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Integrative Approaches in Reducing Steroid Dependency: Exploring Alternative Therapies for Chronic Inflammatory Conditions

Nambi Namusisi H.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Chronic inflammatory diseases, including rheumatoid arthritis (RA), inflammatory bowel disease (IBD), asthma, psoriasis, systemic lupus erythematosus (SLE), and chronic dermatitis—often require prolonged glucocorticoid therapy. While steroids remain highly effective anti-inflammatory agents, long-term use is associated with substantial adverse effects: metabolic dysfunction, osteoporosis, immunosuppression, adrenal suppression, cardiovascular risk, and neuropsychiatric complications. Steroid dependency represents a major clinical challenge, particularly in low-resource settings where biologics may be inaccessible. Integrative medicine combining conventional pharmacotherapy with evidence-based complementary modalities such as acupuncture, phytotherapy, mind–body interventions, nutritional modulation, and physical rehabilitation offer potential steroid-sparing strategies. This review synthesizes mechanistic evidence, clinical trial data, and translational insights supporting integrative approaches in reducing steroid reliance across major inflammatory conditions. We highlight immunomodulatory pathways (NF-κB, MAPK, JAK/STAT, NLRP3 inflammasome), gut microbiome interactions, neuroimmune regulation, and epigenetic mechanisms underpinning these therapies. We propose a practical framework for steroid tapering supported by integrative modalities and outline future research priorities.

Keywords: steroid dependency, glucocorticoids, integrative medicine, acupuncture, herbal medicine

INTRODUCTION

Glucocorticoids (GCs) remain cornerstone therapies for chronic inflammatory and autoimmune diseases, and since their mid-20th-century introduction, they have markedly improved outcomes in rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, asthma, vasculitis, and related dermatologic/hematologic disorders [1]. Their clinical utility stems from rapid, potent immunomodulation via genomic and non-genomic actions. Mechanistically, GCs bind cytoplasmic glucocorticoid receptors, translocate to the nucleus, and remodel transcription by inducing anti-inflammatory programs while repressing pro-inflammatory signaling. Central effects include inhibition of NF-κB and AP-1 activity with downstream reduction of cytokines such as TNF-α, IL-1β, and IL-6, alongside induction of mediators like annexin-1 and IL-10, decreased leukocyte trafficking, lysosomal membrane stabilization, and suppression of T-cell activation collectively enabling fast symptom control and disease stabilization [2]. However, sustained GC exposure carries substantial dose- and duration-dependent toxicity across metabolic, endocrine, musculoskeletal, cardiovascular, neuropsychiatric, and immune systems, including iatrogenic Cushing's syndrome, insulin resistance/type 2 diabetes, osteoporosis and fractures, hypertension and elevated cardiovascular risk, hypothalamic–pituitary–adrenal (HPA) axis suppression, infection susceptibility, and psychiatric disturbances [3]. This cumulative toxicity contributes materially to long-term morbidity and mortality in autoimmune populations. A key challenge is steroid dependency, where tapering triggers disease flare and/or adrenal insufficiency; in RA and IBD, ~30–40% may develop prolonged reliance, and chronic low-dose dependence remains common in asthma and SLE despite disease-modifying agents. Although biologics and targeted synthetic therapies (e.g., anti-TNF, anti-IL-6, anti-integrin, JAK inhibitors) provide steroid-sparing benefits, barriers include high cost and limited LMIC access, safety concerns, monitoring demands, and refractory/intolerant patients. Hence, integrative steroid-sparing strategies combining optimized pharmacotherapy with metabolic, nutritional, microbiome, lifestyle, and precision approaches are increasingly prioritized [4].

