www.idosr.org Nyambura

©IDOSR PUBLICATIONS

ISSN: 2579-079X

International Digital Organization for Scientific Research IDOSR JST/26/1130000
IDOSR JOURNAL OF SCIENCE AND TECHNOLOGY 12(1):93-97, 2026.
https://doi.org/10.59298/IDOSR/JST/26/113.9397

Phytochemical Antioxidants in Immune System Regulation: Mechanistic Insights and Translational Potential

Nyambura Achieng M.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Phytochemical antioxidants, encompassing diverse plant-derived molecules such as polyphenols, carotenoids, organosulfur compounds, and certain alkaloids, represent a crucial interface between diet and immune system regulation. While their early recognition centered on the ability to neutralize reactive oxygen species (ROS), contemporary evidence highlights far broader immunological roles. These compounds modulate redox-sensitive transcription factors such as Nrf2, enhance endogenous antioxidant defense, and suppress pro-inflammatory programs mediated by NF-κB. They further influence MAPK and JAK-STAT pathways, restrict inflammasome activation, and engage in bidirectional interactions with the gut microbiota, ultimately shaping both innate and adaptive immune responses. Preclinical data provide consistent mechanistic insights, demonstrating that compounds such as resveratrol, curcumin, quercetin, epigallocatechin gallate (EGCG), and lutein regulate cytokine production, macrophage polarization, and T cell differentiation. However, translating these findings into consistent clinical outcomes remains challenging due to low bioavailability, variable dosing regimens, pleiotropic biological effects, and heterogeneous clinical trial designs. This review therefore synthesizes mechanistic evidence, critically evaluates clinical data, and addresses pharmacokinetic, formulation, and safety considerations. It further outlines research priorities aimed at bridging laboratory discoveries with therapeutic applications, emphasizing the translational potential of phytochemical antioxidants as adjuncts in immune modulation and disease prevention.

Keywords: Phytochemical antioxidants, Immune regulation, Redox signaling, NF-κB and Nrf2 pathways, Translational potential

INTRODUCTION

Plants produce a staggering diversity of secondary metabolites that humans have ingested for millennia. A substantial subset commonly called phytochemical antioxidants includes flavonoids (quercetin, catechins), stilbenes (resveratrol), diarylheptanoids (curcumin), carotenoids (β-carotene, lutein), organosulfur compounds (allicin derivatives), and other phenolics [1]. Historically these compounds were studied for their ability to neutralize ROS; more recently they are recognized as modulators of redox-sensitive signaling and immune cell behavior [2]. Interest surged with emerging understandings that controlled redox signaling governs immune activation, resolution, and tissue repair, and that dysregulated oxidative/inflammatory crosstalk contributes to chronic inflammatory, infectious, and autoimmune diseases [3]. Contemporary work links phytochemicals to specific molecular switches (e.g., Nrf2 activation, NF-κB inhibition) and to clinically relevant endpoints-though translating bench findings into consistent clinical benefit remains a challenge [4].

2. Major classes of phytochemical antioxidants and immune-relevant activities

2.1 Polyphenols (flavonoids, stilbenes, phenolic acids)

Polyphenols constitute the most intensively investigated class of dietary antioxidants. Structurally diverse, they include flavonoids such as quercetin, catechins like epigallocatechin gallate (EGCG), stilbenes such as resveratrol, and a wide range of phenolic acids [5]. These compounds not only scavenge free radicals but also regulate key immune signaling pathways. Quercetin has been shown to downregulate pro-inflammatory cytokines, while EGCG interferes with T cell activation and macrophage function [6]. Resveratrol, through modulation of sirtuin and NF-κB pathways, exerts both anti-inflammatory and immunometabolic effects [7]. Animal models demonstrate that polyphenols can reduce leukocyte infiltration into inflamed tissues, lower oxidative burden, and promote resolution mediators such as specialized pro-resolving lipid derivatives [8]. The cumulative evidence positions polyphenols as

modulators of innate and adaptive responses, capable of both suppressing excessive inflammation and supporting immune resilience.

