

REVIEW

Open Access



Systematic review of preclinical and clinical evidence of Sacha inchi

Terence Yew Chin Tan^{1†}, Puteri Sofia Nadira Megat Kamaruddin^{2†}, Siti Hajar Muhamad Rosli¹, Han Yin Lim², Janice Sue Wen Chan^{1*}, Wan Ahmad Syazani Mohamed², Puspawathy Krishnan¹, Mohd Naeem Mohd Nawi², Ida Farah Ahmad¹, Nur Es Naini Awalludin³ and Sophia Rasheeqa Ismail²

[†]Terence Yew Chin Tan and Puteri Sofia Nadira Megat Kamaruddin contributed equally to this work.

*Correspondence:

Janice Sue Wen Chan
janice.cs@moh.gov.my

¹Herbal Medicine Research Centre, Institute for Medical Research, National Institutes of Health, Shah Alam, Selangor, Malaysia

²Nutrition, Metabolic and Cardiovascular Research Centre, Institute for Medical Research, National Institutes of Health, Shah Alam, Selangor, Malaysia

³Research Review and Approval Unit, Sector for Ethics and Research Surveillance, Office of NIH Manager, National Institutes of Health, Shah Alam, Selangor, Malaysia

Abstract

Background Sacha inchi (*Plukenetia volubilis*), a member of the Euphorbiaceae family, has long been valued for its nutritional and medicinal properties, including use in food and cosmetic industries as a poultice to soften, revitalize, and rejuvenate the skin. Its health benefits are attributed to its rich content of essential nutrients and phytocompounds.

Objective This review systematically explores and compiles current scientific evidence on the efficacy of Sacha inchi.

Methods Publications were identified and selected according to the PRISMA guidelines, with predetermined inclusion criteria. Databases searched included Web of Science, CENTRAL, LILACS, Scopus, PubMed®, and EBSCOhost.

Results Thirteen articles were included, primarily using oil-based extracts or products, with treatment durations ranging from one month to 20 months in human studies and 75 min to 3.5 months in animal studies. Clinical findings support the benefits of Sacha inchi for metabolic syndrome, cognitive enhancement, dry eye syndrome, and dermatological health, while animal studies suggest potential effects in managing hypertension, hyperlipemia, and offering neuroprotection.

Conclusions However, there remains a lack of comprehensive evaluation of specific formulations or extracts in both clinical and preclinical settings. Further research is needed, particularly regarding safety data at higher doses and for prolonged use.

Keywords Sacha inchi, *Plukenetia volubilis*, Efficacy, Inca peanut

1 Introduction

Sacha inchi (*Plukenetia volubilis*), a member of the Euphorbiaceae plant family, is native to Central and South America [1]. Traditionally valued for its nutritional and health benefits, Sacha inchi has gained prominence for its moisturizing and anti-aging effects, leading to its widespread inclusion in cosmetic products [2]. Over the years, its utilization has expanded beyond Central and South America into Europe, the Asia–Pacific region, and Africa, reflecting a growing global interest.



© The Author(s) 2026. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Commonly known as “Inca peanut” or “mountain peanut”, this perennial plant reaches a height up to 2 m and features alternate, heart-shaped, serrated leaves (10–12 cm long and 8–10 cm wide) with 2- to 6-cm petioles [3]. The seeds are the primary part of the plant used for consumption, as they contain a significant proportion of lipids, which vary depending on cultivation, extraction, and processing methods [4–8].

Sacha inchi is particularly rich in polyunsaturated fatty acids (PUFAs) (77.5–84.4%) while also having smaller percentages of monounsaturated fatty acids (MUFAs) (8.4–13.2%) and saturated fatty acids (SFAs) (6.8–9.1%) [9, 10]. Amongst the essential health benefits of PUFA such as for cardiovascular health, anti-inflammatory, brain function, and immune function through the effects of several omega-3 and omega-6 fatty acids. Alpha-Linolenic Acid (ALA), an omega-3 fatty acid, is the most abundant PUFA in Sacha inchi, comprising approximately 33.4–50.8% of its total fat content, depending on the source and processing method [11–13]. Whereas Linoleic Acid (LA), an omega-6 fatty acid, makes up about 13.77–35.2% of the total fat content in Sacha inchi [11, 13].

The phytochemical profile of Sacha inchi includes tannins [14, 15], saponins [14–16], phytic acid [17], and a variety of phenolic compounds such as flavonoids (isorhamnetin glucoside, luteolin, and apigenin) and secoiridoid derivatives [9, 16, 18–20]. Additionally, it contains tocopherols [16, 19–26] and phytosterols [9, 21, 27].

Given its rich nutritional and phytochemical composition, Sacha inchi has been extensively studied for its antioxidant, anti-inflammatory, and disease-prevention properties [28–31]. Despite the increasing body of literature, there has been no systematic review that evaluates the health effects of Sacha inchi using a structured framework based on both animal and human studies. Therefore, the aim of this systematic review is to consolidate and critically assess the available scientific evidence regarding the efficacy of Sacha inchi.

2 Research method

This review followed the procedures outlined in the Cochrane Handbook for Systematic Reviews (The Cochrane Collaboration, Oxford, UK) [32] of Interventions and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [33]. This systematic literature review was planned and conducted following the PRISMA protocol. The PRISMA Checklist can be found in Table S1. The International Prospective Register of Systematic Reviews (PROSPERO) has registered the systematic review (CRD42023466086), and the study protocol can be accessed at <https://www.crd.york.ac.uk/PROSPERO/view/CRD42023466086>.

3 Eligibility criteria

We included studies that evaluated the efficacy of any formulation, dosage, utilization, or application of Sacha inchi, and articles written in English only. Experimental studies such as randomized and non-randomized controlled studies, quasi-experiment studies, crossover trials or single-arm studies, mixed method studies, case reports/series, animal studies, and conference abstracts were also included. We excluded *in vitro*, *in silico* studies as well as reviews and editorials.

3.1 Outcome measures

3.1.1 Efficacy measures

The efficacy of Sacha inchi was evaluated according to the following outcome domains:

- (a) Cardiovascular health: Changes in cholesterol levels, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, or very low-density lipoprotein, and blood pressure (systolic or diastolic)
- (b) Weight and body composition: Changes in body mass index (BMI), body weight, and waist or hip circumferences
- (c) Metabolic health and glucose regulation: Changes in fasting/random blood glucose, insulin levels, and Homeostasis Model Assessment of Insulin Resistance (HOMA) index
- (d) Dermatological effects: Changes in overall skin health and acne conditions
- (e) Ophthalmological effects: Changes in overall eye health
- (f) Inflammatory response and immune modulation: Changes in C-reactive protein (CRP), interleukin-6 (IL-6), uric acid, and other inflammatory markers
- (g) Neurological and cognitive health: Changes in cognitive function or neurological conditions

3.1.2 Safety measures

The safety of Sacha inchi was assessed in the included efficacy studies, where available, according to the following outcome domains:

- (a) Risk findings
- (b) Toxicological studies
- (c) Allergic reactions
- (d) Special population
- (e) Environmental impact assessment
- (f) Safety level

3.2 Search strategies

By using the guided PICO framework, we identified keywords that formulated the fundamental research questions before we systematically searched six databases, including Web of Science (WoS), Cochrane Central Register of Controlled Trials (CENTRAL), Latin America and the Caribbean Literature on Health Sciences (LILACS), Scopus, PubMed®, and EBSCOhost from inception up to 3rd October 2023. To ensure thorough coverage, we included all possible synonyms, medical subject headings (MeSH), related expressions, and keyword variations for 'Human', 'In Vivo', 'Sacha inchi', and 'Efficacy', together with the Boolean operators (Table S2). The comparator element was not specified in this study because there were no specific comparisons to be made; any comparison could be used to assess the efficacy of Sacha inchi. The selected databases were chosen for broad subject coverage and advanced search capabilities.

3.3 Study selection, data extraction, and management

All identified references were imported into EndNote X9 software [34] and duplicate entries were removed prior to the screening stage. Records were screened based on the aforementioned eligibility criteria. Five pairs of authors (WASM & TYCT, JSWC &

MNMN, HYL & SHMR, IFA & PK, NENA & PSNMK) independently screened titles and abstracts in duplicates to identify potentially eligible studies. Subsequently, PSNMK and TTYC reviewed the shortlisted abstracts and full texts to confirm inclusion. We indicate our study selection process in a PRISMA diagram (Fig. 1). All author pairs (WASM & TYCT, JSWC & MNMN, HYL & SHMR, IFA & PK, NENA & PSNMK) independently extracted all data from each included study using standardized data collection forms, which essentially covered study design, study population, intervention details, comparison details, and outcomes. Specifically, we extracted the following information: (i) author, year; (ii) plant part; (iii) type of extract; (iv) animal species (for in vivo studies); (v) administration route; (vi) dosage and formulation; (vii) comparator type; and (viii) safety findings (if available from included papers. All extracted data were evaluated by PSNMK and TTYC for accuracy.