Although glucocorticoids provide rapid anti-inflammatory efficacy, their long-term use imposes a substantial clinical and public health burden. Steroid-induced metabolic syndrome, cardiovascular disease, osteoporosis, and infection risk significantly increase healthcare utilization and reduce quality of life. Importantly, many patients remain trapped in cycles of dose escalation and taper failure due to disease flare or adrenal suppression [5]. Current steroid-sparing approaches, including biologics and JAK inhibitors, are not universally accessible and carry independent safety concerns. In resource-limited settings, chronic glucocorticoid therapy often persists as the primary anti-inflammatory strategy due to economic constraints. Even in high-income settings, incomplete therapeutic response or safety limitations restrict widespread replacement of glucocorticoids. Furthermore, steroid dependency reflects both immunologic persistence and endocrine dysregulation [5]. Prolonged GC exposure suppresses endogenous cortisol production, impairing physiologic stress responses and complicating withdrawal. The lack of standardized tapering protocols and predictive biomarkers for successful discontinuation exacerbates the problem. Despite the magnitude of steroid-related morbidity, there remains insufficient integration of molecular insights, metabolic interventions, and multidisciplinary strategies into clinical practice. The absence of comprehensive frameworks addressing immunologic control, endocrine recovery, and systemic toxicity reduction perpetuates reliance on glucocorticoids. Thus, there is an urgent need to critically evaluate the mechanisms underlying steroid dependency, assess limitations of current steroid-sparing pharmacotherapies, and explore integrative approaches capable of minimizing long-term glucocorticoid exposure without compromising disease control [6]. This review synthesizes current evidence on glucocorticoid (GC) dependence in chronic inflammatory and autoimmune diseases, with a focus on mechanisms, harms, and practical pathways to reduce long-term steroid reliance while preserving durable remission. It will (i) clarify key molecular and immunologic actions of GCs that drive rapid disease control, and (ii) interrogate the pathophysiology of steroid dependency, including persistent inflammatory signaling, compensatory immune activation, and hypothalamic–pituitary–adrenal (HPA) axis suppression that complicates tapering and withdrawal. The review also evaluates the systemic toxicity of chronic GC exposure, particularly metabolic (e.g., steroid-induced diabetes, weight gain), cardiovascular (hypertension, atherothrombotic risk), skeletal (osteoporosis, fractures), and neuropsychiatric complications, highlighting how these adverse effects compound baseline inflammatory risk, worsen long-term morbidity, and increase healthcare costs. In parallel, it critically appraises established steroid-sparing pharmacologic strategies (biologics and JAK inhibitors), balancing efficacy against safety concerns and real-world limitations, including affordability and access barriers in low- and middle-income countries (LMICs) that perpetuate chronic GC use. Beyond conventional agents, the review explores emerging integrative steroid-sparing approaches like metabolic modulation, microbiome-targeted therapies, lifestyle interventions, and precision medicine to strengthen inflammatory control and metabolic resilience. Finally, it identifies key research gaps and future directions, emphasizing biomarker development to predict taper success, individualized risk stratification, and multimodal intervention models that integrate immunologic and endocrine recovery frameworks for safer, more sustainable long-term management.

Pathophysiology of Steroid Dependency

Steroid dependency is driven by overlapping molecular and systemic mechanisms that blunt glucocorticoid responsiveness and sustain inflammation. A key factor is glucocorticoid receptor (GR) resistance, characterized by reduced GR expression, a disrupted GR-α/GR-β balance that favors inhibitory signaling, and enhanced MAPK-driven GR phosphorylation that limits receptor function [7]. This is compounded by chronic NF-κB activation, which promotes pro-inflammatory gene transcription and further antagonizes glucocorticoid effects. In parallel, persistent immune dysregulation maintains disease activity, notably through Th17/Treg imbalance, sustained cytokine signaling (especially IL-6 and TNF-α), and activation of the NLRP3 inflammasome, all of which perpetuate tissue inflammation and increase reliance on steroids for control [8]. Neuroendocrine disruption also contributes, as prolonged steroid exposure suppresses the hypothalamic–pituitary–adrenal (HPA) axis and impairs normal cortisol feedback, reducing endogenous stress-hormone support during flares. Finally, gut microbiome alterations and dysbiosis with increased intestinal permeability facilitate translocation of lipopolysaccharide (LPS), amplifying systemic inflammation [9]. Collectively, these pathways create a self-reinforcing cycle of reduced steroid efficacy and ongoing immune activation, suggesting that multimodal strategies targeting receptor signaling, immune pathways, neuroendocrine recovery, and microbiome restoration could lower steroid requirements.

Rationale for Integrative Medicine

Integrative medicine prioritizes a whole-systems approach to disease control by combining complementary strategies that work alongside standard therapy. Key aims include multimodal immune modulation to rebalance dysregulated immune responses, reduction of systemic inflammation to limit downstream tissue injury, and restoration of homeostasis to stabilize physiological function [10]. It also seeks to enhance patient resilience, supporting adaptive capacity under ongoing inflammatory or autoimmune stress, while minimizing cumulative drug toxicity, including effects mediated through the neuroimmune axis. In practice, this framework does not advocate abrupt replacement of corticosteroids; instead, it supports careful, stepwise steroid tapering while sustaining clinical

stability [11]. By targeting multiple interconnected pathways (immune, inflammatory, metabolic, and neuroendocrine), integrative approaches can help maintain symptom control, reduce flare risk, and potentially lower long-term adverse effects associated with prolonged steroid exposure. Overall, the rationale is to achieve durable disease management with fewer trade-offs, using coordinated interventions that reinforce endogenous regulatory mechanisms and improve tolerability of conventional treatment over time [12].