2.2 Curcuminoids

Curcumin, derived from turmeric, is a prominent phytochemical studied for its dual antioxidant and anti-inflammatory activities. Its molecular actions include suppression of NF-κB, inhibition of the NLRP3 inflammasome, and modulation of JAK/STAT and MAPK pathways [9]. These effects translate into reduced production of pro-inflammatory mediators, protection against oxidative injury, and reprogramming of macrophage polarization from M1 (pro-inflammatory) to M2 (repair-oriented) [9]. Curcumin also exerts neuroimmune effects by reducing microglial activation, suggesting utility in neuroinflammatory disorders [10]. Despite challenges with bioavailability, novel formulations-such as nanoparticles and adjuvant combinations-have enhanced its clinical potential.

2.3 Carotenoids

Carotenoids, including β-carotene, lutein, and lycopene, are lipid-soluble antioxidants that accumulate in membranes and protect against oxidative lipid damage. Their immunological functions extend to stabilizing cell membranes, supporting epithelial barrier integrity, and modulating phagocyte signaling [11]. Lutein, for example, has been associated with improved mucosal immunity, while lycopene reduces oxidative stress–induced cytokine production [12]. Carotenoids also influence adaptive immunity by affecting lymphocyte proliferation and antibody responses [12]. Given their photoprotective role, carotenoids further contribute to immune defense at barrier sites such as the skin and eye [13].

2.4 Organosulfur compounds and others

Sulfur-containing phytochemicals, notably allicin and related compounds from garlic, as well as glucosinolate derivatives from cruciferous vegetables, provide additional immunoregulatory benefits [14]. These compounds can enhance phagocytic efficiency, stimulate natural killer (NK) cell cytotoxicity, and modulate cytokine secretion. Studies in vitro and in vivo suggest that organosulfur compounds act as both antioxidants and mild electrophiles, triggering adaptive stress responses that bolster immune resilience [15]. Together, these lesser-studied phytochemicals expand the repertoire of natural immunomodulators with translational promise.

3. Molecular mechanisms linking antioxidant phytochemicals to immune regulation

3.1 Direct ROS scavenging and redox buffering

Many phytochemicals directly neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS), thereby preventing oxidative damage to DNA, proteins, and lipids [16]. However, due to limited bioavailability and low tissue concentrations, this direct scavenging contributes only partially to their in vivo efficacy. Their more significant impact arises from modulation of redox-sensitive signaling pathways that shape immune cell function.

3.2 Activation of Nrf2-dependent cytoprotective programs

Nrf2 is a transcription factor central to antioxidant defense. Phytochemicals such as resveratrol, EGCG, and curcumin activate Nrf2 by modifying Keap1 or engaging upstream kinases, releasing Nrf2 to drive the expression of genes like HO-1 and NQO1 [17]. This enhances endogenous antioxidant systems, reduces oxidative stress in immune cells, and indirectly restrains inflammatory signaling cascades. By fortifying epithelial and immune cell resilience, Nrf2 activation contributes to balanced immune responses [18,19].

3.3 Inhibition of NF-κB and downstream inflammatory gene programs

NF-κB controls transcription of numerous pro-inflammatory mediators, including TNF-α, IL-1β, and IL-6 [20]. Polyphenols and curcumin suppress NF-κB activation by blocking IκB degradation, inhibiting upstream kinases, or reducing ROS-mediated signaling [21]. This leads to attenuation of cytokine storms in models of infection and inflammatory disease. Such inhibition is pivotal in restoring homeostasis during dysregulated immune activation.

3.4 Modulation of inflammasomes (NLRP3) and pyroptosis

The NLRP3 inflammasome drives IL-1β and IL-18 release, amplifying inflammation and pyroptotic cell death [22]. Curcumin, quercetin, and resveratrol inhibit NLRP3 priming and assembly through suppression of mitochondrial ROS and NF-κB activity [23]. By limiting inflammasome-driven pathology, phytochemicals demonstrate potential for treating metabolic, autoimmune, and neuroinflammatory disorders.

