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REVIEW

Traditional and culturally relevant foods with anti-inflammatory potential in systemic lupus erythematosus: A systematic review

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ABSTRACT

Introduction: Systemic lupus erythematosus is a chronic autoimmune disease characterised by systemic inflammation and immune dysregulation. While pharmacological treatments are essential, their adverse effects have prompted growing interest in complementary nutritional strategies. This systematic review explored the impact of key nutritional components and dietary interventions on the inflammatory processes in lupus and identified traditional and culturally relevant foods as potential sources of anti-inflammatory nutrients. **Methods:** A systematic search was conducted in PubMed and Scopus for studies published between 2013 and 2023 to examine the relationship between nutrition and lupus. Outcomes were assessed based on both inflammatory biomarkers and clinical disease activity scores. In addition, traditional and culturally relevant food sources containing these nutrients were identified to support culturally adapted dietary strategies. **Results:** A total of 25 studies were included: six randomised controlled trials, three non-randomised trials, and 16 observational studies. Intervention studies examined vitamin D, omega-3 fatty acids, and probiotics on markers such as C-reactive protein, interleukins, and disease activity scores. Observational studies assessed links between dietary quality, micronutrient status, and disease progression. Vitamin D deficiency was prevalent and associated with increased inflammation, while supplementation improved immune function. Omega-3 fatty acids and probiotics showed benefits, although dosage variation limited comparability. Locally available fish and other marine products, leafy greens, nutrient-dense legumes, and traditional fermented foods were recognised as culturally relevant dietary sources of these nutrients. **Conclusion:** Nutritional interventions demonstrated potential in improving outcomes, but heterogeneity across studies limits firm conclusions. Future culturally adapted trials are needed to validate long-term efficacy.

Keywords: diet, immunity, inflammation, lupus

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterised by immune system dysregulation, chronic inflammation, and involvement of multiple organs. Despite advances in pharmacological therapies, SLE continues to be a significant cause of morbidity and mortality due to its unpredictable nature and associated complications (Ross *et al.*, 2022). The disease disproportionately affects women of childbearing age, particularly in regions with limited access to healthcare, exacerbating its burden (Bradyanova *et al.*, 2024).

Globally, the prevalence of SLE in 2022 was estimated at 43.7 per 100,000 population, with an annual incidence of approximately 5.14 per 100,000 (Duarte-García *et al.*, 2022; Fatoye, Gebrye & Mbada, 2022; Gergianaki *et al.*, 2017; Tian *et al.*, 2023). Patients of Asian ethnicity are reported to have a higher incidence and more severe disease manifestations than Caucasian populations (Yap & Chan, 2015). In Indonesia, data from the national health information system (SIRS) reported 2,166 hospitalised SLE patients in 2016, with a case fatality rate of up to 25% (Ditjen P2P Kementerian Kesehatan, 2018; Rifai *et al.*, 2018). These figures reflect a substantial disease burden and highlight the importance of accessible, culturally relevant management approaches.

Traditional treatments, mainly involving immunosuppressive and anti-inflammatory drugs, often come with substantial side effects, such as increased susceptibility to infections and organ toxicity. Consequently, there is a growing interest in exploring adjunctive non-pharmacological strategies, including dietary interventions, to manage SLE symptoms and improve patient outcomes (Knippenberg *et al.*, 2022).

Recent literature emphasises the potential role of specific nutrients and dietary patterns in modulating inflammation and immune function in autoimmune diseases like SLE (Akbar *et al.*, 2017). For example, omega-3 fatty acids have demonstrated potent anti-inflammatory properties, reducing markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in rheumatic conditions (Poggioli *et al.*, 2023). Similarly, a Mediterranean diet rich in antioxidants, polyphenols, and healthy fats has been shown to be effective in reducing cardiovascular risk and systemic inflammation among SLE patients (Gavilán-Carrera, Gavilán-Carrera & Aguilera-Fernández, 2024). Other studies have investigated the influence of micronutrients, including vitamin D and methyl donors, on deoxyribonucleic acid (DNA) methylation and immune regulation, providing insights into their potential therapeutic values (Nikolova-Ganeva *et al.*, 2022).

Despite these promising findings, the application of dietary strategies remains limited by the heterogeneity in study designs, a lack of standardised clinical guidelines, and insufficient consideration of cultural dietary practices (da Mota *et al.*, 2024). Moreover, the interaction between genetic predisposition, environmental factors, and diet in shaping the progression of SLE is not yet fully understood (Montoya *et al.*, 2023). These gaps hinder the translation of nutritional evidence into context-specific interventions that can be effectively implemented in real-world settings.

In the Indonesian context, studies report that SLE patients commonly present with nutritional deficiencies, including inadequate intakes of vitamin D, folate, and vitamin B12, along with suboptimal energy and fibre intakes (Handono *et al.*, 2014; Miranda *et al.*, 2018; Sari, 2019; Yanih, 2016). These findings point to the need for culturally tailored nutrition strategies that align with local dietary habits and nutritional needs. In particular, little is known about the anti-inflammatory potential of traditional and culturally relevant foods commonly consumed in non-Western populations.

The term "traditional and culturally relevant foods" refers to food items that are commonly consumed within a specific culture or region and integrated into long-standing culinary practices (Alqurashi *et al.*, 2025; Wu *et al.*, 2023). In the context of Indonesia, these foods are aligned with local dietary habits and cultural preferences, which include items like locally available fish, leafy greens, legumes, and fermented products. While global studies emphasise nutrients, few efforts have been made to identify regionally accessible foods that naturally contain these bioactive compounds.

This systematic review aimed to evaluate the effects of key nutritional components and dietary interventions on inflammation in SLE and to identify traditional and culturally relevant foods, particularly those widely consumed in Indonesia, that may serve as practical sources of beneficial nutrients. By bridging global scientific evidence with local dietary practices, this study sought to inform culturally appropriate dietary strategies that may support long-term disease management and improve the quality of life for individuals with SLE.

METHODOLOGY

Study design and registration

This systematic literature review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page *et al.*, 2021) (Figure 1). The study protocol was registered in the PROSPERO database under the registration number CRD42024614149, ensuring adherence to international standards for transparency and methodological rigour in systematic reviews.

