl<sub>4</sub>-induced oxidative stress. PSP extract significantly reduced pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and MMP-3 (Majid *et al.* 2018; Ambara *et al.* 2023; Subawa *et al.* 2023; Dong *et al.* 2025; Yen *et al.* 2025). These effects are mediated through modulation of NF- $\kappa$ B, MAPK, and Akt-eNOS pathways, enhancement of antioxidant defenses via Nrf2 activation, and suppression of ROS generation (Giampieri *et al.* 2023). It also proved by Majid *et al.* (2018) that PSP extract can lower NO. Besides, decreased MMP-3 (stromelysin-1) levels help protect connective tissue and cartilage by reducing leukocyte migration, TNF- $\alpha$  and IL-1 $\beta$ , and ROS production (Pulik *et al.* 2023).

Majid *et al.* (2018) employed ethanolic and methanolic extraction at a dose of 300 mg/kg Body Weight (BW) and reported reductions in IL-1 $\beta$  ( $\downarrow$  to 4.28 pg/mL), IL-6 ( $\downarrow$  to 21.28 pg/mL), and Nitric Oxide (NO) ( $\downarrow$  to 38.73  $\mu$ M/mL). In contrast, Subawa *et al.* (2023) used aqueous extract at 400 mg/kg BW/day for 9 days, resulting in a significant decrease in IL-1 $\beta$  ( $-1.26$  ng/mL). Meanwhile, Dong *et al.* (2025) used a hot ethanolic-citric acid extraction at 40 mg/kg BW for 14 days, producing marked reductions in TNF- $\alpha$  ( $309.65 \pm 1.34$  ng/L) and IL-1 $\beta$  ( $30.88 \pm 0.46$  ng/L) (Majid *et al.* 2018; Subawa *et al.* 2023; Jawi *et al.* 2024). These discrepancies in dosage (200–400 mg/kg BW), solvent type (aqueous vs. organic), and duration (9 days to 3 months) may influence the concentration, stability, and bioavailability of bioactive compounds, such as anthocyanins.

Organic solvent extractions yield more anthocyanins, while aqueous or mixed methods

**Table 3. Number of included studies by category and quality**

Study category	Number of studies	Study quality	Explanation
Anti-inflammatory outcomes	14 studies	6 high quality, 8 moderate	All 14 studies measured TNF- $\alpha$ , IL-6, IL-1 $\beta$ , and NF- $\kappa$ B. Six showed strong methodology, eight moderate, and all reported significant reductions in pro-inflammatory markers.
Supporting endogenous antioxidant outcomes	10 studies	5 high quality, 5 moderate	Ten studies assessed antioxidant enzymes (SOD, CAT, GPx) and five were high quality and five moderate. Most showed increased endogenous antioxidant activity.
Anti-lipid peroxidation outcomes	14 studies	6 high quality, 8 moderate	All 14 studies assessed lipid peroxidation via MDA; six were high quality and eight moderate. All showed reduced MDA levels, confirming the antioxidant potential of purple sweet potato anthocyanins.

SOD: Superoxide Dismutase; CAT: Catalase; GPx: Glutathione Peroxidase; MDA: Malondialdehyde; TNF- $\alpha$ : Tumor Necrosis Factor-Alpha; IL-6: Interleukin-6; IL-1 $\beta$ : Interleukin-1 Beta; NF- $\kappa$ B: Nuclear Factor Kappa B

offer better safety and scalability. Dose and duration influence outcomes, with shorter treatments reducing IL-1 $\beta$  and longer treatments needed for systemic markers like TNF- $\alpha$ . Hot ethanolic-citric acid extract (40 mg/kg for 14 days) strongly lowered TNF- $\alpha$  and IL-1 $\beta$  in rats (Dong *et al.* 2025), whereas aqueous extract (400 mg/kg/day for 9 days) effectively reduced IL-1 $\beta$  with good safety (Subawa *et al.* 2023). Future research should standardize extraction and dosing protocols and include clinical trials to verify these effects in humans. Variations in extraction methods, dosages (40–400 mg/kg BW), and intervention durations (9 days–3 months) affect PSP anthocyanin stability, bioavailability, and cross-study comparability. With some studies showing unclear bias, standardized extraction and dosing in well-designed human trials are needed to confirm PSP's therapeutic potential as a natural anti-inflammatory agent.

#### **Anthocyanin-rich *Ipomoea batatas* L. boosts endogenous antioxidants**

Multiple studies have shown that PSP markedly enhances SOD, GPx, and CAT activity, highlighting its strong capacity to counter oxidative stress. Jawi *et al.* (2024) found that 200 mg/day of aqueous PSP extract for 3 months significantly increased SOD activity to 5.22 U/mL and suggested a protective effect against oxidative damage, while Dewangga *et al.* (2022) reported SOD improvement to 75.2 U/mL using steamed and blended PSP in Wistar rats. Unlike studies using solvent-based extraction, Dewangga *et al.* (2022) used thermal processing (steaming) and mechanical blending, resulting in a whole food-based preparation containing anthocyanins, which was directly administered to animals (Dewangga *et al.* 2022). In Sprague-Dawley rats with HFD-induced obesity, Majid *et al.* (2018) observed a 16.85% increase in SOD after ethanolic PSP extract treatment. Similarly, Wang *et al.* (2017a) reported that AB-8 resin-purified PSP anthocyanins elevated SOD to 330 $\pm$ 7.53 U/mg protein in C57BL/6 mice that confirming the strong antioxidative effect of PSP across various models and extraction methods. Only a limited study, such as Elvana *et al.* (2016), reported the highest GPx level (19.39 $\pm$ 7.06 mU/mL) using fermented PSP extract produced via 36-hour tapai fermentation, suggesting enhanced bioactive compound availability. Similarly, Majid *et al.* (2018) observed a 16.32% increase in CAT

activity after ethanolic PSP extract administration, further supporting its role in mitigating oxidative stress through enzymatic antioxidant pathways.

