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Review Article

Critically Analysing Plant-based Bioactives as Anti-inflammatory Agents: A molecular Phytopharmacology Perspective Coupled with Bibliometric Data

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Abstract
This study presents a critical, mechanistic, and bibliometric analysis of plant-derived bioactive compounds for the treatment of inflammation. From a molecular phytopharmacological perspective, this review critically examines the anti-inflammatory potential of key phytochemical classes, including polyphenols, alkaloids, glycosides, tannins, and essential oils, highlighting their ability to modulate cytokines and signalling pathways such as NF-κB, MAPK, and COX/LOX. Using the Scopus database (2020–2024); 17,129 publications were evaluated to identify global research trends, co-authorship networks, and journal participation. China and India demonstrated the highest research output, while Portugal, Turkey, and Italy showed notable international collaboration and influence. A preference for open-access publishing was also observed, enhancing visibility and citation impact. Integrating bibliometric and mechanistic insights, the analysis underscores a growing shift toward evidence-based and integrative approaches in phytochemical research. Overall, plant bioactives represent a promising, multi-targeted strategy for developing safer anti-inflammatory therapeutics.

Keywords: anti-inflammatory activity, bibliometric analysis, medicinal plant, NF-κβ, polyphenol

1. INTRODUCTION

According to the World Health Organization, inflammation is a complex biological response of the immune system to infectious agents, damaged cells, or pollutants. It is a natural defensive mechanism that can assist the body in getting rid of dangerous substances, repairing damaged tissue, and starting the healing process. Infections, wounds, exposure to toxins etc. can cause inflammation [1]. Key chemical mediators of inflammation include cytokines such as tumor necrosis factor-α (TNF-α), interleukins (IL; mainly including IL-1β, IL-6, IL-1), prostaglandins (PGs), histamine, and nitric oxide (NO) [2]. There are two types of inflammation: acute and chronic. Acute inflammation is localized and short-lived, but chronic inflammation is broad and long-lasting. Acute inflammation is beneficial, while chronic inflammation is linked to several disease pathologies, including cancer, cardiovascular disorders, and arthritis [3].

Bioactive substances naturally present in plants, known as phytochemicals, play a key role in regulating inflammatory pathways. Phytochemicals are classified into various categories, including phenolic, flavonoid, alkaloid, glycoside, and tannin [4]. These compounds have anti-inflammatory activities by inhibiting proinflammatory cytokines, downregulating nuclear factor kappa β activation (NF-κB), suppressing key inflammatory enzymes such as cyclooxygenase (COX), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS), and modulating intracellular signalling pathways such as mitogen-activated protein kinases (MAPK) [5] and Janus kinase/signal transducers and activators of transcription (JAK/STAT) [6]. The development of novel anti-inflammatory drugs is drawn to phytochemicals because of their great diversity and relative safety. Numerous experimental studies have shown that diets enriched with plant-based foods are linked to a lower risk of developing chronic inflammatory illnesses. Additionally, phytochemicals have multi-targeted actions and synergistic effects when used in combination, which increases their therapeutic activity. Some have advanced to clinical trials, where they have demonstrated favorable results in inflammatory disorders while presenting fewer side

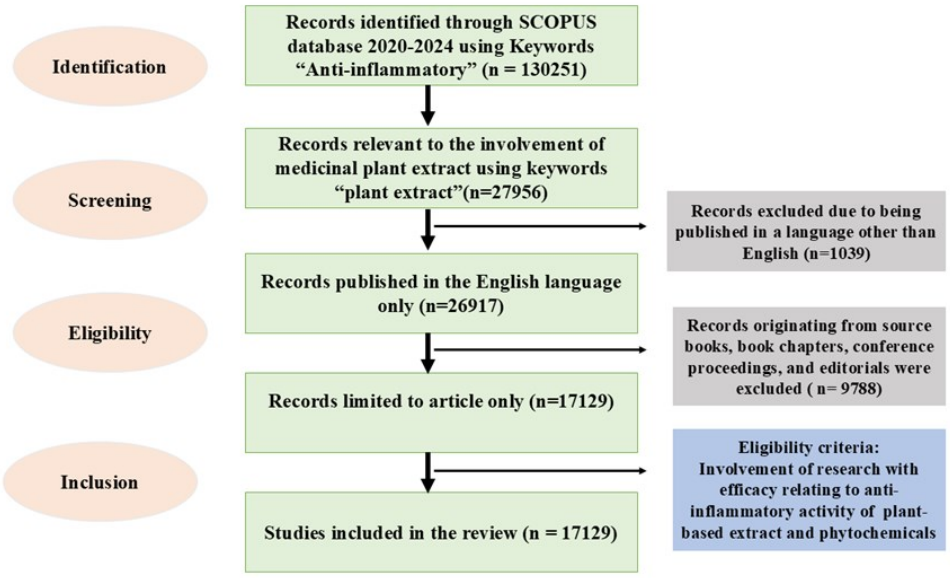


Figure 1. Details of data mining from the Scopus database (2020–2024).

effects than standard therapies [7].

Several review articles have been published highlighting the role of various classes of bioactives and medicinal plants in combating inflammation. Such review articles have basically focused on the pre-clinical findings associated with plant extracts, enriched fractions, and isolated pure bioactives. With the growing popularity of plant-based products, the mechanism must be well elucidated for such plant-based entities. In this regard, this article is the first of its kind where an elaborate, vivid description of the mechanistic pathways involved and the possible intervening points are presented on one roof. This article also presents a comprehensive package on the work done so far (2020–2024) in combating inflammation using plant-based bioactives, including plant extracts. This comprehensive package has been divided into two parts. In the first part, a vivid cellular mechanism has been presented for a deeper understanding of the complex cascadic pathways involved in inflammation and the possible interventions in which various classes of bioactives can provide. The second part presents a research landscape through bibliometric analysis to unveil the current research landscape in terms of identifying active research groups, countries, and journals involved. Such strategic identification shall help young and less experienced researchers to adopt a proactive approach in their research and look to strengthen their research linkages and networking.

2. DATA MINING

The Scopus database was searched using the parameters shown in Figure 1 to extract the data required for analyzing research trends on the anti-inflammatory effect of medicinal plant extracts. Five years, from 2020 to 2024, were chosen for data collection. As compared to other scientific databases, Scopus data mining has several benefits, as the authors have demonstrated in their earlier works. All crude data were extracted from Scopus using the keywords "anti-inflammatory" to generate the master data pool regarding all published works on anti-inflammatory activity (n=130,251). Scopus search returned 13,0251 publication records for "anti-inflammatory," out of which 27,956 publications related to medicinal plant extract. Among 27,956 publications; 17,129 publications comprised research papers (in English language) that were considered for this review.

3. PUBLICATION TREND

The trend in the quantity of papers published between 2020 and 2024 indicates a continuous increase, indicating that interest in publishing and conducting research related to anti-inflammatory activity of phytochemicals have grown over time (Figure 2). The number of articles increased from

52% in 2020 to 2024. This noteworthy increase suggests that research output or publication activity has increased significantly. Over the past years, the application of phytochemicals for controlling inflammation has attracted significant scientific attention. The number of publications specifically about medicinal plants is generally increasing because it is believed that phytochemicals have lower toxicity profiles and fewer adverse consequences. From 3,520 articles in 2023 to 4,257 in 2024, there is a notable increase, indicating that research on medicinal plants is getting increased attention because with the rising incidence of chronic diseases linked to inflammation, including cardiovascular diseases, diabetes, cancer, and neurodegeneration, researchers are turning to plant-based bioactives and other alternative therapeutic approaches.

4. MEDIATORS OF INFLAMMATION

A variety of chemical mediators initiate, control, and eliminate the inflammatory response. During inflammation, immune cells, endothelial cells, and injured tissues release it. Below is a brief overview of the major types of inflammatory mediators.

4.1. Eicosanoid

Eicosanoids are active mediators of inflammation, produced from arachidonic acid, a key component of membrane phospholipids in all cells. They are synthesized in response to immune activation or cell damage, have a short half-life, and act locally at the site of injury. Two major enzymatic pathways, COX and LOX, catalyze the conversion of arachidonic acid into distinct lipid mediators. While COX-derived PGs and thromboxanes are primarily involved in vasodilation, vascular permeability, and pain induction, LOX-derived leukotrienes (LTs) mainly mediate leukocyte recruitment and bronchoconstriction, showing a more pronounced role in allergic and asthmatic responses. While multiple studies have established the pivotal role of COX and LOX pathways in inflammation, there remains a degree of inconsistency and evolving interpretation regarding the precise contributions of specific eicosanoids. The COX enzyme exists in two isoforms: COX-1 and COX-2. The COX-2-derived PGs are the dominant mediators of inflammatory pain and swelling, whereas COX-1 is largely protective [8].

Among different PGs (PGG2, PGH2, PGI2, PGD2, PGE2), the pro-inflammatory role of PGE2 is via upregulation of IL-1β and suppression of macrophage phagocytic activity. In contrast, evidence suggests that PGE2 can also exert anti-inflammatory or immunomodulatory effects, particularly in the resolution phase, by inhibiting excessive neutrophil infiltration and promoting tissue repair [9]. These dual effects of PGE2 reveal a complicated dynamic regulation. The findings also showed that 15d-PGJ2 suppresses iNOS and TNF-α expression, adding an important dimension to this discussion. The anti-inflammatory nature of 15d-PGJ2 contrasts with the pro-inflammatory roles of other PGs, implying that COX-derived mediators may transition from promoting to resolving

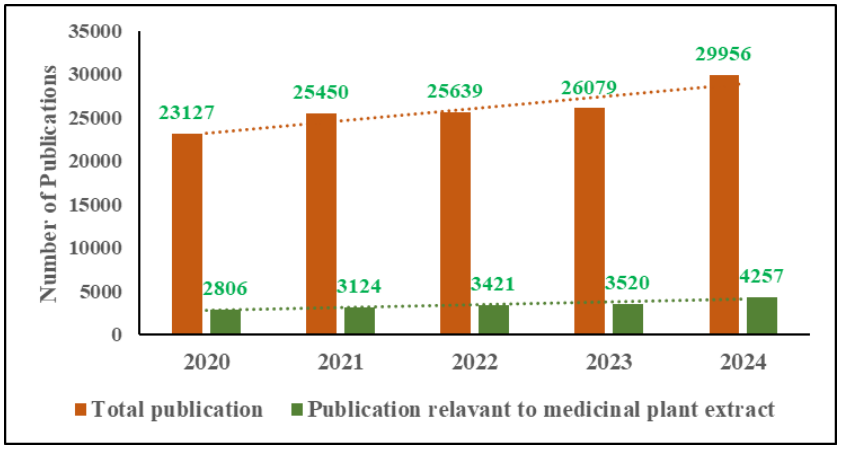


Figure 2. Total number of publications on anti-inflammatory studies of medicinal plant extract during 2020 to 2024.

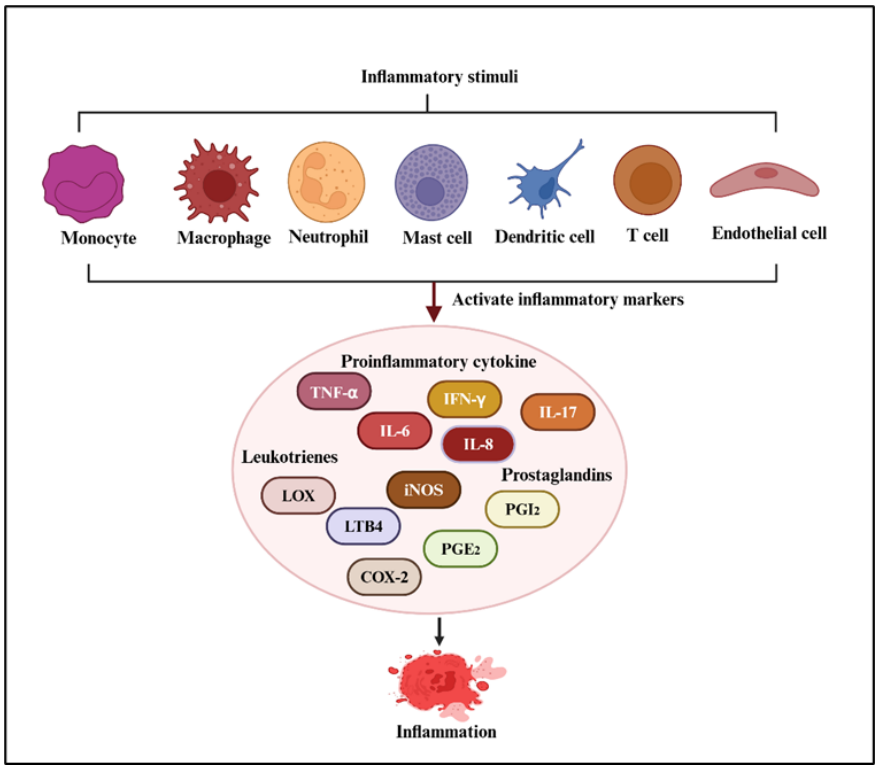


Figure 3. Inflammatory cells triggering inflammatory markers for initiating an inflammatory response.

inflammation as the tissue microenvironment changes. However, the physiological relevance of 15d-PGJ2 is still under discussion [10]. In the case of leukotrienes, [11] emphasized that elevated LTB4 levels correlate with chronic inflammatory disorders such as arthritis and diabetes. Nonetheless, some studies propose that LTB4 may also participate in host defense mechanisms, particularly in early bacterial clearance. During infection, LTB4 modulation seems to determine its pathogenic versus protective balance. Moreover, emerging data suggest cross-talk between COX and LOX pathways, where PGE2 can inhibit 5-LOX activity, further complicating the understanding of their independent versus cooperative roles. Overall, while both COX and LOX pathways are essential for initiating inflammation, their mediators differ in timing, target cells, and long-term impact. A critical balance between these pathways is vital. COX products can both promote and resolve inflammation, whereas LOX products primarily amplify and sustain inflammatory responses.

