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Review

Pantothenic Acid (Vitamin B5) Supplementation in Rheumatological Diseases: A Review

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Abstract: Background: Pantothenic acid (PA), the dietary precursor of coenzyme A, plays a central role in mitochondrial metabolism, lipid regulation, and the synthesis of steroid hormones and neurotransmitters. Although PA has been traditionally applied in areas such as wound healing and immunomodulation, its potential therapeutic relevance in rheumatology has not been well characterized. Objective: To provide an updated overview of the clinical effectiveness, safety, and research gaps related to PA supplementation in rheumatic diseases. Methods: A structured search was performed across PubMed/MEDLINE, Web of Science, SciELO, and LILACS for human studies published up to July 2024. Eligible articles investigated PA supplementation in patients with rheumatic diseases and reported clinical outcomes. Key data relating to population characteristics, dosage, treatment duration, outcomes, and adverse effects were extracted. Results: Seven studies involving 183 participants were included: two focused on osteoarthritis (OA), one on fibromyalgia (FM), and four addressing systemic lupus erythematosus (SLE). PA was administered using heterogeneous regimens, generally in combination with other micronutrients, at doses ranging from 12.5 mg to 12 g/day and over variable follow-up durations. Clinical improvement was reported in most studies, especially in cutaneous lupus, in which substantial resolution of lesions was frequently observed. Benefits in fatigue in SLE and pain reduction in OA and FM were also noted. Adverse events were rare and predominantly mild. Conclusions: Available clinical evidence suggests that PA supplementation may provide symptomatic benefit in selected rheumatic diseases, with a favorable safety profile. However, current data remain limited by small sample sizes, lack of standardized protocols, and frequent co-supplementation. Well-designed randomized clinical trials—especially in SLE and OA—are required to determine therapeutic efficacy, optimal dosing, and mechanistic pathways.

Keywords: Vitamin B5; pantothenic acid; pantothenate; rheumatic diseases; systemic lupus erythematosus; osteoarthritis; fibromyalgia

1. Introduction

Pantothenic acid (PA), traditionally referred to as vitamin B5, is an essential water-soluble micronutrient required for the biosynthesis of coenzyme A (CoA), a central cofactor involved in mitochondrial energy production, fatty-acid β-oxidation, acetylation reactions, lipid metabolism, steroidogenesis, and neurotransmitter synthesis. Its metabolic relevance extends to immune regulation, epithelial repair, and redox balance, processes

that are critically involved in the pathophysiology of rheumatologic diseases [1,2]. Historically, PA has been used in dermatology and wound healing, but its therapeutic implications for systemic inflammation and autoimmunity have received limited attention [1].

Given its influence on mitochondrial bioenergetics, fatty-acid metabolism, acetyl-CoA generation, and redox pathways, PA may exert anti-inflammatory and immunomodulatory effects relevant to fatigue, pain, immune dysfunction, and epithelial integrity—features commonly observed in rheumatic diseases. Clinical symptoms associated with PA insufficiency or suboptimal levels—fatigue, musculoskeletal discomfort, mood disturbance, sensory symptoms, and impaired immune responses—overlap with several rheumatologic conditions [1].

A growing body of research has focused on vanin-family pantetheinases, especially vanin-1, an enzyme regulating PA homeostasis through pantetheine cleavage and cysteamine generation. Vanin-1 activity affects oxidative stress responses, leukocyte migration, and inflammatory cascades, and its expression is increased in tissues relevant to rheumatologic pathophysiology such as cartilage and renal epithelium [3]. Notably, urinary vanin-1 has emerged as a potential biomarker of active lupus nephritis, reinforcing the biological plausibility of interventions affecting PA metabolism [4].

More recent investigations have explored PA supplementation in osteoarthritis (OA), fibromyalgia (FM), and systemic lupus erythematosus (SLE), reporting benefits in pain, stiffness, fatigue, depression, and cutaneous manifestations, although findings remain limited by small sample sizes, heterogeneous dosing, and confounding by co-supplementation [5–8]. Early clinical studies from the mid-20th century documented substantial improvement in cutaneous lupus with high-dose PA or panthenol—often combined with vitamin E—demonstrating reductions in erythema, scaling, and lesion size [9–11].

An important historical point concerns the discrepancy in the nomenclature of B-complex vitamins, particularly between North American and continental European scientific traditions. Pantothenic acid was originally designated as vitamin B3 in the 1930s–1940s, as the third nitrogen-containing B vitamin to be identified, while nicotinic acid/nicotinamide ("niacin") was designated vitamin B5, based on chronological discovery [12]. Although American literature gradually shifted after the 1990s—promoting the widespread use of the designations niacin = B3 and pantothenic acid = B5—no formal IUPAC ruling has ever altered the classical nomenclature. Consequently, many textbooks and academic sources from continental Europe (e.g., Russia, Germany, France) continue to use PA = B3 and niacin = B5, occasionally causing confusion among international readers [12]. This historical discrepancy is directly relevant to early dermatologic and rheumatologic studies on PA, which were authored during the period in which PA was universally referred to as vitamin B3, not B5 [9–11]. Recognizing this nomenclature divergence is essential, as it prevents misinterpretation of older literature and ensures accurate comparison of clinical interventions across historical and contemporary studies.