3.5 Effects on MAPK, JAK-STAT, and other kinases

Phytochemicals exert broad influence on kinase signaling networks. By dampening MAPK pathways (ERK, JNK, p38) and JAK-STAT cascades, they reduce immune cell proliferation and cytokine responsiveness [24]. These changes alter T helper cell balance, suppress pro-inflammatory Th1/Th17 subsets, and promote regulatory T cell phenotypes, shifting immunity toward resolution and tolerance [25].

3.6 Epigenetic and metabolic reprogramming

Beyond classical signaling, phytochemicals influence epigenetic mechanisms including histone acetylation, DNA methylation, and microRNA regulation. These changes reshape immune transcriptional programs, enabling long-

term modulation of cell function [26]. Additionally, many compounds alter immune cell metabolism, favoring oxidative phosphorylation over glycolysis, a shift associated with anti-inflammatory states [27].

3.7 Interaction with gut microbiota and barrier function

A growing body of evidence highlights the role of the gut microbiome in mediating phytochemical effects. Many polyphenols are metabolized by gut bacteria into bioactive phenolic acids and urolithins that exert systemic immunoregulatory actions [28]. Conversely, phytochemicals promote beneficial microbial taxa, enhance gut barrier integrity, and reduce systemic inflammation by limiting microbial translocation [29]. This bidirectional relationship underscores the importance of diet–microbiota–immune interactions in shaping clinical outcomes.

4. Immune cell–level effects: innate and adaptive immune systems

4.1 Macrophages and neutrophils

Macrophages and neutrophils serve as first-line defenders against infection, yet their excessive activation fuels tissue injury [30]. Phytochemicals regulate this balance by suppressing pro-inflammatory cytokines such as TNF-α and IL-6 while enhancing anti-inflammatory mediators like IL-10 [31]. Polyphenols and curcumin promote a shift from M1 (inflammatory) to M2 (repair-oriented) macrophage phenotypes, facilitating tissue healing [32]. In neutrophils, compounds such as quercetin and EGCG dampen excessive oxidative bursts, thereby limiting collateral tissue damage, while maintaining phagocytic efficiency and resolution functions [33].

4.2 Dendritic cells (DCs)

DCs link innate and adaptive immunity through antigen presentation. Several phytochemicals impair over-maturation of DCs by downregulating costimulatory molecules (CD80, CD86) and pro-inflammatory cytokines (IL-12, IL-23) [34]. This reduces inappropriate T cell priming during inflammatory states, contributing to tolerance and resolution without abolishing necessary immune surveillance.

4.3 T lymphocytes

T cell responses are profoundly influenced by phytochemicals. Flavonoids and carotenoids can blunt hyperactive Th1 and Th17 responses while enhancing regulatory T cell (Treg) activity [35]. Additionally, phytochemicals affect T cell metabolism, promoting oxidative phosphorylation over glycolysis, a shift associated with controlled immune activation [36]. These effects are particularly relevant in autoimmune and chronic inflammatory diseases.

4.4 B cells and antibody responses

Phytochemicals show dual actions on B cells. In some contexts, they enhance antibody production and improve vaccine responsiveness, highlighting adjuvant potential [37]. Conversely, in autoimmunity, they may reduce pathogenic antibody generation by modulating B cell proliferation and differentiation [38]. Outcomes are highly dependent on compound type, dose, and disease state.

4.5 Natural killer (NK) cells

NK cells are crucial for antiviral and antitumor immunity. Moderate doses of phytochemicals, including resveratrol and carotenoids, enhance NK cytotoxicity and interferon-γ production [39]. This immunostimulatory effect suggests potential applications in cancer prevention and viral infections, while avoiding overstimulation that could provoke immunopathology.