4.2. Cytokine and Chemokine

Proinflammatory cytokines such as TNF-α and ILs are widely recognized as mediators of inflammation and pathological pain [2]. Emerging evidence suggests that their roles are more complex. For instance, IL-1β is a well-established pro-inflammatory cytokine released by monocytes, macrophages, fibroblasts, and endothelial cells during infection or injury. However, studies differ regarding its extent of involvement in chronic pain, some reporting a direct role in nociceptor sensitization, while others suggest it primarily acts upstream by modulating glial activation. Similarly, IL-6 has been shown to play a central role in the neuronal response to nerve injury and is crucial in the development of neuropathic pain following peripheral nerve damage. Nevertheless, its role remains controversial, while most studies highlight its pro-inflammatory and pronociceptive functions, recent findings propose that IL-6 can also exhibit neuroprotective or anti-inflammatory properties by promoting neuronal survival and tissue repair under specific conditions [12]. This duality underscores the need to reinterpret IL-6 not merely as a pathogenic mediator but as a context-sensitive cytokine influencing both damage and recovery phases of inflammation. While TNF-α is widely recognized for promoting leukocyte adhesion and migration by upregulating adhesion molecules and chemokines [13], discrepancies exist regarding its temporal influence. Some experimental data

indicate that early TNF-α signaling is necessary for effective pathogen clearance and tissue repair, whereas sustained overproduction leads to chronic inflammation and neuropathic pain. This time-dependent dichotomy reflects a broader challenge in targeting TNF-α therapeutically, as its inhibition may relieve pain but also impair host defense. Chemokines, such as monocyte chemoattractant protein-1 (MCP-1) and IL-8, are well-established in directing immune cell chemotaxis [14]; however, recent work has revealed that certain chemokines also participate in inflammation resolution by recruiting regulatory T cells and facilitating immune cell clearance. These findings challenge the long-held notion of chemokines as purely pro-inflammatory molecules, suggesting instead that they act as dynamic regulators of both initiation and resolution phases of inflammation. Collectively, these studies reveal a growing consensus that cytokines and chemokines act not as unidirectional pro-inflammatory agents but as modulators with diverse functions.

4.3. Nitric oxide (NO)

As one of key signaling molecules, NO regulates vascular tone and inflammatory responses [15]. Its exact role in inflammation remains controversial. While NO derived from endothelial (eNOS) and neuronal (nNOS) sources exerts cytoprotective and anti-inflammatory effects, inducible nitric oxide synthase (iNOS) derived NO often contributes to tissue injury and chronic inflammation. Some studies suggest that low basal levels of NO from eNOS promote vasodilation and inhibit leukocyte adhesion, thereby limiting inflammatory progression. Conversely, excessive NO production from iNOS has been implicated in the amplification of oxidative stress and tissue cytotoxicity, particularly during chronic inflammatory diseases. A particularly intriguing aspect is also reported cross-regulation between iNOS and COX-2. While earlier research established that iNOS upregulation

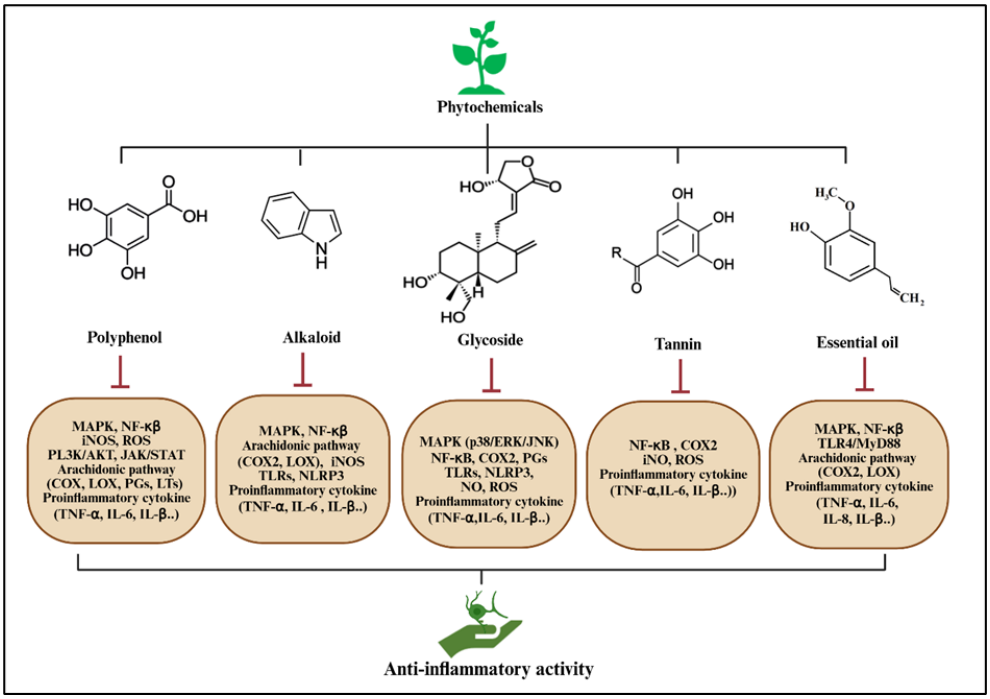


Figure 4. Pictorial representation of different signalling pathways as possible intercepting points by different classes of plant-based bioactives. The shown chemical structures are for gallic acid, indole, andrographolide, tannic acid and eugenol representing polyphenol, alkaloid, glycoside, tannin, and essential oil, respectively.

Abbreviation: MAPK: mitogen-activated protein kinase, NF-κβ: nuclear factor kappa B, iNOS: inducible nitric oxide syanthase, ROS: reactive oxygen species, PL3K/AKT: Phosphoinositide 3-kinase / Protein Kinase B, JAK/STAT: Janus kinase/signal transducer and activator of transcription, COX: cyclooxygenase. LOX: lipoxygenase, PGs: prostaglandins, LTs: leukotrienes, TNF-α: Tumor necrosis factor α, IL-6: interleukin 6, IL-β: interleukin β, TLRs: toll-like receptors, NLRP3: NOD-like receptor protein 3, p38/ERK/JNK: p38 mitogen-activated protein kinase/ extracellular signal-regulated kinase/ c-Jun N-terminal kinase, TLR4: toll-like receptor 4, MyD88: myeloid differentiation factor 88, COX2: cyclooxygenase 2.

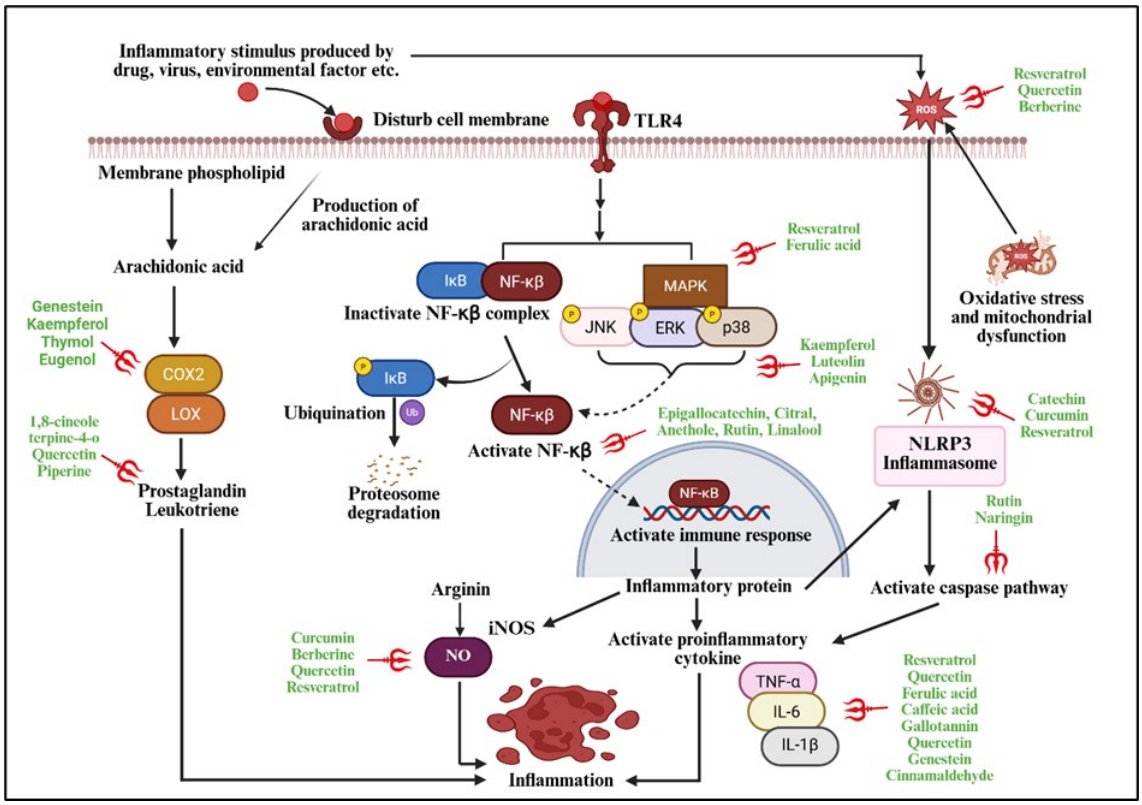


Figure 5. An illustrative mechanism of phytochemicals exhibiting anti-inflammatory activity through activating and deactivating different signalling pathways.

"Trishul – a divine mythological weapon, as per Indian belief". Abbreviation: TLR4: toll-like receptor 4, MAPK: mitogen-activated protein kinase, p38/ERK/JNK: p38 mitogen-activated protein kinase/extracellular signal-regulated kinase/ c-Jun N-terminal kinase, NF-κβ: nuclear factor kappa B, IκB: Inhibitory kappa B, NO: nitric oxide, iNOS: inducible nitric oxide synthase, ROS: reactive oxygen species, COX2: cyclooxygenase2. LOX: lipoxygenase, TNF-α: Tumor necrosis factor α, IL-6: interleukin 6, IL-1β: interleukin 1β, NLRP3: NOD-like receptor protein 3.

enhances COX-2 activity and PGE2 synthesis, thereby exacerbating inflammatory damage [16]. More recent studies indicate that COX-derived PGs can reciprocally modulate NO synthesis, suggesting a bidirectional feedback loop. This finding introduces novelty to the understanding of inflammatory signaling, implying that NO and PGs act in a dynamic manner rather than as independent mediators. Thus, the apparent contradictions in NO's inflammatory role reflect its chemical versatility and the complexity of its interactions with other mediators, such as COX-2.

4.4. Nuclear Factor-κβ (NF-κB)

NF-κB is a family of inducible transcription factors that regulate a wide range of genes involved in immune and inflammatory responses [17]. The NF-κB pathway responds to diverse stimuli, including ligands from cytokine receptors, the tumor necrosis factor receptor superfamily, pattern-recognition receptors, and antigen receptors on T- and B-cells. Traditionally, NF-κB has been viewed as a pro-inflammatory transcription factor because of its role in inducing cytokines, chemokines, and adhesion molecules that promote inflammation. However, growing evidence suggests that NF-κB exhibits a dual and context-dependent role, functioning not only as a promoter of inflammation but also as a regulator of immune homeostasis, tissue repair, and cell survival under certain physiological conditions. Studies supporting its pathogenic role emphasize that persistent or dysregulated NF-κB activation contributes to chronic inflammatory and autoimmune diseases, as well as to tumor progression [18]. Still, contrasting research indicates that transient NF-κB activation can protect cells from apoptosis and aid in recovery from acute inflammation, underscoring the importance of activation timing and intensity. Recent discoveries have also revealed that NF-κB does not act in isolation but interacts closely with pathways such as MAPK, JAK-STAT, and PI3K-

Table 1. Selected potential compounds and their target pathways involved in anti-inflammatory activity.