The present review synthesizes available human evidence on PA supplementation in rheumatic diseases, contextualizes mechanistic pathways linking PA to inflammation and immune regulation, and identifies gaps requiring rigorous modern investigation.

2. Materials and Methods

2.1. Search Strategy

A structured search was performed across PubMed/MEDLINE, Web of Science, SciELO, and LILACS for human studies published up to July 2024". To ensure methodological rigor, the review followed the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), although no protocol was prospectively registered. The study selection process is summarized in a PRISMA 2020 flow diagram (Figure 1). The search strategy employed combinations of the terms "pantothenic acid", "pantothenate", "vitamin B5", and "dexpanthenol" paired with disease-related descriptors such as "rheumatic", "rheumatologic", "osteoarthritis", "fibromyalgia", "systemic lupus erythematosus", "rheumatoid arthritis", "myositis", "spondyloarthritis", "Sjogren's syndrome", "systemic sclerosis", and "vasculitis". Equivalent strategies were adapted for each database. No language restrictions were applied, and reference lists of included articles were manually inspected to identify additional studies. A single record retrieved during the search could not be accessed in full text or abstract despite multiple attempts; therefore, although acknowledged, it was not included in the analysis.

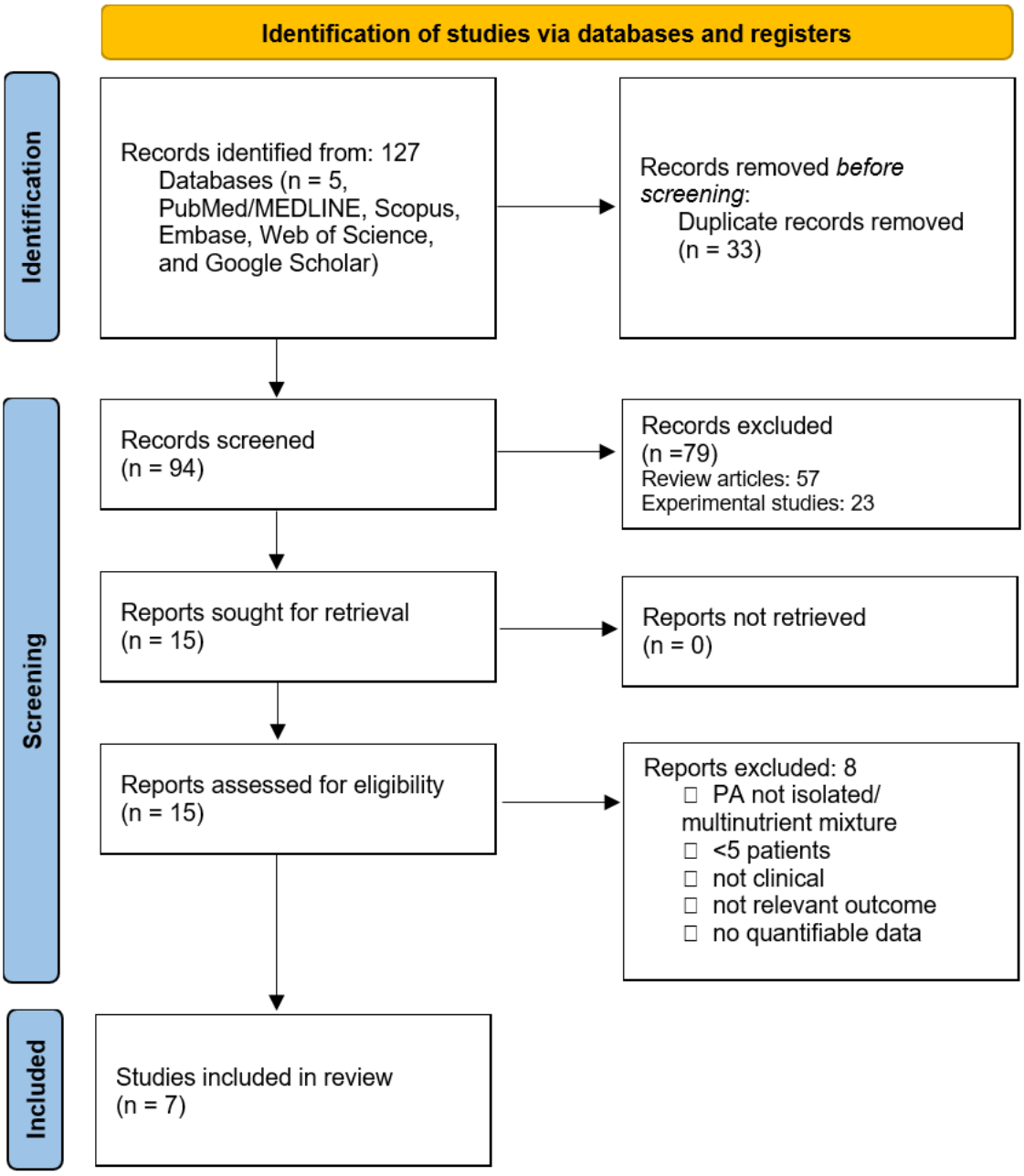

Figure 1. Flowchart of the included studies.