Steaming or boiling may degrade heat-sensitive compounds but can increase phenolic extractability, retaining significant antioxidant activity. Ethanol extraction yields higher anthocyanin levels than aqueous methods, enhancing antioxidant efficacy (Tena & Asuero 2022). Consistent increases in antioxidant enzymes across models suggest a broad protective effect, while resin-purified or fermented extracts may offer greater stability and absorption. Thus, PSP holds considerable promise as a dietary antioxidant intervention capable of supporting redox balance, protecting against oxidative insults, and contributing to chronic disease prevention.

#### **Anthocyanin-rich *Ipomoea batatas* L. lowering lipid peroxidation**

The hepatoprotective effects of PSP are well established in CCl<sub>4</sub>-induced liver injury models. Wang *et al.* (2017a) reported a dose-dependent reduction in MDA levels, with anthocyanin-rich PSP (100 mg/kg BW for 10 days) lowering MDA to 5.15 $\pm$ 0.48  $\mu$ M. This confirms the hepatoprotective antioxidant role of PSP, especially when rich in anthocyanins. Subawa *et al.* (2023) similarly reported a marked reduction in MDA levels ( $\sim$ 2.77 ng/mL) after administering 400 mg/kg BW aqueous PSP orally via nasogastric tube for 9 consecutive days (Subawa *et al.* 2023). These studies reinforce the short-term effectiveness of PSP in oxidative stress modulation linked to liver damage.

PSP extract shows strong antioxidant protection not only in chemical-induced but also in physiological and environmental stress models. Dewangga *et al.* (2022) reported decreased MDA to 1.9 nmol/mL after low-dose PSP (5.2 mg/day) during maximal physical activity. Similarly, Dwi *et al.* (2020) found that PSP anthocyanins (40–80 mg/kg BW) reduced MDA to 0.41 $\pm$ 0.06  $\mu$ M in cigarette smoke-exposed rats, while Rahman *et al.* (2023) confirmed a consistent dose-dependent MDA decline (20, 40, and 80 mg/kg for 8 weeks). Across chemical and physiological models, PSP consistently reduced MDA in diet-induced oxidative stress. Setiawan and Nadhil (2019) reported up to 71% reduction in HFD induced rats (120–480 mg/kg BW), and Jawi *et al.* (2024) observed similar effects with 200 mg/mL PSP for

3 months in HCD induced rats. Collectively, these studies demonstrate PSP's dual antioxidant and lipid-lowering properties suggesting potential vascular protective effects (Jawi *et al.* 2024; Dwi *et al.* 2020).

These studies consistently show that anthocyanin-rich PSP extract markedly lowers lipid peroxidation, as reflected by reduced MDA levels across various pathological models, including liver injury, diet induced inflammation, physical stress, and environmental toxins. Aqueous and fermented extracts appear most suitable for long-term use in supplements and functional foods due to their safer preparation, minimal solvent residue, and better bioavailability (Elvana *et al.* 2016; Jawi *et al.* 2024). Thus, PSP represents a promising natural intervention for reducing oxidative stress, mitigating cardiovascular risk, and potentially slowing the progression of degenerative joint disorders.

### Study limitations

The observed reductions in MDA and other anti-inflammation markers suggest promising bioactivity, but due to this heterogeneity. A key limitation highlighted in this review is the lack of standardized protocols across studies due to variations in extraction methods, dosages, treatment durations, and the forms of PSP used (aqueous, fermented, or whole food), as well as differences in oxidative stress or inflammation models. The difference of protocols makes it difficult to directly compare results or draw definitive conclusions about efficacy so the findings can only indicate potential benefits rather than confirm consistent therapeutic efficacy.

### CONCLUSION

Administration of anthocyanins extract from PSP shows potential antioxidant and anti-inflammatory effects in various disease models. PSP anthocyanin extracts show antioxidant and anti-inflammatory effects, reducing oxidative stress markers (MDA) and pro-inflammatory mediators (TNF- $\alpha$ , IL-1 $\beta$ , IL-6, NO, MMP-3) while enhancing enzymes like SOD, GPx, and CAT. Benefits are consistent across disease models despite variations in extraction, dosage, and duration such as hot ethanolic-citric acid extracts are most potent, while aqueous and fermented forms balance safety and efficacy for long-term use. Lack of standardized protocols

remains limitations across studies so future research should focus on developing extraction techniques, dosage, and conducting human clinical trials to validate the PSP's potential.

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This research was independently funded by the authors. No potential conflict of interest was identified in relation to this study.

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