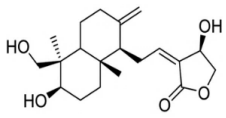
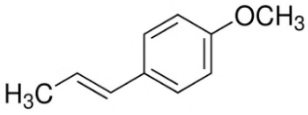
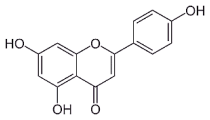
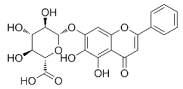
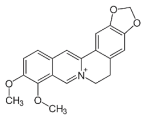
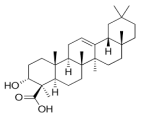
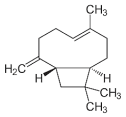
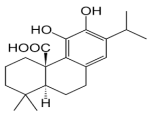
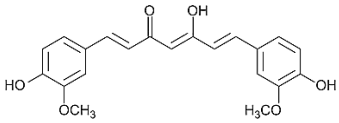
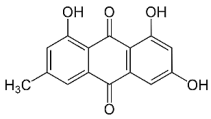
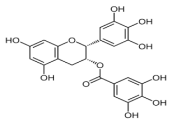
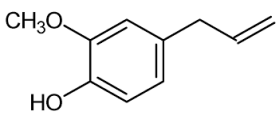
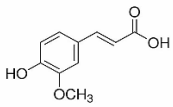
Phytochemical	Structure	Intercepted/Modulated Pathway or Target
Andrographolide		NF-κB, JAK/STAT, MAPK
Anethole		TNF-α, IL-1β, IL-17
Apigenin		NF-κB, STAT1, MAPK
Baicalin		NF-κB, Nrf2, MAPK
Berberine		NF-κB, AMPK, MAPK, 5-LOX, PGE_2
Boswellic acid		5-LOX, NF-κB
β-caryophyllene		PI3K/Akt / MAPK
Carnosic acid		NF-κB, Nrf2/HO-1
Curcumin		NF-κB, COX-2, iNOS, MAPK
Emodin		NF-κB, TLR4/MyD88, NLRP3
Epigallocatechin		NF-κB, JAK/STAT, Nrf2/HO-1
Eugenol		NF-κB, COX-2, NLRP3
Ferulic acid		5-LOX, PGE_2

Table 1. *Cont.*

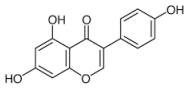
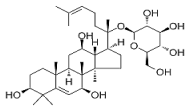
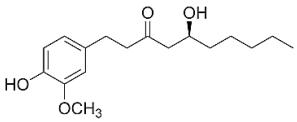
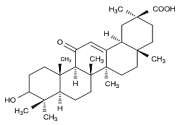
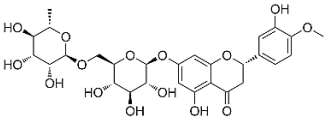
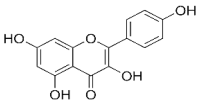
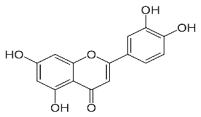
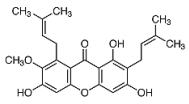
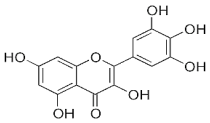
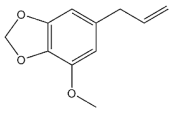
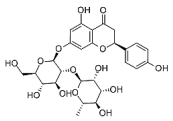
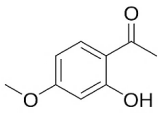
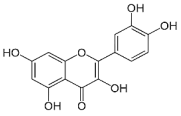
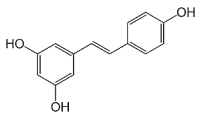
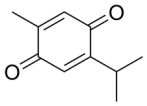
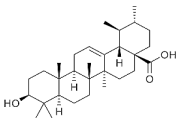
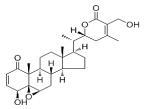
Phytochemical	Structure	Intercepted/Modulated Pathway or Target
Genistein		NF-κB, JAK/STAT, MAPK
Ginsenoside		NF-κB, Nrf2/Keap1
Gingerol		NF-κB, COX-2, LOX, NLRP3
Glycyrrhizin		NF-κB, TLR4
Hesperidin		NF-κB, Nrf2/HO-1, MAPK
Kaempferol		NF-κB, MAPKs (p38/ERK/JNK)
Luteolin		NF-κB, PI3K/Akt, Nrf2
α-Mangostin		NF-κB, MAPK, SIRT1, COX-2/iNOS
Myricetin		NLRP3, NF-κB, STAT1
Myristicin		NO, IL-6
Naringin		NF-κB, TLR4, MAPK, JAK/STAT
Paeonol		NF-κB, MAPK, PI3K/Akt, NLRP3
Quercetin		NF-κB, MAPK, NLRP3

Table 1. *Cont.*

Phytochemical	Structure	Intercepted/Modulated Pathway or Target
Resveratrol		NF-κB, SIRT1, AP-1, STAT3
Thymoquinone		NF-κB, MAPKs (ERK/JNK/p38), COX-2, iNOS
Ursolic acid		NF-κB, TLR4/MyD88; NLRP3, PI3K-AKT
Withaferin A		NF-κB, Akt/ERK, TLR4, iNOS/COX-2

NF-κB: Nuclear factor kappa B, JAK/STAT: Janus kinase-signal transducer and activator of transcription, MAPK: Mitogen-activated protein kinase, TNF-α: Tumor necrosis factor-alpha, IL-1β: Interleukin-1 beta, IL-17: Interleukin-17, STAT1: Signal Transducer and Activator of Transcription 1, Nrf2: Nuclear factor erythroid 2-related factor 2, AMPK: AMP-activated protein kinase, 5-LOX: 5-lipoxygenase, PGE_2: Prostaglandin E_2, PI3K/Akt: phosphatidylinositol 3-kinase/Protein Kinase B (PKB), HO-1: Heme-oxygenase 1, COX-2: cyclooxygenase 2, iNOS: Inducible Nitric Oxide Synthase, TLR4/MyD88: Toll-like Receptor 4/Myeloid differentiation primary response 88, NLRP3: NOD-like receptor pyrin domain containing 3, Keap1: Kelch-like ECH-associated protein 1, p38/ERK/JNK: p38/Extracellular signal-regulated kinase/c-Jun N-terminal kinase, NO: Nitric oxide, IL-6: Interleukin-6, AP-1: Activator Protein-1.

Akt, forming an intricate network that determines whether the outcome is pro-inflammatory or anti-apoptotic. Overall, NF-κB remains central to the inflammatory process, its precise role appears to depend on cellular context, activation duration, and molecular interactions, making it both a promising and challenging target for anti-inflammatory therapy.

5. INFLAMMATORY CELL

The body uses a variety of cell receptors to identify various foreign substances, including bacteria, viruses, parasites, chemicals, and antigenic compounds. Once identified, several pro-inflammatory pathways are activated, resulting in the release of cytokines and the activation of immune cells, such as lymphocytes and macrophages, which are responsible for the removal of foreign objects. if the body doesn't get rid of these foreign substances in the early stage, inflammation worsens, which is also known as the chronic phase, caused by the overproduction of cytokines, chemokines, and inflammatory enzymes. The inflammation initiated a series of immune cells, such as macrophages, mast cells, dendritic cells, vascular endothelial cells, neutrophils, monocytes, and T cells. These cells trigger several inflammatory mediators, which are depicted in Figure 3.

5.1. Monocyte

The initiation and development of inflammation depend on the recruitment of monocytes and their subsequent differentiation into macrophages [19]. From the blood, migration of monocytes into different tissues can develop into macrophages. They differentiate into either macrophages (essential role in phagocytosis and inflammation) or dendritic cells (involved in antigen presentation and triggering adaptive immunity). Additionally, they contribute to tissue cleansing by engulfing infections and dead cells. Monocytes can either stimulate pro-inflammatory or anti-inflammatory responses, depending on the signals they receive. They promote the additional immune cells to the site and worsen the inflammatory response through the production of cytokines, including TNF-α, IL-1, and IL-6 [20].

5.2. Macrophage

Macrophages are tissue-derived phagocytes and are produced from either circulating monocytes or embryonic progenitors. All organs and connective

tissues contain macrophages, which are termed according to their location. For example, the central nervous system has microglial cells, the liver contains kupffer cells, the lung comprises alveolar macrophages, and the bone consists of osteoclasts. Macrophage plays a vital role in the initiation, regulation, and elimination of inflammation [21]. Toll-like receptors and NOD-like receptors are two examples of pattern recognition receptors found in macrophages. These receptors help macrophages identify damage-associated molecular patterns generated by damaged cells or pathogen-associated molecular patterns found on microorganisms. To regulate immunological or inflammatory responses, activated macrophages release pro-inflammatory cytokines such as IL-1, IL-6, TNF-α, interferon-α/ß, IL-10, IL-12, and IL-18. These cytokines stimulate the production of adhesion molecules on endothelial cells, which facilitates leukocyte recruitment and immune cell entrance. Macrophages also generate chemokines like monocyte chemoattractant protein 1 and IL-8, which regulate neutrophils and monocytes toward the site of inflammation by forming a chemotactic gradient [22].

5.3. Neutrophil

Neutrophil plays a key role in phagocytosis, engulfing or digesting pathogens. Sometimes, they form neutrophil extracellular traps to trap or kill microbes. Neutrophil extracellular cells are essential for controlling inflammation and maintaining tissue homeostasis. During the inflammatory process, neutrophils exhibit a variety of functions, including generating reactive oxygen species and secreting proteases, chemokines, and cytokines, which recruit and activate other immune cells [23]. After performing their function, neutrophils usually go through apoptosis, or programmed cell death, and macrophages remove them. When it is not working properly due to excessive activity, it can lead to chronic inflammation and tissue damage [24].

5.4. Mast Cell

Mast cells are another important inflammatory initiator, particularly in parasite infections, allergic inflammation, and some autoimmune diseases [25]. They produced histamine, heparin, protease, chymase, etc. Rapid degranulation and histamine release from these cells cause vasodilation and increase local vascular permeability, which permits leukocytes and plasma proteins to enter the tissue. Additionally, mast cells generate other chemicals such as PGs, LTs, and cytokines that promote and increase the inflammatory response [26]. Mast cells secrete proteases, which may interact with plasma

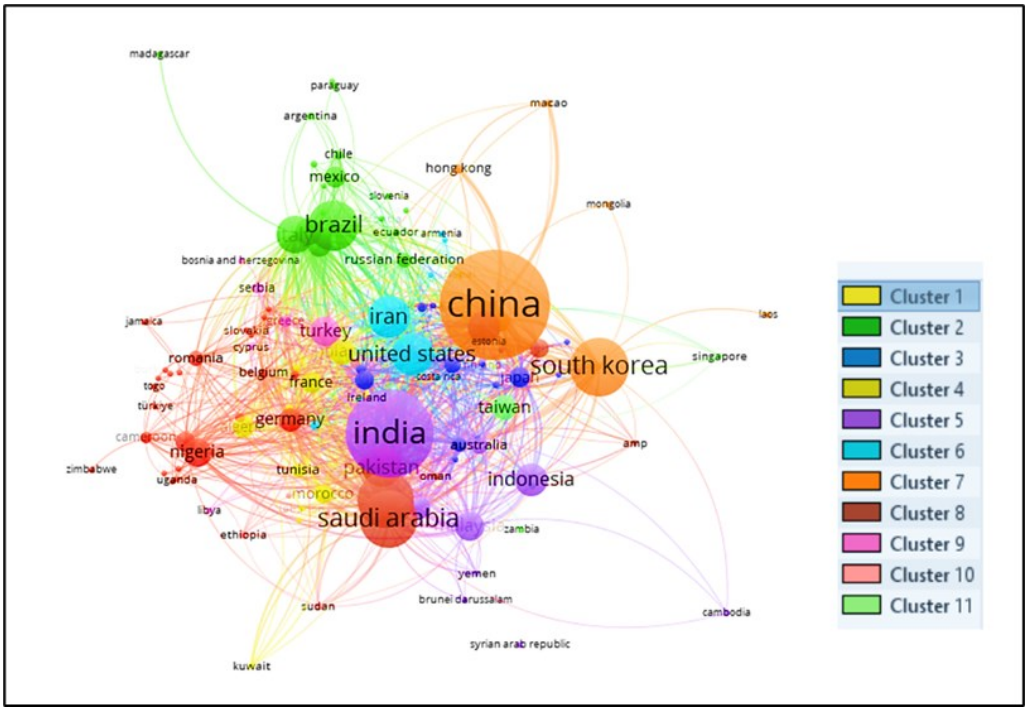


Figure 6. Collaboration network of countries.

Table 2. Ranking of the top 10 countries based on the number of publications, and also indicating their collaborative link strength.

Country	Documents	Citation	Total Link Strength
China	3,724	50,420	1,168
India	2,607	23,443	1,247
South korea	1,354	14,661	580
Egypt	1,354	14,661	580
Saudi arabia	1,300	16,103	2,229
United states	802	11,512	1,092
Pakistan	703	8,095	619
Italy	642	9,731	619
Germany	307	4,132	493
Malaysia	437	4,256	479

albumin to produce histamine-releasing peptides, which in turn may promote inflammation and mast cell activation. The inflammatory processes are facilitated by mast cell-derived histamine, TNF-α, and IL-6, whereas the control of inflammation is mediated by IL-10. Activated mast cells release a variety of pro-inflammatory chemicals and contain nine different types of toll-like receptors [27]. For example, it has been demonstrated that toll-like receptor 2 activation causes TNF, IL-6, IL-13, IL-4, and IL-5 to be secreted, whereas toll-like receptor 4 activation causes TNF, IL-6, IL-13, and IL-1β to be expressed.

5.5. Dendritic Cell

Dendritic cells are essential for immunological defense because they are the primary mediator between innate and adaptive immunity. They also have pattern recognition receptors, just like macrophages, and react to tissue injury as well as microbial infection. In their activated state, they start releasing inflammatory cytokines, including IL -12 and TNF-α. They connect innate and adaptive immunity by linking to neighbouring lymph nodes in their active state and presenting antigens to native T cells [28].

5.6. T Cell

It has been shown that T cells act in two forms such as CD4+ T cells stimulate B cells to make virus-specific antibodies, whereas CD8+ T cells can destroy virus-infected cells and release interferon-γ and TNF-α [29]. When inflammation occurs, T cells get activated and, depending on the cytokines released around the inflammatory loci, develop into different T-cell subsets, such as T-helper 1, 2, 17, and regulatory T cells. In response to infections, T-helper cells generally produce a range of pro-inflammatory cytokines and chemokines by triggering NF-κB signalling, which attracts leukocytes and lymphocytes to the site of inflammation. All of these immune cells then express and secrete more chemokines and cytokines, increasing the inflammatory process [30].