3.4 Risk of bias assessment

3.4.1 Risk of bias in randomized trials 2.0

We employed the second version of the Cochrane RoB tool (RoB 2.0) [35] to assess RoB in included trials. RoB 2.0 is an update of a previous version of the Cochrane RoB tool, which was released in 2008 and assesses five domains covering various aspects of trial

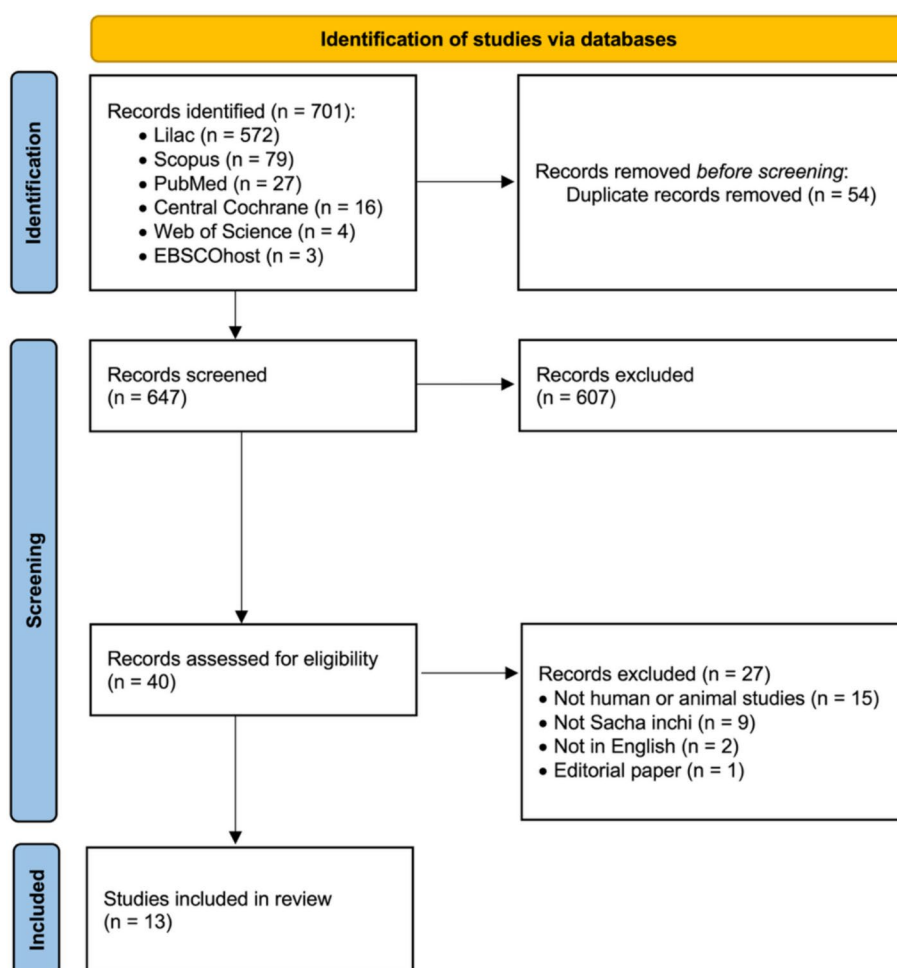


Fig. 1 The PRISMA flowchart of the study identification process from screening to data synthesis

design, conduct, and reporting. Several signaling questions would be addressed in each domain until enough information was gathered to determine the RoB level of a trial. Ratings were made for LOW RoB, HIGH RoB, or SOME CONCERNS for each domain, and finally, an overall risk of bias rating was justified. The RoB was conducted by two independent reviewers, and inconsistencies were reconciled through discussion.

3.4.2 Risk of bias in non-randomized studies of intervention (ROBINS-I)

For interventional studies, we evaluated risk of bias using the ROBINS-I framework, which examines multiple aspects of study design and conduct. The assessment generates both domain-specific and overall RoB ratings, classified from low to critical risk. In doing so, it considers elements such as the influence of confounding factors, the soundness of the methodology approach, and the quality of reporting, particularly in relation to the assignment of interventions [36].

3.4.3 Systematic review centre for laboratory animal experimentation (SYRCLE)

We assessed the methodological quality of animal studies using SYRCLE's RoB tool. This instrument includes ten criteria(s) that address potential sources of bias, such as selection, performance, detection, attrition, reporting, and other study-specific issues. For every study, each domain of the RoB tool will be rated as "yes," "no," and "unclear," corresponding to low, high, or unclear risk of bias, respectively, with accompanying explanations provided for each judgment [37].

Every pair of authors underwent pre-testing of the RoB assessment tools using a sample of studies before the full assessment to ensure consistent interpretation of the criteria. Five pairs of authors (WASM & TYCT, JSWC & MNMN, HYL & SHMR, IFA & PK, NENA & PSNMK) independently assessed each included study for RoB. In cases of disagreement, a third author (PSNMK) facilitated a discussion to reach a consensus.

3.5 Data synthesis

We conducted a descriptive analysis of all included studies and categorized them based on reported health outcomes. Due to the limited number of studies assessing the same outcomes, a quantitative analysis was not feasible.

4 Results

4.1 Study inclusion

The database search revealed 701 articles published up to 3rd October 2023. After 54 duplicates were removed, 647 articles were further screened based on the eligibility criteria. This process involved manually screening and excluding 607 articles due to unsuitable study design, for example, nutritional content analysis, agricultural studies, and phytochemical studies. Subsequently, we assessed 40 full-text articles, of which 27 studies were excluded for ineligibility. A total of 13 articles were then included in this systematic review. The overall study identification process is outlined in Fig. 1.

4.2 Characteristics of included studies

A total of 13 studies were included, comprising nine human intervention studies and four animal studies. Four out of thirteen studies were conducted in Thailand (30.8%), three in Peru (23.0%), two in China (15.4%), and Colombia, with one study each in Japan

(7.7%) and Finland (7.7%), respectively. Although most studies were unclear on the plant part used, the majority of studies used oil-based extracts or products ($n=10$, 76.9%), while others used boiled-Sacha inchi ($n=1$), microemulsion ($n=1$), and shell extract ($n=1$). Duration of treatment ranges from one month to 20 months for human studies and 75 min to 3.5 months for animal studies. The study characteristics are presented in Fig. 2, with further details of each study presented in Table S3.

4.3 Cardiovascular health

Effects of cardiovascular health were observed in four human clinical interventions [38–41] studies and two animal studies [42, 43]. Table 1 summarizes the characteristics and outcomes of the included studies in relation to cardiovascular health.

All four human clinical studies evaluated the efficacy of oral consumption of Sacha inchi oil (SIO) [38–41]. Two of these studies (reported across three articles, with two based on the same trial [38, 39]) explored the effects of a single dosing of SIO, while the other evaluated the impact of daily morning SIO intake over a 4-month intervention period [40]. The study designs included two cluster-randomized trials conducted exclusively in male participants [38, 39], and two randomized controlled trials involving healthy participants [40, 41].

In terms of glycemic outcomes, one study reported that 38% of participants showed a reduction in the incremental area under the curve for glucose (iAUC-G) following postprandial SIO consumption [38]. Although no overall difference in postprandial Sirtuin 1 (SIRT-1) gene expression was observed between the group receiving a high-fat diet with SIO and the high-fat meal (HFM) alone, subgroup analysis among participants with above-median glucose (AHG) revealed meaningful associations [38]. In this subgroup, SIRT-1 expression was negatively correlated with glucose levels ($r = -0.724$, $p = 0.012$) and iAUC-G ($r = -0.665$, $p = 0.025$), and positively correlated with the postprandial insulin sensitivity index (ISI) ($r = 0.636$, $p = 0.035$) [38].

As for lipid outcomes, short-term consumption of SIO reversed the postprandial increase in total cholesterol (TC) in metabolically healthy participants when compared to those who consumed only HFM ($p = 0.037$) [39]. However, a longer-term intervention

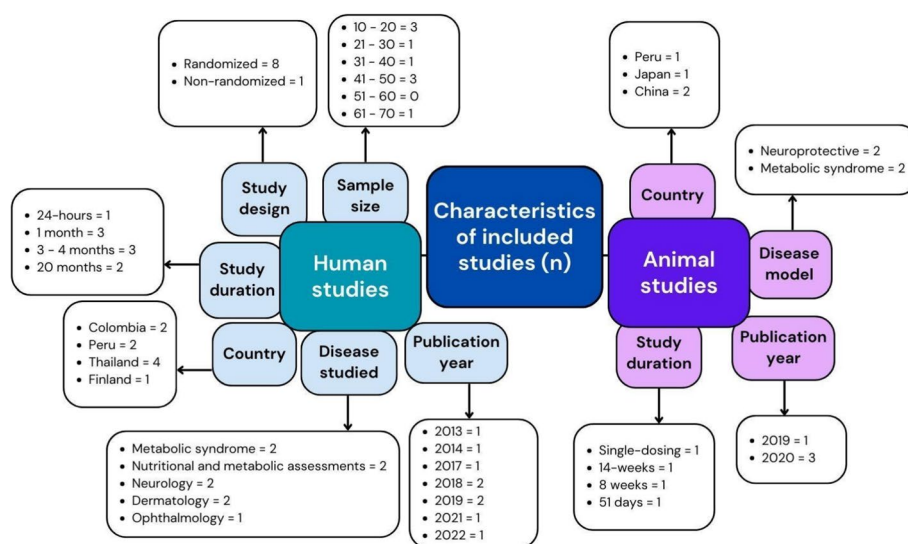


Fig. 2 Characteristics of included studies

Table 1 Characteristics of studies evaluating the effects of Sacha inchi on cardiovascular health

