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Article

Cannabinoids in Inflammation-Related Therapeutic Research: A Systematic Review of Mechanisms, Evidence Maturity, and Translational Barriers

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Abstract. Cannabinoid research has expanded rapidly in inflammation-related therapeutic contexts, but the evidence remains heterogeneous in compounds, formulations, models, and outcome measures. This systematic review synthesizes recent evidence on the anti-inflammatory and immunomodulatory actions of cannabinoids, evaluates the maturity of that evidence, and identifies barriers to clinical translation. A systematic Scopus search covering 2022–2026 identified 79 eligible English-language Articles and Reviews available through Open Access; data were synthesized through a structured matrix and thematic coding. The evidence was predominantly preclinical, drawn mainly from in vivo animal models (40.5%) and in vitro cell-based systems (22.8%), with smaller ex vivo or human-derived (10.1%) and computational (7.6%) shares, and cannabidiol was the most frequently examined compound (46.8%). The literature most consistently linked cannabinoids with modulation of inflammatory signaling, oxidative stress, immune responses, and tissue injury through NF-κ B, NLRP3, Nrf2, CB1/CB2, and PPAR pathways, while direct clinical validation, pharmacokinetic characterization, and long-term safety data remained limited. Restricting the search to Open Access records is acknowledged as a potential source of selection bias. Cannabinoids show plausible anti-inflammatory and immunomodulatory potential, but the evidence remains translationally immature. Progress requires standardized preparations, exposure-informed dosing, human-relevant models, mechanism-linked endpoints, and adequately designed clinical studies.

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1. Introduction

Cannabis-derived compounds have attracted biomedical interest for their potential to modulate inflammation, oxidative stress, immune activity, and tissue injury. Experimental evidence identifies anti-inflammatory actions of cannabidiol (CBD) in models of interstitial cystitis and intestinal, pain-related, and cytokine-driven inflammation [1-3]. Comparable benefits are reported in imiquimod-induced psoriasis [4], while CBD-loaded solid lipid nanoparticles suppress proinflammatory cytokines and free radicals in vitro [5]. Neuroinflammation studies further report attenuation of glial activity and inflammatory mediators in autoimmune encephalomyelitis, Parkinson disease, and neurodegeneration models [6-8], and CBD- or THC-enriched preparations reduce neuroinflammation after spinal cord injury and in Alzheimer-related models [9-10]. Interest has also expanded beyond CBD to cannabigerol (CBG), cannabigerolic acid (CBGA), acidic cannabinoids, and *Cannabis sativa* matrices with documented anti-inflammatory synergy [11-13].

Multi-component preparations and terpenes contribute additional activity in human keratinocytes and inflamed immune cells [14-16], and paired cannabidiol and beta-caryophyllene treatment shows anti-inflammatory synergy in vitro [17]. Nevertheless, differences in composition, dose, formulation, biological model, and outcome measurement limit comparison across this rapidly growing literature [18-19], and the predominance of preclinical designs restricts direct clinical inference [20-21].

Several published reviews have synthesized cannabinoid evidence for narrower purposes, including neurodegeneration and clinical pharmacology challenges [20], [22], age-related pain [21], immune modulation [23], and formulation or product-quality appraisal [18-19]. None of these reviews integrates inflammation-focused mechanistic evidence with an explicit assessment of evidence maturity and translational barriers across compounds, formulations, models, and outcome measures. An inflammation-focused synthesis is therefore needed to distinguish mechanistic promise from evidence that is sufficiently mature for therapeutic translation.

To guide that assessment, evidence maturity is operationally defined in this review as the degree to which an inflammation-related cannabinoid finding satisfies four cumulative conditions, namely reproducible mechanistic demonstration, chemical standardization of the intervention, characterization of exposure or pharmacokinetics, and validation in clinically relevant models or human studies. This definition allows the evidence to be graded along a translational continuum instead of being treated as uniformly established. The review window of 2022–2026 was chosen because it captures the most recent wave of cannabinoid research, a period marked by renewed regulatory appraisal of CBD, rapid growth of preclinical studies, and expanding formulation technology [18], [23-24]. Restricting the synthesis to this window therefore reflects the current state of the field and its most recent methodological standards.

Accordingly, this systematic review examines cannabinoids specifically within inflammation-related therapeutic research and addresses five questions. RQ1 asks what study designs, biological models, and cannabinoid interventions characterize the included literature. RQ2 asks which anti-inflammatory and immunomodulatory effects and mechanisms are reported. RQ3 asks how mature

and methodologically robust the evidence is. RQ4 asks which development opportunities are most relevant to inflammation-focused therapy. RQ5 asks which barriers limit translation into clinically meaningful interventions.

To answer these questions, the evidence was collected through a PRISMA-aligned search of a single bibliographic database, screened against predefined eligibility criteria, extracted into a structured evidence matrix, and appraised with adapted risk-of-bias instruments. Because inflammation-related terms were mandatory in the search strategy, the corpus should be interpreted as evidence on inflammation-associated cannabinoid research rather than as a representation of the entire therapeutic cannabinoid field. The complete search strategy, selection outcomes, and appraisal procedures are reported in Section 2.

2. Methods

The review proceeded through three systematic stages. The initial stage covered the formulation of the research questions, the definition of eligibility criteria, and the execution of the database search. The implementation stage addressed title and abstract screening, full-text eligibility assessment, and structured data extraction into an evidence matrix. The final stage comprised quality appraisal, thematic synthesis, and interpretation of the findings against the research questions. Data were collected with a standardized extraction form, interpreted through non-mutually exclusive thematic coding, and analyzed descriptively against predefined indicators for study design, intervention characterization, and outcome relevance. The overall procedure is illustrated in Figure 1.