Acupuncture as a Steroid-Sparing Strategy

Acupuncture is emerging as a steroid-sparing strategy by dampening inflammation through multiple pathways, including reduced NF-κB signaling; lowered pro-inflammatory cytokines (TNF-α, IL-1β, IL-6); increased IL-10; vagal stimulation via the cholinergic anti-inflammatory pathway; HPA-axis regulation; and inhibition of microglial activation. Electroacupuncture may further suppress systemic inflammation through the vagus–adrenal axis. Clinically, randomized trials in rheumatoid arthritis report improved DAS28 scores and reduced CRP when acupuncture is added to DMARDs [13]. Controlled studies in asthma show improved FEV1 and lower reliance on rescue steroids, while acupuncture plus moxibustion has reduced disease activity indices in ulcerative colitis. In dermatitis and psoriasis, symptom and pruritus reductions are reported, with modest decreases in steroid dose in some studies; however, evidence is limited by heterogeneous designs, small sample sizes, and lack of standardized protocols [14]. Phytotherapy also offers pleiotropic immunomodulation: curcumin inhibits NF-κB and JAK/STAT, suppresses COX-2, and may act epigenetically via HDAC inhibition, with clinical signals for improved RA outcomes, remission maintenance in IBD, and reduced PASI in psoriasis. Boswellia (5-LOX inhibition) shows evidence in asthma and IBD, licorice modulates cortisol metabolism but risks mineralocorticoid effects, and ashwagandha reduces IL-6 and TNF-α. Traditional Chinese formulas may target cytokine cascades, but safety requires attention to CYP450 interactions, quality control, and pharmacovigilance [15].

Nutritional and Microbiome-Modulating Interventions

Nutritional and microbiome-modulating strategies can meaningfully complement steroid-sparing management across inflammatory diseases. Mediterranean-style, anti-inflammatory dietary patterns are associated with lower inflammatory biomarkers (e.g., reduced IL-6 and CRP), improved rheumatoid arthritis (RA) outcomes, and fewer steroid-related flares. Omega-3 fatty acids support inflammation control by inhibiting eicosanoid production, improving asthma control, and reducing steroid requirements in RA. Probiotics and prebiotics help restore gut-barrier integrity and reshape immune regulation by modulating the Th17/Treg balance; clinically, they show benefit particularly in mild-to-moderate ulcerative colitis [16]. Vitamin D also plays an immunomodulatory role and may enhance steroid responsiveness in asthma, potentially supporting lower systemic exposure. Beyond diet, physical therapy and exercise provide broad anti-inflammatory benefits, including decreased TNF-α, increased IL-10, improved mitochondrial function, and reduced adipose-driven inflammation. In RA and systemic lupus erythematosus (SLE), structured rehabilitation can reduce flare frequency and improve the feasibility of steroid tapering. Likewise, pulmonary rehabilitation improves asthma control and may reduce the need for systemic steroid bursts, reinforcing the value of integrated lifestyle and supportive-care interventions.

Clinical Framework for Steroid Tapering Using Integrative Care

A clinical framework for steroid tapering using integrative care follows a stepwise model designed to maintain disease control while safely reducing corticosteroid exposure. First, stabilize the underlying condition using standard-of-care therapy. Once clinical stability is achieved, introduce an evidence-based integrative modality as an adjunct (selected to match the patient's diagnosis, risk profile, and preferences). Throughout the process, closely monitor objective inflammatory activity using validated markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and when relevant, fecal calprotectin to detect subclinical relapse early [17]. Steroids are then tapered gradually, typically by reducing the dose by 5–10% every 2–4 weeks, with the pace individualized based on symptom control, biomarker trends, and prior flare history. Concurrently, assess for adrenal insufficiency, especially with long-term use, by watching for suggestive symptoms and using appropriate clinical evaluation when indicated. If inflammation worsens or withdrawal symptoms emerge, adjust the taper schedule and refine integrative components to support disease stability. Effective implementation requires multidisciplinary collaboration (e.g., physicians, pharmacists, nurses, dietitians, and integrative practitioners) to ensure coordinated monitoring, patient education, and timely treatment adjustments [18].