Study type	Author, year	Intervention (dose, frequency, and administration route)	Control (dose, frequency, and administration route)	Intervention/control duration	Study outcome
Human intervention studies	Alayon 2018	HFM with 15 mL SIO per oral once	HFM per oral once	One day for each group (with a 2-week washout period)	– Postprandial glucose: lower increase in 38.1% of participants – Postprandial SIRT-1 expression: increased expression in AHG group correlating with better insulin sensitivity ($p=0.035^*$) and lower glucose levels ($p=0.012^*$) – Total cholesterol: SIO prevented increase post-HFM (iAUC: 0.27 vs. -0.18 mmol/L/4 h, $p=0.037$) – HDL-C & TAG: No postprandial improvement with SIO in both groups
	Gonzales 2013	SIO 10 mL or 15 mL single oral administration	Sunflower oil 10 mL or 15 mL, single oral administration	One time	– ΔTAG: Reduced 2 h post-prandial with sunflower oil; slight increase with SIO – ΔTRL-cholesterol: Reduced within 24 h with a greater and earlier drop with SIO
	Gonzales 2014	SIO 10 or 15 mL per oral once daily	Sunflower oil 10 or 15 mL, per oral once daily	4 months	– HDL-C: Higher at month-4 with SIO vs. sunflower oil ($p<0.05$; 95% CI) – SBP: Reduced at month-2 in both groups ($p<0.01$; 95% CI); no between-group differences – DBP: Reduced at month-2 ($p<0.05$; 95% CI) and remained lower; no between-group differences – TAG: Unchanged throughout with both oils
Animal intervention studies	Li 2020a	SISE 400 mg/kg daily, per oral	Saline administration, standard diet without intervention	2-week acclimatization followed by 51-day treatment	– SBP: Reduced with SISE (166 ± 16 vs. 190 ± 10 mmHg, $p<0.05$; 95% CI) – LVWT: Decreased in SHR and high-salt WKY, indicating reduced cardiac hypertrophy
	Li 2020b	SIO 0.5, 1.0, and 1.5 mL/kg/day, daily, per oral	1. Normal chow diet 10 kcal% fat 2. High-fat diet 45 kcal% fat	1-week acclimatization followed by 8-week treatment	Liver TG: Reduced with SIO, similar to fish oil

AHG—Above-Median Glucose Group; DBP—Diastolic Blood Pressure; Δ TAG—Change in Triacylglycerol levels; Δ TRL-cholesterol—Change in Triacylglycerol-Rich Lipoprotein cholesterol levels; HDL-C—High-Density Lipoprotein Cholesterol; HFM—High-Fat Meal; iAUC—Incremental Area Under the Curve for Glucose; ISI—Insulin Sensitivity Index; LVWT—Left Ventricular Wall Thickness; SBP—Systolic Blood Pressure; SHR—Spontaneously Hypertensive Rats; SIO—Sacha inchi oil; SIRT-1—Sirtuin 1; SISE—Sacha inchi shell extract; TAG—Triacylglycerol; TG—Triglycerides; WKY—Wistar-Kyoto rats

of daily SIO intake over four months demonstrated a significant reduction in serum TC levels ($p<0.01$) [40]. Similarly, serum low-density lipoprotein cholesterol (LDL-C) levels showed a significant reduction starting from month 2 among participants consuming either SIO or sunflower oil ($p<0.01$) [40].

While no significant changes were initially observed in HDL-cholesterol (HDL-C) or triacylglycerol (TAG) levels postprandially with SIO intake [39], prolonged consumption over four months led to a significant increase in HDL-C levels compared to sunflower oil [40]. TAG levels, on the other hand, remained unchanged throughout the study period in both the SIO and sunflower oil groups [40]. Postprandial TAG levels remained elevated

up to 4 h following intake, particularly among metabolically unhealthy participants [39]. Additionally, at 2 h post-ingestion, plasma delta TAG levels decreased with sunflower oil but showed a slight increase with SIO in healthy individuals [41].

Lastly, regarding changes observed in TRL-cholesterol, both SIO and sunflower oil demonstrated a reduction in plasma TRL concentrations over a 24-h period, with a greater effect observed in the SIO group. However, the reductions were observed earlier in participants consuming SIO (at 1 h) as compared to those who consumed sunflower oil (at 2 h) [41].

In two separate studies, the effects of Sacha inchi interventions were evaluated for their impact on systolic blood pressure (SBP) and lipid metabolism. In the first study, Spontaneously Hypertensive Rats (SHR) male Wistar Kyoto (WKY) rats were treated for 51 days following a two-week acclimatization period [42]. In this study, both groups received Sacha inchi Shell Extract (SISE) orally at 400 mg/kg/day, while the control groups received saline and a standard diet [42]. SISE significantly reduced systolic blood pressure (SBP) in SHR rats compared to controls (166 ± 16 mmHg vs. 190 ± 10 mmHg, $p < 0.05$), and also decreased left ventricular wall thickness (LVWT) in both SHR and high-salt diet WKY rats, indicating attenuation of cardiac hypertrophy [42]. In a separate study, eight-week-old male Sprague–Dawley (SD) rats were fed either a normal chow diet or a high-fat diet for 8 weeks, following a one-week acclimatization period, and were administered SIO orally at doses of 0.5, 1.0, or 1.5 mL/kg/day. SIO treatment significantly reduced liver TAG, with effects comparable to those observed with fish oil supplementation [43].

4.4 Weight management and body composition

No studies evaluated the effects of Sacha inchi on weight management and body composition.

4.5 Metabolic health and glucose regulation

Two human intervention studies evaluated the effects of metabolic health and glucose regulation Alayón et al. (2018) and Gonzales et al. (2014) [38, 40] which have been summarized in Table 2. The study by Alayón et al. (2018) employed a randomized crossover

Table 2 Characteristics of studies evaluating the effects of Sacha inchi on metabolic health and glucose regulation

Author, year	Intervention (dose, frequency, and administration route)	Control (dose, frequency, and administration route)	Intervention/control duration	Study outcome
Alayón 2018	HFM with 15 mL SIO per oral once, observed 1- and 4-h post-meal	HFM per oral once, observed 1- and 4-h post-meal	Once (with a 2-week washout between groups)	– iAUC-G: reduced in 38.1% of participants with SIO in HFM – SIRT-1 & ISI: positive correlation ($r = 0.636$, $p = 0.035$) suggests higher insulin sensitivity – Postprandial glucose: higher at 4 h with HFM + SIO versus HFM alone ($p = 0.017$) – Fasting & 1 h samples: no differences in glucose, insulin, or lipid levels between treatments
Gonzales 2014	SIO 10 or 15 mL per oral once daily	Sunflower oil 10 or 15 mL, per oral once daily	4 months	– Blood glucose: remained unchanged; no differences in fasting levels – Serum insulin: increased with both SIO and sunflower oil, with no differences between interventions

design with a 2-week washout period, where participants ($n=42$) consumed either a HFM alone or HFM with 15 mL of SIO, followed by postprandial assessments at 1 and 4 h. Gonzales et al. (2014) conducted a randomized, double-blind trial in which participants ($n=30$) consumed 10 or 15 mL of SIO or sunflower oil per oral once daily for 4 months.

The incorporation of SIO into HFM exhibited diverse effects on glucose metabolism and insulin sensitivity. Alayón et al. (2018) reported that 38.1% of participants consuming HFM with SIO experienced a reduction in the Incremental Area Under the Curve for Glucose (iAUC-G), suggesting a decreased postprandial glucose response compared to HFM alone. Additionally, Sirtuin 1 (SIRT-1) expression in peripheral blood mononuclear cells (PBMCs) was positively correlated with improved insulin sensitivity, as indicated by an association with the Insulin Sensitivity Index (ISI) ($r=0.636$, $p=0.035$). This finding implies that higher SIRT-1 expression may enhance insulin sensitivity. However, serum postprandial glucose levels at 4 h were significantly higher in the HFM + SIO group (4.77 mmol/L, IQR: 4.59–5.11) compared to HFM alone (4.62 mmol/L, IQR: 4.18–4.93; $p=0.017$). No significant differences were observed in fasting or 1-h serum glucose, insulin, or lipid levels between treatments. Similarly, Gonzales et al. (2014) found no changes in fasting glucose levels during interventions with either SIO or sunflower oil, though serum insulin levels increased during both treatments without significant differences between them.

HFM—High-Fat Meal; iAUC-G—Incremental Area Under the Curve for Glucose; ISI—Insulin Sensitivity Index; SIO—Sacha Inchi Oil; SIRT-1—Sirtuin 1

4.6 Dermatological effects

Two studies exploring the dermatological effects of SIO Soimee 2019 [44] and Suthiphasil 2018 [45]. Table 3 summarizes characteristics of studies evaluating the effects of Sacha inchi on skin. Soimee et al. investigated the topical application of SIO for improving skin hydration and appearance in individuals with dry skin, while Suthiphasil 2018 evaluated the effects of orally administered SIO in combination with erythromycin for the treatment of acne vulgaris.