Eligibility criteria

To capture studies relevant to dietary interventions and their anti-inflammatory effects in SLE, the inclusion criteria were defined to focus on SLE in humans; examine the impact of dietary components, specific nutrients, or dietary patterns, and nutrition status on inflammation or disease activity; report quantitative or qualitative outcomes related to inflammation, clinical symptoms, or biochemical markers; and be published in journals written in English. The exclusion criteria were studies that used animal subjects and *in vitro* research methods; studies involving research subjects who were children, pregnant women, or breastfeeding mothers; editorials, commentaries, or conference abstracts lacking primary data; and duplicate publications or articles without full text. Outcomes of interest included both inflammatory biomarkers [e.g., CRP, interleukin-6 (IL-6), interleukin-17 (IL-17), tumour necrosis factor alpha (TNF-α), anti-double stranded deoxyribonucleic acid (anti-dsDNA)] and clinical disease activity scores [e.g., Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)], in accordance with the objective of evaluating anti-inflammatory effects.

Search strategy

A comprehensive search strategy was developed to identify relevant studies across multiple databases, including PubMed and Scopus. Search terms were constructed using a combination of

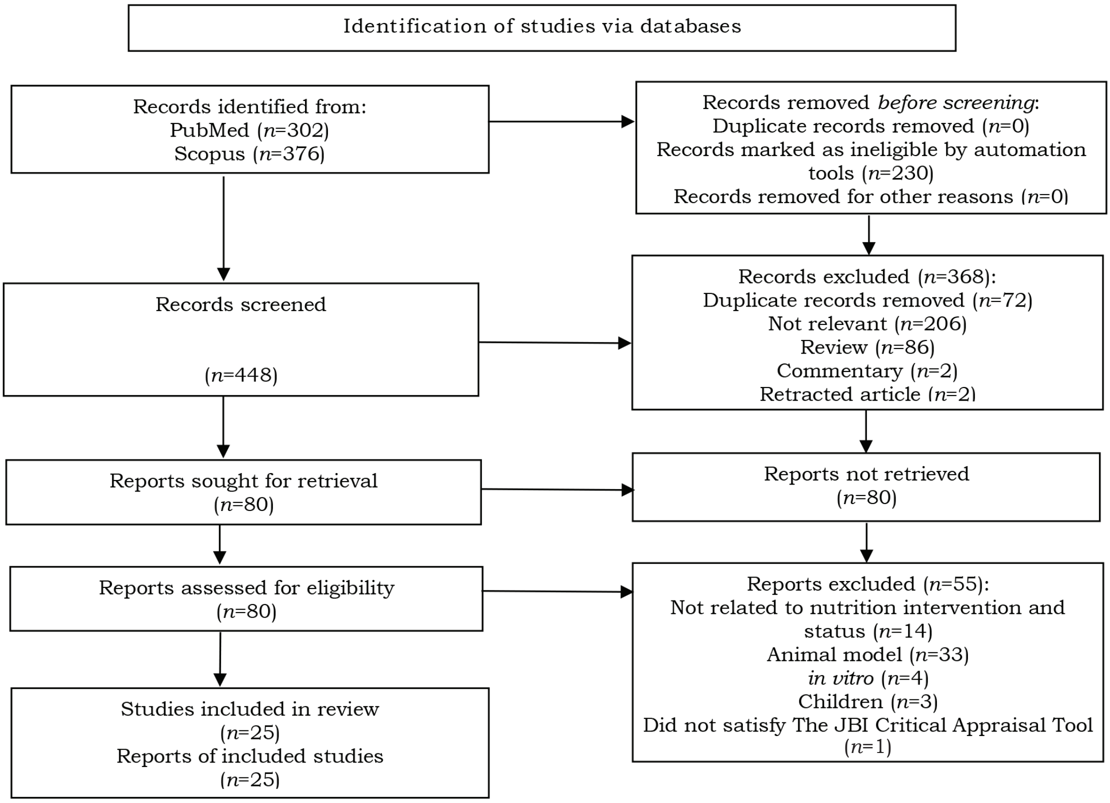

Figure 1. Data collection flow

Medical Subject Headings (MeSH) and free-text terms related to "systemic lupus erythematosus", "dietary intervention", "nutrition", and "inflammation". Boolean operators (AND, OR) were used to combine search terms (Table 1). The search period covered publications from 2013 to 2023, ensuring inclusion of the most recent and pertinent research.

The use of quotation marks ("") around certain keywords was intended to search for phrases as complete units. To refine the search results in the Publish or Perish (PoP) software (version 8.8, Melbourne, Victoria, Australia), the following keywords were entered into the Title Word column: (lupus OR "Lupus Erythematosus, Systemic") AND (diet OR dietary OR nutrient OR nutrients OR food OR nutrition OR nutritional OR fat OR fatty OR fats OR omega OR carbohydrate OR carbohydrates OR protein OR fibre OR "vitamin D" OR "vitamin B" OR folate OR folic OR methyl OR "Diet Therapy" OR "Nutritional Status" OR "Nutrition Therapy" OR dysbiosis OR "gut microbiota"). Simultaneously, the keywords inflammation OR inflammatory OR inflammaging were entered into the Keyword column.

Study selection process

All identified articles were organised into a table using Microsoft Excel and duplicates were removed. Two pairs of independent reviewers (four authors in total) screened the titles and abstracts for relevance. Full-text versions of potentially eligible studies were retrieved and assessed against the eligibility

Table 1. Keyword formulation

Concept 1	*Diet*
Keywords	diet OR dietary OR nutrient OR nutrients OR food OR nutrition OR nutritional OR fat OR fatty OR fats OR omega OR carbohydrate OR carbohydrates OR protein OR fibre OR "vitamin d" OR "vitamin b" OR folate OR folic OR methyl OR dysbiosis OR "gut microbiota"
MeSH	"Diet Therapy" OR "Nutritional Status" OR "Nutrition Therapy"
Concept 2	Inflammation
Keywords	inflammation OR inflammatory OR inflammaging
MeSH	-
Concept 3	Lupus
Keywords	Lupus
MeSH	"Lupus Erythematosus, Systemic"

MeSH: Medical Subject Headings

criteria. Discrepancies were resolved through discussion among the involved authors.