5.7. Endothelial Cell

A significant role for vascular endothelial cells in the inflammatory process is well established. They serve as a barrier and control the movement of immune cells, blood flow in the healthy state. When there is inflammation, immune cells like mast cells or macrophages release cytokines (such as TNF-α and IL-1) that trigger the activation of endothelial cells [31]. In the activated state, adhesion molecules, such as intercellular adhesion molecule 1, vascular cell adhesion molecule 1, selectins, and chemokines (monocyte chemoattractant protein 1) are expressed on the surface of endothelial cells. Additionally, endothelial cells generate PGs and NO, which affect blood artery permeability and vascular tone and promote redness, swelling, and inflammation. In chronic inflammation, endothelial

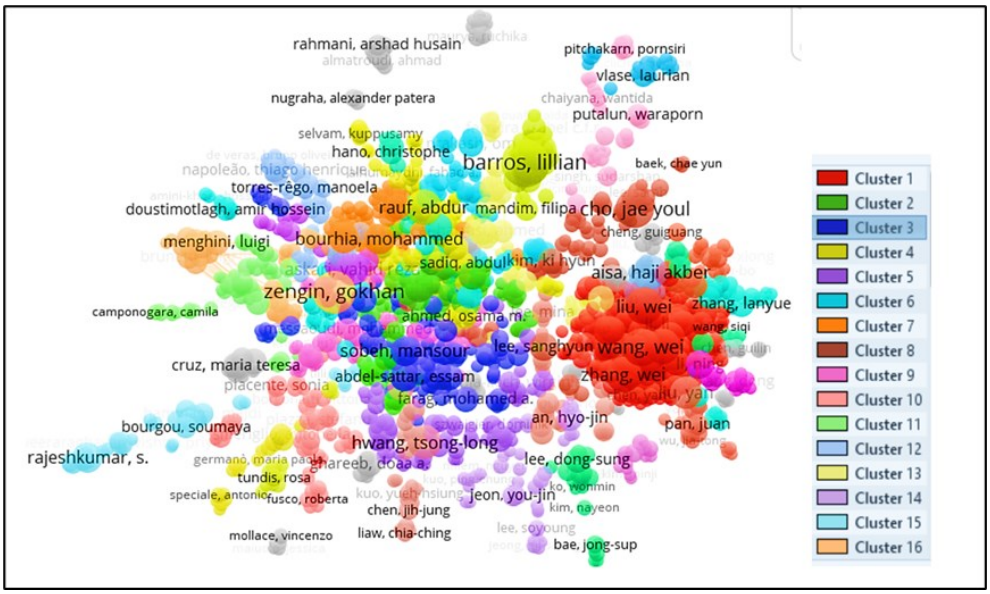


Figure 7. Co-authorship network of authors with a minimum of 5 publications based on average publications per year.

cells may be involved in vascular dysfunction, clot formation, or tissue damage [32].

6. PHYTOCHEMICALS REGULATE PATHWAYS INVOLVED IN ANTI-INFLAMMATORY RESPONSE

When the inflammatory response is induced, arachidonic acid is released from the cell membrane by cytosolic phospholipase A2. Arachidonic acid is a polyunsaturated fatty acid that is metabolised to PG and thromboxane by COX and LOX pathways in different cells. The PGs, especially PGE2, amplify the pain mechanism and enhance vascular permeability, whereas the LTs contract the smooth muscles of blood vessels, enhance vascular permeability, and mediate proinflammatory and allergic responses. Phytochemicals inhibit the expression of the COX2 and LOX pathways, showing anti-inflammatory activity. Several cellular signalling cascades are involved in the anti-inflammatory activity of phytochemicals (Figure 4). These include Toll-like receptor 4, the mitogen-activated protein kinase (MAPK) pathway, and NF-κB, which lead to the subsequent increase of target genes related to inflammation. MAPK plays a key role in regulating gene transcription and transcription factor activities involved in inflammation. The different groups of MAPKs are extracellular signal-related kinases, like (extracellular signal-related kinases (ERK))-1/2, c-Jun amino-terminal kinases (JNK1/2/3), p38-MAP kinase (α, β, δ, and γ). MAPK signalling is activated by stress and mitogens. For instance, stress stimulates the JNK and p38 cascades, whereas mitogens and growth factors activate the ERK1/2 pathway. The complex structure of the MAPK pathway interacts with various pathways, including NF-κβ [33]. In the cytoplasm, NF-κB is found in an inactive, non-DNA-binding form because it is associated with inhibitors of nuclear factor kappa B (IκB), which are inhibitor proteins. IκB kinase (IKK) phosphorylates IκB proteins in response to inflammatory stimuli, which causes subsequent ubiquitination, the breakdown of the inhibitory proteins, and the activation of the NF-κB dimer. Later, this can translocate into the nucleus and trigger the production of several genes linked to inflammation, including COX-2 and pro-inflammatory cytokines (IL-1, IL-2, IL-6, and TNFα) and chemokines, further activating endothelial cells. The additional pathway activated in endothelial cells, such as iNOS, which produces NO in response to inflammatory stimuli, and iNOS-mediated NO production is often associated with inflammation and can contribute to local tissue destruction. So, primarily NF-κβ regulates the inflammatory response of a cell to multiple stimuli. Thus, the inhibition of NF-κB can be of great

benefit in controlling inflammatory conditions. Reactive oxygen species (ROS) induced inflammation via the expression of inflammatory cytokines, including IL-1β, which has been linked with NOD-like receptor protein 3 (NLRP3) inflammasome. The NLRP3 inflammasome is activated by ROS, which are generated by a variety of stimuli such as oxidative stress and mitochondrial malfunction, resulting in caspase activation and inflammation. Pro-inflammatory cytokines, including IL-1β and IL-18, are released as a result of this activation, which promotes inflammation. There are several recent works on the anti-inflammatory action of phytochemicals listed below, and their mechanistic intercept pathway is shown in Figure 5.

6.1. Polyphenol

Polyphenols are a diverse group of secondary plant metabolites known to exhibit a wide range of biological activities, including antiviral, antimicrobial, anticancer, antioxidant, neuroprotective, and anti-inflammatory effects. Among these, the anti-inflammatory potential of polyphenols has been the most extensively investigated. Polyphenols exert anti-inflammatory effects primarily by modulating cytokine production and regulating multiple intracellular signalling pathways, such as MAPKs (p38, ERK1/2, and JNK), NF-κB, and the arachidonic acid cascade (via the inhibition of COX and LOX enzymes) [34].

Polyphenols are broadly classified into several categories, including simple phenolics, flavonoids, and phenolic acids. Most phenolic compounds are abundant in plants and are products of their secondary metabolic pathways. Numerous studies have demonstrated their importance in attenuating inflammation through diverse mechanisms. Among phenolic compounds, resveratrol is the most extensively studied for its anti-inflammatory effects. It regulates inflammatory responses by modulating key signalling pathways such as NF-κB, MAPK, and the arachidonic acid cascade [35]. Experimental evidence suggests that resveratrol exerts anti-inflammatory effects through the activation of AMP-activated protein kinase (AMPK) and the inhibition of NF-κB-induced COX -2 signalling in RAW 264.7 macrophages [36]. The phenolic compounds oxyresveratrol, norartocarpetin, and artocarpesin from *Artocarpus heterophyllus* (jackfruit) demonstrated potent anti-inflammatory activity by suppressing iNOS and COX-2 expression in lipopolysaccharide (LPS)-activated macrophages and by significantly reducing NO and PGE_2 levels [37]. Similarly, Ali et al. [38] identified five phenolic compounds from *Eucalyptus maculata* resin, of which 1,6-dicinnamoyl-O-α-D-glucopyranoside showed notable inhibition of NO generation, COX-2, TNF-α, and NF-κB expression in vitro. In another study, phenolic compounds isolated from *Habenaria*

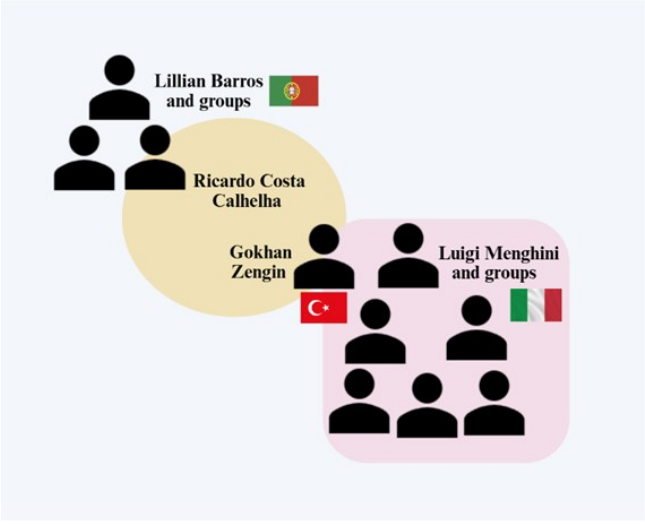


Figure 8. A visual summary of the leading research groups represented by the top 10 co-authors based on bibliometric analysis.

Table 3. Top 10 co-authors and their corresponding link strength.

Author	Documents	Citation	Total Link Strength	H-Index
Lillian Barros	57	751	272	95
Gökhan Zenin	45	994	243	72
Maria Inês Dias	34	432	192	41
Ricardo Costa Calhelha	38	515	181	58
Luigi Menghini	17	289	157	37
Claudio Ferrante	16	279	153	35
Giustino Orlando	15	267	152	37
Luigi Brunetti	15	267	152	36
Annalisa Chiavaroli	15	267	152	33
Sheila Leone	15	267	152	37

digitata exhibited strong antioxidant and anti-inflammatory activities, with 5-methylpyrimidine-2,4-diol being the most potent. These compounds inhibited COX-2 and 5-LOX enzymes in a carrageenan-induced pleurisy model in mice, confirming in vivo relevance [39]. Further, Aydemir et al. [40] identified phenolic substances such as *p*-coumaric acid, hyperoside, and hesperidin from *Astragalus gymnolobus* methanolic extracts, which showed significant cytotoxic, antioxidant, and anti-inflammatory potential supported by molecular docking studies. The study by Benarba et al. [41] reported that methanolic extracts of *Telephium imperati L.*, rich in phenolic compounds, exhibited strong antioxidant, anti-inflammatory, and anticancer properties.

Flavonoids, also known as hydroxylated polyphenols, represent a major subclass of polyphenols with well-documented anti-inflammatory effects. They modulate the production and activity of various cytokines by inhibiting the expression of pro-inflammatory mediators such as TNF-α, IL-1β, IL-6, and IL-8 in different cell types, including human peripheral blood mononuclear cells, mast cells, astrocytes, synovial cells, and LPS -activated mouse macrophages [42][43]. Several individual flavonoids, such as quercetin [44][45], curcumin [46], genistein, apigenin [47], kaempferol, and epigallocatechin-3-gallate [48], exhibit potent anti-inflammatory activity. These compounds regulate cytokine expression (IL-1β, TNF-α, IL-6, and IL-8), inhibit transcription factors (NF-κB and activator protein-1), suppress adhesion molecules (ICAM, VCAM, and E-selectin), and block key enzymes (NO synthase, COX-2, and LOX) involved in inflammation. Phenolic acids such as chlorogenic acid, rosmarinic acid, and ellagic acid, abundant in medicinal and edible plants, also exhibit pronounced anti-inflammatory activity. These compounds modulate key inflammatory pathways, including NF-κB, MAPK, and NLRP3 inflammasome signalling, and have been shown to influence gut microbiota composition, highlighting a possible gut–immune axis in their mechanism of action [49]-[51].

Recent studies have focused on polyphenol-enriched extracts and novel formulations to enhance bioavailability and therapeutic potential. For example, a seabuckthorn-derived polyphenol–phospholipid complex demonstrated significant *in vivo* anti-inflammatory activity in Sprague–Dawley rats [52]. Extracts rich in polyphenols from *Cirsium japonicum* [53] and *Withania adpressa* [54] showed potent antioxidant, anti-inflammatory, and analgesic properties. A recent innovation is a sustained-release pure polyphenol capsule designed for osteoarthritis treatment, which achieved a single-dose therapeutic effect in mouse and dog models by modulating the microenvironment and inhibiting the p38 MAPK pathway [55]. Collectively, these studies highlight the diverse pharmacological potential of polyphenolic compounds derived from various plant species. The identification of specific bioactive molecules provides valuable leads for further drug development and mechanistic studies. Most investigations were restricted to preliminary

biological assays without extensive pharmacokinetic or toxicity evaluations, leaving their clinical relevance uncertain. Future research should focus on mechanistic elucidation, formulation development, and clinical validation of these phenolic compounds.

6.2. Alkaloid

The basic nitrogen-containing chemical compounds known as alkaloids are primarily found in plants. They have diverse structural classes, such as indole, quinolone, isoquinoline, pyridine, pyrrolidines, and piperidines. Alkaloids have a wide range of physiological and pharmacological characteristics, such as analgesic, anti-inflammatory, antioxidant, anti-tumor, and antibacterial actions. Current studies related to the anti-inflammatory properties of alkaloids are described below. It was noted that certain isoquinolines, such as berberine, tetrandrine, dauricine, sinomenine, and lycorine, could alter the NF κB, COX 2, iNOS, TNF α, IL-6, STAT, and MAPK pathways. Berberine reduces inflammation in lipopolysaccharide-induced human dental pulp fibroblasts by inhibiting the NF-κB signalling pathway [56]. It also decreases the expression of K-ras, c-Raf, and p-38/ERK-phosphorylation and blocks the overproduction of IL-6 and TNF-α in fibroblast-like rheumatoid arthritis synoviocytes. Furthermore, it suppressed NLRP3, caspase-1, and ASC mRNAs in the NLRP3 inflammasome cascade and decreased the release of proinflammatory cytokines (IL-1α, IL-1β, IL-6, and TNF-α) [57]. Tetrandrine has anti-inflammatory and antioxidant properties through the PI3K/AKT/NF-κB signaling pathway [58]. In lipopolysaccharide-induced RAW 264.7 cells, tetrandrine also suppresses the production of IL-6, IL-1β, and TNF-α by inhibiting NF-κβ [59]. It also inhibits the phosphorylation of IκBα and NF-κB p65, reducing inflammation in chondrogenic ATDC5 cells and lipopolysaccharide-induced macrophage RAW 264.7 cells [60]. Sinomenine inhibits the JNK and NF-κB signaling pathways to produce its anti-inflammatory action. Through NF-κB activity inhibition, it suppresses TNF-α mRNA and IL-1β mRNA expression in synovial cells [61]. The six quinoline alkaloids, avicenines (A–F), found in *Zanthoxylum avicennae* fruits inhibited the production of pro-inflammatory cytokines IL-1β and IL-6 in macrophages, which are used to treat a variety of inflammatory conditions [62]. Moreover, quinoline alkaloid from Watheria indica suppressed NF-kb and iNOS pathways [63]. The indole alkaloid evodiamine from *Evodia rutaecarpa* has anti-inflammatory activity by decreasing the expression of proinflammatory mediators COX-2, iNOS, IL-6, and TNF-α via AKT/Nrf2/HO-1 activation and inhibiting NF-κB p65 phosphorylation in lipopolysaccharide-stimulated BV-2 cells [64].