Soimee 2019 investigated the moisturizing and irritation effects of SIO on human skin. Conducted with 13 participants, the study compared SIO with olive oil using a regression model, where each oil was applied to the lower legs for 14 days, followed by a 2-day

Table 3 Characteristics of studies evaluating the effects of Sacha inchi on skin

Author, year	Intervention (dose, frequency, and administration route)	Control (dose, frequency, and administration route)	Intervention/control duration	Study outcome
Soimee 2021	Cold-pressed SIO was topically applied to the skin of the lower leg of the participant	Olive oil was applied to the skin of the other lower leg of the same participant	14-day application	– Moisture retention: higher with SIO than olive oil – Skin irritation: no erythema, scaling, or edema with either oil – Skin hydration: comparable improvement with SIO
Suthiphasil 2018	6 mL SIO after meals daily (number of meals not specified) and erythromycin 250 mg (1 tablet) four times a day	Erythromycin 250 mg (1 tablet) four times a day	4 weeks	– Acne lesions: SIO with erythromycin showed better reduction in inflammatory and non-inflammatory lesions than the control

SIO—Sacha inchi oil

discontinuation. The results showed that SIO was as effective as olive oil in improving skin hydration and dry skin appearance. Corneometer® readings indicated a statistically significant increase in hydration after 14 days of application ($P < 0.01$), rising from an average baseline of 36.7 AU to 44.9 ± 1.7 AU for SIO and 45.6 ± 1.7 AU for olive oil. Two days after discontinuation, SIO showed slightly better moisture retention (40.4 ± 2.9 AU) compared to olive oil (39.1 ± 3.5 AU), with both values still significantly higher than baseline ($P < 0.05$). Neither oil caused irritation, with no observed cases of erythema, scaling, or edema. Additionally, SIO did not induce the release of pro-inflammatory cytokines (TNF- α and IL-1 α) or disrupt keratin 1 expression in the stratum corneum, suggesting it does not compromise skin barrier integrity. These findings support the potential of SIO as a mild, active moisturizing ingredient suitable for dry skin care, owing to its fatty acid profile and its ability to maintain skin barrier function and homeostasis. However, further research with a larger sample size and extended duration is needed to confirm these dermatological benefits.

The preliminary study by Suthiphasil 2018 [45], the therapeutic potential of oral SIO combined with erythromycin was assessed in the treatment of acne vulgaris over a four-week intervention period, with follow-up assessments extending to eight weeks. Acne severity was evaluated by physicians using the Acne Global Severity Grading System, along with inflammatory and non-inflammatory acne lesion counts. Five participants received both SIO and erythromycin, and the intervention led to a statistically significant reduction in both types of acne lesions. Inflammatory lesions decreased from an average of 7.75 ± 8.25 at baseline to 3.0 ± 6.0 by week 8, while non-inflammatory lesions dropped from 22.5 ± 30.03 to 8.75 ± 19.17 over the same period ($p < 0.05$). Severity grading also improved significantly, decreasing from 3.25 ± 0.5 at baseline to 2.5 ± 1.0 at week 4 and 1.5 ± 1.0 at week 8 ($p < 0.05$). Patient self-assessments, measured using a Visual Analogue Scale (VAS) ranging from 0 (disease-free) to 10 (severe disease), showed similar improvements, with scores falling from 6.75 ± 1.5 at baseline to 4.25 ± 3.04 at week 2 and 1.75 ± 0.5 at week 4. However, two participants reported adverse effects, including nausea, vomiting, and mild abdominal discomfort; one withdrew from the study. These results suggest potential anti-inflammatory and therapeutic benefits of SIO in acne management. Nonetheless, as this was a preliminary study without a control group, definitive conclusions about efficacy cannot be drawn. Further randomized controlled trials are needed to confirm the safety and effectiveness of SIO as an adjunct treatment for acne.

4.7 Ophthalmological effects

There was one study, Laihia 2019 [46], which evaluated the effects of Sacha inchi on moderate or severe dry eye conditions, used a novel emulsion eye drop formulation with Sacha inchi seed oil. It targeted three aetiologic factors for biophysical protection of the ocular surface for recovery from damage, inflammation, and symptoms. Findings showed Sacha inchi microemulsion (SIME) eyedrop improved the tear osmolarity and fluorescein tear break-up time (TBUT) with increased 1.7 s compared to hyaluronic acid (HA) (increased 0.87 s) with p -value 0.0025. Other positive findings by SIME include improved ocular protection index (OPI) (p -value of 0.0026), reduction in corneal staining (p -value 0.014), reduction in nasal conjunctival staining (p -value 0.043), decrease in conjunctival redness (p -value 0.001) and lid redness (p -value 0.012) when compared

with HA. As measured by the ocular surface disease index, both SIME and HA had comparable symptom relief. We summarized its characteristics on its eye effects in Table 4.

4.8 Neurological and cognitive health

There were five studies that evaluated the effects of Sacha inchi on neurological and cognitive health perspectives [47–49]. We summarized the characteristics and outcomes of the included studies on neurological and cognitive health in Table 5.

Two studies conducted in Thailand explored the effects of Sacha inchi consumption on cognitive function. Firstly, a non-randomized, single-arm trial by Nokdhes and Sittiprapaporn (2017) investigated the impact of SIO supplementation in adults aged 20–55. Participants consumed six capsules of SIO daily (two capsules after each meal) for one month. The results demonstrated a significant increase in Theta, Alpha, and Beta brainwave activity, as measured by cognitive functional tests (Theta: $2.37 \pm 0.31 \mu\text{V}$ to $4.27 \pm 0.54 \mu\text{V}$, $p=0.014$; Alpha: $2.49 \pm 0.41 \mu\text{V}$ to $4.33 \pm 0.52 \mu\text{V}$, $p=0.02$; Beta: $2.14 \pm 0.42 \mu\text{V}$ to $4.73 \pm 0.61 \mu\text{V}$, $p=0.014$).

Secondly, a randomized controlled trial (RCT) by Sittiprapaporn and Suyajai (2022) examined the effects of Sacha inchi-enriched eggs in 40 children aged 6–12. Participants were randomly assigned to consume either a boiled Sacha inchi-based omega-3,6,9 enriched egg (treatment group) or a normal egg (placebo group) daily for 12 weeks. The study employed various cognitive, behavioral, and brain electrical activity assessments. The findings indicated that the Sacha inchi-enriched eggs significantly reduced response time compared to baseline ($p<0.05$). Furthermore, topological distribution analysis revealed a slight increase in the mean amplitude of N1, suggesting enhanced central nervous system activity. Collectively, these studies suggest that Sacha inchi consumption may have a beneficial impact on cognitive function in both healthy children and adults.

Three animal studies have indicated potential neuroprotective effects of Sacha inchi. Herrera-Calderon et al. (2019) [50] examined the effects of oral SIO administration in a Bagg Albino inbred strain C (Balb/C) mouse model of epilepsy. Mice treated with 500 to 1000 mg/kg of SIO exhibited a significant reduction in seizure onset, duration, severity, and frequency compared to the control group ($p<0.05$). Notably, the effects of SIO were comparable to those observed with diazepam (1 mg/kg). Furthermore, the study revealed that SIO (1000 mg/kg) significantly increased GABA levels ($73 \pm 1.1 \text{ ng/g tissue}$)

Table 4 Characteristics of studies evaluating the effects of Sacha inchi on the eye

Au- thor, year	Intervention (dose, frequency, and ad- ministration route)	Control (dose, fre- quency, and adminis- tration route)	Interven- tion/control duration	Study outcome
Laihia 2019	Part 1: 1 drop SIME 4 times on the worst eye at 2-h intervals, for 1 day	Part 1: No control for the other eye	Part 1: 1 day	– TFBUT: greater improvement with SIME than HA ($p=0.0025$) – OPI: Improved with SIME than HA ($p=0.0026$)
	Part 2: 1 drop SIME 3 times a day on 1 randomized eye	Part 2: 0.2% HA eye drops, 1 drop on the other eye, 3 times per day	Part 2: 10 days	– Corneal staining: reduced with SIME than HA ($p=0.014$) – Nasal conjunctival staining: re- duced with SIME than HA ($p=0.043$)
	Part 3: 1 drop SIME 3 times a day for both eyes	Part 3: 0.2% HA eye drops, 1 drop, 3 times per day on both eyes	Part 3: 30 days	– Redness: decreased conjunc- tival ($p=0.001$) and lid redness ($p=0.012$) with SIME – Symptom relief: comparable between SIME and HA

HA—Hyaluronic Acid; OPI—Ocular Protection Index; SIME—Sacha inchi Microemulsion; TFBUT – Tear Film Break-Up Time

Table 5 Characteristics of studies evaluating the effects of Sacha inchi on neurological and cognitive health

Study type	Author, year	Intervention (dose, frequency, and administration route)	Control (dose, frequency, and administration route)	Intervention/control duration	Study outcome
Human inter-vention studies	Nok-dhes 2017	6 SIO capsules containing 4 g per day, per oral (2 capsules per meal: breakfast, lunch, and dinner)	No control	1 month consumption	– Brainwave activity: increased alpha ($p=0.02$), Theta ($p=0.014$), and Beta ($p=0.014$) – Delta & Gamma: no significant changes
	Sit-tiprapaporn 2022	2 boiled chicken eggs enriched with omega-3 3,6,9 derived from Sacha inchi, per oral daily	2 normal chicken eggs per oral daily	12 weeks of consumption	– Cognitive ability: no differences in accuracy between groups – Response time: reduced with enriched eggs after 12 weeks ($p<0.05$)
Animal inter-vention studies	Her-rera-Calde-ron 2019	SIO, 250, 500, or 1000 mg/kg as a single dose, per oral	1. Diazepam 1 mg/kg as a single dose, subcutaneously 2. No treatment	15-day ac-climatization followed by a one-time dosing and 30-min observation	– Seizure reduction: SIO (1000 mg/kg) lowered seizure frequency/duration, comparable to diazepam (1 mg/kg) – GABA levels: Increased with SIO (1000 mg/kg) – MDA levels: reduced with SIO (1000 mg/kg)
	Islam 2020	GNO or SIO treated for 14 weeks. The dose, route, and frequency were not mentioned	Corn oil treated for 14 weeks. The dose, route, and frequency were not mentioned	1-week acclimatiza-tion followed by 14-week treatment	– Brain DHA levels: increased with GNO (1.85×) and DHA (3.67×) compared to corn oil – Memory efficiency: Improved with GNO (1.99×) and DHA (2.34×) vs. corn oil – DHA-PC levels: significantly in-creased with GNO/DHA treatment – Memory function: significantly improved with GNO/DHA vs. corn oil

CO—Corn Oil; DHA—Docosahexaenoic Acid; DHA-PC—Docosahexaenoic Acid-Phosphatidylcholine; GABA—Gamma-Aminobutyric Acid; GNO—Green Nut Oil; MDA—Malondialdehyde; SIO—Sacha inchi oil

and decreased MDA levels ($1.1 \pm 0.03 \mu\text{mol/g}$ brain tissue) relative to the negative control ($p<0.01$ and $p<0.05$, respectively). A high dose of SIO (1000 mg/kg) demonstrated protective effects against pentylenetetrazole (PTZ)-induced seizures in mice, resulting in 100% survival (6/6 mice), comparable to a safe dose of diazepam. The antioxidant capacity of Sacha inchi was also demonstrated through its dose-dependent inhibition of 2,2-diphenylpicrylhydrazyl (DPPH) radicals and malondialdehyde. This antioxidant activity is suggested to reduce the direct inactivation of glutamine synthase, a process associated with the abnormal release of excitatory neurotransmitters such as glutamic acid.