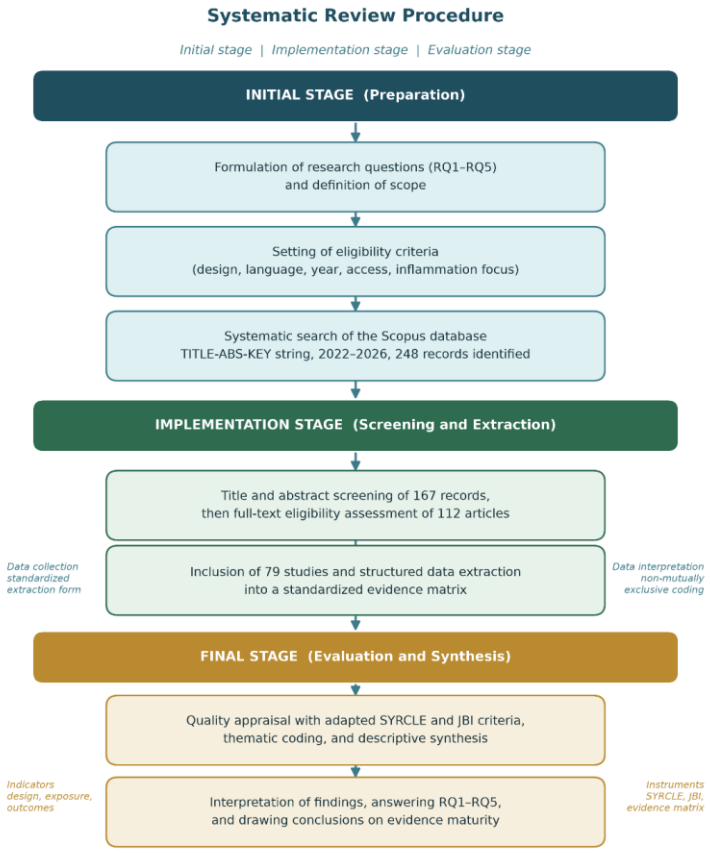


Figure 1. Flowchart of the systematic review procedure

2.1. Search Strategy and Selection Criteria

A systematic search was conducted in Scopus, which served as the single bibliographic database for this review, using the TITLE-ABS-KEY field with the string TITLE-ABS-KEY((cannabinoid OR cannabidiol OR CBD OR "Cannabis sativa") AND (inflamm* OR "anti-inflammatory" OR immunomodulat* OR neuroinflamm*) AND (therapeutic OR pharmacolog* OR biological OR mechanism OR translational)). The search identified 248 publications, and filtering by publication year (2022–2026), document type (Article or Review), language (English), and Open Access status yielded 167 records for screening. Eligibility required an explicit connection between a cannabinoid intervention or exposure and an inflammation-related mechanism, marker, condition, or therapeutic implication. Following title screening, full-text assessment, and final eligibility evaluation, 79 English-language Articles and Reviews published in 2022–2026 and available through Open Access were included in the synthesis.

2.2. Screening and Eligibility

The 167 records underwent title and abstract screening, followed by full-text assessment against the predefined research scope and eligibility criteria. In total, 112 articles proceeded to detailed evaluation, and 79 studies met the final criteria and were included for systematic data extraction and thematic synthesis. The complete selection process is presented in the PRISMA 2020 flow diagram (Figure 2).

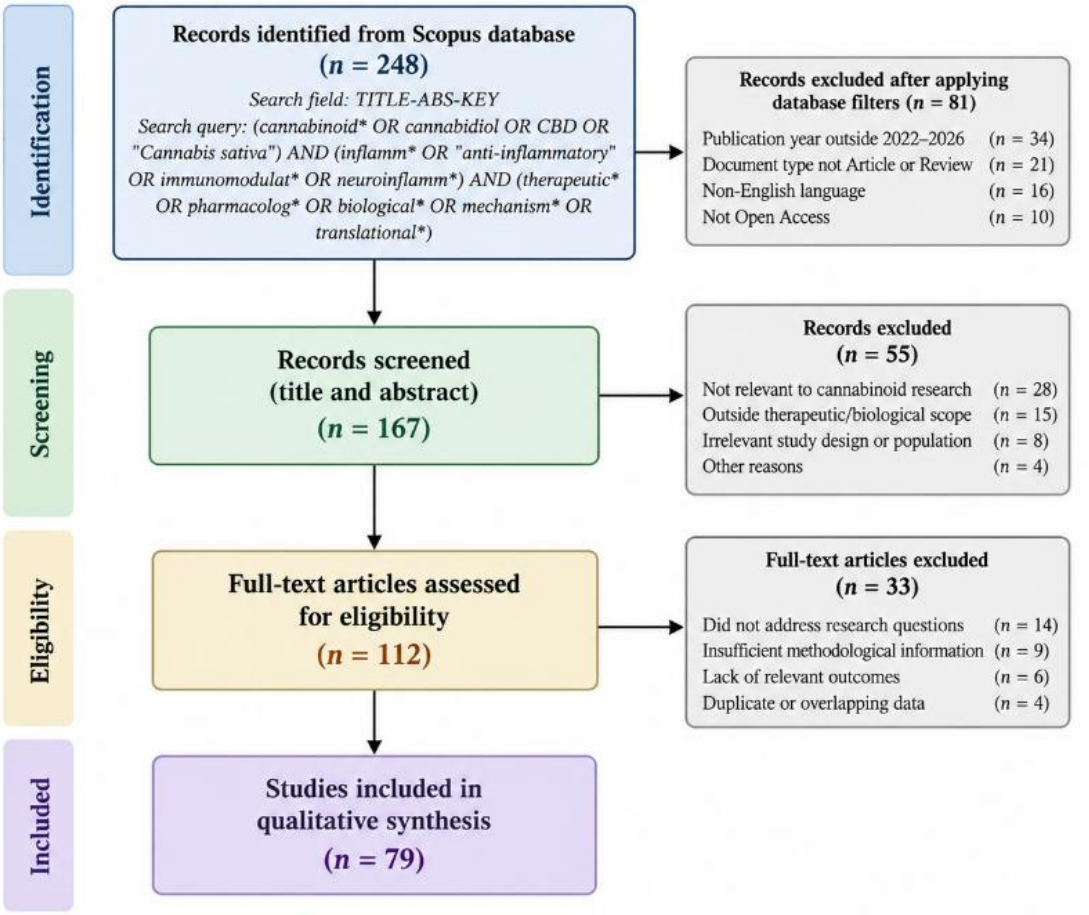


Figure 2. PRISMA 2020 flow diagram of the study selection process

2.3. Data Extraction Process
Data from the 79 included studies were extracted into a structured evidence matrix covering authorship, year, study design, biological model or sample, cannabinoid or preparation, inflammation-related condition, research techniques, inflammatory or immunological outcomes, proposed mechanisms, strengths, limitations, opportunities, and translational barriers. Study-specific differences were retained to avoid treating heterogeneous compounds, preparations, and models as directly equivalent.

2.4. Synthesis of Findings
The extracted evidence was analyzed for recurring patterns, convergence, inconsistency, and gaps in inflammation-related cannabinoid research. Study characteristics were coded descriptively, whereas thematic domains were non-mutually exclusive, allowing one study to inform more than one mechanism or translational issue. The synthesis distinguished demonstrated outcomes within the reported model from broader therapeutic interpretation and from evidence supporting clinical translation.

2.5. Quality Assessment
The methodological quality of the 79 included studies was appraised using criteria adapted from two standard instruments, namely the SYRCLE risk-of-bias tool for in vivo animal studies and the Joanna Briggs Institute (JBI) critical appraisal checklists for in vitro, ex vivo, human-derived, computational, and review-based evidence. The appraisal domains covered selection and allocation, performance and detection bias, attrition, outcome reporting, analytical transparency, and reproducibility. Reporting of randomization, blinding, and sample-size justification varied substantially across the corpus, and these weaknesses were considered when interpreting evidence strength and translational relevance. Consistent with the objective of mapping evidence maturity, appraisal outcomes were used descriptively to weight the strength of each conclusion rather than to exclude studies. This review was not prospectively registered in a registry such as PROSPERO, and this absence of pre-registration is acknowledged as a limitation of the review process.

2.6. Study Limitations
Several limitations of the review process deserve explicit acknowledgement. The search relied on a single database, and restricting retrieval to Open Access articles may have excluded credible subscription-based studies, creating a risk of publication and selection bias. These constraints may limit the comprehensiveness of the corpus and the generalizability of the synthesis. Future updates should therefore extend the search to PubMed/MEDLINE and Web of Science, consider grey literature, and adopt prospective protocol registration.

3. Results and Discussion
3.1. Research Characteristics and Methodological Patterns
The 79 included studies used animal, cell-based, human-derived, ex vivo, computational, analytical, and review designs. As summarized in Figure 3, in vivo animal studies formed the largest design category (40.5%), followed by in vitro cell-based systems (22.8%), literature-based reviews (15.2%), ex vivo or human-derived preparations (10.1%), and computational approaches (7.6%). Rodent models dominated the biological samples, since mice (26.6%) and rats (17.7%) together accounted for nearly half of the corpus, while human cells or human tissue represented only 13.9%. Experimental models were concentrated in neuroinflammation, intestinal inflammation, inflammatory pain, skin inflammation, and tissue injury [6], [25-26]. This distribution shows a field whose translational distance remains considerable, because the models closest to human physiology are precisely those least represented [20-21].