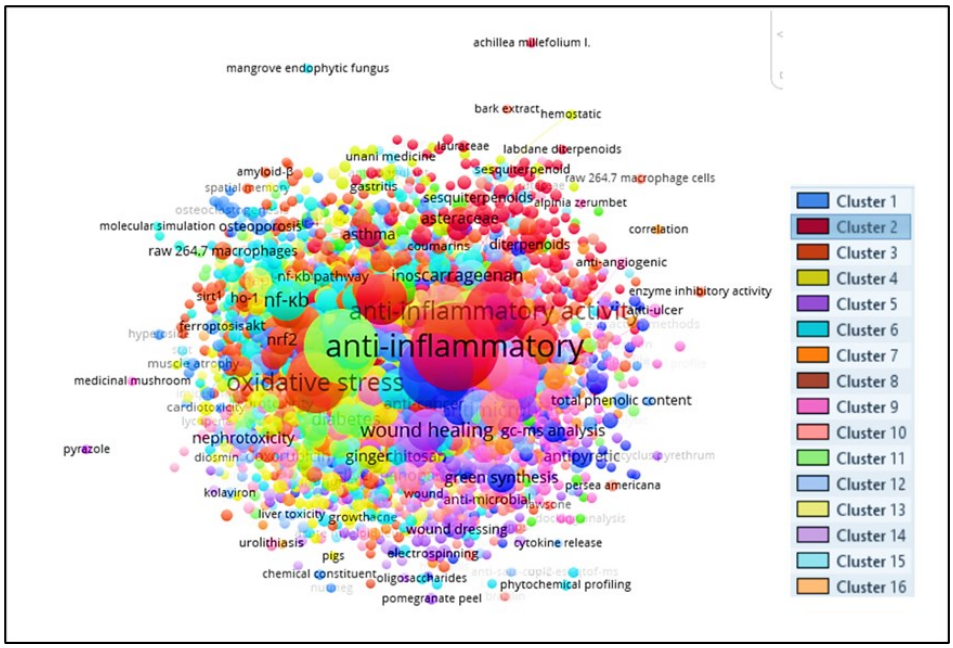


Figure 9. Network visualization of author's keyword with a minimum of 5 co-occurrences.

Table 4. Top 10 keywords with a minimum of 5 occurrences.

Keywords	Occurrence	Total Link Strength
Anti-inflammatory	2,739	7,660
Antioxidant	1,710	5,284
Inflammation	1,664	4,790
Anti-inflammatory activity	1,028	2,260
Oxidative stress	944	2,854
Antioxidant activity	608	1,631
Molecular docking	581	1,646
Anti-inflammation	550	1,278
Apoptosis	440	1,302
Cytotoxicity	397	1,221

Rhynchophylline, another indole alkaloid from *Uncaria rhynchophylla,* has been identified for its anti-inflammatory properties by modulating MAPK/NF κB pathways [65]. It can inhibit the production of IL-1β and TNF-α in lipopolysaccharide-induced dopaminergic neurons and glial cells. Additionally, it can prevent the phosphorylation of p38 MAPK, block the nuclear translocation of NF-κB, and inhibit its transcriptional function in hypoxia-induced vascular endothelial cell damage [66][67]. Pei et al. [68] found that diterpenoid alkaloids from Delphinium ajacis have potent anti-inflammatory activity by reducing NO production in lipopolysaccharide-induced BV-2 microglial cells. Tang et al. [69] found that the alkaloids from black pepper showed anti-inflammatory activity by preventing the activation of the NF-κβ pathway in murine macrophages. The purine alkaloid theophylline exhibited anti-inflammatory activity by decreasing the release of phosphodiesterase and neuropeptides. It also inhibits the adenosine receptor, increases the release of IL-10, and prevents the transcriptional expression of NF-κB as well as the activation of T cells and inflammatory cells [70][71].

6.3. Glycoside

Glycosides are organic compounds that can be isolated from either plants or animals. Based on glycosidic bond, they can be linked by an N-, S-, or C-glycosidic bond to form C-glycosides, thioglycosides, and glycosylamines, respectively. There is another classification based on the aglycone portion, such as flavonoid glycosides, anthraquinon glycosides, triterpene glycosides, kaempferol glycosides, phenylpropanoid, β-sistosterol, and saponine. In both animal and cell models, glycosides exhibit strong anti-inflammatory properties. They often work by restoring immunological responses, increasing antioxidant defenses (Nrf2), and inhibiting important inflammatory pathways (NF-κB/MAPK). Kaempferol-based glycoside from Siraitia grosvenorii that was isolated from monk fruit showed dose-dependent anti-inflammatory properties by triggering the Nrf2/HO-1 antioxidant response and blocking the TLR4/NF-κB/MyD88 pathway in lipopolysaccharide-activated macrophages and OA-treated HepG2 cells [72]. Wu et al. [73] reported that the glycoside-rich extract from *Picrorhiza scrophulariiflora* inhibits NO production, iNOS expression, IL-1β, and IL-6 transcription of lipopolysaccharide-activated RAW 264.7 cells. Luteolin glycoside, aucubin, and sweroside main components responsible for the anti-inflammatory effect of the extract. According to earlier research, steviol and stevioside may influence the expression of cytokines by inhibiting IkBα/NF-κB signalling pathway, resulting reduction of the production of pro-inflammatory cytokines induced by lipopolysaccharide [74]. Additionally, Xu et al. reported that stevia glycosides regulate the NF-κB/MAPK pathway, enhance antioxidant capacity, reduce inflammation, and apoptosis of diquat-induced IPEC-J2 cells [75]. Iridoid glycosides from *Cornus officinalis* showed

neuroprotective activity in rats with brain injury by increasing antioxidant levels and reducing lipid peroxidation and proinflammatory marker levels by inhibiting NF-κB and STAT3 expression [76]. In lipopolysaccharide-stimulat RAW 264.7 macrophages, phenylethanoid glycoside, from the flowers of Hosta plantaginea, significantly reduced inflammation by blocking the NF-κB signalling pathway and reducing NO, TNF-α, PGE2, IL-1β, and IL-6 [77]. Another phenylethanoid glycoside, like tubuloside A from Cistanche tubulosa, reduced NF-κB activation and upregulated the Nrf2/HO-1 antioxidant pathway to inhibit diclofenac-induced hepato-renal oxidative damage in rats [78].

6.4. Tannin

Tannins come from a variety of sources. They are present in several wild herbs, plants, fruit, tree wood, and bark. There are two primary categories of tannins: condensed and hydrolyzable. They showed anti-inflammatory effects by reducing proinflammatory mediators through inhibition of NF-κB and MAPK pathways and regulating the immune response. There are several new studies on the anti-inflammatory properties of tannin, some of which even address their mode of action or pinpoint the compounds that enable this effect. Among hydrolysable tannins, extract from Sumach (*Rhus coriaria*) has demonstrated anti-inflammatory, immunomodulatory, and anti-apoptotic properties in addition to the ability to cure, prevent, and reverse necrotizing enterocolitis [79]. Furthermore, hydrolysable tannin of Terminalia chebula showed potent anti-inflammatory activity by blocking NF-κB and MAPK signalling, reducing NO, ROS, cytokines, COX-2, iNOS, and TNF-α in both model collagen-induced arthritis in mice and lipopolysaccharide-stimulated RAW 264.7 macrophages [80]. Additionally, the hydrolyzable gallotannin found in chestnut spiny burs tannin extract exhibited anti-inflammatory properties and cryoprotection [81]. Gallnut-derived tannic acid reduced inflammation, NF-κB activation, and airway hyperresponsiveness in a mouse model of ovalbumin-induced asthma [82]. Curcumin nanoparticles coated with tannic acid show strong anti-inflammatory and anti-fibrotic properties through downregulating the expression of the TGF β and NF κB genes in human tenocyte cell cultures [83]. There was evidence that a randomized placebo -controlled clinical trial revealed that 14 days of oral tannin supplements dramatically decreased the pro-inflammatory chemokine macrophage inflammatory protein-1α, which was linked to changes in gut Bifidobacteria [84]. Reports show that tannins improve the gut microbiota in both healthy individuals and disease models, promoting bacteria that produce anti-inflammatory metabolites and correlate with improved immune responses.

6.5. Essential Oil

Essential oils (EOs) possess anti-inflammatory activity depending on their chemical composition. The anti-inflammatory activity of essential oils is shown by affecting arachidonic metabolism, cytokine production, and the regulation of proinflammatory gene expression through inhibition of the NF-κβ pathway. De Cicco et al. [85] reported

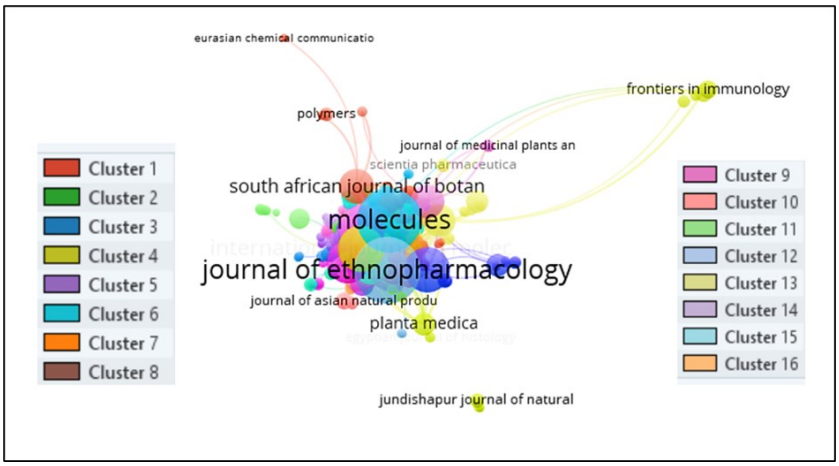


Figure 10. Visualization network of bibliographic coupling of journals with a minimum of 5 publications.

Table 5. Top 10 journals along with their link strength.

Source	Documents	Citation	Total Link Strength	Impact Factor	Citescore
Journal of Ethnopharmacology	809	11,968	158	5.4	10.4
Molecules	754	10,973	134	4.6	8.6
Frontiers in Pharmacology	322	3,781	79	4.8	8.9
Natural Product Research	260	1,652	89	2.0	5.2
South African Journal of Botany	161	1,989	186	2.7	5.3
Inflammopharmacology	148	1,429	199	5.2	8.4
International Journal of Biological Macromolecules	135	2,506	71	8.5	10.3
Food and Function	97	1,932	108	5.4	NA
ACS Omega	77	1,526	69	4.3	7.1
Journal of Inflammation Research	34	555	62	4.5	6.5

NA: Not available

that Chamomile EO from *Matricaria* chamomilla L. showed anti-inflammatory activity by inhibiting the proinflammatory cytokines TNF-α and IL-6 and modulating macrophages and human $CD4^+$ T cells-mediated immune response. Results also revealed that these effects are associated with suppression of NF-κB activation and stimulation of the NRF2 signalling pathway. Another study found that 8 EO from sage (*Salvia officinalis*), coriander (*Coriandrum sativum*), rosemary (*Rosmarinus officinalis*), black cumin (*Nigella sativa*), prickly juniper (*Juniperus oxycedrus*), geranium (*Pelargonium graveolens*), oregano (*Origanum vulgare*), and wormwood (*Artemisia herba-alba*) exerted anti-inflammatory activity by inhibiting NF -κB activation and decreasing inflammatory mediators such as IL-6, IL-1β, TNF-α, and COX-2 mRNA expression in lipopolysaccharide-stimulated THP-1 macrophages [86]. Linalool is an active constituent of *Lavandula angustifolia* Mill. downregulated the mRNA and protein levels of IL-6, IL-8, IL-β, and TNFα of THP-1 cells, pro-inflammatory cytokines resulting in inhibition of both NF-κB and inflammasome [87]. In addition, Horváth et al. [88] found that lavender and eucalyptus EO decrease pro-inflammatory cytokine mRNA expression, IL-6, and IL-8 secretion of T24 cells. The same authors also reported that different components of EO regulate NF-κB pathway and but others other pathways such as MAPK as well. Among the 21 essential oils from citrus peels, those extracted from *Citrus japonica* and *Citrus maxima* have been found to have potent anti-inflammatory properties through the reduction of inflammatory mediators (NO) and proinflammatory cytokines (TNF-α, COX-2, iNOS, IL-1β, and IL-6) in lipopolysaccharide-stimulated RAW 264.7 cells [89]. Zhao et al. [90] reported the protective effects of cinnamon oil and eucalyptus oil on lipopolysaccharide-induced inflammation by reducing IL-1β, TNF-α, and NF-κB levels and increasing IL-10 levels.