Challenges & Barriers

Key barriers to advancing integrative, steroid-sparing therapies include the lack of large, multicenter randomized controlled trials, substantial variability in herbal preparations (dose, purity, and bioactive composition), and regulatory gaps that limit quality assurance and pharmacovigilance. Uptake is further constrained by skepticism among conventional clinicians, often driven by inconsistent evidence and safety concerns, alongside limited insurance coverage that reduces patient access and continuity of care. Future directions should prioritize systems-biology frameworks that capture multi-pathway effects, integrating microbiome and metabolomics data to link interventions with mechanistic and clinical outcomes. Epigenetic profiling can help identify responder signatures

and clarify long-term immunometabolic impacts, enabling more personalized integrative protocols tailored to patient phenotypes and risk profiles. Trials should incorporate clearly defined, standardized outcome measures and clinically meaningful steroid-sparing endpoints (e.g., cumulative steroid dose reduction, flare rates, and adverse-event profiles) to improve comparability and translation into practice [19]. Ethical and global health considerations are central: in low- and middle-income countries where biologics are frequently unaffordable, culturally adapted integrative approaches may offer more accessible adjunct options [20]. Nonetheless, implementation must remain evidence-based, with robust safety monitoring, product standardization, and equitable governance to protect patients and avoid widening health disparities.

CONCLUSION

In conclusion, integrative steroid-sparing strategies remain promising but under-validated adjuncts, constrained by sparse multicenter RCT evidence, heterogeneity in herbal product quality, and weak regulatory oversight. These limitations fuel clinician skepticism, complicate pharmacovigilance, and, together with limited insurance coverage, restrict equitable access and sustained use. The next phase of the field should shift from single-target claims to mechanism-informed, clinically anchored evaluation using systems-biology designs that combine microbiome–metabolomics readouts with epigenetic and immunometabolic profiling. Such integration can clarify causal pathways, improve safety stratification, and identify responder phenotypes, enabling personalized, culturally appropriate protocols. Critically, future trials must adopt standardized outcomes and pragmatic, patient-relevant steroid-sparing endpoints (dose reduction, flare control, and adverse-event burden) to support comparability, guideline uptake, and real-world implementation. In LMIC contexts where biologics are often unaffordable, evidence-based integrative approaches could expand therapeutic options, but only if coupled with rigorous standardization, active safety monitoring, and ethical governance that prioritizes patient protection and health equity.

REFERENCES

1. Boers, M.: Viewpoint: Glucocorticoids in the treatment of rheumatoid arthritis: points to (re)consider. Rheumatol. Oxf. Engl. 62, 3534–3537 (2023). https://doi.org/10.1093/rheumatology/kead309
2. Margaret L M, Shernan G H, Armin R, Todd E D, Claudio G B, John E W, et al (2018). Validation of minnesota acute GVHD risk score and identification of new factors associated with initial response to steroids: not all GVHD is created equal. Blood, 132, 67, https://doi.org/10.1182/blood-2018-99-113085
3. Exogenous (iatrogenic) Cushing syndrome: Most frequent uses of glucocorticoids and outcomes, including recommendations for recovery (postchemotherapy, asthma treatments, chronic use on rheumatoid, and/or skeletal disorders). In: Cushing Syndrome. pp. 65–103. Elsevier (2026)
4. Celalettin U, Jacqueline B, Debra A M, Eris T, Marisa M, Armin R, et al (2020). Necessity for treatment of steroid refractory severe GIT GVHD: patience of providers. *Bone marrow transplantation*, *55*, *(4)*, *833-835*.
5. Hofbauer, L.C., Compston, J.E., Saag, K.G., Rauner, M., Tsourdi, E.: Glucocorticoid-induced osteoporosis: novel concepts and clinical implications. Lancet Diabetes Endocrinol. 13, 964–979 (2025). https://doi.org/10.1016/S2213-8587(25)00251-7
6. Mao, X., Wu, S., Huang, D., Li, C.: Complications and comorbidities associated with antineoplastic chemotherapy: Rethinking drug design and delivery for anticancer therapy. Acta Pharm. Sin. B. 14, 2901–2926 (2024). https://doi.org/10.1016/j.apsb.2024.03.006
7. Shernan G H, Ashraf S, Armin R, Brian C B, Margaret L M, Celalettin U, et al (2019). RNA Sequencing of Intestinal Biopsies Expands the T Cell-Centric Paradigm of Steroid-Refractory Acute Graft-Versus-Host Disease. *Biology of Blood and Marrow Transplantation*, *25*, *(3)*, *S295*.
8. Xu Lou, I., Zhou, H., Wan, H.: The critical role of Th17 cells and IL-17A in autoimmune and inflammation-associated neurological diseases: mechanisms and therapeutic perspectives. Front. Immunol. 16, (2025). https://doi.org/10.3389/fimmu.2025.1656422
9. Margaret L M, Shernan G H, Armin R, Todd E D, Bruce B, Daniel J W (2017). Pediatric Acute GVHD Grade, Risk Prediction and Response to Upfront Steroids in 370 Children Treated at the University of Minnesota. *Blood*, *130*, *4486*. https://doi.org/10.1182/blood.V130.Suppl_1.4486.4486
10. Garaci, E., Russo, M.A., Pariano, M., Puccetti, M., Fabi, C., Balucchi, S., et al: Innovative Approaches to Medical Rehabilitation: Regeneration, Immune Training, Homeostasis, and Microbiome Synergy. Int. J. Mol. Sci. 26, (2025). https://doi.org/10.3390/ijms26178687
11. Dantzer, R., Cohen, S., Russo, S.J., Dinan, T.G.: Resilience and immunity. Brain. Behav. Immun. 74, 28–42 (2018). https://doi.org/10.1016/j.bbi.2018.08.010
12. Alum, E. U., Ibiam, U. A. and Ugwu, O. P. C. A Comprehensive Review of Treatment Approaches and Perspectives for Management of Rheumatoid Arthritis. *INOSR Scientific Research*. 2023; 10(1):12-17. https://doi.org/10.59298/INOSRSR/2023/2.2.13322