CBD was the most frequently investigated compound (46.8% of studies), while CBG, THC, CBN, CBGA, acidic cannabinoids, terpenes, phytocomplexes, and whole-plant preparations appeared in smaller subsets [11], [12], [27]. Neurological and neuropsychiatric records examined glial responses, receptor interactions, autophagy, cognition, behavior, and inflammatory markers [28-30]. Related evidence extended to neuroprotection in hepatic encephalopathy, schizophrenia, cognitive decline, and chemotherapy-related affective outcomes [31-33], and to inflammatory-marker changes in anxiety and depression models [34-35].

Hepatic, metabolic, musculoskeletal, regenerative, oncological, dermatological, oral, and veterinary contexts were represented by a smaller and more heterogeneous group of studies [36-38]. Further records addressed pericarditis and colorectal tumorigenesis [39-40], veterinary medicine and animal production [41-43], and regenerative and dermatological applications [44-45]. A closing subset examined gingival and skin keratinocyte responses and murine colitis [46-47].

Other records contributed evidence on membrane interactions, phytochemical composition, extract characterization, regulation, industrial hemp composition, and byproduct utilization [48-50]. These contextual records also appraised regulatory aspects, industrial commodity chemistry, and large-animal byproduct feeding [24], [51-52]. All contextual records were used to characterize the breadth and maturity of the evidence base and were not treated as equivalent to direct demonstrations of anti-inflammatory efficacy.

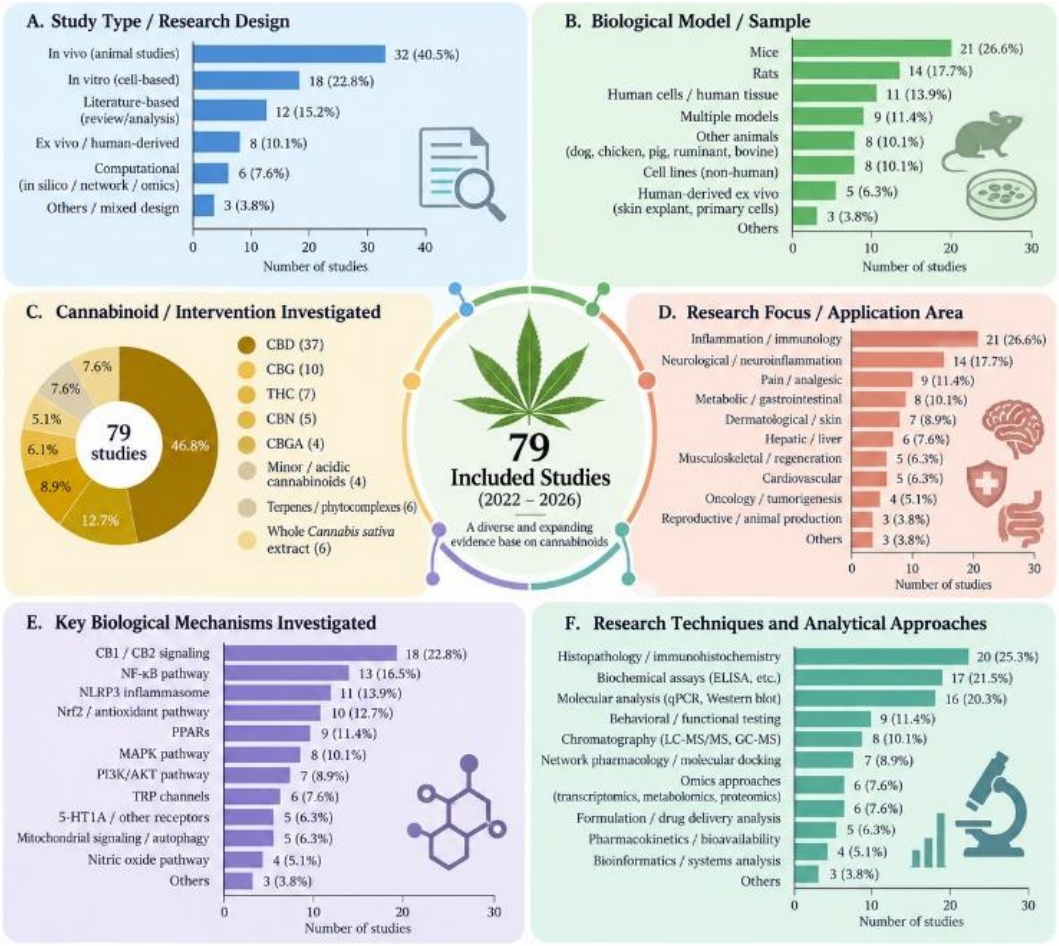


Figure 3. Research characteristics and methodological patterns of the 79 included studies

The included studies also concentrated mechanistic attention on CB1/CB2 signaling (22.8%), NF-κ B activation (16.5%), the NLRP3 inflammasome (13.9%), Nrf2-mediated antioxidant responses (12.7%), and PPARs (11.4%) [53-55]. Methodologically, histopathology and immunohistochemistry (25.3%), biochemical cytokine assays (21.5%), and molecular analyses such as qPCR and Western blotting (20.3%) carried most of the evidence [8], [56-57], complemented by chromatographic, transcriptomic, and network-pharmacology approaches [58-60]. By contrast, pharmacokinetic and bioavailability assessment accounted for only 5.1% of studies and formulation analysis for 6.3% [18], [61]. This disproportion matters because dose, exposure, and tissue distribution determine whether mechanistic effects can be reproduced in patients, so their scarcity weakens exposure-based interpretation of the reported findings. The methodological diversity broadens mechanistic coverage but reduces direct comparability, since divergent models, endpoints, and analytical techniques yield findings that cannot be pooled quantitatively.

3.2. Research Findings and Evidence Profile

Across the included literature, cannabinoids were associated with reduced inflammatory mediators or inflammatory injury in neurological, intestinal, dermatological, and musculoskeletal contexts [2], [26], [62], and comparable protection is documented in dermatitis and skin-barrier models [63-64]. As visualized in Figure 4, several studies also connected inflammation control with changes in oxidative stress, mitochondrial regulation, immune signaling, or tissue-barrier integrity [10], [54], [65], including gut-organ protection after ischemic injury [9], [66]. Evidence beyond CBD included anti-inflammatory findings for CBG-rich preparations, acidic cannabinoids, phytocannabinoid and terpene combinations, and multi-component matrices [12], [13], [15]. These findings remain model-specific, and differences in composition, dose, comparator, and disease context prevent a uniform efficacy conclusion.