The most potent compounds showing anti-inflammatory activity are in Table 1. While extensive *in vitro* and *in vivo* evidence supports the anti-inflammatory efficacy of phytochemicals, most studies remain preclinical. Moreover, many studies rely on crude extracts, making it difficult to attribute biological activity to specific compounds.

Future research should therefore emphasize structure–activity relationships, advanced formulation strategies (e.g., nano-encapsulation, phospholipid complexes), and well-designed clinical trials to translate these promising findings into effective anti-inflammatory therapeutics.

7. BIBLIOMETRIC STUDY

In academic research, literature reviews are crucial to evaluate the overall status of an area, collecting and identifying existing knowledge, and finding knowledge gaps. The number of academic journals and publications (such as articles, reports, and conference papers) has grown rapidly in recent years, leading to an exponential expansion in scientific knowledge. As a result, it is now highly challenging for researchers to use standard literature review techniques (such as narrative, critical, and meta-analysis) to identify specific gaps and track the state, advancements, and progress of that field. In any research field, bibliometric analysis has become an essential tool for assessing the scientific outputs of various scientific items (such as papers, authors, keywords, journals, institutions, and countries) and analyzing how the relationships and interactions between these items have changed the intellectual, social, and conceptual structure of the field over time. A bibliometric overview provides a thorough visualization of current research related to the anti-inflammatory activity of medicinal plant extract (period: 2020–2024). This approach aims to help researchers grasp the current state of academic research, identify patterns in research collaboration, and pinpoint potential international partners for future projects.

7.1. Collaborative Countries

The analysis highlights diverse collaborative activities among various countries, shedding light on the global research network surrounding the anti -inflammatory activity of medicinal plants. Using the VOS viewer, collaborative networking among other nations was investigated as seen in Figure 6. Out of the 232 countries identified, only 118 countries could meet the minimum threshold of 5 publications arranged in 11 clusters. Each country is depicted as a circle, with interconnecting lines of varying thickness representing collaborative links. The thickness of these lines reflects the intensity of collaboration; the thicker the line, the stronger the research partnership. Similarly, the size of each circle reflects how frequently that nation appears in the dataset, providing a clear indication of its productivity and prominence in terms of publishing output. Table 2 indicate that China has the highest number of publications. The reason behind this China is one of the world's most biodiverse countries, with vast ecosystems. The country has a long history of using medicinal and agricultural plants (e.g., traditional Chinese medicine), which encourages scientific investigation into native flora. In addition, India also offers a wealth of Ayurvedic expertise, more plant resources, and more publications. Overall, Saudi Arab, Egypt, China, and India have the greatest cumulative link strength, with 2229, 1262, 1247, and 1168, respectively.

7.2. Analysis of Authorship

Figure 7 shows that a total of 82,846 researchers were found during the authors' analysis. Only 2,092 co-authors out of this total produced the minimum of 5 papers throughout the time frame assigned (2020–2024). The 50 clusters comprise the complete co-authorship network. Similar levels of co-author participation are indicated by the networking, which is encouraging when searching for potential collaboration partners. The authors with the highest output are shown in Table 3. Lillian Barros, with an h-index of 95 from Portugal, has produced the most research. Strong networking is visible in Portugal, where Lillian Barros collaborates with Maria Inês Dias and Ricardo Costa Calhelha from the same institute, Instituto Politécnico de Bragança. A strong research group is also evident in Italy, including Luigi Menghini, Claudio Ferrante, Giustino Orlando, Luigi Brunetti, Annalisa Chiavaroli, and Sheila Leone from the University of G. d'Annunzio Chieti and Pescara. Gökhan Zenin from Turkey, with an h-index of 72, collaborates closely with the Italian research group and also with Ricardo Costa Calhelha from Portugal. Portugal and Italy show particular interest in inflammatory activity due to the high prevalence of inflammation-related chronic diseases and their strong tradition of studying natural bioactive compounds with anti-inflammatory potential [91] [92]. Figure 8 presents a schematic representation

of the top 10 active research groups identified in the bibliometric analysis.

7.3. Analysis Co-occurrence of Keywords

Keywords help researchers by making their work easier through databases, indexing systems, and search engines. Properly selected keywords make the study more visible and accessible to the appropriate audience. Keyword co-occurrence describes situations in which authors frequently employ the same words or phrases in many publications, suggesting common study themes or areas of interest. out of the 31,718 keywords, only 2,324 cooccurrences of the author's keywords fulfilled the threshold of at least 5 keywords related to this topic spread across 16 clusters, as seen in Figure 9. The top five keywords were detected based on their link strength, such as anti-inflammatory> antioxidant> inflammation> oxidative stress> anti-inflammatory activity. Overall, the occurrence of keywords is depicted in Table 4. The most explored topics related to the anti -inflammatory activity of medicinal plant extracts have been identified in the keywords.

7.4. Analysis of Journal Participation

From 2020 to 2024, 2192 journals published research articles and reviews on the previously mentioned topic. Only 553 journals could meet the threshold of a minimum of five publications spread across 36 clusters, as depicted in Figure 10. The Journal of Ethnopharmacology published the most and had the most publications (809), as shown in Table 5. Others include Molecules (754), Antioxidants (312), International Journal of Molecular Science (329), and Frontiers in Pharmacology (322). The results demonstrated a notable inclination among researchers toward publishing in open-access journals. Among the ten journals identified in the bibliometric analysis, 60% were classified as open access, highlighting a rising tendency for research projects to receive institutional or agency support to cover publication fees. Open-access outlets enhance the reach and visibility of scientific work, offering significant advantages to both readers and early-stage researchers. The average impact factor of these ten journals, which published studies related to anti-inflammatory research, was 4.74 reflecting the strong quality and relevance of the research being produced in this area. In addition, 90% of these journals were ranked in the Q1 quartile (top 25% globally), emphasizing their academic excellence, reputation, and citation impact. Publishing in such high-ranking journals is widely viewed as a mark of distinction, helping authors build professional

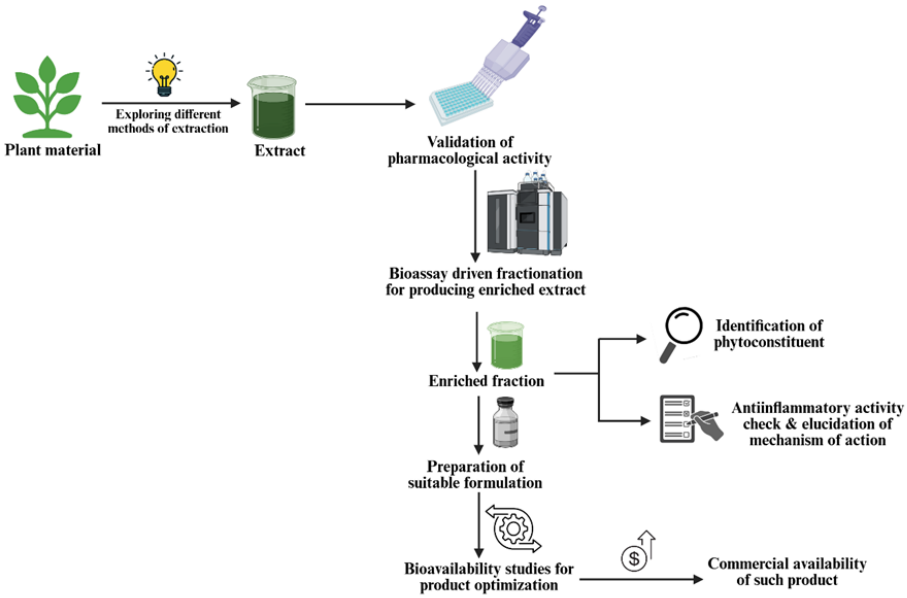


Figure 11. Roadmap illustrating options and opportunities for plant-based bioactives in anti-inflammatory treatment.

credibility and recognition within the scientific community. Overall, these findings indicate that plant-based bioactive research in inflammation management is gaining considerable recognition from high-impact journals, thereby enhancing its global visibility and inspiring further contributions from emerging scientists.

8. FUTURE PROSPECTIVE

The information present in this article provides a magnified look at the mechanistic pathway leading to inflammation, which is expected to provide a broader picture of inflammation to the researchers. This intern shall help the researcher navigate through the possible targets that can be hit plant plant-based bioactives to control inflammation. In this regard, a schematic diagram depicting the various optoions and oppurtunities available with plant based bioactives to be used for the treatment of various diseases is depicted in Figure 11 as a roadmap for new researchers.

9. CONCLUSIONS

Inflammation is associated with the progression of almost all diseases and severely impacts the diseased person. Controlling inflammation also forms a part of providing symptomatic relief for such cases, where direct treatment of the occurring disease is not possible. In this regard, there shall always be a need for anti-inflammatory agents that can mitigate the inflammatory storm inside the body. A clear insight into various plant-based bioactives and their multimodal approach towards inflammation has been vividly described in this article. The elastic compilation is expected to provide clarity and productive thought in the minds of researchers, thus inspiring them to explore new ventures in plant-based bioactives as anti-inflammatory agents.

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Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] A. L. Kiss. (2022). "Inflammation in Focus: The Beginning and the End". *Pathology & Oncology Research.* **27**. 10.3389/pore.2021.1610136.

[2] S. Kany, J. T. Vollrath, and B. Relja. (2019). "Cytokines in Inflammatory Disease". *International Journal of Molecular Sciences.* **20** (23): 6008. 10.3390/ijms20236008.

[3] V. P. Chavda, J. Feehan, and V. Apostolopoulos. (2024). "Inflammation: The Cause of All Diseases". *Cells.* **13** (22): 1906. 10.3390/cells13221906.

[4] D. Koche, R. Shirsat, and M. Kawale. (2016). "An Overview of Major Classes of Phytochemicals: Their Types and Role in Disease Prevention". *Hislopia Journal.* **9** (1-2): 1-11.

[5] S. Saleem. (2024). "Targeting MAPK Signaling: A Promising Approach for Treating Inflammatory Lung Disease". *Pathology – Research and Practice.* **254** : 155122. 10.1016/j.prp.2024.155122.

[6] S. Samra, J. R. E. Bergerson, A. F. Freeman, and S. E. Turvey. (2025). "JAK–STAT Signaling Pathway, Immunodeficiency, Inflammation, Immune Dysregulation, and Inborn Errors of Immunity". *Journal of Allergy and Clinical Immunology.* **155** (2): 357-367. 10.1016/j.jaci.2024.09.020.

[7] P. A. Pawase, C. Goswami, R. Shams, V. K. Pandey, A. Tripathi, S. Rustagi, and G. Darshan. (2024). "A Conceptual Review on Classification, Extraction, Bioactive Potential, and Role of Phytochemicals in Human Health". *Future Foods.* **9** : 100313. 10.1016/j.fufo.2024.100313.

[8] A. Yamaguchi, E. Botta, and M. Holinstat. (2022). "Eicosanoids in Inflammation in the Blood and the Vessel". *Frontiers in Pharmacology.* **13** : 997403. 10.3389/fphar.2022.997403.

[9] A. E. F. Sheppe and M. J. Edelmann. (2021). "Roles of Eicosanoids in Regulating Inflammation and Neutrophil Migration as an Innate Host Response to Bacterial Infections". *Infection and Immunity.* **89** (8): e00095-21. 10.1128/IAI.00095-21.

[10] C. N. Koyani, W. Windischhofer, C. Rossmann, G. Jin, S. Kickmaier, F. R. Heinzel, K. Groschner, A. Alavian-Ghavanini, W. Sattler, and E. Malle. (2014). "15-Deoxy-Δ12,14-PGJ2 Promotes Inflammation and Apoptosis in Cardiomyocytes via the DP2/MAPK/TNF-α Axis". *International Journal of Cardiology.* **173** (3): 472-480. 10.1016/j.ijcard.2014.03.086.

[11] W. Tian, X. Jiang, D. Kim, T. Guan, M. R. Nicolls, and S. G. Rockson. (2020). "Leukotrienes in Tumor-Associated Inflammation". *Frontiers in Pharmacology.* **11** : 1289. 10.3389/fphar.2020.01289.

[12] K. K. Kummer, M. Zeidler, T. Kalpachidou, and M. Kress. (2021). "Role of IL-6 in the Regulation of Neuronal Development, Survival, and Function". *Cytokine.* **144** : 155582. 10.1016/j.cyto.2021.155582.

[13] G. Harvanová, S. Duranková, and J. Bernasovská. (2023). "The Role of Cytokines and Chemokines in the Inflammatory Response". *Polish Journal of Allergology.* **10** (3): 210-219. 10.5114/pja.2023.131708.

[14] H. Li, M. Wu, and X. Zhao. (2022). "Role of Chemokine Systems in Cancer and Inflammatory Diseases". *MedComm.* **3** (2): e147. 10.1002/mco2.147.

[15] P. Tripathi, P. Tripathi, L. Kashyap, and V. Singh. (2007). "The Role of Nitric Oxide in Inflammatory Reactions". *FEMS Immunology and Medical Microbiology.* **51** (3): 443-452. 10.1111/j.1574-695X.2007.00329.x.

[16] S. Papi, F. Ahmadizar, and A. Hasanvand. (2019). "The Role of Nitric Oxide in Inflammation and Oxidative Stress". *Immunopathologia Persa.* **5** (1): e08. 10.15171/ipp.2019.08.