One study, Islam et al. (2020), investigated the neuroprotective effects of green nut oil (GNO) extracted from Sacha inchi seeds in a senescence-accelerated mouse P8 (SAMP8) model of dementia. Mice were supplemented with GNO for 14 weeks. It was reported that GNO supplementation significantly enhanced the brain distribution of docosahexaenoic acid (DHA) by 1.85-fold in SAMP8 mice, comparable to the 3.67-fold increase seen in mice supplemented with DHA directly. Furthermore, GNO and DHA improved memory efficiency by 1.99-fold and 2.34-fold, respectively, compared to corn oil-fed controls ($p<0.05$). The study also noted significant improvements in the spatial distribution of other free fatty acids, including linoleic acid, oleic acid, eicosapentaenoic acid,

docosapentaenoic acid, and adrenic acid. GNO supplementation restored decreased brain distribution levels of DHA-phosphatidylcholines, a lipid crucial for optimal neuronal function and synaptic membrane protein regulation, which are typically reduced in dementia. The Mass spectrometry revealed increase of DHA-phosphatidylcholine (DHA-PC) distribution by 16:0_22:6 and 18:0_22:6 in GNO/DHA-treated SAMP8 mice than corn oil (CO)-treated mice ($p < 0.05$) in hippocampus, cerebellum, cerebral cortex, caudate putamen, and ventral striatum, with a significant improvement of memory function with GNO/DHA as compared to CO. These findings suggest that GNO, derived from Sacha inchi seeds, may mitigate dementia progression by improving memory function and neuronal signaling. The authors attributed these neuroprotective effects to the high concentration of omega-3 polyunsaturated fatty acids present in SIO.

4.9 Risk of bias assessment

We summarized the overall bias assessments of the 13 included studies in Fig. 2. The overall RoB across randomized human studies varied considerably by domain. Most were judged to have low risk for missing outcome data, while fewer achieved low risk in the randomization process and outcome measurement. A notable proportion of studies had high RoB in outcome measurement, and many lacked sufficient methodological detail, resulting in a large number of domains with unclear RoB assessments.

For the non-randomized human study, RoB was generally low across most domains, particularly in selection bias, classification of interventions, deviations from intended interventions, measurement of outcomes, and reporting bias.

Among animal studies, the RoB also varied across domains. Most were assessed as low risk in baseline characteristics, incomplete outcome data, and selective reporting. Similarly, random sequence generation and random housing were frequently judged as low risk. However, allocation concealment and blinding were less consistently addressed. As with the human studies, several domains lacked sufficient information to allow for a definitive RoB judgment. Detailed summary figures for all the assessments are found in Appendix A (Fig. 3).

on of included studies assessed using the respective risk-of-bias tool (total = 100% per domain per tool).

4.10 Safety assessment

From the included studies, one human study [44] which tested the topical application of SIO for its effect on skin hydration and reported two safety-related findings. Firstly, applying SIO twice daily was found to be safe over 14 days. Secondly, pretreatment of tissues with the oil before ultraviolet (UV) irradiation did not lead to an excessive secretion of cytokines when compared to ultraviolet B (UVB)-irradiated tissues without pretreatment, indicating that the tested oil does not disturb the skin's barrier function. Another human study [40] reported several side effects associated with oral consumption of SIO during the first 4 weeks, with nausea ($n = 14$) and eructation ($n = 5$) being the most common. Other minor side effects included hot flashes, headache, cramping, and constipation. However, these symptoms diminished over time, with only two subjects continuing to report side effects by week 17. One experienced headache and nausea, while the other experienced nausea alone.

DOMAINS	ROB2 (n = 8 studies)	ROBINS-I (n = 1 study)	SYRCLE (n = 4 studies)
SELECTION BIAS			
Randomisation process	25% LOW 62.5% SOME CONCERNS 12.5% HIGH		75% LOW 25% SOME CONCERNS
Baseline characteristics		100% LOW	100% LOW
Allocation concealment			25% LOW 75% SOME CONCERNS
CONFOUNDING BIAS			
Confounding bias		100% SOME CONCERNS	
CLASSIFICATION BIAS			
Classification of interventions		100% LOW	
PERFORMANCE BIAS			
Deviations from intended interventions	25% SOME CONCERNS 75% HIGH	100% LOW	
Random housing			75% LOW 25% SOME CONCERNS
Blinding of caregivers/investigators			75% SOME CONCERNS 25% HIGH
MEASUREMENT BIAS			
Measurement bias	25% LOW 25% SOME CONCERNS 50% HIGH	100% SOME CONCERNS	
Random outcome assessment (Detection Bias)			50% LOW 50% SOME CONCERNS
Blinding of outcome assessment (Detection Bias)			100% SOME CONCERNS
ATTRITION BIAS			
Bias due to missing outcome data	87.5% LOW 12.5% HIGH	100% SOME CONCERNS	87.5% LOW
REPORTING BIAS			
Selective reporting	12.5% LOW 37.5% SOME CONCERNS 50% HIGH	100% LOW	100% LOW

*Percentages in each domain represent the proportion of included studies assessed using the respective risk-of-bias tool (total = 100% per domain per tool).

Fig. 3 Overall summary of risk of bias assessments of all included studies

5 Discussion

5.1 Summary of included studies

In summary, Sacha inchi has shown potential benefits for metabolic syndrome, cognitive enhancement, ophthalmology (dry eyes), and dermatology through clinical studies. Animal studies demonstrated effects on hypertension, hyperlipidemia, and neuroprotection. Although this plant has been extensively studied for its nutritional composition, the active phytochemicals responsible for its health benefits are not fully defined. However, previous studies have postulated that the therapeutic effects are likely contributed by bioactive compounds composed of tannins, phenolic acids, flavonoids, and lignans. [51]

In the studies evaluating metabolic health, weight changes were not evaluated, potentially due to the interventions' short duration, small sample size, and doses unlikely to produce measurable changes in body weight over the study interval. For metabolic health, Sacha inchi has shown positive effects due to its high alpha-linolenic acid and linolenic acid content, which play a role in insulin sensitivity and sirtuin-1 expression [52]. Sacha inchi also contains a certain amount of ω -3 fatty acids and antioxidants that have been shown to reduce triglyceride accumulation and fat droplet distribution in the liver [53]. Another study has shown that extra virgin SIO can improve pancreatic β -cell function and protect it from apoptosis due to its antioxidant (superoxide dismutase) and anti-inflammatory (NF- κ B, TNF- α , and IL-6) effects [54]. The existing scientific evidence for Sacha inchi as a treatment agent for metabolic syndrome is encouraging, but it is considered preliminary in terms of the strength of evidence. The available efficacy data from human trials demonstrate consistent and significant positive effects on key

cardiometabolic risk factors, particularly blood pressure (systolic and diastolic) and the lipid profile (improving Total Cholesterol, LDL-C, and HDL-C) [55]. However, the evidence is attenuated by two major limitations. First, while Sacha inchi shows strong anti-inflammatory and antioxidant activity in various models, the impact on glycemic control markers, such as fasting blood glucose and HOMA-IR, remains inconsistent or statistically non-significant across human studies. Second, the available research mainly consists of small-scale, short-term human trials and supportive animal model experiments, rather than the large-scale, long-duration RCTs necessary to establish definitive clinical efficacy and long-term safety for a formal therapeutic recommendation.

The role of omega-3 fatty acids for neurocognitive effects has been highlighted in a systematic review, which included 69 RCTs and 19 observational studies that show its short-term benefits in visual attention, working memory, executive function, and communication [56]. The role of arachidonic acid (AA) and docosapentaenoic acid (DPA) has been shown to reduce the rate of cognitive decline among older adults [57], which explained the Sacha inchi role in cognitive development and function, since it contains ω -6 fatty acids that can be converted into arachidonic acid (AA) but do not contain docosapentaenoic (DPA) in its ω -3 fatty acids like fish oil [53]. Based on its composition, the evidence for Sacha inchi's neurocognitive benefits is mechanistically plausible but clinically limited, primarily relying on its omega-3 content, which is a critical structural component of neuronal cell membranes [29]. From our review, Its consumption is widely hypothesized to support brain structure, neurotransmission, and reduced neuroinflammation through evidence from animal studies. However, the clinical translation still remains in the foundational stage.