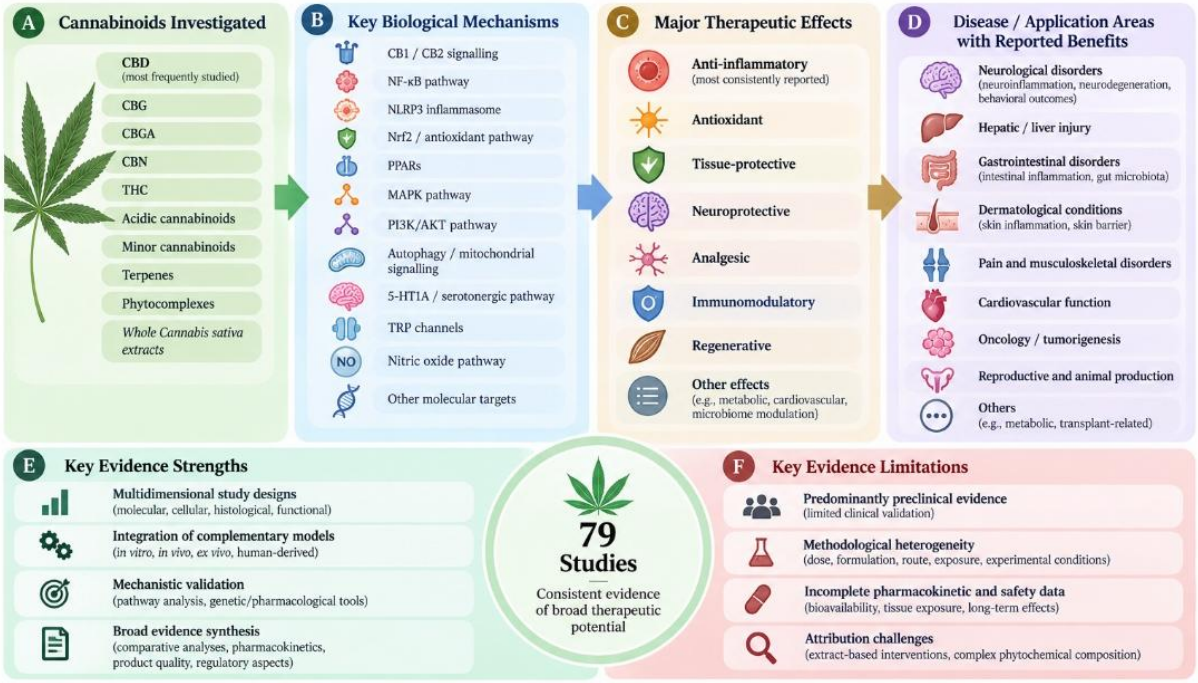


Figure 4. Research findings and evidence profile of the 79 included studies

The evidence base was strengthened when studies combined functional outcomes with molecular, biochemical, histological, or pharmacokinetic measurements. Examples include mechanistic validation in rheumatoid arthritis and psoriasis models and multi-omics analysis in neuropathic pain

[4], [67-68]. Transcriptomic and pharmacokinetic-pharmacodynamic assessments further strengthened mechanistic interpretation [58], [61]. Human-derived or ex vivo models added translational relevance in bovine endometritis, human keratinocytes, and ex vivo human skin [15], [64], [69]. These designs improve mechanistic interpretation but do not substitute for controlled clinical evidence.

The principal weakness of the corpus is its preclinical and model-based predominance [20], [21]. Variation in cannabinoid identity, extract composition, dose, formulation, route, exposure duration, model, and inflammatory endpoint limited comparison and generalizability [18], [19], [57]. Multi-component interventions further complicated attribution to a single cannabinoid or terpene [12], [15], [70]. Clinical validation, pharmacokinetic characterization, bioavailability, tissue exposure, drug interactions, and long-term safety were insufficiently addressed across much of the corpus [18], [20], [71].

The synthesis also identifies a recurring relationship between cannabinoid exposure and modulation of inflammatory signaling, oxidative stress, immune activity, and tissue integrity, implicating NLRP3, NF-κB, Nrf2, CB1/CB2, PPARs, and nitric oxide pathways [53], [54], [72]. However, pathway involvement is not equivalent to therapeutic efficacy, and the reported response remains conditional on cannabinoid composition, exposure, biological model, and disease context [3], [26], [57]. The evidence nonetheless supports moving beyond a predominantly CBD-centered perspective toward defining which cannabinoid, at what exposure, and through which biological network a clinically meaningful outcome is produced [7], [11], [73]. Combination and entourage-related approaches illustrate this complexity, because current designs rarely include the single-agent comparators needed to distinguish genuine synergy from additive effects [12], [14], [17].

3.3. Therapeutic Opportunities and Priority Research Directions

The most defensible therapeutic opportunity lies in inflammation-related conditions for which mechanistic and functional outcomes converge, including neuroinflammation, inflammatory pain, intestinal inflammation, skin inflammation, and selected tissue-injury contexts [2], [4], [6]. Delivery systems such as nanoemulsions, solid lipid nanoparticles, and polymer-based formulations may improve exposure or targeting, but their translational value requires independent pharmacokinetic and safety validation [5], [74-75]. Research beyond CBD may clarify whether CBG, acidic cannabinoids, terpenes, or standardized combinations offer distinct advantages [11], [13], [16].

Priority research should connect a chemically characterized intervention to an inflammation-specific mechanism, an exposure measure, and a clinically relevant outcome. This requires standardized composition and reporting, optimized dose and route, pharmacokinetic assessment, human-relevant models, and trials designed for defined inflammatory indications. Combination studies should test synergy against appropriate single-agent comparators instead of assuming an entourage effect [12], [15], [17].

A precision approach remains more defensible than generalized efficacy claims, because variation in dose response, formulation, route, pharmacokinetics, and biological context makes a uniform cannabinoid strategy implausible [3], [26], [27]. Indication-specific biomarkers and exposure-response analysis may help identify relevant patient groups, therapeutic windows, and stopping rules, but these approaches still require prospective clinical validation [61], [76]. The major opportunities and corresponding research directions are summarized in Table 1.

Table 1. Therapeutic Opportunities and Research Directions

Opportunity	Key direction	Key references
Clinical translation	Clinical trials and human-relevant validation	[20], [21], [76]
Precision treatment	Dose, route, formulation, PK, and biomarker optimization	[61], [76]
Advanced delivery	Nanoformulations, targeted, and topical delivery systems	[5], [74], [75]
Combination strategies	Multi-cannabinoid, cannabinoid and terpene combinations	[12], [15], [17]
Beyond CBD	CBG, CBGA, CBN, acidic and minor cannabinoids	[11], [13], [27]
Human-relevant models	Human-derived and translational experimental models	[15], [64], [69]
Standardization	Chemotypes, extraction, formulations, analytical methods, and quality control	[19], [57], [60]
Sustainable applications	Cannabis biomass and agricultural byproduct utilization	[49], [52]

3.4. Translational Barriers and Standardization Challenges

The central translational barrier is the distance between promising preclinical anti-inflammatory findings and reliable evidence in humans [20], [21], [76]. Animal, cellular, and ex vivo studies support biological plausibility in several conditions [2], [4], [26]. However, they cannot establish clinical efficacy, and responses vary with compound, dose, formulation, route, exposure, receptor context, and disease model [18], [57], [77]. Human studies must therefore test clearly characterized interventions against indication-specific inflammatory and clinical endpoints.

Methodological heterogeneity constitutes a second major barrier. Differences in *Cannabis* chemotype, extraction procedure, cannabinoid concentration, formulation, dosing, analytical method, and outcome definition reduce reproducibility [19], [57], [60]. Whole-plant and multi-component preparations create an additional attribution problem, because observed effects may arise from one constituent, from several constituents, or from their interaction [12], [14], [70]. Uncertainty in bioavailability, tissue exposure, metabolism, and drug interactions further constrains translation [18], [61], [71].