[17] T. Lawrence. (2009). "The Nuclear Factor NF -κB Pathway in Inflammation". *Cold Spring Harbor Perspectives in Biology.* a001651. 10.1101/cshperspect.a001651.

[18] M. S. Hayden and S. Ghosh. (2012). "NF-κB, the First Quarter-Century: Remarkable Progress and Outstanding Questions". *Genes*

& Development. **26** (3): 203-234. 10.1101/gad.183434.111.

[19] R. M. Kratofil, P. Kubes, and J. F. Deniset. (2017). "Monocyte Conversion during Inflammation and Injury". *Arteriosclerosis, Thrombosis, and Vascular Biology.* **37** (1): 35 -42. 10.1161/ATVBAHA.116.308198.

[20] S. P. Dash, S. Gupta, and P. P. Sarangi. (2024). "Monocytes and Macrophages: Origin, Homing, Differentiation, and Functionality during Inflammation". *Heliyon.* **10** (8): e29686. 10.1016/j.heliyon.2024.e29686.

[21] S. Watanabe, M. Alexander, A. V. Misharin, and G. R. S. Budinger. (2019). "The Role of Macrophages in the Resolution of Inflammation". *Journal of Clinical Investigation.* **129** (7): 2619-2628. 10.1172/JCI124615.

[22] P. Rodríguez-Morales and R. A. Franklin. (2023). "Macrophage Phenotypes and Functions: Resolving Inflammation and Restoring Homeostasis". *Trends in Immunology.* **44** (12): 986-998. 10.1016/j.it.2023.10.004.

[23] C. Rosales. (2018). "Neutrophil: A Cell with Many Roles in Inflammation or Several Cell Types?". *Frontiers in Physiology.* **9** : 113. 10.3389/fphys.2018.00113.

[24] A. Herrero-Cervera, O. Soehnlein, and E. Kenne. (2022). "Neutrophils in Chronic Inflammatory Diseases". *Cellular and Molecular Immunology.* **19** (2): 177-191. 10.1038/s41423-021-00832-3.

[25] C. Chompunud Na Ayudhya, S. Roy, M. Thapaliya, and H. Ali. (2020). "Roles of a Mast Cell-Specific Receptor MRGPRX2 in Host Defense and Inflammation". *Journal of Dental Research.* **99** (8): 882-890. 10.1177/0022034520919107.

[26] X. Wang, P. Zhang, Y. Tang, Y. Chen, E. Zhou, and K. Gao. (2024). "Mast Cells: A Double-Edged Sword in Inflammation and Fibrosis". *Frontiers in Cell and Developmental Biology.* **12** : 1466491. 10.3389/fcell.2024.1466491.

[27] D. Elieh Ali Komi, S. Wöhrl, and L. Bielory. (2020). "Mast Cell Biology at the Molecular Level: A Comprehensive Review". *Clinical Reviews in Allergy and Immunology.* **58** (3): 342-365. 10.1007/s12016-019-08769-2.

[28] J. Liu, X. Zhang, Y. Cheng, and X. Cao. (2021). "Dendritic Cell Migration in Inflammation and Immunity". *Cellular and Molecular Immunology.* **18** (11): 2461-2471. 10.1038/s41423-021-00726-4.

[29] A. Skapenko, J. Leipe, P. E. Lipsky, and H. Schulze-Koops. (2005). "The Role of the T Cell in Autoimmune Inflammation". *Arthritis Research & Therapy.* **7** (Suppl 2): S4. 10.1186/ar1505.

[30] M. A. Moro-García, J. C. Mayo, R. M. Sainz, and R. Alonso-Arias. (2018). "Influence of Inflammation in the Process of T Lymphocyte Differentiation: Proliferative, Metabolic, and Oxidative Changes". *Frontiers in Immunology.* **9** : 339. 10.3389/fimmu.2018.00339.

[31] J. Galle, T. Quaschning, S. Seibold, and C. Wanner. (2003). "Endothelial Dysfunction and Inflammation: What Is the Link?". *Kidney International Supplements.* **63** (84): S45-S49. 10.1046/j.1523-1755.63.s84.12.x.

[32] J. Xue, Z. Zhang, Y. Sun, D. Jin, L. Guo, X. Li, D. Zhao, X. Feng, W. Qi, and H. Zhu. (2023). "Research Progress and Molecular Mechanisms of Endothelial Cell Inflammation in Vascular-Related Diseases". *Journal of Inflammation Research.* **16** : 3593-3617. 10.2147/JIR.S418166.

[33] R. Pal, S. Mukherjee, A. Khan, M. Nathani, S. Maji, R. Tandey, S. Das, A. Patra, and V. Mandal. (2024). "A Critical Appraisal on the Involvement of Plant-Based Extracts as Neuroprotective Agents (2012–2022): An Effort to Ease the Decision-Making Process for Researchers". *Naunyn-Schmiedeberg's Archives of Pharmacology.* **397** (12): 9367-9415. 10.1007/s00210-024-03266-6.

[34] J. M. Peter and A. W. Thomas. (2008). "Protective and Pathogenic Functions of Macrophage Subsets". *Nature Reviews Immunology.* **11** (11): 723-737. 10.1038/nri3073.

[35] Z. Q. Ren, S. Y. Zheng, Z. Sun, Y. Luo, Y. T. Wang, P. Yi, Y. S. Li, C. Huang, and W. F. Xiao. (2025). "Resveratrol: Molecular Mechanisms, Health Benefits, and Potential

Adverse Effects". *MedComm.* **6** (6): e70252. 10.1002/mco2.70252.

[36] C. O. Yi, B. T. Jeon, H. J. Shin, E. A. Jeong, K. C. Chang, J. E. Lee, D. H. Lee, H. J. Kim, S. S. Kang, G. J. Cho, W. S. Choi, and G. S. Roh. (2011). "Resveratrol Activates AMPK and Suppresses LPS-Induced NF-κB-Dependent COX-2 Activation in RAW 264.7 Macrophage Cells". *Anatomy and Cell Biology.* **44** (3): 194-203. 10.5115/acb.2011.44.3.194.

[37] W. Thaweesest, V. Buranasudja, R. Phumsuay, C. Muangnoi, O. Vajragupta, B. Sritularak, P. Rashatasakhon, and P. Rojsitthisak. (2022). "Anti-Inflammatory Activity of Oxyresveratrol Tetraacetate, an Ester Prodrug of Oxyresveratrol, on Lipopolysaccharide-Stimulated RAW 264.7 Macrophage Cells". *Molecules.* **27** (12): 3922. 10.3390/molecules27123922.

[38] D. E. Ali, R. A. E. Gedaily, S. M. Ezzat, M. A. E. El Sawy, M. R. Meselhy, and E. Abdel-Sattar. (2023). "In Silico and In Vitro Anti-Inflammatory Study of Phenolic Compounds Isolated from Eucalyptus maculata Resin". *Scientific Reports.* **13** : 28221. 10.1038/s41598-023-28221-y.

[39] H. H. Almasoudi, M. S. Jan, M. H. Nahari, A. Y. M. Alhazmi, A. S. Binshaya, O. Abdulaziz, M. H. Mahnashi, M. Ibrar, R. Zafar, and A. Sadiq. (2024). "Phenolic Phytochemistry, In Vitro, In Silico, In Vivo, and Mechanistic Anti-Inflammatory and Antioxidant Evaluations of Habenaria digitata". *Frontiers in Pharmacology.* **15** : 1346526. 10.3389/fphar.2024.1346526.

[40] E. Aydemir, E. Odabaş Köse, M. Yavuz, A. C. Kilit, A. Korkut, S. Özkaya Gül, C. Sarikurkcu, M. E. Celep, and R. S. Göktürk. (2024). "Phenolic Compound Profiles, Cytotoxic, Antioxidant, Antimicrobial Potentials, and Molecular Docking Studies of Astragalus gymnolobus Methanolic Extracts". *Plants.* **13** (5): 658. 10.3390/plants13050658.

[41] B. Benarba, K. Belhouala, C. Korkmaz, M. T. Küçükaydın, S. Küçükaydın, and M. E. Duru. (2024). "Phenolic Profile, Antioxidant, Anti-Inflammatory, and Anticancer Activities of Telephium imperati L". *Journal of Phytology.* **16** : 216-225. 10.25081/jp.2024.v16.9334.

[42] N. Yahfoufi, N. Alsadi, M. Jambi, and C. Matar. (2018). "The Immunomodulatory and Anti-Inflammatory Role of Polyphenols". *Nutrients.* **10** (11): 1618. 10.3390/nu10111618.

[43] J. M. Al-Khayri, G. R. Sahana, P. Nagella, B. V. Joseph, F. M. Alessa, and M. Q. Al-Mssallem. (2022). "Flavonoids as Potential Anti-Inflammatory Molecules: A Review". *Molecules.* **27** (9): 2901. 10.3390/molecules27092901.

[44] M. S. Sung, E. G. Lee, H. S. Jeon, H. J. Chae, S. J. Park, Y. C. Lee, and W. H. Yoo. (2012). "Quercetin Inhibits IL-1β-Induced Proliferation and Production of MMPs, COX-2, and PGE2 by Rheumatoid Synovial Fibroblasts". *Inflammation.* **35** (4): 1585-1594. 10.1007/s10753-012-9473-2.

[45] C. H. Kang, Y. H. Choi, S. K. Moon, W. J. Kim, and G. Y. Kim. (2013). "Quercetin Inhibits Lipopolysaccharide-Induced Nitric Oxide Production in BV2 Microglial Cells by Suppressing the NF-κB Pathway and Activating the Nrf2-Dependent HO-1 Pathway". *International Immunopharmacology.* **17** (3): 808-813. 10.1016/j.intimp.2013.09.009.

[46] Y. Lin, H. Liu, L. Bu, C. Chen, and X. Ye. (2022). "Review of the Effects and Mechanisms of Curcumin in the Treatment of Inflammatory Bowel Disease". *Frontiers in Pharmacology.* **13** : 908077. 10.3389/fphar.2022.908077.

[47] K. Charrière, V. Schneider, M. Perrignon-Sommet, G. Lizard, A. Benani, A. Jacquin-Piques, and A. Vejux. (2024). "Exploring the Role of Apigenin in Neuroinflammation: Insights and Implications". *International Journal of Molecular Sciences.* **25** (9): 5041. 10.3390/ijms25095041.

[48] A. James, K. Wang, and Y. Wang. (2023). "Therapeutic Activity of Green Tea Epigallocatechin-3-Gallate on Metabolic Diseases and Non-Alcoholic Fatty Liver Disease: Current Updates". *Nutrients.* **15** (13): 3022. 10.3390/nu15133022.

[49] Y. Xiong, Z. Cheng, Y. Zhang, T. Liu, Z. Wan, C. Xia, B. Zhou, C. Shan, D. Song, and F. Miao. (2025). "Ellagic Acid Alleviates DSS-Induced Ulcerative Colitis by Inhibiting ROS/NLRP3 Pathway Activation and Modulating Gut Microbiota in Mice". *European Journal of Nutrition.* **64** (1): 1-15. 10.1007/s00394-024-03577-7.

[50] Q. Wang, K. Xu, X. Cai, C. Wang, Y. Cao, and J. Xiao. (2023). "Rosmarinic Acid Restores Colonic Mucus Secretion in Colitis Mice by Regulating Gut Microbiota-Derived Metabolites and Activation of Inflammasomes". *Journal of Agricultural and Food Chemistry.* **71** (11): 4571-4585. 10.1021/acs.jafc.2c08444.

[51] J. Zeng, D. Zhang, X. Wan, Y. Bai, C. Yuan, T. Wang, D. Yuan, C. Zhang, and C. Liu. (2020). "Chlorogenic Acid Suppresses miR-155 and Ameliorates Ulcerative Colitis through the NF-κB/NLRP3 Inflammasome Pathway". *Molecular Nutrition & Food Research.* **64** (23): 2000452. 10.1002/mnfr.202000452.

[52] D. D. Gore, N. Mishra, D. Kumar, G. Jena, S. M. Jachak, K. Tikoo, A. K. Bansal, and I. P. Singh. (2025). "Anti-Inflammatory Activity, Stability, Bioavailability, and Toxicity Studies of Seabuckthorn Polyphenol-Enriched Fraction and Its Phospholipid Complex (Phytosomes)". *International Journal of Biological Macromolecules.* **297** : 139919. 10.1016/j.ijbiomac.2025.139919.

[53] H. H. Kim, S. H. Jeong, M. Y. Park, P. B. Bhosale, A. Abusaliya, H. W. Kim, J. K. Seong, D. I. Kim, S. J. Lee, K. I. Park, and G. S. Kim. (2024). "Potential Antioxidant and Anti-Inflammatory Properties of Polyphenolic Compounds from Cirsium japonicum Extract". *International Journal of Molecular Sciences.* **25** (2): 785. 10.3390/ijms25020785.

[54] A. M. Salamatullah. (2023). "Antioxidant, Anti-Inflammatory, and Analgesic Properties of Chemically Characterized Polyphenol-Rich Extract from Withania adpressa Coss. ex Batt". *Life.* **13** (1): 109. 10.3390/life13010109.

[55] S. Wei, Z. Shou, D. Yang, L. Sun, Y. Guo, Y. Wang, X. Zan, L. Li, and C. Zhang. (2024). "Ultra-Long-Term Anti-Inflammatory Polyphenol Capsule to Remodel the Microenvironment for Accelerating Osteoarthritis Healing by Single Dosage". *Advanced Science.* **11** (48): 202407425. 10.1002/advs.202407425.

[56] J. Song, Q. Wu, J. Jiang, D. Sun, F. Wang, B. Xin, and Q. Cui. (2020). "Berberine Reduces Inflammation of Human Dental Pulp Fibroblasts via the miR-21/KBTBD7 Axis". *Archives of Oral Biology.* **110** : 104630. 10.1016/j.archoralbio.2019.104630.