2.2. Eligibility Criteria

Studies were considered eligible when they evaluated pantothenic acid, calcium pantothenate, panthenol, or dexpanthenol, administered either alone or within multicomponent formulations, in human participants diagnosed with any rheumatic disease. Eligible studies were required to report clinical outcomes, including symptoms, disease activity, cutaneous manifestations, pain, fatigue, stiffness, flare frequency, or functional parameters. Accepted study designs comprised randomized or non-randomized trials, open-label or prospective studies, cohort studies, and case series with at least five participants. Articles were excluded if they involved animal or in vitro models, narrative reviews, editorials, opinions, conference abstracts without original data, or case reports with fewer than five patients. Studies in which pantothenic acid could not be quantified or its contribution to clinical outcomes could not be determined were also excluded. These eligibility criteria were intentionally broad; therefore, the inclusion of only seven clinical studies reflects the scarcity of published human data on pantothenic acid in rheumatic diseases rather than an unduly restrictive selection process.

2.3. Study Selection

The selection process adhered to the PRISMA structure. After identification of all records, duplicates were removed, and titles and abstracts were screened by two independent reviewers (JFC and ATAM). Full-text versions of potentially eligible studies were obtained and assessed for inclusion. Disagreements were resolved through discussion until consensus was reached. Of the 127 records initially identified, 94 remained after duplicate removal, 15 were eligible for full-text evaluation, and seven studies met all criteria and were included in the final synthesis.

2.4. Data Extraction

Data extraction was performed independently by the reviewers using a structured approach. Extracted variables included authorship, publication year, country, study design, sample size and demographics, disease characteristics, pantothenic acid dosage and formulation, route and duration of administration, presence of co-supplementation, and reported clinical outcomes. Additional information on adverse events, withdrawals, and methodological limitations was collected when available. Because of extensive heterogeneity across studies—particularly regarding dosing, outcome measures, and design—meta-analysis was not feasible, and findings were synthesized narratively.

2.5. Risk of Bias Considerations

Given the diverse nature of the included literature, risk of bias was assessed narratively. Key aspects included the presence or absence of randomization, allocation concealment, blinding, sample size adequacy, co-supplementation, and consistency in outcome reporting. Many older studies lacked methodological elements required by contemporary research standards, such as validated outcome instruments or controlled designs, which is addressed in detail in the Discussion. For one historical publication without accessible text, author contact or archive retrieval was not possible; therefore, although cited historically, it was excluded from the qualitative synthesis.

3. Results

3.1. Overview of Included Studies

A total of seven clinical studies, comprising 183 participants, fulfilled all eligibility criteria and were included in the final synthesis [5–11]. Despite the broad search strategy and inclusive eligibility criteria, only seven clinical studies fulfilled all requirements, underscoring how limited the current clinical literature on pantothenic acid in rheumatic diseases remains. These investigations evaluated pantothenic acid (PA) or related formulations in osteoarthritis (OA), fibromyalgia (FM), and systemic lupus erythematosus (SLE), including discoid, subacute cutaneous, and systemic forms. The studies were conducted in the United States, the United Kingdom, and Hong Kong, over several decades [5–11]. Sample sizes ranged from 12 to 46 participants, and demographic data were incompletely reported in some of the older studies. Across all trials, PA was rarely administered as monotherapy, and dosing regimens varied substantially, from 12.5 mg/day in combination with B-complex formulations to 10–12 g/day of high-dose therapy in SLE and cutaneous lupus [5–11]. One additional study in rheumatoid arthritis was identified but could not be retrieved in abstract or full text and is therefore mentioned but not analyzed [12]. Table 1 summarizes all included studies.

3.2. Osteoarthritis Studies

Two studies assessed PA in osteoarthritis [5,6]. An early open-label prospective study from the United Kingdom administered 12.5 mg/day of PA plus vitamin B-complex to patients with OA and reported that 20 of 26 participants (77%) experienced improvement in stiffness and pain within 14 days, with benefits maintained during an 18-month follow-up; mild asthenia occurred in 3 of 26 patients (12%) [6]. In contrast, a later double-blind, randomized, placebo-controlled trial evaluated 50 mg of PA plus 30 mg of L-cysteine twice daily versus placebo over 12 weeks in knee OA, including 40 patients with long-standing disease (1–54 years of duration) [5]. This trial found no significant differences between the active and placebo groups in global outcomes. Adverse events—such as headache, sleepiness, depression, memory loss, flatulence, and abdominal pain—led to withdrawal in 6 of 40 participants (15%) [5]. These contrasting results highlight the heterogeneity in study design, co-supplementation, and outcome assessment, and make it difficult to isolate a specific therapeutic effect of PA in OA.