Table 2. Major Research Challenges and Translational Barriers

Challenge	Key issue	Key references
Preclinical predominance	Limited human generalizability	[20], [21]
Clinical validation	Insufficient evidence for definitive efficacy	[21], [76]
Methodological heterogeneity	Differences in dose, formulation, route, and outcomes	[19], [57], [77]
Standardization gaps	Variable preparations and analytical procedures	[27], [60]
Attribution problem	Unclear contribution of individual constituents	[12], [14], [70]
Pharmacokinetics and exposure	Incomplete bioavailability and tissue-exposure data	[18], [61], [71]
Long-term safety	Limited chronic toxicity and interaction data	[18], [78]
Causal validation	Molecular changes may not establish functional benefit	[53], [67]
Formulation validation	Uncertainty in stability, biodistribution, and scalability	[5], [79]
Regulatory translation	Need for coordinated clinical and regulatory pathways	[24]

Additional barriers include long-term safety, toxicology, causal validation, formulation readiness, and regulatory consistency. Molecular changes alone do not establish meaningful functional or clinical benefit, and advanced delivery or combination approaches require evidence on stability, biodistribution, scalability, comparative effectiveness, and human safety [5], [71], [79]. Standardization is therefore a scientific prerequisite for comparing anti-inflammatory effects, not merely a manufacturing concern. Translation ultimately depends on coordinated chemical standardization, mechanism-linked outcomes, pharmacokinetic validation, and rigorous clinical trials rather than on broad claims drawn from heterogeneous preclinical findings. Table 2 summarizes these barriers and the evidence gaps that sustain them.

3.5. From Mechanistic Convergence to Translational Maturity

Inflammation-related applications span neurological, pain, dermatological, gastrointestinal, cardiovascular, and tissue-injury contexts [2], [6], [26]. Translation depends not only on biological activity but also on solubility, stability, bioavailability, tissue penetration, and targeted exposure [18], [71], [74]. The practical objective is therefore to match a characterized cannabinoid or formulation with a defined inflammatory indication, a biological target, an exposure profile, and a measurable clinical outcome.

Potential anti-inflammatory activity should not be equated with established clinical efficacy. Most direct evidence in this corpus came from experimental or review-based studies, while controlled human evidence remained comparatively limited [21], [22], [76]. Differences in interventions and endpoints further restrict extrapolation, and molecular convergence across pathways does not guarantee functional benefit in patients [53], [67]. Future work should therefore prioritize evidence quality and clinical relevance rather than adding further heterogeneous preclinical studies.

3.6. Implications for Research and Translational Development

The field's central task is to move from demonstrating inflammation-related biological activity to establishing reproducible, exposure-linked, and clinically meaningful benefit. Current confidence is constrained by preclinical predominance, inconsistent characterization of preparations, limited pharmacokinetic evidence, sparse long-term safety data, and insufficient controlled clinical validation [18], [19], [20].

Future studies should prioritize chemically standardized preparations, validated analytical methods, exposure-informed dosing, human-relevant models, mechanism-linked inflammatory endpoints, and adequately powered clinical trials. These elements would clarify the pathway from composition to exposure, mechanism, functional response, and clinical benefit.

Overall, the included studies support biological plausibility for cannabinoid modulation of inflammation, but they do not justify claims about the entire therapeutic cannabinoid field. The decisive questions are which cannabinoid or standardized formulation works for a defined inflammatory indication, at what exposure, through which verified mechanism, and with what level of human evidence.

4. Conclusion

This systematic review set out to characterize inflammation-related cannabinoid research and to judge the maturity of its evidence. With respect to RQ1, the 79 included studies were dominated by preclinical designs, with in vivo animal models accounting for 40.5% and in vitro cell-based systems for 22.8%, mice and rats representing almost half of all biological samples, and CBD examined in 46.8% of the work. With respect to RQ2, the most consistent findings were the modulation of inflammatory signaling, oxidative stress, immune responses, and tissue-barrier function, linked to NF-κB, NLRP3, Nrf2, CB1/CB2, and PPAR pathways and extended across CBG, acidic cannabinoids, terpenes, and standardized multi-component preparations. With respect to RQ3, the evidence remains translationally immature, because pharmacokinetic assessment appeared in only 5.1% of the studies, controlled human clinical validation was scarce, and preparation, dosing, and endpoint reporting varied widely.

With respect to RQ4, the most credible opportunities lie in chemically standardized preparations, exposure-informed dosing, human-relevant models, mechanism-linked inflammatory endpoints, and adequately powered trials for defined indications. With respect to RQ5, translation is constrained by methodological heterogeneity, attribution problems in multi-component preparations, incomplete pharmacokinetic and long-term safety data, and the absence of coordinated clinical and regulatory pathways. Cannabinoids are therefore plausible but not yet proven anti-inflammatory agents, and their clinical value will be established only through indication-specific, standardized, reproducible, and clinically validated evidence.

References

[1] Peskar, D., Kerec Kos, M., Tavčar, Š., Lakota, K., Kojc, N., Veranič, P., & Erman, A. (2026). CBD promotes structural and functional epithelial restoration and alleviates inflammation in a mouse model of interstitial cystitis. *Pharmaceutics*, *18*(4), 458.

[2] Singh, M. K., Sen, S., Singh, S., Aftab, N., Kumar, B., Gupta, N., ... & Verma, R. S. (2025). Therapeutic potential of cannabidiol-rich Cannabis sativa to mitigate the severity of inflammation and pain: A pre-clinical study. *Journal of Ethnopharmacology*, 120856.

[3] Shi, Q., Wu, Q., Wang, Q., Zhu, S., Guo, M., & Xia, Y. (2025). Cannabidiol finds dihydrocannabidiol as its twin in anti-inflammatory activities and the mechanism. *Journal of ethnopharmacology*, *337*, 118911.

[4] Kim, M. S., Lee, J. H., Kim, S. W., & Bang, C. H. (2024). Cannabidiol Alleviates Imiquimod-Induced Psoriasis by Inhibiting JAK2–STAT3 in a Mouse Model. *Biomedicines*, *12*(9), 2084.

[5] Alcantara, K. P., Malabanan, J. W. T., Nalinratana, N., Thitikornpong, W., Rojsitthisak, P., & Rojsitthisak, P. (2024). Cannabidiol-loaded solid lipid nanoparticles ameliorate the inhibition of proinflammatory cytokines and free radicals in an in vitro inflammation-induced cell model. *International Journal of Molecular Sciences*, *25*(9), 4744.

[6] Videtta, G., Sasia, C., Quadrino, S., Brighenti, V., Bertarini, L., Caroli, C., ... & Galeotti, N. (2026). A sesquiterpene-rich essential oil from Cannabis sativa L. attenuates symptoms and neuroinflammation in experimental autoimmune encephalomyelitis model through a CB2-mediated signalling. *Phytomedicine*, 158068.

[7] Fowler, D. K., Savage, T. M., & Mackie, D. I. (2026). Cannabidiol and other non-psychotropic cannabinoids from Cannabis sativa as therapeutics for microglial-mediated neuroinflammation and neurodegeneration. *Journal of Cannabis Research*.

[8] Nascimento, G. C., Bálico, G. G., de Mattos, B. A., Dos-Santos-Pereira, M., Oliveira, I. G. C., Queiroz, M. E. C., ... & Del-Bel, E. (2025). Cannabidiol improves L-DOPA-induced dyskinesia and modulates neuroinflammation and the endocannabinoid, endovanilloid and nitrergic systems. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *141*, 111456.

[9] Del Core, J., Jure, I., Sofrás, F. M. S., Pietranera, L., Ronchetti, S., Roig, P., ... & Labombarda, F. (2025). Cannabidiol/tetrahydrocannabinol-enrich extract decreases neuroinflammation and improves locomotor outcome following spinal cord injury. *Neuroscience*, *573*, 468-481.