In terms of SIO effects on dry eyes, a recent prospective, randomized, and comparative study was conducted on patients undergoing cataract surgery with postoperative discomfort such as persistent dry eyes, which showed that the combination of hyaluronic acid/trehalose/SIO eye drops showed relief in dry eye symptoms based on the ocular surface disease index (OSDI) questionnaire. However, there are limitations to this study which is the eye drops is a mixture, the administration is in addition to standard postoperative drops, and the questionnaire can be influenced by the cataract surgery's positive impact [58]. However, a meta-analysis that included 18 RCTs showed the benefit of omega-3 in dry eye disease in comparison with placebo when measuring OSDI mean changes, but no improvement on corneal staining, TBUT, or Schirmer's score, with a major limitation of high heterogeneity ($I^2 > 60\%$), which makes the findings inconclusive [59].

The application of SIO in skincare is attributed to its high antioxidant effects due to the omega-3 content. In an in vitro study to determine the antiaging activity of SIO in facial serum form, findings showed its ability to inhibit neutrophil elastase and collagenase activity with no irritation on human skin [60]. A recent study on mice with atopic dermatitis has shown that SIO has an upregulatory effect on the protein expression of filaggrin and loricrin and exerts inhibitory effects on the protein expression and phosphorylation levels of P38, ERK, NF- κ B, and I κ B α , which further explains its mechanism of action for antioxidant and anti-inflammatory benefits [61].

From the included articles, safety assessment was few but did not show any significant toxicity. This is further supported by the general toxicity and genotoxicity study of powdered Sacha inchi for 14 days (2000 mg/kg), 90 days (50, 250, and 500 mg/kg/day), and

micronucleus test (2000 mg/kg) did not report any morbidity, mortality, or micronucleus formation [62]. However, the processing methods of Sacha inchi, such as roasting, are important to reduce its phytotoxins (alkaloids, lectins (carbohydrate-binding proteins), and saponins which may cause deoxyribonucleic acid (DNA) mutations [15, 63].

5.2 Strengths

The strength of this systematic review lies in its comprehensive approach, encompassing various study designs such as animal studies, non-randomized clinical trials, and randomized clinical trials. We conducted quality analyses tailored to each study design using appropriate RoB tools. Recent reviews on Sacha inchi provide overviews of the herb without employing a systematic approach in database search with predetermined keywords. They cover a wide range of research study designs, from in vitro and in vivo efficacy and safety studies to human clinical trials, in addition to offering detailed descriptions of the plant's chemical composition [29]. In contrast, our review was developed systematically, focusing solely on the efficacy and safety aspects. We included only animal and human studies to assess the therapeutic potential of this plant.

5.3 Limitations

However, this review also faces several limitations. Firstly, the lack of adequate randomized clinical trials with consistent outcome measures hinders our ability to perform meta-analyses. Additionally, the inclusion criteria limited articles to those written in English, potentially restricting the representation of global scientific data concerning the efficacy and safety of Sacha inchi. Moreover, we did not incorporate in vitro studies, which could offer valuable insights into emerging potential efficacies. The clinical findings, although they have a small sample size (between 10 and 70 participants), eight out of nine human trials are randomized controlled trials, which showed low risk in nine out of the 13 domains listed for risk of bias assessment. However, there is a need for RCTs to be conducted with larger sample sizes and longer duration of studies for a more comprehensive understanding of the effects and safety of the SIO.

5.4 Recommendations

The findings of this review indicate that SIO may be considered as a dietary supplement to promote cardiometabolic health. Its incorporation into the diet should be viewed as complementary to, rather than a substitute for, a balanced nutrient-rich eating pattern, healthy lifestyle, and established medical therapies. Consultation with qualified healthcare professionals is recommended to ensure appropriate and safe use. Despite the promising observations, the current evidence remains limited. SIO demonstrates potential as a functional food with specific relevance to obesity and non-alcoholic fatty liver disease. [28, 40, 54, 55, 64–66]. However, it is important to build its scientific evidence through the conduct of preclinical and clinical studies prior to its approval for marketed use. Furthermore, regulatory processes are country-specific, and therefore, current findings may not be universally generalizable with respect to their classification, permissible health claims, and utility as either a dietary supplement or functional food.

While current findings are highly encouraging, further large-scale, well-designed randomized controlled clinical trials (RCTs) are essential to fully establish the medicinal efficacy and safety of SIO across diverse populations and clinical conditions. To ensure

reliable clinical outcomes and consistent therapeutic benefits, herbal medicines must be standardized to achieve uniform quality and clearly defined ingredient profiles. Future research must determine the optimal daily dosage of Sacha Inchi oil and seeds for specific health benefits, whereby all relevant non-clinical data, such as pharmacological dose response, pharmacological/toxicological profile, and pharmacokinetics, should be taken into account. Mechanistic studies are also important to determine the interaction of its unique fatty acid ratio (n-6:n-3 is close to ideal, approx. 1:1.25) and its phenolic compounds with cellular pathways (e.g., eNOS pathway for blood pressure), which will further solidify its primary and secondary pharmacodynamics [67].

6 Conclusion

Findings from this review indicate that SIO shows the most consistent evidence for improving lipid profiles, especially in lowering total cholesterol and LDL-C levels, as well as reducing systolic blood pressure and enhancing postprandial insulin sensitivity. Additional benefits were observed for skin hydration, dry eye symptoms, and cognitive function, though these require further validation through larger and longer-term clinical studies. Safety data on SIO remains limited, though available human studies suggest topical use is well-tolerated and does not impair skin barrier function, while mild, self-limiting side effects may occur with oral consumption. However, the number of available studies is very limited and hence lacks substantial scientific evidence to support the plant's pharmacological efficacy and safety for therapeutic applications. Further safety data are needed, especially in higher doses and for extended periods. Both clinical and preclinical research also lack a comprehensive exploration of specific formulations or extracts of Sacha inchi. In essence, while traditional uses suggest promise, more thorough scientific investigation is essential to validate its therapeutic claims and ensure its safe integration into healthcare practices.

Abbreviation

AA	Arachidonic acid
AHG	Above-median glucose
ALA	α -Linolenic acids
ARA	Arachidonic acid
AU	Arbitrary unit
Balb/C	Bagg Albino inbred strain C
BMI	Body mass index
CENTRAL	Cochrane Central Register of Controlled Trials
CO	Corn oil
CRP	C-reactive protein
DBP	Diastolic blood pressure
DHA	Docosahexaenoic acid
DHA-PC	Docosahexaenoic Acid-Phosphatidylcholine
DPA	Docosapentaenoic acid
DPPH	2,2-Diphenylpicrylhydrazyl
DNA	Deoxyribonucleic acid
EPA	Eicosapentaenoic acid
ERK	Extracellular signal-regulated kinases
GABA	Gamma-Aminobutyric Acid
GNO	Green Nut Oil
HA	Hyaluronic acid
HDL-C	High density lipoprotein cholesterol
HFD	High fat diet
HFM	High-fat meal
HOMA	Homeostasis Model Assessment of Insulin Resistance
iAUC	Incremental area under the curve
iAUC-G	Incremental Area Under the Curve for Glucose
IkBa	Inhibitor of nuclear factor kappa B
IL-1 α	Interleukin 1-alpha

IL-6	Interleukin-6
IQR	Interquartile range
ISI	Insulin Sensitivity Index
ITT	Intention-to-treat
LA	Linoleic acid
LDL-C	Low-density lipoprotein cholesterol
LILACS	Latin America and the Caribbean Literature on Health Sciences
LTCC	L-Type Voltage-Gated Calcium Channel
LVWT	Left ventricular wall thickness
MDA	Malondialdehyde
MeSH	Medical subject heading
MH	Metabolically healthy
MU	Metabolically unhealthy
MUFAs	Monounsaturated fatty acids
NF- κ B	Nuclear factor kappa B
OPI	Ocular protection index
OSDI	Ocular surface disease index
p38 MAPK	P38 mitogen-activated protein kinase
PBMC	Peripheral Blood Mononuclear Cells
PP	Per-protocol
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	The International Prospective Register of Systematic Reviews
PTZ	Pentylentetrazole
PUFAs	Polyunsaturated fatty acids
RCTs	Randomized controlled trials
RoB	Risk of bias
RoB 2.0	The Cochrane Risk of Bias tool 2
ROBINS-I	Risk Of Bias In Non-randomized Studies—of Interventions
SAMP8	Senescence-Accelerated Mouse-Prone 8
SBP	Systolic blood pressure
SD	Sprague-Dawley
SFAs	Saturated fatty acids
SHR	Spontaneous Hypertensive rats
SI	Sacha inchi
SIME	Sacha inchi microemulsion
SIO	Sacha inchi oil
SIRT-1	Sirtuin 1
SISE	Sacha inchi shell extract
SYRCLE	Systematic Review Centre for Laboratory Animal Experimentation
TAG	Triacylglycerol
TBUT	Tear break-up time
TC	Total cholesterol
TG	Triglycerides
TNF- α	Tumor necrosis factor
TRL-cholesterol	Triglyceride-rich lipoprotein
UV	Ultraviolet
UVB	Ultraviolet B
VAS	Visual Analogue Scale
WKY	Wistar Kyoto rats
WoS	Web of Science
ω -3 fatty acids	Omega-3 fatty acids
ω -6 fatty acids	Omega-6 fatty acids

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1007/s44187-026-00844-w>.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

Supplementary Material 6.

Supplementary Material 7.

Supplementary Material 8.

Acknowledgements

We would like to thank the Director General of Health Malaysia, Deputy Director General of Health Malaysia (Research and Technical Support), Director of Institute for Medical Research, Head Centre of Herbal Medicine Research Centre, and Nutrition, Metabolic and Cardiovascular Research Centre for their support and permission to publish this article.