3.3. Fibromyalgia Study

Fibromyalgia was evaluated in a randomized, double-blind, placebo-controlled pilot trial using an intravenous micronutrient formulation known as "Myers' cocktail", which included dexpanthenol and panthenol as PA derivatives among other vitamins and minerals [7]. In this study of 34 patients, predominantly women, the active treatment group exhibited statistically and clinically significant improvements in tender point count, pain, depression scores, and quality of life after eight weeks, compared with placebo [7]. No adverse effects were reported in the intervention group, suggesting a favorable tolerability profile [7]. However, because the infusion combined multiple micronutrients, including magnesium, B-complex vitamins, and vitamin C, the specific contribution of PA cannot be determined, although the observed improvements are consistent with the hypothesis that correcting micronutrient deficits and supporting mitochondrial metabolism may alleviate FM symptoms [7].

3.4. Systemic Lupus Erythematosus and Cutaneous Lupus Studies

Four studies explored the role of PA in lupus, including discoid, subacute cutaneous, and systemic forms [8–11]. In an open prospective trial from Hong Kong, 12 women with SLE received 10 g/day of PA for up to two years and showed improvement in fatigue within four weeks, followed by reductions in pyrexia and fewer major flares over longer follow-up [8]. In many patients, background SLE medications could be tapered, and no adverse effects were reported [8].

Historical dermatologic series from the United States described high-dose calcium pantothenate or panthenol, often combined with vitamin E 400 mg/day, for the treatment of cutaneous lupus [9–11]. In one open trial of 42 patients with longstanding SLE, high-dose PA (0.5–3 g/day initially, then 8–12 g/day) plus vitamin E resulted in improvement of skin lesions in all patients, with 70–100% clearing of cutaneous lesions in many cases and good long-term control over 2–36 months of follow-up [9]. Another series of 46 patients with discoid, subacute, and systemic lupus treated with PA doses ranging from 0.5 to 10 g/day reported clinical improvement in 2 of 9 patients with acute lupus, 9 of 10 with subacute lupus, and 17 of 27 with discoid lupus, with only one case of lesion aggravation [10]. A smaller study of 14 patients with discoid lupus treated with 200–400 mg/day of PA for six months documented marked responses particularly in subacute lupus, with 2 of 14 non-responders, 3 of 14 requiring phenol cauterization of residual lesions, and 1 of 14 developing a new lesion during follow-up [11]. Collectively, these findings suggest a consistent therapeutic signal in cutaneous lupus, especially in subacute and discoid forms, albeit in uncontrolled historical series.

3.5. Safety Profile

Across all studies, the safety profile of PA appeared favorable. In the OA trials, adverse effects were generally mild and limited to a subset of participants, with symptoms such as headache, sleepiness, mood changes, flatulence, and abdominal pain leading to withdrawal in a minority [5,6]. In the Myers' cocktail fibromyalgia trial, no adverse events were recorded in the active treatment arm [7]. The lupus studies—particularly the high-dose regimens, with up to 10–12 g/day of PA—reported no serious treatment-related toxicity, and historical reports emphasized good tolerability over prolonged administration [8–11]. Nonetheless, the absence of systematic laboratory monitoring and standardized adverse event reporting in older studies warrants cautious interpretation and underscores the need for modern safety assessments.

3.6. GRADE Assessment

A GRADE-based evaluation of all seven included clinical studies demonstrated overall very low certainty of evidence for most outcomes. The main factors contributing to downgrading were serious methodological limitations (absence of randomization, lack of blinding, heterogeneous interventions), small sample sizes, and potential publication bias. Only one study (the intravenous micronutrient trial in fibromyalgia) reached "low" certainty due to somewhat greater methodological rigor, although indirectness remained a concern because PA was not administered as monotherapy. The full GRADE summary is presented in Table 2.

Table 1. Summary of clinical studies evaluating pantothenic acid (PA) in rheumatic diseases.