[10] Hickey, J. P., Collins, A. E., Nelson, M. L., Chen, H., & Kalisch, B. E. (2024). Modulation of oxidative stress and neuroinflammation by cannabidiol (CBD): Promising targets for the treatment of Alzheimer's disease. *Current Issues in Molecular Biology*, *46*(5), 4379-4402.

[11] Fuentes, G. M., Echarte, S. M., Parise, A. R., Ramírez, C. L., & Orallo, D. E. (2026). Cannabigerol And Cannabigerolic Acid: Biosynthesis, Pharmacology, And Translational Perspectives.? A Critical Review. *Phytomedicine Plus*, 100965.

[12] Strnad, O., Nejedlý, T., Svoboda, P., Mertlíková-Kaiserová, H., Malý, M., Malý, M., ... & Viktorová, J. (2025). Phytocannabinoids as anti-inflammatory agents: Synergistic effects when combined with Cannabis sativa matrices. *Journal of Ethnopharmacology*, 121134.

[13] Singh, S. K., Antoine, C., Tse, C., Ji, L., Reed, M., Carter, W. G., ... & Bid, H. K. (2026). Therapeutic potential of acidic cannabinoids: an update. *Journal of Cannabis Research*, *8*(1), 25.

[14] Al-Khazaleh, A. K., Zhou, X., Bhuyan, D. J., Münch, G. W., Al-Dalabeeh, E. A., Jaye, K., & Chang, D. (2024). The neurotherapeutic arsenal in cannabis sativa: insights into anti-neuroinflammatory and neuroprotective activity and potential entourage effects. *Molecules*, *29*(2), 410.

[15] Fumagalli, M., Martinelli, G., Paladino, G., Rossini, N., Ciriello, U., Nicolaci, V., ... & Sangiovanni, E. (2025). Beyond cannabidiol: the contribution of Cannabis sativa phytocomplex to skin anti-inflammatory activity in human skin keratinocytes. *Pharmaceuticals*, *18*(5), 647.

[16] Tan, K. B., Alexander, H. D., Linden, J., Murray, E. K., & Gibson, D. S. (2024). Anti-inflammatory effects of phytocannabinoids and terpenes on inflamed Tregs and Th17 cells in vitro. *Experimental and Molecular Pathology*, *139*, 104924.

[17] Mazzantini, C., El Bourji, Z., Parisio, C., Davolio, P. L., Cocchi, A., Pellegrini-Giampietro, D. E., & Landucci, E. (2024). Anti-inflammatory properties of cannabidiol and beta-caryophyllene alone or combined in an in vitro inflammation model. *Pharmaceuticals*, *17*(4), 467.

[18] Banerjee, S., Saharan, V. A., Banerjee, D., Ram, V., Kulhari, H., Pooja, D., & Singh, A. (2025). A comprehensive update on cannabidiol, its formulations and drug delivery systems. *Phytochemistry Reviews*, *24*(4), 2723-2757.

[19] Mouton, M., Gerber, M., & Van der Kooy, F. (2024). Cure-All cannabidiol? The cannabidiol content of commercial products. *Phytomedicine plus*, *4*(1), 100520.

[20] Komedera, M., Wojda, U., & Kiryk, A. (2026). Cannabinoids in Alzheimer's disease: animal–human evidence and clinical pharmacology challenges. *Frontiers in Behavioral Neuroscience*, *20*, 1833021.
[21] Pulone, S., Moulton, C., Nucera, S., Ilari, S., Muscoli, C., & Tasciotti, E. (2026). Therapeutic use of cannabinoids in age-related pain: Current evidence and clinical perspectives. *Pharmacological Research*, 108130.
[22] Jha, S. K., Nelson, V. K., Suryadevara, P. R., Panda, S. P., Pullaiah, C. P., Nuli, M. V., ... & Jafari, S. M. (2024). Cannabidiol and neurodegeneration: From molecular mechanisms to clinical benefits. *Ageing Research Reviews*, *100*, 102386.
[23] Mujahid, K., Rasheed, M. S., Sabir, A., Nam, J., Ramzan, T., Ashraf, W., & Imran, I. (2025). Cannabidiol as an immune modulator: A comprehensive review. *Saudi Pharmaceutical Journal*, *33*(3), 11.
[24] Gupta, P., Singh, A., Shafi, S., Ralli, T., Pottoo, F. H., Sultana, Y., & Kohli, K. (2024). Cannabis sativa in phytotherapy: reappraisal of therapeutic potential and regulatory aspects. *Current pharmaceutical biotechnology*, *25*(1), 58-76.
[25] Aalidaeijavadi, Z., Khodagholi, F., & Haghparast, A. (2026). Potential effects of cannabidiol on formalin-induced inflammatory pain in morphine-dependent rats. *Journal of Psychiatric Research*.
[26] Anderson, B. D., Sepulveda, D. E., Nachnani, R., Cortez-Resendiz, A., Coates, M. D., Beckett, A., ... & Raup-Konsavage, W. M. (2024). High cannabigerol hemp extract moderates colitis and modulates the microbiome in an inflammatory bowel disease model. *The Journal of pharmacology and experimental therapeutics*, *390*(3), 331-341.
[27] Khouchlaa, A., Khouri, S., Hajib, A., Zeouk, I., Amalich, S., Msairi, S., ... & Bouyahya, A. (2024). Health benefits, pharmacological properties, and metabolism of cannabinol: A comprehensive review. *Industrial Crops and Products*, *213*, 118359.
[28] de Rezende, V. L., Mathias, K., Gonçalves, C. L., de Bitencourt, R. M., Barichello, T., & Petronilho, F. (2026). Beyond neurons: Impact of cannabidiol on glial cells in ischemic stroke. *Neural Regeneration Research*, *21*(10), 4560-4566.
[29] Okrah, E. A., Allan, C., Doblin, M. S., & Annesley, S. J. (2025). Cannabidiol and Parkinson's disease: Investigating receptor interactions and their therapeutic implications. *Pharmacology & Therapeutics*, 108943.
[30] Ntsapi, C., Weyers, M., Chinheya, R., Jim, T., & Matsabisa, M. (2025). Exploring cannabinoid modulation on autophagy mechanisms in Alzheimer's disease: A review. *Frontiers in Pharmacology*, *16*, 1748368.
[31] Liu, Y. (2024). Alzheimer's disease, aging, and cannabidiol treatment: A promising path to promote brain health and delay aging. *Molecular Biology Reports*, *51*(1), 121.
[32] Völker, J. S. D., Micluţia, I. V., & Vinași, R. C. (2024). Investigating Cannabidiol's potential as a supplementary treatment for schizophrenia: A narrative review. *European Journal of Pharmacology*, *979*, 176821.
[33] Mostafa, D. M., Hassan, A. A., Aboghadeer, A. R., Mansour, S. Z., & Abdel-Hamid, G. R. (2025). Cannabidiol and low-dose γ-radiation regulate alterations consequences of hepatic-encephalopathy induced by thioacetamide: neuroprotective and anti-inflammatory role. *Immunopharmacology and Immunotoxicology*, *47*(5), 631-644.
[34] Raïch, I., Lillo, J., Rebassa, J. B., Griñán-Ferré, C., Bellver-Sanchis, A., Reyes-Resina, I., ... & Navarro, G. (2025). Cannabidiol as a multifaceted therapeutic agent: mitigating Alzheimer's disease pathology and enhancing cognitive function. *Alzheimer's Research & Therapy*, *17*(1), 109.
[35] Poudel, B., Bany, B. M., Hales, D. B., & Cheatwood, J. L. (2024). Effects of Cannabidiol (CBD) on Doxorubicin-Induced anxiety and Depression-like behaviors and mRNA expression of inflammatory markers in rats. *Brain sciences*, *14*(10), 999.