13. Li, N., Guo, Y., Gong, Y., Zhang, Y., Fan, W., Yao, K., et al: The Anti-Inflammatory Actions and Mechanisms of Acupuncture from Acupoint to Target Organs via Neuro-Immune Regulation. J. Inflamm. Res. 14, 7191–7224 (2021). https://doi.org/10.2147/JIR.S341581
14. Wang, D., Wang, Q., Wang, Y., Li, T., Tian, M.: Effects of acupuncture and moxibustion on ulcerative colitis: An overview of systematic reviews. Heliyon. 10, e27524 (2024). https://doi.org/10.1016/j.heliyon.2024.e27524
15. Hamid A.A, Kaushal T., Ashraf R., Singh A, Gupta A. C, Prakash O. M, et al (2017). (22β, 25R)-3β-Hydroxy-spirost-5-en-7-iminoxy-heptanoic acid exhibits anti-prostate cancer activity through caspase pathway. *Steroids 119, 43-52*. https://doi.org/10.1016/j.steroids.2017.01.001
16. Gioia, C., Lucchino, B., Tarsitano, M.G., Iannuccelli, C., Di Franco, M.: Dietary Habits and Nutrition in Rheumatoid Arthritis: Can Diet Influence Disease Development and Clinical Manifestations? Nutrients. 12, 1456 (2020). https://doi.org/10.3390/nu12051456
17. Swaminathan, L., Kaatz, S., Chubb, H., Tae, K., Ramesh, M.S., Fadel, R., et al: Impact of Early Corticosteroids on Preventing Clinical Deterioration in Non-critically Ill Patients Hospitalized with COVID-19: A Multi-hospital Cohort Study. Infect. Dis. Ther. 11, 887–898 (2022). https://doi.org/10.1007/s40121-022-00615-x
18. Hamid A A, Mohammad H, Arjun S, Balakishan B, Prema G V, Jayanta S, et al (2014). Synthesis of novel anticancer agents through opening of spiroacetal ring of diosgenin. Steroids, 87, 108-118. https://doi.org/10.1016/j.steroids.2014.05.025
19. Son, J.W., Shoaie, S., Lee, S.: Systems Biology: A Multi-Omics Integration Approach to Metabolism and the Microbiome. Endocrinol. Metab. 35, 507–514 (2020). https://doi.org/10.3803/EnM.2020.303
20. Ekpang II, J. E., Ekpang, P. O., Ainebyoona, C., Nwagu, K. E., Nwuruku, O. A., & Muhammad, K. (2025). Toward an ethical future for orphan drugs: balancing access, affordability, and innovation. *Journal of Medical Economics*, *28*(1), 1869–1886. https://doi.org/10.1080/13696998.2025.2577514

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