Author/Year	Country	Study Design	Sample Size & Population	Disease	PA Dose/Formulation	Duration	Main Outcomes	Adverse Effects
Annand, 1962 [6]	UK	Open-label prospective	26 adults with OA	Osteoarthritis	12.5 mg/day PA + B-complex	Up to 18 months	77% improved pain and stiffness within 14 days; sustained benefit during follow-up	Mild asthenia (12%)
Haslock & Wright, 1971 [5]	UK	Double-blind RCT	40 patients with knee OA	Osteoarthritis	PA 50 mg + L-cysteine 30 mg, BID	12 weeks	No significant benefit versus placebo	Headache, sleepiness, depression, memory issues, GI symptoms (15% withdrawal)
Ali et al., 2009 [7]	USA	Randomized, double-blind pilot trial	34 patients with FM	Fibromyalgia	IV "Myers' Cocktail" including dexpanthenol	8 weeks	Improved pain, tender points, depression and quality of life compared with placebo	None reported
Leung, 2004 [8]	Hong Kong	Prospective open-label	12 women with SLE	Systemic lupus erythematosus	10 g/day PA	Up to 2 years	Improved fatigue within 4 weeks; fewer febrile episodes and flares; reduced medication use	None reported
Welsh, 1952 [9]	USA	Open clinical series	42 patients with lupus	Cutaneous/systemic lupus	0.5–3 g/day initially, then 8–12 g/day PA + vitamin E	2–36 months	Marked clinical improvement; 70–100% clearing of lesions	None reported
Goldman, 1950 [10]	USA	Open case series	46 patients	Discoid, subacute and acute lupus	0.5–10 g/day PA	Not reported	Improvement in 2/9 acute, 9/10 subacute and 17/27 discoid lupus	One case of lesion worsening
Goldman, 1948 [11]	USA	Open-label	14 patients	Discoid lupus	200–400 mg/day PA	6 months	Marked responses, especially in subacute forms; 2 non-responders	One new lesion reported

BID = duas vezes ao dia; FM = fibromyalgia; GI = gastrointestinal; IV = intravenous; OA = osteoarthritis; PA = pantothenic acid; RCT = randomized controlled trial; SLE = systemic lupus erythematosus; UK = United Kingdom; USA = United States.

Table 2. Certainty of evidence (GRADE) for clinical studies evaluating pantothenic acid (PA) in rheumatic diseases.

Study	Disease/Outcome	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty (GRADE)
Annand, 1962 [6]	Osteoarthritis—pain and stiffness	Serious	Serious	Not serious	Serious	Likely	**Very low**
Haslock & Wright, 1971 [5]	Osteoarthritis—global outcomes	Serious	Serious	Not serious	Serious	Likely	**Very low**
Ali et al., 2009 [7]	Fibromyalgia—pain, tender points, quality of life	Serious	Not serious	Serious	Serious	Likely	**Low**
Leung, 2004 [8]	SLE—fatigue and flare frequency	Serious	Serious	Not serious	Serious	Likely	**Very low**
Welsh, 1952 [9]	Cutaneous lupus—lesion improvement	Very serious	Serious	Not serious	Serious	Likely	**Very low**
Goldman, 1950 [10]	Discoid/subacute/acute lupus—lesion response	Very serious	Serious	Not serious	Serious	Likely	**Very low**
Goldman, 1948 [11]	Discoid lupus—lesion improvement	Very serious	Serious	Not serious	Serious	Likely	**Very low**

3.7. General Findings

Taken together, these seven studies suggest that PA supplementation may confer symptomatic benefits in selected rheumatic diseases, notably cutaneous lupus, with additional signals in SLE-related fatigue, fibromyalgia symptoms, and OA-related pain and stiffness [5–11]. However, the evidence base is constrained by small sample sizes, heterogeneous dosing regimens, co-supplementation with other vitamins and amino acids, non-standardized outcome measures, and limited use of randomized, blinded designs. The additional, non-analyzed report in rheumatoid arthritis [12] illustrates that the potential spectrum of PA use in rheumatology may be broader than currently documented. Overall, these limitations highlight the urgent need for well-designed randomized controlled trials using standardized dosing, validated clinical endpoints, and systematic safety evaluation to clarify the therapeutic role of PA in rheumatologic practice.

4. Discussion

This narrative review highlights both foundational and contemporary evidence on pantothenic acid (PA) supplementation in rheumatic diseases, reframing these findings within the evolving field of immunometabolism. As the essential precursor to coenzyme A (CoA), PA supports multiple biochemical processes relevant to inflammation and tissue repair, including mitochondrial bioenergetics, fatty-acid oxidation, acetyl-CoA homeostasis, and steroidogenesis. Clinically, insufficient PA may manifest as fatigue, musculoskeletal discomfort, and impaired barrier integrity—features commonly seen in chronic inflammatory disorders and thus supportive of supplementation strategies [1]. In addition to these established mechanisms, PA also contributes to sphingolipid and phospholipid biosynthesis, epigenetic acetylation processes, and antioxidant regulation, offering broader biochemical plausibility for its contribution to immune and tissue homeostasis. In comparison, although other B vitamins (such as B3 and B6) exhibit anti-inflammatory effects, PA is unique due to its obligatory incorporation into CoA-dependent metabolic pathways.