Author contributions

Conceptualization, Terence Yew Chin Tan and Puteri Sofia Nadira Megat Kamaruddin; Methodology, Terence Yew Chin Tan, Sophia Rasheeqa Ismail, and Puteri Sofia Nadira Megat Kamaruddin; Software, Puteri Sofia Nadira Megat Kamaruddin; Formal analysis, Terence Yew Chin Tan, Sophia Rasheeqa Ismail, and Puteri Sofia Nadira Megat Kamaruddin; Investigation, Terence Yew Chin Tan, Sophia Rasheeqa Ismail, Puteri Sofia Nadira Megat Kamaruddin, Wan Ahmad Syazani Mohamed, Janice Sue Wen Chan, Mohd Naeem Mohd Nawi, Han Yin Lim, Siti Hajar Muhamad Rosli, Ida Farah Ahmad, Puspawathy Krishnan, and Nur Es Naini Awalludin; Writing—original draft preparation, Terence Yew Chin Tan, and Puteri Sofia Nadira Megat Kamaruddin; Writing—review and editing, Terence Yew Chin Tan, Sophia Rasheeqa Ismail, Puteri Sofia Nadira Megat Kamaruddin, Wan Ahmad Syazani Mohamed, Janice Sue Wen Chan, Mohd Naeem Mohd Nawi, Han Yin Lim, Siti Hajar Muhamad Rosli, Ida Farah Ahmad, Puspawathy Krishnan, and Nur Es Naini Awalludin; Project administration, Terence Yew Chin Tan and Puteri Sofia Nadira Megat Kamaruddin.

Funding

The authors declare that no funds, grants, or other support was received during the preparation of this manuscript.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent to publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 28 July 2025 / Accepted: 21 January 2026

Published online: 29 January 2026

References

1. Araújo-Dairiki TB, Chaves FCM, Dairiki JK. Seeds of sacha inchi (*Plukenetia volubilis*, Euphorbiaceae) as a feed ingredient for juvenile tambaqui, *Colossoma macropomum*, and matrinxã, *Brycon amazonicus* (Characidae). *Acta Amazon.* 2018;48(1):32–7.
2. Polaris Market Research. Sacha Inchi Protein Market Share, Size, Trends, Industry Analysis Report, By Form (Powder, Liquid); By Application (Cosmetics, Pharmaceuticals, Food & Beverages, Dietary Supplements); By Region; Segment Forecast, 2023–2032 2023 [Available from: <https://www.polarismarketresearch.com/industry-analysis/sacha-inchi-protein-market#:~:text=The%20global%20sacha%20inchi%20protein,and%20is%20like%20flaxseed%20oil>].
3. Hanssen HP, Schmitz-Hübsch M. Sacha Inchi (*Plukenetia volubilis* L.) Nut Oil and Its Therapeutic and Nutritional Uses. *Nuts Seeds Health Disease Prevention.* 2011:991–4.
4. Kim D-S, Joo N. Nutritional composition of sacha inchi (*Plukenetia volubilis* L.) as affected by different cooking methods. *Int J Food Prop.* 2019;22(1):1235–41.
5. Singanusong R, Jiamyangyuen S. Effects of maturity on chemical composition and antioxidant activity of sacha inchi (*Plukenetia volubilis* L.) cultivated in Northern Thailand. *Walailak J Sci Technol (WJST).* 2020;17(9):998–1009.
6. Supriyanto S, Imran Z, Ardiansyah R, Auliyai B, Pratama A, Kadha F. The effect of cultivation conditions on sacha inchi (*Plukenetia volubilis* L.) seed production and oil quality (Omega 3, 6, 9). *Agronomy.* 2022;12(3):636.
7. Triana-Maldonado DM, Torijano-Gutiérrez SA, Giraldo-Estrada C. Supercritical CO₂ extraction of oil and omega-3 concentrate from sacha inchi (*Plukenetia volubilis* L.) from Antioquia, Colombia. *Grasas Aceites.* 2017;68(1):e172.
8. Zanqui AB, Silva CMD, Morais DRd, Santos JM, Ribeiro S, Eberlin MN, et al. Sacha inchi (*Plukenetia volubilis* L.) oil composition varies with changes in temperature and pressure in subcritical extraction with n-propane. *Industrial Crops and Products.* 2016;87:64–70.
9. Chirinos R, Zuloeta G, Pedreschi R, Mignolet E, Larondelle Y, Campos D. Sacha inchi (*Plukenetia volubilis*): a seed source of polyunsaturated fatty acids, tocopherols, phytosterols, phenolic compounds and antioxidant capacity. *Food Chem.* 2013;141(3):1732–9.
10. Maurer NE, Hatta-Sakoda B, Pascual-Chagman G, Rodriguez-Saona LE. Characterization and authentication of a novel vegetable source of omega-3 fatty acids, sacha inchi (*Plukenetia volubilis* L.) oil. *Food Chem.* 2012;134(2):1173–80.
11. Afifah DN, Salam DA, Nugraheni F, Resti N, Purwanti R, Anjani G, et al. Analysis of the nutritional and fatty acid profile of sacha inchi tempe (*Plukenetia volubilis* L.) using different cooking methods. *Frontiers in Nutrition.* 2025;12.
12. Jitpinit S, Siraworakun C, Sookklay Y, Nuithitikul K. Enhancement of omega-3 content in sacha inchi seed oil extracted with supercritical carbon dioxide in semi-continuous process. *Heliyon.* 2022;8(1):e08780.
13. Maya I, Winardi DO, Amalia E, Mita SR, Kusumawulan CK, Putriana NA, et al. Physicochemical characteristics, fatty acid profile, and in vitro antioxidant activity evaluation of Sacha Inchi seed oil from Indonesia. *Cosmetics.* 2023;10(6):171.
14. Rawdkuen S, Murdayanti D, Ketnawa S, Phongthai S. Chemical properties and nutritional factors of pressed-cake from tea and sacha inchi seeds. *Food Biosci.* 2016;15:64–71.