[36] Chauhan, S. B., Singh, I., Dahiya, K., & Jain, C. (2026). Cannabidiol as a Modulator of the Gut-Liver Axis: Clinical and Pharmacological Insights into Hepatic and Metabolic Disorder Therapies. *Current Reviews in Clinical and Experimental Pharmacology*.
[37] Zhan, Z., Jiang, Y., Chen, S., Yang, Q., Pan, G., Liu, Y., ... & Lin, C. (2025). Cannabidiol attenuates the LPS/D-Galactosamine-induced acute liver injury by inhibiting parkin-mediated ubiquitination of MFN2. *Journal of Ethnopharmacology*, 121067.
[38] Yazdanpanah, Z., Sobhani, H., Vossoughinia, S., Sahebi, S., Jalali, J., & Rahbardar, M. G. (2026). Medicinal plants in the management of muscle loss and sarcopenia: A narrative review of preclinical and clinical evidence from eight species. *Phytomedicine*, 157958.
[39] Bonaventura, A., Vecchié, A., Mauro, A. G., Del Buono, M. G., Weber, B. N., Toldo, S., & Abbate, A. (2026). Updates on Pathophysiology of Pericarditis to Guide Development of Therapeutics. *Current Cardiology Reports*, *28*(1), 58.
[40] Liu, Z. (2025). Cannabidiol (CBD) and colorectal tumorigenesis: potential dual modulatory roles via the serotonergic pathway. *Current Oncology*, *32*(7), 375.
[41] Benjamin, E. T., Maria Teresa, S. E., Alexander, N. S., Stephanie, S. A., Martín, S. C., & Sylvia, A. B. (2026). Randomized and Blind Evaluation of the Efficacy of a Full-Spectrum Oral Cannabis sativa Oil Extract, Standardized Based on CBD-A, CBD and THC-A, THC in Canines with Chronic Osteoarthritis. *Animals*, *16*(6), 900.
[42] Richter, G., & Hazzah, T. (2025). Cannabis and veterinary medicine. *Veterinary Clinics: Small Animal Practice*, *55*(6), 1137-1158.
[43] Fallahi, S., Śmieszek, A., Bobak, Ł., Lipińska, A., Asghar, M. U., Olejnik, K., & Opaliński, S. (2025). Dose-dependent effects of cannabidiol in drinking water on yolk fatty acid profile and hepatic expression of polyunsaturated fatty acids (PUFAs)-related genes in laying hens: insights into the cannabidiol (CBD) systemic and molecular mechanisms of action. *BMC Veterinary Research*, *21*(1), 662.
[44] Buchaim, R. L., Dias, L. C., De Sousa, F. G. C. P., Morais, S. D. S., Jacintho, A. J., Paulini, M. R., ... & Buchaim, D. V. (2025). Exploring Cannabidiol's Role in Regenerative Medicine: Focus on Neural and Skeletal Tissues. *Biomedicines*, *13*(10), 2490.
[45] Lee, J. H., Yoon, J. Y., Kim, D. H., Kwon, Y. G., Kim, G. H., Park, B. J., & Suh, D. H. (2024). Potential of cannabidiol as acne and acne scar treatment: novel insights into molecular pathways of pathophysiological factors. *Archives of Dermatological Research*, *316*(7), 428.
[46] Bahraminia, M., Laaboudi, F. Z., Romanet, C., Zhang, Z., Chakir, J., Béland, F., & Rouabhia, M. (2025). Evaluation of the Effects of Tetrahydrocannabinol (THC) and Cannabidiol (CBD) on Gingival and Skin Keratinocyte Growth, Migration, Metabolic Activity, and Pro-Inflammatory Cytokine Secretion. *Biomedicines*, *13*(10), 2541.
[47] Godbole, S. S., Sun, D., Coates, M. D., Himmelberger, V. J., Roopchand, D. E., & Raup-Konsavage, W. M. (2025). Orally administered CBD/CBG hemp extract reduces severity of ulcerative colitis and pain in a murine model. *Journal of Clinical Medicine*, *14*(17), 6095.
[48] Velez-Saboyá, C. S., López-Pérez, F. A., Rodríguez-Huerta, L. G., Sierra-Valdez, F. J., Romero-Arias, J. R., Barrio, R. A., & Ruiz-Suárez, J. C. (2026). Cannabidiol (CBD) Induces Lipid Microdomain Disruption or Budding in Ternary Mixtures. *The Journal of Physical chemistry. B*, *130*(14), 3960.
[49] Gargiulo, E., Romano, B., Formisano, C., Fiorentino, N., Somma, F., Maresca, D. C., ... & Chianese, G. (2025). From waste to value: evaluation of chemical composition and anti-inflammatory activity of Cannabis sativa stem extracts. *Fitoterapia*, 106894.
[50] Singh, M. K., Singh, S., Mishra, S., Shankar, U., Maurya, A., Sahu, K. S., ... & Verma, R. S. (2025). Investigating the phytochemical diversity and anti-inflammatory activity of a non-psychoactive genotype of Cannabis sativa L. from India. *Microchemical Journal*, *211*, 113111.