Data extraction

To ensure consistency in data extraction, a standardised data extraction form was developed. The extracted data included study characteristics (author, year, study design, sample size, and population); type of dietary intervention or specific nutrient or indicators/ parameters of nutritional status studied; the outcomes measured, including inflammatory markers, disease activity, and symptom improvement; and key findings encompassing both quantitative and qualitative results.

Data extraction was conducted independently by two review authors, with other authors verifying the accuracy and consistency of the extracted data. Discrepancies were identified and resolved through discussion among the involved authors. In addition to extracting study-level data, a targeted mapping of Indonesian food sources known to contain nutrients identified as beneficial in the included studies was conducted. Food composition data were obtained from the Indonesian Food Composition Table (TKPI) and the USDA database and were cross-referenced with local dietary patterns.

Quality assessment

The methodological quality of the included studies was evaluated using the Joanna Briggs Institute (JBI) critical appraisal tools, which are tailored to various study designs such as randomised controlled trials (RCTs), cohort studies, and cross-sectional studies. Each study was assessed based on criteria like randomisation, blinding, and reliability of outcome measurements. The review authors assessed each indicator with a response of "yes», "no», "unclear" or "not applicable." These responses determined the overall appraisal by the review authors to categorise the study as "include», "exclude" or "seek further information". (Barker *et al.*, 2023).

Data synthesis and analysis

Due to the heterogeneity among the included studies in terms of dietary interventions, outcome measures, and study designs, a narrative synthesis was conducted. Key findings were thematically categorised into (1) specific nutritional interventions in SLE, including supplementation with vitamin D, omega-3 fatty acids, synbiotics, low-

Table 2. Research on nutritional interventions in systemic lupus erythematosus (SLE)

Author (Year)	*Research design*	*Subjects*	*Nutritional intervention*	*Intervention target*	*Key results*
Bello *et al.*, 2013	RCT	85 SLE patients (mean age 47 years; 55% Caucasian, 38% African-American, 94% female)	3 g Omega-3 (Lovaza, GSK) versus placebo for 12 weeks	Endothelial function, disease activity, inflammatory markers (sICAM-1, sVCAM-1, IL-6), and fasting lipid profile	Omega-3 supplementation did not improve endothelial function, disease activity, or inflammatory markers (sICAM-1, sVCAM-1, IL-6) compared to the placebo group. However, it increased LDL cholesterol levels without improving the LDL/HDL ratio.
Kamen & Oates, 2015	RCT	9 SLE patients older than 18 years with vitamin D levels [(25(OH)D) < 20 ng/ml]	Group 1 (control): 400 IU Vitamin D3 daily; Group 2 (treatment): 5,000 IU daily	Vitamin D levels (25(OH) D) and flow-mediated dilation (FMD)	Vitamin D3 supplementation (5,000 IU daily) led to significant increases in vitamin D levels, with half of the subjects achieving levels ≥32 ng/ml. Improved flow-mediated dilation (FMD) was observed in those with higher final vitamin D concentrations.
Reynolds *et al.*, 2016	Non-RCT	22 SLE patients with vitamin D deficiency [vitamin D levels (25(OH)D) < 20 ng/ml] and 18 patients with normal vitamin D levels (>30 ng/ml)	High-dose oral cholecalciferol (400,000 IU followed by 20,000 IU weekly for 12 weeks)	Serum 25(OH)D and endothelial function	High-dose cholecalciferol supplementation significantly improved endothelial function, which was associated with increased serum 25(OH)D levels, independent of disease activity.
Marinho *et al.*, 2017	RCT	24 SLE patients (1 male and 23 females)	Vitamin D supplementation for 6 months	FoxP3 expression, IL-17A-producing T- cells, disease activity, serum vitamin D levels, and calcium metabolism	Six months of vitamin D supplementation significantly increased serum 25(OH)D levels and improved the FoxP3/IL-17A ratio, suggesting enhanced immune regulation. No significant changes were observed in serum phosphorus or calcium levels.
Curado Borges *et al.*, 2017	RCT	49 female SLE patients (22 treatment group, 27 control group)	Daily intake of EPA (1080 mg) + DHA (200 mg) for 12 weeks. Two omega-3 fatty acid tablets were taken once daily (540 mg EPA and 100 mg DHA)	Disease activity index, damage index, fasting lipid/glucose profiles, standard laboratory tests, cytokines (IL-6, IL-10), adipokines (leptin, adiponectin), protein, CRP, BMI, and medications used	Omega-3 fatty acid supplementation reduced CRP concentrations but showed no significant effects on cytokines (IL-6, IL-10), adipokines (leptin, adiponectin), or lipid/glucose profiles.

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Table 2. Research on nutritional interventions in systemic lupus erythematosus (SLE) *(continued)*

Author (Year)	*Research design*	*Subjects*	*Nutritional intervention*	*Intervention target*	*Key results*
Scrivo *et al.*, 2017	Non-RCT	28 patients (13 with RA and 15 with SLE)	A low-sodium diet (<5 g sodium chloride/day for 3 weeks) vs. a normal-sodium diet (>5 g sodium chloride/day for 2 weeks)	24-hour urinary sodium excretion, peripheral blood Th17 and Treg cell function, and serum cytokine levels	The low-sodium diet led to a progressive decrease in Th17 cells, reaching statistical significance at T5 (the end of the 5-week study period: 3 weeks of low-sodium intake followed by 2 weeks of normal-sodium intake). Treg cell percentages increased at T1 (1 week), T3 (3 weeks), and T5, compared to baseline (T0). Serum IL-9 levels were significantly reduced at T5. No significant changes were observed in apoptosis or proliferation.
Partan *et al.*, 2019	RCT	32 SLE subjects	Rasbora fish oil (500 μL capsules, one daily for 90 days)	Serum vitamin D levels, IL-1, IL-6, IL-17 levels, and clinical assessment of SLE	Supplementation with Rasbora fish oil significantly increased serum vitamin D levels compared to the control group. This was followed by a notable decrease in inflammatory markers, including IL-1, IL-6, and IL-17 levels.
Magro *et al.*, 2021	Non-RCT	31 SLE patients (13 with vitamin D deficiency and 18 with insufficiency)	Vitamin D3 (8000 IU/day for 8 weeks)	Disease activity, fatigue, anti-dsDNA titres, interferon gene expression, sleep quality, functional disability, and steroid use	Vitamin D3 supplementation improved disease activity and fatigue over 12 months, with a significant decrease in anti-dsDNA titres. While interferon gene expression scores decreased, the reduction was not statistically significant.
Widhani *et al.*, 2022	RCT	46 SLE patients (23 in synbiotic group and 23 in placebo group)	Synbiotic supplementation	Faecal microbiota composition, hs-CRP, IL-6, and IL-17 levels measured at baseline and after 60 days	Synbiotic supplementation increased the Firmicutes: Bacteroidetes ratio and improved butyrate metabolism, indicating enhanced gut microbiota function. Inflammatory markers showed positive trends: hs-CRP did not increase in the synbiotic group, while IL-6 levels decreased. In contrast, the placebo group showed no significant changes. A significant improvement in SLE disease activity was observed in the synbiotic group, while no changes were seen in the placebo group.