15. Srichamnong W, Ting P, Pitchakarn P, Nuchuchua O, Temviriyannukul P. Safety assessment of *Plukenetia volubilis* (Inca peanut) seeds, leaves, and their products. *Food Sci Nutr*. 2018;6(4):962–9.
16. Fanali C, Dugo L, Cacciola F, Beccaria M, Grasso S, Dachà M, et al. Chemical characterization of sacha inchi (*Plukenetia volubilis* L.) oil. *J Agric Food Chem*. 2011;59(24):13043–9.
17. Bueno-Borges LB, Sartim MA, Gil CC, Sampaio SV, Rodrigues PHV, Regitano-d'Arce MAB. Sacha inchi seeds from sub-tropical cultivation: effects of roasting on antinutrients, antioxidant capacity and oxidative stability. *J Food Sci Technol*. 2018;55(10):4159–66.
18. Kyaw T NT, Khaing M, San P, Kyaing K, Thet T, Htun E. Studies on nutritional compositions of sacha inchi seed and physico-chemical characteristics of sacha inchi oil. *Int Euro Extended Enablement Sci Eng Manage (IEEESEM)*. 2019;7(8).
19. Ramos-Escudero F, Morales MT, Ramos Escudero M, Muñoz AM, Cancino Chavez K, Asuero AG. Assessment of phenolic and volatile compounds of commercial Sacha inchi oils and sensory evaluation. *Food Res Int*. 2021;140:110022.
20. Xuan TD, Gangqiang G, Minh TN, Quy TN, Khanh TD. An overview of chemical profiles, antioxidant and antimicrobial activities of commercial vegetable edible oils marketed in Japan. 2018. *Foods*. <https://doi.org/10.3390/foods7020021>.
21. Chasquibol NA, del Aguila C, Yácono JC, Guinda Á, Moreda W, Gómez-Coca RB, et al. Characterization of glyceridic and unsaponifiable compounds of Sacha Inchi (*Plukenetia huayllabambana* L.) Oils. *J Agric Food Chem*. 2014;62(41):10162–9.
22. Chirinos R, Pedreschi R, Domínguez G, Campos D. Comparison of the physico-chemical and phytochemical characteristics of the oil of two *Plukenetia* species. *Food Chem*. 2015;173:1203–6.
23. Cisneros FH, Paredes D, Arana A, Cisneros-Zevallos L. Chemical composition, oxidative stability and antioxidant capacity of oil extracted from roasted seeds of Sacha-inchi (*Plukenetia volubilis* L.). *J Agric Food Chem*. 2014;62(22):5191–7.
24. Follegatti-Romero LA, Piantino CR, Grimaldi R, Cabral FA. Supercritical CO₂ extraction of omega-3 rich oil from Sacha inchi (*Plukenetia volubilis* L.) seeds. *J Supercrit Fluids*. 2009;49(3):323–9.
25. Liu Q, Xu YK, Zhang P, Na Z, Tang T, Shi YX. Chemical composition and oxidative evolution of Sacha Inchi (*Plukenetia volubilis* L.) oil from Xishuangbanna (China). *Grasas Aceites*. 2014;65(1):e012.
26. Takeyama E, Fukushima M. Physicochemical properties of *Plukenetia volubilis* L. seeds and oxidative stability of cold-pressed oil (Green Nut Oil). *Food Sci Technol Res*. 2013;19(5):875–82.
27. Chirinos R, Zorrilla D, Aguilar-Galvez A, Pedreschi R, Campos D. Impact of roasting on fatty acids, tocopherols, phytosterols, and phenolic compounds present in *Plukenetia huayllabambana* seed. *J Chem*. 2016;2016.
28. Abd Rahman IZ, Nor Hisam NS, Aminuddin A, Hamid AA, Kumar J, Ugusman A. Evaluating the potential of *Plukenetia volubilis* Linneo (Sacha Inchi) in alleviating cardiovascular disease risk factors: a mini review. *Pharmaceutics*. 2023;16(11):1588.
29. Cárdenas DM, Gómez Rave LJ, Soto JA. Biological activity of Sacha Inchi (*Plukenetia volubilis* Linneo) and potential uses in human health: a review. *Food Technol Biotechnol*. 2021;59(3):253–66.
30. Kittibunchakul S, Hudthagosol C, Sanporkha P, Sapwarobol S, Temviriyannukul P, Suttisansanee U. Evaluation of Sacha Inchi (*Plukenetia volubilis* L.) by-products as valuable and sustainable sources of health benefits. *Horticulturae*. 2022;8(4):344.
31. Mhd Rodzi NAR, Lee LK. Sacha Inchi (*Plukenetia Volubilis* L.): recent insight on phytochemistry, pharmacology, organoleptic, safety and toxicity perspectives. *Heliyon*. 2022;8(9):e10572.
32. Cochrane. Cochrane Handbook for Systematic Reviews of Interventions version 6.5 (Updated August 2024)2024.
33. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
34. Team TE. EndNote X9 ed. Philadelphia, PA: Clarivate Analytics; 2013.
35. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:14898.
36. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
37. Hooijmans CR, Rovers MM, de Vries RBM, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol*. 2014;14(1):43.
38. Alayón AN, Ortega Ávila JG, Echeverri Jiménez I. Carbohydrate metabolism and gene expression of sirtuin 1 in healthy subjects after Sacha inchi oil supplementation: a randomized trial. *Food Funct*. 2018;9(3):1570–7.
39. Alayón AN, Ortega Ávila JG, Echeverri Jiménez I. Metabolic status is related to the effects of adding of sacha inchi (*Plukenetia volubilis* L.) oil on postprandial inflammation and lipid profile: randomized, crossover clinical trial. *J Food Biochem*. 2019;43(2):e12703.
40. Gonzales GF, Gonzales C. A randomized, double-blind placebo-controlled study on acceptability, safety and efficacy of oral administration of sacha inchi oil (*Plukenetia volubilis* L.) in adult human subjects. *Food Chem Toxicol*. 2014;65:168–76.
41. Gonzales GF, Gonzales C, Villegas L. Exposure of fatty acids after a single oral administration of sacha inchi (*Plukenetia volubilis* L.) and sunflower oil in human adult subjects. *Toxicol Mech Methods*. 2013;24(1):60–9.
42. Li P, Cai X, Xiao N, Ma X, Zeng L, Zhang LH, et al. Sacha inchi (*Plukenetia volubilis* L.) shell extract alleviates hypertension in association with the regulation of gut microbiota. *Food Funct*. 2020;11(9):8051–67.
43. Li P, Huang J, Xiao N, Cai X, Yang Y, Deng J, et al. Sacha inchi oil alleviates gut microbiota dysbiosis and improves hepatic lipid dysmetabolism in high-fat diet-fed rats. *Food Funct*. 2020;11(7):5827–41.
44. Soimee W, Nakayai W, Charoensit P, Grandmottet F, Worasakwutiphong S, Phimmuan P, et al. Evaluation of moisturizing and irritation potential of sacha inchi oil. *J Cosmet Dermatol*. 2021;19(4):915–24.
45. Suthiphasil P, Rintha J, Nararatwanchai T, Sittiprapaporn P, editors. Comparative study of oral administration of Sacha Inchi oil extraction with erythromycin versus oral erythromycin on the treatment of Acne Vulgaris. In: 2018 international conference on digital arts, media and technology (ICDAMT); 2018.
46. Laihia J, Järvinen R, Wylegala E, Kaarniranta K. Disease aetiology-based design of multifunctional microemulsion eye drops for moderate or severe dry eye: a randomized, quadruple-masked and active-controlled clinical trial. *Acta Ophthalmol*. 2020;98(3):244–54.
47. Islam A, Takeyama E, Mamun MA, Sato T, Horikawa M, Takahashi Y, et al. Green nut oil or DHA supplementation restored decreased distribution levels of DHA containing phosphatidylcholines in the brain of a mouse model of dementia. *Metabolites*. 2020;10(4):153.
48. Nokdhes YN, Sittiprapaporn P, editors. Effect of Sacha Inchi on human brain functions and brainwaves alteration. In: 2017 International conference on digital arts, media and technology (ICDAMT); 2017.

49. Sittirapaporn P, Suyajai P. Topographical distribution of the human brain to *Plukenetia volubilis*-based omega-3,6,9 enriched egg consumption. 2022. 2022;11(4):13.
50. Oscar H-C, Ricardo Ángel Y-P, Johnny Aldo T-J, Edwin E-R, César F-Q, Victor C-C, et al. Neuroprotective effect of Sacha Inchi Oil (*Plukenetia volubilis* L.) in an experimental model of epilepsy. *Pharmacognosy J*. 2019;11(6s).
51. Chirinos R, Necochea O, Pedreschi R, Campos D. Sacha inchi (*Plukenetia volubilis* L.) shell: an alternative source of phenolic compounds and antioxidants. *Int J Food Sci Technol*. 2016;51(4):986–93.
52. Long C, Zhao ZX, Willing BP, Sheng XH, Wang XG, Xiao LF, et al. Alpha-linolenic acid supplementation improves testosterone production in an aged breeder rooster model: role of mitochondrial modulation and SIRT1 activation. *Mol Nutr Food Res*. 2024;68(22):e2400522.
53. Samrit T, Osotprasit S, Chaivichien A, Suksomboon P, Chansap S, Athipornchai A, et al. Cold-pressed Sacha inchi oil: high in Omega-3 and prevents fat accumulation in the liver. *Pharmaceuticals*. 2024;17(2):220.
54. Wongmanee N, Rojanaverawong W, Boonsong T, Hanchang W. Antihyperglycemic effect of extra virgin sachu inchi oil in type 2 diabetic rats: mechanisms involved in pancreatic β -cell function and apoptosis. *J Tradit Complement Med*. 2024;14(2):148–61.
55. Mhd Rodzi NAR, Mohd Sopian M, Lee LK. Effects of Sacha Inchi (*Plukenetia volubilis* L.) oil supplementation on hyperglycaemia, hypertension and hyperlipidaemia (3Hs) patients: a preliminary human trial. *Plant Foods Hum Nutr*. 2025;80(1):80.
56. Sherzai D, Moness R, Sherzai S, Sherzai A. A systematic review of Omega-3 fatty acid consumption and cognitive outcomes in neurodevelopment. *Am J Lifestyle Med*. 2023;17(5):649–85.
57. de Oliveira Otto MC, Wu JHY, Thacker EL, Lai HTM, Lemaitre RN, Padhye N, et al. Circulating Omega-3 and Omega-6 fatty acids, cognitive decline, and dementia in older adults. *J Alzheimers Dis*. 2023;95(3):965–79.
58. Pereira A, Teixeira-Martins R, Coelho-Costa I, Lima-Fontes M, Pinheiro-Costa J, Macedo JP. High molecular weight hyaluronic acid, trehalose and Sacha inchi oil drops in post-cataract dry eye symptoms. *Revista Sociedade Portuguesa de Oftalmologia*. 2024.
59. O'Byrne C, O'Keeffe M. Omega-3 fatty acids in the management of dry eye disease-An updated systematic review and meta-analysis. *Acta Ophthalmol*. 2022.
60. Maya I, Sriwidodo S, Mita SR, Kusumawulan CK, Putriana NA, Amalia E, et al. Formulation and evaluation of facial serum containing Sacha Inchi oil (*Plukenetia volubilis* L.) from Indonesia as an anti-aging: stability, in vitro, and skin irritation assessments. *Cosmetics*. 2024;11(6):226.
61. Zhang Y, Zhao W, Liao J, Zhang Y, Wang L, Li P, et al. Evaluation of the therapeutic effect of Sacha inchi oil in atopic dermatitis mice. *Int Immunopharmacol*. 2024;138:112552.
62. Rodeiro I, Ramirez D, Flores D. Sacha Inchi (*Plukenetia volubilis* L.) powder: acute toxicity, 90 days oral toxicity study and micronucleus assay in rodents. *J Pharm Pharmacogn Res*. 2018;6(1):17–26.
63. Torres Sánchez EG, Hernández-Ledesma B, Gutiérrez LF. Sacha inchi oil press-cake: physicochemical characteristics, food-related applications and biological activity. *Food Rev Int*. 2023;39(1):148–59.
64. Garmendia F, Pando R, Ronceros G. [Effect of sachu inchi oil (*plukenetia volubilis* l) on the lipid profile of patients with hyperlipoproteinemia]. *Rev Peru Med Exp Salud Publica*. 2011;28(4):628–32.
65. En CY. Effect of Sacha Inchi oil on human blood pressure and lipid profile: a preliminary study in Malaysia. *Jurnal Gizi dan Pangan*. 2024;19(1):61–8.
66. Sa-nguanpong P, Wetprasit P, Chatturong U, Chootip K, Kantip N, Tochampa W, et al. Protective effects of Sacha inchi meal protein hydrolysate against oxidative stress and endothelial dysfunction via MDA suppression and SOD activation in L-NAME-induced hypertensive rats. *Eur J Med Chem Rep*. 2025;15:100297.
67. National Committee for R, Development of Herbal M. Guideline for Herbal Medicine Research, First Edition. Shah Alam, Selangor: Ministry of Health, Malaysia; 2023.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.