Because Th17 cells and IL-17–driven inflammation play pivotal roles in the pathogenesis of multiple rheumatic diseases, the mechanistic discussion was expanded to explore how pantothenic acid may influence Th17 biology through metabolic, epigenetic, and redox-dependent pathways. Coenzyme A availability regulates intracellular acetyl-CoA pools, which directly affect histone acetylation and the transcriptional programs governing RORγt-dependent Th17 differentiation [13]. In parallel, CoA-dependent mitochondrial metabolism and reactive oxygen species (ROS) signaling shape T-cell activation and IL-17 production, while redox imbalance favors Th17 polarization and impairs regulatory T-cell (Treg) development, linking metabolic state to inflammatory lineage commitment [14]. In addition, lipid metabolism—another CoA-dependent process—modulates membrane composition and signaling platforms involved in T-cell receptor activation and differentiation, further connecting vitamin B5 metabolism to adaptive immune regulation [15]. Collectively, these mechanisms provide a biologically coherent framework by which pantothenic acid insufficiency could favor Th17-skewed immunity and, conversely, how metabolic repletion might shift immune balance toward regulatory phenotypes in autoimmune rheumatic diseases. A schematic integration of these immunometabolic pathways is shown in Figure 2.

A key mechanistic connection lies in the vanin-1 pantetheinase pathway. Vanin-1 activity generates cysteamine, a modulator of oxidative stress responses and inflammatory signaling. Expression by both leukocytes and renal tubular cells has prompted interest in its urinary secretion as a biomarker of lupus nephritis activity [3,4]. Preclinical studies also suggest that altered vanin-1 signaling may contribute to chondrogenesis dynamics and aberrant mineralization, linking this axis to degenerative joint conditions and soft-tissue calcification [3]. Although a direct causal chain from PA supplementation to vanin-1 modulation remains hypothetical, this axis offers a compelling biological rationale for biomarker-driven interventional trials. Importantly, PA's role in regulating oxidative stress and immune activation may intersect with vanin-1–mediated redox pathways, strengthening the mechanistic framework for testing PA in SLE. A schematic representation of these proposed mechanisms and their relevance to immunoregulation in rheumatic diseases is presented in Figure 2.

Among the clinical data, cutaneous lupus exhibits the most consistent therapeutic signal. Small series and uncontrolled interventions report rapid and sustained improvements in dermatologic lesions with PA-based regimens [9–11]. Despite considerable variability in dosing, administration route, and co-supplementation, the recurrence of response patterns—alongside reductions in fatigue and flare frequency—suggests potential adjunctive utility in selected systemic lupus erythematosus (SLE) phenotypes [8–11]. Future research should incorporate validated dermatologic scoring systems, blinded outcome assessment, and stratification according to cutaneous subtype (acute, subacute, discoid) to refine treatment expectations. Historical use of high-dose PA in

these studies, without significant toxicity, further supports its safety profile and justifies renewed evaluation under controlled contemporary designs.