CONCLUSIONS

Phytochemical antioxidants are far more than passive ROS scavengers: they engage conserved redox-sensitive pathways (Nrf2, NF-κB), inflammasomes, kinase networks, and the gut microbiome to reprogram immune responses. Preclinical mechanistic data are compelling, and selected clinical results suggest potential benefit in defined contexts. However, inconsistent clinical outcomes reflect bioavailability constraints, heterogenous formulations, and insufficiently rigorous trials. Addressing these gaps-through standardized preparations, PK-PD mapping, and targeted RCTs-will determine whether phytochemical antioxidants can be reliably harnessed as immunomodulatory therapeutics or adjuvants.

REFERENCES

1. Ochulor Okechukwu C., Njoku Obioma U., Uroko Robert I and Egba Simeon I. Nutritional composition of *Jatropha tanjorensis* leaves and effects of its aqueous extract on carbon tetrachloride induced oxidative stress in male Wistar albino rats. Biomedical Research 2018; 29(19): 3569-3576
2. Agu, P. C., Christopher, N. N., Nwiziogo, F. C., Okafor, M. U., *et al.* (2025). Historical and ethnopharmacological perspectives on African medicinal plants: From traditional remedies to computational drug discovery. *Scientific African*, *30*, e02941. https://doi.org/10.1016/j.sciaf.2025.e02941
3. Bellanti F, Coda ARD, Trecca MI, Lo Buglio A, Serviddio G, Vendemiale G. Redox imbalance in inflammation: the interplay of oxidative and reductive stress. Antioxidants. 2025;14(6):656. doi:10.3390/antiox14060656
4. Uhuo E N, Egba S I, Nwuke P C, Obike C A and Kelechi G K. Antioxidative properties of Adansonia digitata L. (baobab) leaf extractexert protective effect on doxorubicin induced cardiac toxicity in Wistar rats. Clinical Nutrition Open Science 2022; 45:3-16