dsDNA: Anti-double stranded deoxyribonucleic acid; C3: Complement-3; Complement-4 (C4); CRP: C-reactive protein; DHA: Docosahexaenoic acid; EPA: Eicosapentaenoic acid; FMD: Flow mediated dilatation; IL-1: Interleukin-1; IL-10: Interleukin-10; IL-17A: Interleukin-17A; IL-6: Interleukin-6; IU: International unit; LDL: Low density lipoprotein; RCT: Randomised controlled trial; LDL/HDL: Low density lipoprotein and high density lipoprotein ratio; RA: Rheumatoid arthritis; sICAM-1: Soluble intercellular adhesion molecule-1; sVCAM-1: Soluble vascular cell adhesion molecule-1; Th17: T-helper 17 sodium diets, and specific food sources (Table 2); and (2) the relationship between nutritional status, dietary quality and patterns (e.g., Mediterranean diet), specific nutrient intakes, and gut microbiota composition with SLE outcomes (Table 3).

Table 3. Research examining the relationship between nutritional status and systemic lupus erythematosus (SLE)

Author (Year)	*Research design*	*Subjects*	*Indicators/ Parameters*	*Key findings*
Mandal *et al.*, 2014	Case-control	79 SLE patients (50 undergoing treatment, 29 untreated) and 100 healthy controls	Plasma vitamin D3 levels, IFN-α, IFN-α gene expression, anti-dsDNA, and SLE disease activity (SLEDAI)	Plasma 25-OH vitamin D3 levels were significantly inversely correlated with disease activity, anti-dsDNA, and IFN-α levels. IFN-α levels were positively correlated with IFN-α gene expression. Untreated SLE patients showed significantly higher plasma IFN-α levels compared to treated and healthy controls.
Shahin *et al.*, 2017	Case-control	57 untreated SLE patients and 42 matched controls	Disease activity score (SLEDAI), serum 25(OH)D, IL-17, and IL-23 levels	Serum 25(OH)D levels were significantly lower in SLE patients compared to controls, with 38.6% of SLE patients showing hypovitaminosis D versus 4.8% in controls. Despite this, vitamin D deficiency was not associated with clinical signs of SLE. A negative correlation was observed between serum 25(OH)D and levels of IL-17, IL-23, and ANA in SLE patients.
Rodríguez-Carrio *et al.*, 2017	Case-control	21 SLE patients and 25 healthy controls	Serum total and specific FFA levels, faecal SCFA levels, and gut microbiota composition	The Firmicutes-to-Bacteroidetes (F/B) ratio correlated with serum FFA levels in healthy controls but not in SLE patients. In SLE, there was a decrease in the F/B ratio and an increase in serum FFA levels. Changes in SCFA production were associated with gut dysbiosis, while SCFA levels aligned with FFA levels in healthy subjects. Specific FFAs showed distinct patterns in SLE principal component analysis. Omega-3 levels correlated positively with the F/B ratio in healthy controls but not in SLE patients.
Pocovi-Gerardino *et al.*, 2018	Case-control	92 SLE patients	BMI and the distribution of energy/nutrient intake	53.26% of patients had normal BMI, while 43.48% were overweight. Energy, protein, and fat intakes were significantly lower in the SLE group. Protein and fat contributions to total energy intake were higher, while carbohydrate and fibre intakes were lower than recommended levels. Most SLE patients did not meet the recommended intakes for iron, calcium, iodine, potassium, magnesium, folate, and vitamins E and D, but their sodium and phosphorus intakes exceeded recommendations.

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Table 3. Research examining the relationship between nutritional status and systemic lupus erythematosus (SLE) *(continued)*

Author (Year)	*Research design*	*Subjects*	*Indicators/ Parameters*	*Key findings*
Luo *et al.*, 2018	Cross-sectional	14 patients with active SLE and 17 non-SLE controls	Gut microbiota composition	SLE patients exhibited significant alterations in gut microbiota, with decreased diversity and increased representation of Gram-negative bacteria. Specific bacterial species from the Odoribacter and Blautia genera and an unnamed Rikenellaceae family were altered. However, the Firmicutes/Bacteroidetes ratio did not differ significantly between SLE patients and controls.
Meza-Meza *et al.*, 2019	Case-control	130 female SLE patients	Clinical activity (MEX-SLEDAI), BMI, and calculated energy and nutrient intakes	Overweight SLE patients had significantly higher clinical activity scores and prevalence of active disease compared to non-overweight patients. Being overweight was associated with increased MEX-SLEDAI scores. SLE patients also displayed higher rates of deficiencies in vitamin E, iodine, omega-3, biotin, vitamin K, iron, vitamin D, potassium, folate, pantothenic acid, vitamin A, and zinc.
Pocovi-Gerardino *et al.*, 2019	Cross-sectional	91 patients diagnosed with SLE	Diet quality and hsCRP	Mean serum hsCRP levels exceeded the normal range. SLE patients followed low-quality diets, but no significant correlation was observed between macronutrient intake, micronutrient intake, dietary antioxidants, and serum CRP levels.
Vordenbäumen *et al.*, 2020	Cross-sectional	68 SLE patients	Proportion of omega-6 and omega-3 fatty acids (PUFAs), essential fatty acids (LA, ALA, ARA)	Omega-6 PUFAs were associated with higher CRP, the LA/ALA ratio, and ARA. Conversely, omega-3 PUFAs were linked to lower CRP. Increased consumption of PUFAs from fish (g/day) correlated with higher omega-3 status and reduced self-reported organ damage.
Ma *et al.*, 2021	Case-control	18 untreated female SLE patients and 7 healthy female controls	Gut microbial diversity, immune response, and histidine levels	SLE patients exhibited significant differences in microbial diversity, including alterations in the Turicibacter genus and five other species. There was an increase in serum autoimmune antibodies, cytokine imbalance, and changes in immune cell distribution in the mucosal and peripheral immune systems. This was accompanied by increased expression of SLE-related genes in SLE patients.