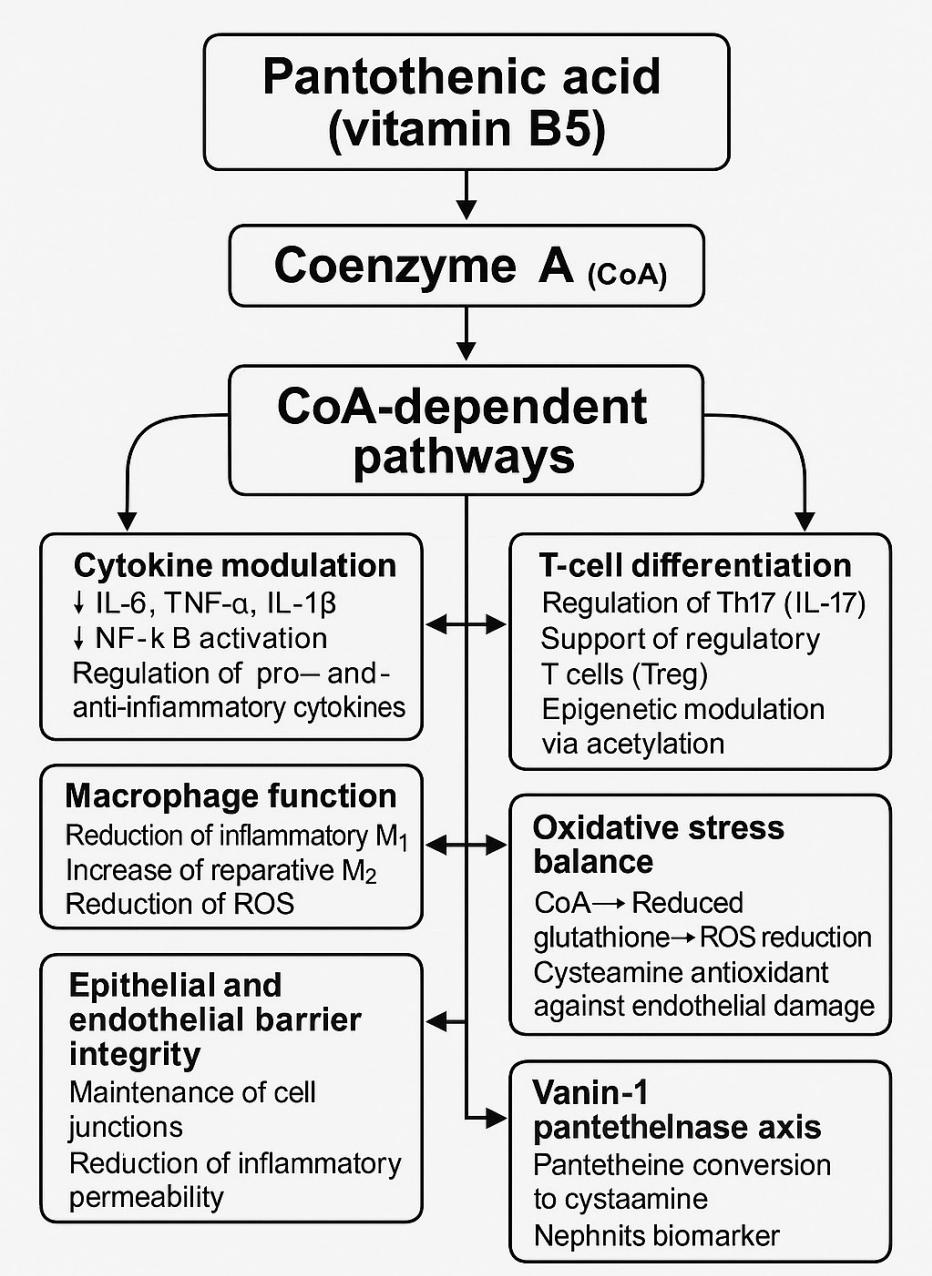

Figure 2. Proposed mechanisms linking pantothenic acid (vitamin B5) and coenzyme A to immunoregulation in rheumatic diseases. Pantothenic acid serves as the precursor for coenzyme A (CoA), which participates in multiple metabolic and cellular processes with direct relevance to immune regulation. Through CoA-dependent pathways, vitamin B5 may modulate pro- and anti-inflammatory cytokines (↓ IL-6, TNF-α, IL-1β; ↓ NF-κB activation), influence T-cell differentiation (downregulation of Th17 activity and support of regulatory T cells), and regulate macrophage function by shifting M_1/M_2 balance and reducing oxidative stress. Additional mechanisms include maintenance of epithelial and endothelial barrier integrity, modulation of oxidative stress via glutathione and cysteamine pathways, adjustments in lipid immunometabolism through fatty-acid β-oxidation, and the activity of the vanin-1 pantetheinase axis, which may also serve as a biomarker in lupus nephritis. Together, these interconnected pathways provide a biologically plausible framework for the potential immunomodulatory effects of pantothenic acid in rheumatic diseases.

In fibromyalgia (FM), preliminary benefit was observed with intravenous multi-micronutrient therapy [7]. Although attribution to PA alone is not possible, mechanistic plausibility is supported by its contributions to CoA-dependent cellular energy and acetylcholine biosynthesis, aligning with FM models of mitochondrial inefficiency and autonomic dysfunction. Comparative studies isolating PA or manipulating PA content within IV

formulations—while incorporating objective endpoints such as actigraphy, pressure pain thresholds, and validated fatigue metrics—would clarify PA-specific effects. Additionally, classical descriptions of pantothenic acid deficiency leading to "burning feet syndrome," a neuropathic condition responsive to PA supplementation, support the hypothesis that PA may influence sensory pathways relevant to FM and autoimmune neuropathies.

Evidence in osteoarthritis (OA) remains inconclusive. One open-label study reported improvements in stiffness and pain with low-dose oral PA combined with B-complex vitamins [6], whereas a randomized controlled trial showed no advantage of PA plus L-cysteine over placebo [5]. Differences in OA phenotype, baseline severity, intervention design, and outcome measurement likely contributed to divergent results. Given the global burden of OA and the scarcity of disease-modifying options, larger rigorously designed trials incorporating standardized pain/function endpoints, imaging modalities, and biomarkers of cartilage turnover are warranted. Potential mechanistic links between CoA-dependent metabolism, chondrocyte bioenergetics, and osteoarthritic cartilage degeneration warrant further exploration.

Safety findings across available studies appear reassuring, with predominantly mild and transient adverse events. Notably, lupus trials utilized supra-nutritional PA doses without major toxicity signals [8–11]. Nonetheless, limited sample sizes, short follow-up intervals, and insufficient systematic reporting of laboratory trends and drug interactions restrict firm conclusions. Because PA participates in acetylation reactions required for the metabolism of several pharmaceutical agents, its potential influence on drug pharmacokinetics—particularly in patients receiving corticosteroids, antimalarials, NSAIDs, or immunosuppressants—should be examined in future studies.