5. Alum, E.U. Unlocking the Secrets of Nature: Phytochemicals as Key Players in Longevity and Healthy Aging. *Cell Biochem Biophys* (2025). https://doi.org/10.1007/s12013-025-01872-6
6. Cialdella-Kam L, Ghosh S, Meaney M, Knab A, Shanely R, Nieman D. Quercetin and green tea extract supplementation downregulates genes related to tissue inflammatory responses to a 12-Week high Fat-Diet in mice. Nutrients. 2017;9(7):773. doi:10.3390/nu9070773
7. Ma C, Wang Y, Dong L, Li M, Cai W. Anti-inflammatory effect of resveratrol through the suppression of NF-κB and JAK/STAT signaling pathways. Acta Biochimica Et Biophysica Sinica. 2015;47(3):207–13. doi:10.1093/abbs/gmu135
8. Singh A, Yau YF, Leung KS, El-Nezami H, Lee JCY. Interaction of polyphenols as antioxidant and Anti-Inflammatory compounds in Brain–Liver–Gut axis. Antioxidants. 2020;9(8):669. doi:10.3390/antiox9080669
9. Kunnumakkara AB, Hegde M, Parama D, Girisa S, Kumar A, Daimary UD, et al. Role of Turmeric and Curcumin in Prevention and Treatment of Chronic Diseases: Lessons Learned from Clinical Trials. ACS Pharmacology & Translational Science. 2023;6(4):447–518. doi:10.1021/acsptsci.2c00012
10. Yu Y, Shen Q, Lai Y, Park SY, Ou X, Lin D, et al. Anti-inflammatory effects of curcumin in microglial cells. Frontiers in Pharmacology. 2018;9. doi:10.3389/fphar.2018.00386
11. Syed, A., Elgorban, A.M., Bahkali, A.H. *et al.* Therapeutic Potential of products derived from *Pluchea lanceolata* for Alzheimer's Disease Treatment. *J Mol Neurosci* **75**, 122 (2025). https://doi.org/10.1007/s12031-025-02409-5
12. Ugwu, CE., Sure, SM., Dike, CC., Okpoga, NA and Egba, SI. Phytochemical and *in vitro* antioxidant activities of methanol leave extract of *Alternanthera basiliana*. Journal of Pharmacy Research, 2018; 12(6): 835-839
13. Aja PM, Uti DE, Egba SI, Ugwu OP-C. The Role of Phytochemicals in Age-Related Cognitive Decline: A Natural Solution for Brain Health. *Natural Product Communications*. 2025;20(6). doi:10.1177/1934578X251350761
14. Alum, E. U. (2024). Climate change and its impact on the bioactive compound profile of medicinal plants: implications for global health. *Plant Signaling & Behavior*, *19*(1), 2419683. doi: 10.1080/15592324.2024.2419683. Epub 2024 Oct 26. PMID: 39460932; PMCID: PMC11520564.
15. Miękus N, Marszałek K, Podlacha M, Iqbal A, Puchalski C, Świergiel AH. Health benefits of Plant-Derived sulfur compounds, glucosinolates, and organosulfur compounds. Molecules. 2020;25(17):3804. doi:10.3390/molecules25173804
16. Grudzien M, Rapak A. Effect of natural compounds on NK cell activation. Journal of Immunology Research. 2018;2018:1–11. doi:10.1155/2018/4868417
17. Uroko Robert Ikechukwu., Agbafor Amarachi, Uchenna Oluomachi Nancy, Achi Ngozi Kalu, Egba Simeon Ikechukwu**,** Nweje-Anyalowu Paul Chukwuemaka and Ngwu Ogochukwu Rita. Evaluation of Antioxidant Activity of Aqueous Extracts of Palm Friuts *(Elaeis guineensis)* Asian Journal of Biochemistry, 2017; 12: 49-57
18. Yu C, Xiao JH. The Keap1-Nrf2 System: A Mediator between Oxidative Stress and Aging. Oxidative Medicine and Cellular Longevity. 2021;2021(1). doi:10.1155/2021/6635460
19. Kim JY, Surh YJ. The role of NRF2 in cellular innate immune response to inflammatory injury. Toxicological Research. 2009;25(4):159–73. doi:10.5487/tr.2009.25.4.159
20. Liu T, Zhang L, Joo D, Sun SC. NF-κB signaling in inflammation. Signal Transduction and Targeted Therapy. 2017;2(1). doi:10.1038/sigtrans.2017.23
21. Liu M, Wang J, Song Z, Pei Y. Regulation mechanism of curcumin mediated inflammatory pathway and its clinical application: a review. Frontiers in Pharmacology. 2025;16. doi:10.3389/fphar.2025.1642248
22. Huang Y, Xu W, Zhou R. NLRP3 inflammasome activation and cell death. Cellular and Molecular Immunology. 2021;18(9):2114–27. doi:10.1038/s41423-021-00740-6
23. Tőzsér J, Benkő S. Natural compounds as regulators of NLRP3 Inflammasome-Mediated IL-1B Production. Mediators of Inflammation. 2016;2016:1–16. doi:10.1155/2016/5460302
24. Nisar A, Jagtap S, Vyavahare S, Deshpande M, Harsulkar A, Ranjekar P, et al. Phytochemicals in the treatment of inflammation-associated diseases: the journey from preclinical trials to clinical practice. Frontiers in Pharmacology. 2023;14. doi:10.3389/fphar.2023.1177050
25. Mo C, Zeng Z, Deng Q, Ding Y, Xiao R. Imbalance between T helper 17 and regulatory T cell subsets plays a significant role in the pathogenesis of systemic sclerosis. Biomedicine & Pharmacotherapy. 2018;108:177–83. doi:10.1016/j.biopha.2018.09.037
26. Ogugua, Victor N., Njoku, Obioma U., Egba, Simeon I., Uroko, Robert I and Ignatius Glory. In vitro study of nutritional and antioxidant properties of methanol extract of *Nauclea latifolia* root bark. Biomedical Research, 2018; 29(21): 3766-3773
27. Shanley LC, Fitzgerald HK, O'Rourke SA, Dunne A. Endogenous drivers of altered immune cell metabolism. Experimental Biology and Medicine. 2022;247(24):2192–200. doi:10.1177/15353702221134093