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Table 3. Research examining the relationship between nutritional status and systemic lupus erythematosus (SLE) *(continued)*

Author (Year)	*Research design*	*Subjects*	*Indicators/ Parameters*	*Key findings*
Gorczyca *et al.*, 2022	Case-control	30 SLE patients (29 females, 1 male) and 20 healthy controls (19 females, 1 male)	Serum n-3 and n-6 PUFA levels, disease activity (SLEDAI), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complement C3 and C4, ANA titres, anti-dsDNA concentrations, and medications	SLE patients had significantly higher serum linoleic acid (LA) and alpha-linolenic acid (ALA) levels compared to controls. LA concentrations correlated positively with ANA titres and corticosteroid doses. Immunosuppressed patients showed elevated levels of LA, ALA, and arachidonic acid (ARA), but lower eicosapentaenoic acid (EPA) levels. EPA and docosahexaenoic acid (DHA) levels were inversely correlated with anti-dsDNA antibody concentrations.
Shevchuk *et al.*, 2023	Case-control	101 SLE patients and 29 control subjects	Vitamin D, ESR, CRP, IL-6, osteocalcin (OC), C-terminal telopeptide (CTX), and BMD (bone mineral density) in the lumbar spine and hip	Only 7.93% of SLE patients had optimal vitamin D levels, while 62.3% had deficiency and 29.7% had insufficiency. Hypovitaminosis D was associated with higher inflammatory activity (SLEDAI, ESR, CRP, IL-6), greater organ damage severity (DI), cumulative glucocorticoid dose, and decreased BMD. However, vitamin D status was not associated with patients' age or disease duration.
Han & Han, 2016	Cohort	37 SLE participants (30 women and 7 men) from NHANES III (1988–1994), 39,695 total subjects	Serum lycopene levels and mortality	Higher serum lycopene intake was significantly associated with reduced mortality in SLE patients. Mortality, particularly from cardiovascular causes, was lower in the high-lycopene group compared to the low-intake group. There was a significant difference in survival rates between high and low lycopene intake groups.
Correa-Rodríguez *et al.*, 2020	Cross-sectional	193 SLE patients recruited from general outpatient clinics in Andalusia, Spain	Dietary free sugar intake and clinical cardiovascular risk markers (CRP, homocysteine, anti-dsDNA, complement C3/ C4)	Higher free sugar intake was significantly associated with increased SLE complications (in percentage and number) and dyslipidaemia. CRP levels and disease activity (SLEDAI) were also elevated in patients with higher sugar intake.
Pocovi-Gerardino *et al.*, 2020	Cross-sectional	105 women with SLE	Dietary Inflammatory Index score, physical activity, and cardiovascular disease risk markers (e.g., total cholesterol, blood lipid profile)	The Dietary Inflammatory Index score was positively associated with total cholesterol levels, even after adjusting for age, physical activity, and medical care.

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Table 3. Research examining the relationship between nutritional status and systemic lupus erythematosus (SLE) *(continued)*

Author (Year)	*Research design*	*Subjects*	*Indicators/ Parameters*	*Key findings*
Pocovi-Gerardino *et al.*, 2021	Cross-sectional	280 SLE patients	Mediterranean diet adherence, CRP, homocysteine, SLE disease activity, and damage accrual scores	Greater adherence to the Mediterranean diet was linked to improved anthropometric profiles, fewer cardiovascular risk factors, and reduced SLE disease activity and damage accrual scores. Higher Mediterranean diet adherence was inversely associated with dietary inflammatory scores, hsCRP, and SLEDAI. Higher intake of Mediterranean diet foods, including olive oil, fruits, vegetables, fish, and legumes, and lower intakes of red meat, sugar, and pastry products, was associated with decreased SLE disease activity and damage.
Barbhaiya *et al.*, 2021	Cohort	Participants from the Nurses' Health Study (NHS) I (121,700 women, aged 30–55 years in 1976) and NHSII (116,430 women, aged 25–42 years in 1989)	Diet scores (AHEI-2010, aMed, DASH, EDIP), SLE incidence, and dsDNA antibodies	No significant difference in SLE risk was observed between women with the highest and lowest diet scores (AHEI-2010, aMed, DASH, EDIP). However, women with the highest intake of legumes (AHEI-2010) showed a reduced risk of SLE compared to those with the lowest intake.