A major limitation of the available literature is the difficulty in establishing any clear dose–response relationship for PA. Across the seven clinical studies, daily doses ranged from 12.5 mg in combination with other B-complex vitamins to 10–12 g of high-dose PA in lupus, and different formulations (oral PA, calcium pantothenate, panthenol or dexpanthenol) were used, frequently together with other micronutrients or amino acids [5–11]. Clinical improvements in cutaneous lupus and SLE-related fatigue were generally observed at gram-level doses, whereas low-dose regimens in osteoarthritis yielded inconsistent results, and the intravenous micronutrient cocktail in fibromyalgia did not allow isolation of the specific contribution of PA [5–8]. Taken together, these data do not support a simple linear association between dose and clinical response, but rather suggest that supra-physiological doses may be required in some indications and that future trials should incorporate explicit dose-ranging designs to define minimal effective and maximal tolerated doses.

In line with the GRADE analysis, the overall certainty of evidence supporting PA supplementation in rheumatic diseases remains very low, primarily due to small sample sizes, high risk of bias in older studies, heterogeneous dosing, and indirectness of interventions. These limitations reinforce the need for modern, well-powered randomized controlled trials with standardized outcomes and dose-ranging designs.

The present synthesis offers a comprehensive appraisal of all human clinical studies in rheumatic settings to date, integrating mechanistic insight with clinical phenotype and immunometabolic context. However, the interpretability of available data is constrained by small cohorts, heterogeneous interventions, variable dosing, absence of blinding in most studies, and reliance on historical controls in cutaneous lupus research. Additionally, the only OA RCT and a pilot FM RCT evaluated multi-ingredient preparations, obscuring PA's individual contribution [5,7]. Concomitant vitamin use (e.g., B-complex, vitamin E) and differing administration routes (oral vs IV) further complicate effect attribution. Furthermore, additional evidence from Eastern European literature—including a patented panthenol-containing formulation used to accelerate tendon healing in systemic sclerosis and a study showing improved xerophthalmia with a panthenol-containing ophthalmic solution (Stillavit) in rheumatoid arthritis—suggests broader reparative and epithelial-trophic roles for PA that merit investigation.

5. Future Directions

Several priorities emerge for subsequent research:

(1) Clinical trials: Well-powered randomized studies of oral PA monotherapy in lupus and OA, including dose-ranging phases to determine minimal effective and maximal tolerated doses.

(2) Mechanistic exploration: Quantification of CoA-related metabolites, acetyl-CoA, and vanin-1 activity/expression to investigate PA-responsive biological pathways and evaluate vanin-1 as a predictive or pharmacodynamic biomarker in SLE [3,4,16].

(3) Pragmatic FM trials: Assessment of PA as an adjunct to standard care using patient-centered outcomes (pain interference, sleep quality, fatigue) and metabolic profiling to identify responder subgroups with impaired CoA flux.

(4) Expansion to other rheumatic diseases: Systematic evaluation in rheumatoid arthritis, spondyloarthritis, Sjögren's syndrome, myositis, systemic sclerosis, and vasculitides, given shared inflammatory and oxidative mechanisms [17–19].

6. Conclusions

Across multiple decades of research, PA supplementation has shown potential therapeutic value in specific rheumatologic contexts—most notably in cutaneous forms of lupus—while producing preliminary yet promising findings in fibromyalgia and more inconsistent outcomes in osteoarthritis. Safety profiles reported to date are generally acceptable, with mostly mild and transient adverse effects. However, the evidence base remains limited by small sample sizes, heterogeneous dosing regimens, frequent co-supplementation, and the absence of modern randomized designs, which collectively restrict firm conclusions regarding efficacy and optimal treatment strategies.

Given these limitations, PA should be considered an investigational adjunct rather than an established therapy, pending confirmation from contemporary randomized controlled trials. Future studies should incorporate standardized dosing protocols, validated dermatologic and musculoskeletal outcome measures, biomarker integration—particularly CoA-related metabolites and vanin-1—and systematic pharmacovigilance to evaluate potential interactions with immunomodulatory agents.

In the interim, PA supplementation may be cautiously explored as an adjunctive strategy in selected patient populations, provided that dosing, concomitant therapies, and safety parameters are carefully monitored. Robust, well-designed clinical trials are urgently needed to clarify its therapeutic potential and define its role within modern rheumatologic practice.

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J.F.d.C. has done literature search, analysis, writing, and submission. A.T.A.M. has done literature search, analysis and revision. All authors have read and agreed to the published version of the manuscript.

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All data are available at request.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

Artificial Intelligence (ChatGPT) was utilized exclusively to refine the final version of the manuscript, focusing on reviewing the structure and ensuring textual coherence for a final quality check, without contributing to the generation of original scientific content.

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