28. Alum, E.U., Uti, D.E., Ugwu, O.PC., Alum, B. N., Edeh, O.F., Ainbeyoona, C. Unveiling the microbial orchestra: exploring the role of microbiota in cancer development and treatment. *Discov Onc* **16**, 646 (2025). https://doi.org/10.1007/s12672-025-02352-2
29. Kim Y, Lim J, Oh J. Taming neuroinflammation in Alzheimer's disease: The protective role of phytochemicals through the gut–brain axis. Biomedicine & Pharmacotherapy. 2024;178:117277. doi:10.1016/j.biopha.2024.117277
30. Su Y, Gao J, Kaur P, Wang Z. Neutrophils and macrophages as targets for development of nanotherapeutics in inflammatory diseases. Pharmaceutics. 2020;12(12):1222. doi:10.3390/pharmaceutics12121222
31. Akwari, A.A., Okoroh, P.N., Aniokete, U.C., Abba, J.N., Uti, D.E. Phytochemicals as modulators of ferroptosis: a novel therapeutic avenue in cancer and neurodegeneration. *Mol Biol Rep* **52**, 636 (2025). https://doi.org/10.1007/s11033-025-10752-4
32. Deng T, Xu J, Wang Q, Wang X, Jiao Y, Cao X, et al. Immunomodulatory effects of curcumin on macrophage polarization in rheumatoid arthritis. Frontiers in Pharmacology. 2024;15. doi:10.3389/fphar.2024.1369337
33. Pečivová J, Mačičková T, Sviteková K, Nosáľ R. Quercetin inhibits degranulation and superoxide generation in PMA stimulated neutrophils. Interdisciplinary Toxicology. 2012;5(2):81–3. doi:10.2478/v10102-012-0014-5
34. Fujii SI, Liu K, Smith C, Bonito AJ, Steinman RM. The linkage of innate to adaptive immunity via maturing dendritic cells in vivo requires CD40 ligation in addition to antigen presentation and CD80/86 costimulation. The Journal of Experimental Medicine. 2004;199(12):1607–18. doi:10.1084/jem.20040317
35. Kelepouri D, Mavropoulos A, Bogdanos DP, Sakkas LI. The role of flavonoids in inhibiting TH17 responses in inflammatory arthritis. Journal of Immunology Research. 2018;2018:1–11. doi:10.1155/2018/9324357
36. Geltink RIK, Kyle RL, Pearce EL. Unraveling the complex interplay between T cell metabolism and function. Annual Review of Immunology. 2018;36(1):461–88. doi:10.1146/annurev-immunol-042617-053019
37. Facciolà A, Visalli G, Laganà A, Di Pietro A. An Overview of vaccine adjuvants: Current evidence and future perspectives. Vaccines. 2022;10(5):819. doi:10.3390/vaccines10050819
38. Behl T, Kumar K, Brisc C, Rus M, Nistor-Cseppento DC, Bustea C, et al. Exploring the multifocal role of phytochemicals as immunomodulators. Biomedicine & Pharmacotherapy. 2020;133:110959. doi:10.1016/j.biopha.2020.110959
39. Waggoner SN, Reighard SD, Gyurova IE, Cranert SA, Mahl SE, Karmele EP, et al. Roles of natural killer cells in antiviral immunity. Current Opinion in Virology. 2015;16:15–23. doi:10.1016/j.coviro.2015.10.008

CITE AS: Nyambura Achieng M. (2026). Phytochemical Antioxidants in Immune System Regulation: Mechanistic Insights and Translational Potential. IDOSR JOURNAL OF SCIENCE AND TECHNOLOGY 12(1):93-97. https://doi.org/10.59298/IDOSR/JST/26/113.9397