ALA: Alpha-linolenic acid; aMed: Alternate Mediterranean diet score; AHEI-2010: Alternative Healthy Eating Index-2020; anti-dsDNA: Anti-double-stranded DNA; ANA: Anti-nuclear antibody; ARA: Arachidonic acid; BMD: Bone mineral density; BTM: Bone turnover marker ; CVD: Cardiovascular disease ; CTX: Collagen type I C-terminal telopeptide; C3: Complement-3; C4: Complement-4; CRP: C-reactive protein; DI: Damage Index; DASH: Dietary Approaches to Stop Hypertension; EPA: Eicosapentaenoic Acid; EDIP: Empirical dietary index pattern; ESR: Erythrocyte Sedimentation Rate; FFA: Free-fatty acid; GC: Glucocorticoid; hsCRP: High sensitivity C-reactive protein; BMI: Body mass index; IFN-α: Interferon alpha; IL-17: Interleukin-17; IL-23: Interleukin-23; LA: Linoleic acid; NHANES: National Health and Nutrition Examination Survey; NHSII: Nurses' Health Study II; OC: Osteocalcin; PUFA: Polyunsaturated fatty acids; F/B: Firmicutes/bacteroidetes ratio; SCFA: Short-chain fatty acid; DAQ: Dietary antioxidant quality score; MEX-SLEDAI: The Mexican Systemic Lupus Erythematosus Disease Activity Index; NHS: The Nurses' Health Study; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

RESULTS

A systematic review of 25 studies was conducted to assess the role of nutrition in the management of SLE. The included studies comprised six RCTs, three non-randomised clinical trials, and 16 observational studies. Among the RCTs, three specifically assessed clinical SLE activity using validated instruments such as the SLEDAI.

Of the six RCTs, studies by Bello *et al.* (2013), Marinho *et al.* (2017), and Curado Borges *et al.* (2017) evaluated changes in SLEDAI scores, thus offering evidence directly relevant to clinical practice. The findings consistently highlighted the immunomodulatory and anti-inflammatory effects of specific dietary components, including vitamin D, omega-3 fatty acids, probiotics, and methyl donors, in individuals with SLE (Mandal *et al*., 2014; Shevchuk *et al*., 2023).

Vitamin D deficiency was consistently associated with increased inflammatory activity, as indicated by elevated levels of CRP and IL-6 (Marinho *et al*., 2017). Supplementation with vitamin D was found to enhance immune regulation by improving endothelial function and increasing the FoxP3/IL-17A ratio, a critical indicator of immune balance in SLE (Magro *et al*., 2021). Additionally, vitamin D supplementation was linked to improvements in SLEDAI scores, fatigue, and overall patient well-being.

Omega-3 fatty acids were identified as key anti-inflammatory agents, with evidence supporting their role in reducing CRP and ESR (Akbar *et al*., 2017; Poggioli *et al*., 2023). Clinical trials also demonstrated modest improvements in disease activity indices. However, inconsistencies in study designs and dosage variations led to differing outcomes, indicating the need for standardised intervention protocols (Bello *et al*., 2013; Curado Borges *et al*., 2017).

Gut microbiota emerged as an important modulator of immune response. Probiotic and synbiotic interventions were associated with increased microbial diversity and a reduction in pro-inflammatory cytokines such as IL-6 and IL-17 (Luo *et al*., 2018; Widhani *et al*., 2022). Some studies also reported improvements in clinical parameters, though most findings remained concentrated on immunological markers. Fermented foods, which are rich sources of probiotics, showed potential to support gut health and indirectly contribute to systemic inflammation reduction.

Methyl donors, including folate, methionine, and betaine, were highlighted for their roles in epigenetic regulation (Nikolova-Ganeva *et al*., 2023; Vordenbäumen *et al*., 2021). Their intake was associated with changes in DNA methylation patterns relevant to immune regulation, as well as reductions in proteinuria and anti-dsDNA antibodies, markers indicative of disease activity.

In addition to individual nutrients, dietary patterns such as the Mediterranean diet were examined. This pattern, which is characterised by intakes of whole grains, fish, nuts, fruits, and olive oil, was associated with reduced systemic inflammation and cardiovascular risk in SLE patients (Gavilán-Carrera *et al*., 2024; Gioia *et al*., 2020). However, no clinical studies investigating the impact of regional or culturally specific dietary patterns in SLE populations were found. To address this limitation, the present review mapped several traditional and culturally relevant foods commonly consumed in Indonesia, such as locally available fish and other marine products, diverse leafy greens, nutrient-dense legumes, and traditional fermented foods that contain nutrients shown to be beneficial in reviewed studies (Table 4). These foods may serve as practical alternatives in developing culturally adapted dietary interventions. These findings underscore the need for clinical trials that assess regionally adapted dietary strategies for SLE management.

DISCUSSION

This systematic review synthesised evidence on nutritional interventions and nutrient components with potential anti-inflammatory effects in SLE, alongside an exploration of traditional and culturally relevant foods that may

Table 4. Local Indonesian food sources with nutritional potential for addressing lupus needs

Nutrient	*Food sources*
Folate	Goose liver, duck liver, chicken liver, black-eyed pea (*kacang tunggak*), long beans, green beans, red beans, chicken, seaweed, beans
Pantothenic acid	Beef, eggs, chicken liver, sunflower seeds, lamb, goose liver, duck liver, chicken
Biotin	Beef liver, eggs
Potassium	Soybeans, black tea, jasmine tea, s*ukun* flour, saga merah flour, hyacinth bean (*kacang komak*), Pigeon pea (*kacang gude*), ikan *kayu*, *rebung laut*, *ares*, *kawista*, *mentimun suri*
Calcium	Anchovies, *Mujair* fish, g*abus* fish, g*ete* fish, *rebon* shrimp, s*aluang* fish, *bandeng* fish, udang papay, *kelor* leaves, *saga merah*, *belut*, *bekasam*, *ikan mas*, *tempeh*
Lycopene	Tomatoes, guava, watermelon
Magnesium	Sorghum, taro, *sukun*, coconut, tuna, black-eyed pea (*kacang tunggak*), green peas
Omega-3	Tuna, anchovies, red beans, oysters, shrimp, lobster, *nila* fish, *mujair* fish, *kerang simping*, eggs, chicken, milk
Probiotics	Fermented foods (*tempeh*, tofu, *tauco*, *oncom*, *dadih*, *bekasam*, *calo)*
Fibre	*Kacang lebui*, *kacang tunis*, *kacang ercis*, red beans (*banda)*, *tekokak*, *lamtoro*, *oncom*, mango *manalagi*, *pisang gapi*, passion fruit, *melinjo* leaves, cassava leaves
Vitamin A	Fish oil, beef liver, chicken liver, *burung Maleo* eggs, venison, beef lungs, *cakalang* fish, *lehoma* fish, *baronang* fish, *malalugis* fish, chicken eggs, *titang* fish, *bandeng* fish, *kenikir* leaves, *cilembu* sweet potato, *katuk* leaves, cassava leaves, red chili, papaya leaves, cassava leaves, carrots, *andaliman*, *kelor* leaves
Vitamin D	Fish oil, ikan *mas*, eel, trout, *bandeng* fish, milk, eggs, *nila* fish
Vitamin E	Eel, eggs, spinach, cumin seeds, chili, turmeric
Vitamin K	Cilantro leaves, spinach, mustard greens, spinach, cabbage, sweet potato leaves, broccoli, watercress, bitter melon, cloves, lettuce, pumpkin leaves, *kelor* leaves
Iodine	Iodised salt, tuna, seaweed, shrimp, eggs
Iron	*Teripang*, coconut meal, *oncom*, groundnut meal, *lamtoro*, anchovies, *calo* fish, *rebon* shrimp, beef lungs, chicken liver, red beans, soybeans, *seluang* fish, *sintrong* leaves, shrimp
Zinc	Soybeans, red beans (*banda*), *saluang* fish, sago worms, *udang papay*, *cakalang* fish, *koro*, beef, *rebung laut*, *kacang tolo*, *lamtoro*, cassava leaves, *bekasang*, *baronang* fish, *bilih* fish