[51] Taubner, T., Englmaierová, M., Bjelková, M., Skřivanová, V., Bejčková, K., Vít, T., & Růnová, K. (2026). Comparative Analysis of the Chemical Composition of Hemp and Linseed Varieties as Key Industrial Commodities. *Foods*, *15*(12), 2145.
[52] Boonprakob, R., Vimolmangkang, S., & Tummaruk, P. (2024). Impacts of supplementing Cannabis sativa byproducts during the transition period on behaviour, feed consumption, constipation levels, colostrum production and piglet performance in hyperprolific sows. *Theriogenology*, *215*, 272-280.
[53] Jaisankar, D., & Jayaprakash, N. (2026). Cannabidiol as a modulator of NLRP3 inflammasome: Mechanistic insights and therapeutic potential. *Journal of Holistic Integrative Pharmacy*, *7*(2), 338-349.
[54] Lv, B., He, J., Zhan, S., Jin, K., Lei, X., Cheng, X., ... & Lin, Q. (2026). The dual roles of natural cannabidiol in combating oxidative stress and inflammation: a potential intestinal guardian. *Redox Biology*, 104051.
[55] Szkopek, D., Mendel, M., Kinsner, M., Fotschki, B., Juśkiewicz, J., Kozłowski, K., ... & Konieczka, P. (2024). Interaction between peroxisome proliferator-activated receptors and cannabidiol in the gut of chickens applied to different challenge conditions. *International Journal of Molecular Sciences*, *25*(21), 11398.
[56] Wei, Y., Liu, X., Lin, S., Jia, Z., Liu, L., Wang, B., ... & Mei, X. (2026). Unraveling cannabidiol's dual modulatory role in schizophrenia: network pharmacology and in vivo validation of neuroinflammatory and behavioral modulation. *Molecular Neurobiology*, *63*(1), 278.
[57] Bartkowiak-Wieczorek, J., Kujawski, R., Szulc, M., Czora-Poczwardowska, K., Szymczak, J., Gierszewska, J., ... & Grzelak, T. (2026). Evaluation of Anti-Inflammatory Effects of Cannabis sativa Extracts via Possible Modulation of mRNA Levels of Inflammatory Cytokines and Cannabinoid Receptors. *Nutrients*, *18*(7), 1106.
[58] Rokicki, M., Żurowski, J., Sawicki, S., Ocłoń, E., Szmatoła, T., Jasielczuk, I., ... & Gurgul, A. (2024). Impact of long-term cannabidiol (CBD) treatment on mouse kidney transcriptome. *Genes*, *15*(12), 1640.
[59] Irawan, A., & Bionaz, M. (2024). Liver transcriptomic profiles of ruminant species fed spent hemp biomass containing cannabinoids. *Genes*, *15*(7), 963.
[60] Oliveira, I. G. C., Grecco, C. F., de Souza, I. D., & Queiroz, M. E. C. (2024). Current chromatographic methods to determine cannabinoids in biological samples: A review of the state-of-the art on sample preparation techniques. *Green Analytical Chemistry*, *11*, 100161.
[61] Conti, F., Lazzara, F., Thermos, K., Zingale, E., Spyridakos, D., Romano, G. L., ... & Bucolo, C. (2025). Retinal pharmacodynamic and pharmacokinetic profile of cannabidiol in an in vivo model of retinal excitotoxicity. *European Journal of Pharmacology*, *991*, 177323.
[62] Maranta, N., Martinelli, G., Fumagalli, M., Pozzoli, C., Sonzogni, E., Rossini, N., ... & Sangiovanni, E. (2025). Efficacy of non-psychotropic Cannabis sativa L. standardized extracts in a model of intestinal inflammation. *Journal of Cannabis Research*, *7*(1), 74.
[63] Wolińska, R., Zalewska, M., Poznański, P., Nawrocka, A., Kowalczyk, A., Sacharczuk, M., & Bujalska-Zadrożny, M. (2025). Anti-inflammatory activity of Cannabis sativa L. extract in 2, 4-Dinitrochlorobenzene-Induced dermatitis in rats. *Pharmaceuticals*, *18*(3), 370.
[64] Klinngam, W., Loruthai, O., & Vimolmangkang, S. (2025). Cannabidiol Mitigates Pollution-Induced Inflammatory, Oxidative, and Barrier Damage in Ex Vivo Human Skin. *Biomolecules*, *16*(1), 10.
[65] Kato, H., Uratsuji, I., Nakadai, Y., & Ochiai, W. (2026). Protective effects of the phytocannabinoid cannabidiol on disuse-induced muscle atrophy through modulation of proteolysis and mitochondrial regulation. *Biological and Pharmaceutical Bulletin*, *49*(5), 822-831.

[66] de Souza Stork, S., Mathias, K., Gava, F., Joaquim, L., Dos Santos, D., Tiscoski, A. D. B., ... & Petronilho, F. (2025). Full-spectrum Cannabis sativa extract enhances gut-peripheral organ integrity after experimental ischemic stroke. *Inflammopharmacology*, *33*(6), 3279-3305.

[67] Chen, J., Li, G., Zhao, F., Zhang, Y., Mu, Q., Zhang, J., ... & Tang, Y. (2026). Ubiquitin-proteasome-dependent degradation of HIF-1α by cannabidiol disrupts pro-angiogenic synoviocyte-endothelial crosstalk in rheumatoid arthritis. *Phytomedicine*, 158661.

[68] Xu, Y., Yao, L., Guo, Y., Shi, C., Zhou, J., & Hua, M. (2024). The potential antinociceptive effect and mechanism of Cannabis sativa L. extract on paclitaxel-induced neuropathic pain in rats uncovered by multi-omics analysis. *Molecules*, *29*(9), 1958.

[69] Parveen, I., Allen, N. R., Wonfor, R. E., Al-Fadhli, A. A., Forde-Thomas, J. E., Giles, J. L., ... & Nash, D. M. (2025). Characterisation of components of an extract of hemp and preliminary assessment of anti-inflammatory activity in an ex vivo model of bovine endometritis. *South African Journal of Botany*, *180*, 254-264.

[70] Perstwong, N., Phongsopitanun, W., Buranasudja, V., & Vimolmangkang, S. (2025). Enhanced Antibacterial and Anti-Inflammatory Activities of the Combination of Cannabis sativa and Propolis Extracts: An In Vitro Study. *International Journal of Molecular Sciences*, *26*(22), 11181.

[71] Eslam, A. F., Mohtashami, L., Moghimi, P., & Iranshahi, M. (2026). Cannabidiol: Pharmaceutical formulations and biomedical applications. *Iranian Journal of Basic Medical Sciences*, *29*(4), 522.

[72] Hooshmand, S. A. A., Rameshrad, M., Sahebkar, A., & Iranshahi, M. (2025). The effects of cannabidiol on nitric oxide synthases: a narrative review on therapeutic implications for inflammation and oxidative stress in health and disease. *Journal of Cannabis Research*, *7*(1), 71.

[73] Matuka, T., Oriola, A. O., Kar, P., Gondwe, M., Apalata, T., & Oyedeji, A. O. (2026). Cannabis sativa Linn.: A Medicinal Plant with Promising Muscle Relaxant-related Constituents. *Journal of Applied Pharmaceutical Science*, *16*(6), 6-18.

[74] Dos Santos, J. C. C., de Aquino, P. E. A., Rebouças, C. D. S. M., Sallem, C. C., Guizardi, M. P. P., Noleto, F. M., ... & de Barros Viana, G. S. (2025). Neuroprotective effects of a cannabidiol nanoemulsion in a rotenone-induced rat model of Parkinson's disease: Insights into the gut-brain axis. *European Journal of Pharmacology*, *1002*, 177748.

[75] Mdarhri, Y., de-Monte-Vidal, V., de-Almeida-Perez-Pimenta, C., Cuello-Rodríguez, S., Touhami, A., Touhami, F., ... & Díaz-Tomé, V. (2026). Encapsulation of Cannabidiol in Chitosan-Stabilized Argan Oil Nanoemulsion as a Potential Dermal Drug Delivery System for Psoriasis Treatment. *Pharmaceutics*, *18*(3), 286.

[76] Naya, N. M., Kelly, J., Hogwood, A., Abbate, A., & Toldo, S. (2024). Therapeutic potential of cannabidiol (CBD) in the treatment of cardiovascular diseases. *Expert Opinion on Investigational Drugs*, *33*(7), 699-712.

[77] Trigo, G., Coelho, M., Ferreira, C. B., Melosini, M., Lehmann, I. S., Reis, C. P., ... & Santos, S. (2024). Exploring the Biological Activity of Phytocannabinoid Formulations for Skin Health Care: A Special Focus on Molecular Pathways. *International Journal of Molecular Sciences*, *25*(23), 13142.

[78] Koyama, S., Etkins, J., Jun, J., Miller, M., So, G. C., Gisch, D. L., & Eadon, M. T. (2025). Utilization of cannabidiol in post-organ-transplant care. *International Journal of Molecular Sciences*, *26*(2), 699.

[79] Chevalier, M. T., Al-Waeel, M., Alsharabasy, A. M., Rebelo, A. L., Martin-Saldaña, S., & Pandit, A. (2024). Therapeutic polymer-based cannabidiol formulation: tackling neuroinflammation associated with ischemic events in the brain. *Molecular Pharmaceutics*, *21*(4), 1609.