Based on the Indonesian Ministry of Health, Indonesian Food Composition Table/*Tabel Komposisi Pangan Indonesia* (TKPI) (Kementerian Kesehatan RI, 2017); National Nutrient Database for Standard Reference (USDA, 2018)

provide these nutrients. The strength of evidence varied across components: vitamin D and omega-3 fatty acids were the most extensively studied, followed by probiotics and dietary quality, while methyl donors had limited representation in the included studies. Findings also revealed that most interventions were supplementation-based, with few whole-diet interventions, and no trials investigated culturally specific dietary patterns in SLE populations.

Vitamin D was evaluated in the largest number of intervention studies, including multiple RCTs and observational analyses (Tables 2 and 3). Supplementation consistently increased serum 25(OH)D concentrations and was associated with reductions in inflammatory biomarkers such as CRP, IL-6, and IL-17, as well as improvements in endothelial function and fatigue scores (Han, Wu & Guo, 2017; Huang *et al.*, 2020; Kamboj *et al.*, 2025; Mazidi, Rezaie & Vatanparast, 2018; Yu *et al.*, 2018). While not all studies demonstrated significant effects on clinical disease activity indices such as SLEDAI, several showed trends toward improvement.

Deficiency of vitamin D was common among SLE patients in multiple settings, including in Indonesia, where adequate sunlight is available but effective cutaneous synthesis is often reduced due to photosensitivity-related sun avoidance, photoprotective behaviours, urban pollution, disease-related renal involvement, corticosteroid use, and limited dietary vitamin D intake. Studies in pregnant women and the general population in Indonesia have shown that vitamin D intake is frequently below recommended levels (Chee *et al.*, 2022; Hagenau *et al.*, 2008; Handono *et al.*, 2014; Holick, 2007; Santoso, Silaban & Charissa, 2023). This is relevant given the immunomodulatory role of vitamin D in T-cell regulation and B-cell function (Infante *et al.*, 2019; Rizkia, 2023; Zhao *et al.*, 2021). These findings underscore vitamin D as a feasible target for nutritional optimisation in SLE, though long-term effects on sustained disease remission remain to be established.

Omega-3 fatty acids were supported by several RCTs and observational studies, demonstrating reductions in pro-inflammatory cytokines (e.g., IL-6, TNF-α), improvements in lipid profiles, and potential cardiovascular protection (Garcia-So *et al.*, 2019; Hansen *et al.*, 2021; Iverson *et al.*, 2018; Kostoglou-Athanassiou, Athanassiou & Athanassiou, 2020; Shahraki *et al.*, 2023). Effects on clinical disease activity scores were inconsistent, likely due to variations in dosage, eicosapentaenoic acid:docosahexaenoic acid (EPA:DHA) ratio, and study duration. From a cultural adaptation perspective, marine and freshwater sources commonly consumed in Indonesia provide rich omega-3 content. These include tuna and *seluang* (*Rasbora sp.*), a small freshwater fish widely available in Sumatra and parts of Kalimantan. *Seluang* is consumed whole, including bones and viscera, which may increase the intake of not only vitamin D but also omega-3 fatty acids and micronutrients (Partan *et al.*, 2019; Sogandi *et al.*, 2020; Triawanti, Nur'amin & Sanyoto, 2019). Promoting such locally available sources could enhance omega-3 intake in a culturally acceptable and economically feasible way. However, preparation methods that preserve omega-3 content should be emphasised (Devadason *et al.*, 2019; Głuchowski, Czarniecka-Skubina & Rutkowska, 2020).

Interventions involving probiotics or synbiotics showed beneficial effects on gut microbiota composition, reductions in inflammatory cytokines, and, in some cases, improved quality of life scores (Cuervo *et al.*, 2015; Shamekhi *et al.*, 2017; Widhani, 2018; Winkvist *et al.*, 2018). Specific strains, such as *Lactobacillus casei* and *Bifidobacterium longum*, were commonly used, although strain-specific effects remain unclear. In Indonesia, traditional fermented foods, such as *tempeh*, *dadih*, and fermented cassava. offer natural sources of probiotics, although their clinical efficacy in SLE has not been formally studied. Variations in microbial content due to fermentation methods

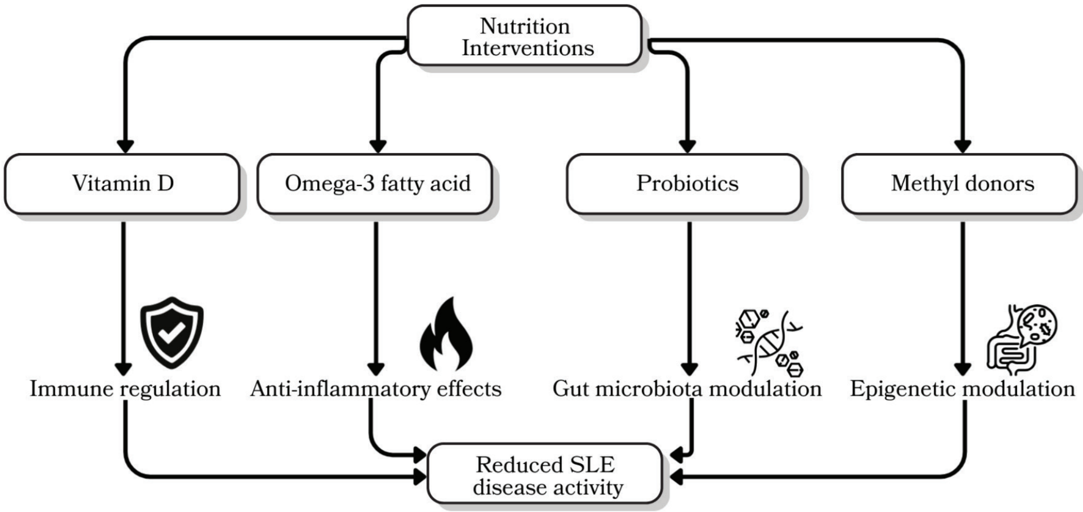

Figure 2. Conceptual framework on nutritional interventions in systemic lupus erythematosus (SLE)

and hygiene practices could influence outcomes (Pamungkas, 2018; Winanti, Bintari & Mustikaningtyas, 2014).

Observational studies assessed dietary patterns, including the Mediterranean diet, low-sodium diet, and scores derived from the Dietary Inflammatory Index (DII). Higher adherence to anti-inflammatory dietary patterns was associated with lower inflammatory markers and, in some studies, improved SLEDAI scores (Nayebi *et al.*, 2022; Pocovi-Gerardino *et al.*, 2018, 2020; Scrivo *et al.*, 2017). However, no studies investigated whole-diet interventions tailored to specific cultural contexts in SLE populations. Given the dietary diversity in Indonesia, identifying local dietary patterns with anti-inflammatory potential is an opportunity to bridge global evidence and local practices. Table 4 in this review maps traditional foods (e.g., cassava leaves, tuna, *tempeh*) to relevant nutrient components, providing a foundation for culturally appropriate dietary strategies.

Only a small number of studies addressed methyl donors (e.g., folate, vitamin B12, choline) in the context of SLE (Nikolova-Ganeva *et al.*, 2023). These nutrients may influence disease processes via DNA methylation and epigenetic regulation, affecting immune cell differentiation and cytokine production (Castellini-Pérez *et al.*, 2024; Mo *et al.*, 2019). Given the limited number of SLE-specific studies, much of the discussion on methyl donors has been extrapolated from other autoimmune conditions. While biologically plausible, current evidence remains insufficient to support clinical recommendations, highlighting the need for targeted trials assessing dietary methyl donor intake and SLE outcomes.

Figure 2 summarises the mechanistic pathways, presenting a conceptual framework of nutritional interventions in SLE. The diagram outlines how vitamin D, omega-3 fatty acids, probiotics, and methyl donors may influence immune regulation, anti-inflammatory responses, gut microbiota, and epigenetic mechanisms, potentially converging toward reduced disease activity. This framework integrates current evidence on biological mechanisms with clinical relevance, supporting the rationale for incorporating these nutrients into culturally adapted dietary strategies for SLE, while acknowledging that the strength of evidence varies across components.

The evidence is limited by the heterogeneity in study designs, interventions, and outcome measures. Most intervention studies were of short duration, used supplementation rather than whole-food approaches, and relied heavily on inflammatory biomarkers, with relatively few incorporating validated clinical endpoints such as SLEDAI. This limits the generalisability of findings to routine clinical practice. Despite these limitations, this review contributes by synthesising available evidence and mapping nutrient–food relationships in an Indonesian context, which may inform future culturally adapted dietary interventions.

In summary, vitamin D, omega-3 fatty acids, probiotics, and potentially methyl donors have plausible roles in modulating inflammation and disease activity in SLE. Traditional Indonesian foods containing these nutrients represent a culturally relevant opportunity for dietary intervention, though direct evidence for their clinical effectiveness in SLE remains lacking. Future studies should prioritise well-designed, long-duration clinical trials that incorporate both biomarker and clinical endpoints and evaluate the feasibility of integrating nutrient-rich traditional foods into comprehensive SLE management strategies.

CONCLUSION

This systematic review demonstrated that specific nutritional interventions, particularly vitamin D, omega-3 fatty acids, probiotics, and, to a lesser extent, methyl donors, have potential roles in modulating inflammation and supporting disease management in SLE through mechanisms involving endothelial function, cytokine regulation, gut microbiota modulation, and epigenetic control. While the Mediterranean diet is the most frequently studied dietary pattern, no clinical trials have evaluated the effects of regional or culturally specific diets on SLE outcomes. To address this gap, this review mapped traditional and culturally relevant foods commonly consumed in Indonesia, such as locally available fish and other marine products, diverse leafy greens, nutrient-dense legumes, and fermented foods, which provide these beneficial nutrients and could inform culturally adapted dietary strategies. However, heterogeneity in study designs, interventions, and outcome measures, particularly the predominance of biomarker endpoints over validated clinical indices, limits the strength of current recommendations. These findings bridge global nutritional evidence with locally accessible food sources, offering a foundation for the development of culturally tailored dietary interventions. Well-designed and long-term clinical trials incorporating both biomarker and clinical endpoints are needed to confirm the effectiveness and feasibility of such strategies in improving outcomes for individuals with SLE.

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Authors' contributions

Olivia A, principal investigator, conceptualised and designed the study, conducted data collection, performed statistical analysis, and had overall responsibility for the study; Kusworini H, contributed to concept and design, critically revised the article, and reviewed the manuscript; Dian H, contributed to concept and design, participated in analysis and interpretation, and critically revised the article; Retno L, participated in data collection, analysis and interpretation, writing the manuscript, and critically revising the article; Holipah, assisted in data collection and statistical analysis; Widya R, contributed to data collection; Ayuningtyas DA, secured funding for the study; Kanthi PT, assisted in obtaining funding. All authors reviewed and approved the final version of the manuscript.

Conflict of interest

Authors declare no conflict of interest.

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