[57] H. Wang, S. Tu, S. Yang, P. Shen, Y. Huang, X. Ba, W. Lin, Y. Huang, Y. Wang, K. Qin, and Z. Chen. (2019). "Berberine Modulates LPA Function to Inhibit the Proliferation and Inflammation of Rheumatoid Arthritis Fibroblast-Like Synoviocytes via the p38/ERK MAPK Pathway Mediated by LPA1". *Evidence-Based Complementary and Alternative Medicine.* **2019** : 2580207. 10.1155/2019/2580207.

[58] G. Bao, C. Li, L. Qi, N. Wang, and B. He. (2016). "Tetrandrine Protects Against Oxygen –Glucose–Serum Deprivation/Reoxygenation -Induced Injury via the PI3K/AKT/NF-κB Signaling Pathway in Rat Spinal Cord Astrocytes". *Biomedicine & Pharmacotherapy.* **84** : 925-930. 10.1016/j.biopha.2016.10.007.

[59] Y. Dang, Y. Xu, W. Wu, W. Li, Y. Sun, J. Yang, Y. Zhu, and C. Zhang. (2014). "Tetrandrine Suppresses Lipopolysaccharide-Induced Microglial Activation by Inhibiting NF-κB and ERK Signaling Pathways in BV2 Cells". *PLoS ONE.* **9** (8): e102522. 10.1371/journal.pone.0102522.

[60] L. N. Gao, Q. S. Feng, X. F. Zhang, Q. S. Wang, and Y. L. Cui. (2016). "Tetrandrine Suppresses Articular Inflammatory Response by Inhibiting Pro-Inflammatory Factors via NF-κB Inactivation". *Journal of Orthopaedic Research.* **34** (9): 1557-1568. 10.1002/jor.23155.

[61] W. D. Lai, S. Wang, W. T. You, S. J. Chen, J. J. Wen, C. R. Yuan, M. J. Zheng, Y. Jin, J. Yu, and C. P. Wen. (2022). "Sinomenine

Regulates Immune Cell Subsets: Potential Neuro-Immune Intervention for Precise Treatment of Chronic Pain". *Frontiers in Cell and Developmental Biology.* **10** : 1041006. 10.3389/fcell.2022.1041006.

[62] K. L. Ji, W. Liu, W. H. Yin, J. Y. Li, and J. M. Yue. (2022). "Quinoline Alkaloids with Anti-Inflammatory Activity from Zanthoxylum avicennae". *Organic & Biomolecular Chemistry.* **20** (20): 4176-4182. 10.1039/D2OB00711H.

[63] F. Liu, T. J. O'Donnell, E.-J. Park, S. Kovacs, K. Nakamura, A. Dave, Y. Luo, R. Sun, M. Wall, S. Wongwiwatthananukit, D. K. Silva, P. G. Williams, J. M. Pezzuto, and L. C. Chang. (2023). "Anti-Inflammatory Quinoline Alkaloids from the Roots of Waltheria indica". *Journal of Natural Products.* **86** (2): 276-289. 10.1021/acs.jnatprod.2c00861.

[64] T. Meng, S. Fu, D. He, G. Hu, X. Gao, Y. Zhang, B. Huang, J. Du, A. Zhou, Y. Su, and D. Liu. (2021). "Evodiamine Inhibits Lipopolysaccharide (LPS)-Induced Inflammation in BV-2 Cells via Regulating AKT/Nrf2-HO-1/NF-κB Signaling Axis". *Cellular and Molecular Neurobiology.* **41** (1): 115-127. 10.1007/s10571-020-00839-w.

[65] R. G. Geetha and S. Ramachandran. (2021). "Recent Advances in the Anti-Inflammatory Activity of Plant-Derived Alkaloid Rhynchophylline in Neurological and Cardiovascular Diseases". *Pharmaceutics.* **13** (8): 1170. 10.3390/pharmaceutics13081170.

[66] L. Chen, Y. Liu, and J. Xie. (2024). "The Beneficial Pharmacological Effects of Uncaria rhynchophylla in Neurodegenerative Diseases: Focus on Alkaloids". *Frontiers in Pharmacology.* **15** : 1436481. 10.3389/fphar.2024.1436481.

[67] Z. Ji-Yin and Z. Shi-Wen. (2010). "Antihypertensive and Neuroprotective Activities of Rhynchophylline: The Role of Rhynchophylline in Neurotransmission and Ion Channel Activity". *Journal of Ethnopharmacology.* **132** (1): 15-27.

[68] Q. Tang, X. Shen, Y.-K. Hao, S.-Y. Yang, J.-T. Fu, T.-Y. Wu, H.-Y. Zhao, B. Qin, Y.-L. Li, Y.-B. Zhang, and G.-C. Wang. (2024). "Diterpenoid Alkaloids from Delphinium ajacis and Their Anti-Inflammatory Activity". *Chemistry & Biodiversity.* **21** (2). 10.1002/cbdv.202301958.

[69] H. Pei, L. Xue, M. Tang, H. Tang, S. Kuang, L. Wang, X. Ma, X. Cai, Y. Li, M. Zhao, A. Peng, H. Ye, and L. Chen. (2020). "Alkaloids from Black Pepper (Piper nigrum L.) Exhibit Anti-Inflammatory Activity in Murine Macrophages by Inhibiting Activation of the NF-κB Pathway". *Journal of Agricultural and Food Chemistry.* **68** (8): 2406-2417. 10.1021/acs.jafc.9b07754.

[70] T. Mitani, T. Takaya, N. Harada, S. Katayama, R. Yamaji, S. Nakamura, and H. Ashida. (2018). "Theophylline Suppresses Interleukin-6 Expression by Inhibiting Glucocorticoid Receptor Signaling in Pre-Adipocytes". *Archives of Biochemistry and Biophysics.* **646** : 98-106. 10.1016/j.abb.2018.04.001.

[71] L. Gallelli, D. Falcone, R. Cannataro, M. Perri, R. Serra, G. Pelaia, R. Maselli, R. Savino, G. Spaziano, and B. D'Agostino. (2017). "Theophylline Action on Primary Human Bronchial Epithelial Cells under Proinflammatory Stimuli and Steroidal Drugs: A Therapeutic Rationale Approach". *Drug Design, Development and Therapy.* **11** : 265-272. 10.2147/DDDT.S118485.

[72] J. Wu, H. Huang, L. Gong, X. Tian, Z. Peng, Y. Zhu, and W. Wang. (2024). "A Flavonoid Glycoside Compound from Siraitia grosvenorii with Anti-Inflammatory and Hepatoprotective Effects In Vitro". *Biomolecules.* **14** (4): 450. 10.3390/biom14040450.

[73] J. Wu, H. Huang, L. Gong, X. Tian, Z. Peng, Y. Zhu, and W. Wang. (2023). "Network Pharmacology Study of Bioactive Components and Molecular Mechanisms of the Glycoside Fraction from Picrorhiza scrophulariiflora against Experimental Colitis". *Drug Design, Development and Therapy.* **17** : 1531-1546. 10.2147/DDDT.S407339.

[74] C. Boonkaewwan and A. Burodom. (2013). "Anti-Inflammatory and Immunomodulatory Activities of Stevioside and Steviol on

Colonic Epithelial Cells". *Journal of the Science of Food and Agriculture.* **93** (15): 3820-3825. 10.1002/jsfa.6287.

[75] Q. Xu, M. Liu, X. Chao, C. Zhang, H. Yang, J. Chen, and B. Zhou. (2023). "Stevioside Improves Antioxidant Capacity and Intestinal Barrier Function while Attenuating Inflammation and Apoptosis by Regulating the NF-κB/MAPK Pathways in Diquat-Induced Oxidative Stress of IPEC-J2 Cells". *Antioxidants.* **12** (5): 1070. 10.3390/antiox12051070.

[76] Y. C. Shi, Y. X. Yu, J. X. Gao, X. Wang, X. Y. Shang, and J. Xu. (2025). "Iridoid Glycoside Dimers from Fruits of Cornus officinalis and Their Anti-Inflammatory Activity". *Frontiers in Chemistry.* **13** : 1558075. 10.3389/fchem.2025.1558075.

[77] L. Yang and J. He. (2022). "Anti-Inflammatory Effects of Flavonoids and Phenylethanoid Glycosides from Hosta plantaginea Flowers in LPS-Stimulated RAW 264.7 Macrophages through Inhibition of the NF-κB Signaling Pathway". *BMC Complementary Medicine and Therapies.* **22** (1): 354. 10.1186/s12906-022-03540-1.

[78] A. Tureyen, H. H. Demirel, E. N. Demirkapi, A. M. Eryavuz, and S. Ince. (2023). "Tubuloside A, a Phenylethanoid Glycoside, Alleviates Diclofenac-Induced Hepato-Nephro Oxidative Injury via Nrf2/HO-1". *Journal of Cellular and Molecular Medicine.* **27** (21): 3404-3413. 10.1111/jcmm.17968.

[79] S. Isik, C. Tayman, U. Cakir, I. Koyuncu, T. Taskin Turkmenoglu, and E. Cakir. (2019). "Sumac (Rhus coriaria) for the Prevention and Treatment of Necrotizing Enterocolitis". *Journal of Food Biochemistry.* **43** (12): e13068. 10.1111/jfbc.13068.

[80] S. P. Ekambaram, J. Aruldhas, A. Srinivasan, and T. Erusappan. (2022). "Modulation of NF -κB and MAPK Signalling Pathways by Hydrolysable Tannin Fraction from Terminalia chebula Fruits Contributes to Its Anti-Inflammatory Action in RAW 264.7 Cells". *Journal of Pharmacy and Pharmacology.* **74** (5): 718-729. 10.1093/jpp/rgab178.

[81] A. Cerulli, A. Napolitano, J. Hošek, M. Masullo, C. Pizza, and S. Piacente. (2021). "Antioxidant and In Vitro Preliminary Anti-Inflammatory Activity of Castanea sativa (Italian Cultivar “Marrone di Roccadaspide” PGI) Burs, Leaves, and Chestnut Extracts and Their Metabolite Profiles by LC-ESI/LTQ-Orbitrap/MS/MS". *Antioxidants.* **10** (2): 278. 10.3390/antiox10020278.

[82] N. Rajasekar, A. Sivanantham, A. Kar, S. Mukhopadhyay, S. K. Mahapatra, S. G. Paramasivam, and S. Rajasekaran. (2021). "Anti-Asthmatic Effects of Tannic Acid from Chinese Natural Gall Nuts in a Mouse Model of Allergic Asthma". *International Immunopharmacology.* **98** : 107847. 10.1016/j.intimp.2021.107847.

[83] G. Molinaro, F. Fontana, R. Pareja Tello, S. Wang, S. López Cérda, G. Torrieri, A. Correia, E. Waris, J. T. Hirvonen, G. Barreto, and H. A. Santos. (2023). "In Vitro Study of the Anti-Inflammatory and Antifibrotic Activity of Tannic Acid-Coated Curcumin-Loaded Nanoparticles in Human Tenocytes". *ACS Applied Materials & Interfaces.* **15** (19): 23012-23023. 10.1021/acsami.3c05322.

[84] S. Molino, A. Pisarevsky, S. Badu, Q. Wu, F. López Mingorance, P. Vega, J. P. Stefanolo, J. Repetti, G. Ludueña, P. Pepa, J. I. Olmos, M. Rodriguez Fermepin, T. Uehara, E. Viciani, A. Castagnetti, T. Savidge, and M. M. Piskorz. (2022). "Randomized Placebo-Controlled Trial of Oral Tannin Supplementation on COVID-19 Symptoms, Gut Dysbiosis, and Cytokine Response". *Journal of Functional Foods.* **99** : 105356. 10.1016/j.jff.2022.105356.

[85] P. De Cicco, G. Ercolano, C. Sirignano, V. Rubino, D. Rigano, A. Ianaro, and C. Formisano. (2023). "Chamomile Essential Oils Exert Anti-Inflammatory Effects Involving Human and Murine Macrophages: Evidence to Support a Therapeutic Action". *Journal of Ethnopharmacology.* **311** : 116391. 10.1016/j.jep.2023.116391.

[86] R. B. Pereira, F. Z. Rahali, R. Nehme, H. Falleh, M. Ben Jemaa, I. Hamrouni Sellami, R. Ksouri, S. Bouhallab, F. Ceciliani, L. Abdennebi-Najar, and D. M. Pereira. (2023).

"Anti-Inflammatory Activity of Essential Oils from Tunisian Aromatic and Medicinal Plants and Their Major Constituents in THP-1 Macrophages". *Food Research International.* **167** : 112678. 10.1016/j.foodres.2023.112678.

[87] V. M. But, A. E. Bulboacă, V. Rus, T. Ilyés, M. L. Gherman, and S. D. Bolboacă. (2023). "Anti-Inflammatory and Antioxidant Efficacy of Lavender Oil in Experimentally Induced Thrombosis". *Thrombosis Journal.* **21** (1): 45. 10.1186/s12959-023-00516-0.

[88] A. Horváth, E. Pandur, K. Sipos, G. Micalizzi, L. Mondello, A. Böszörményi, P. Birinyi, and G. Horváth. (2022). "Anti-Inflammatory Effects of Lavender and Eucalyptus Essential Oils on an In Vitro Cell Culture Model of Bladder Pain Syndrome Using T24 Cells". *BMC Complementary Medicine and Therapies.* **22** (1): 236. 10.1186/s12906-022-03604-2.

[89] J. Yang, S. Y. Lee, S. K. Jang, K. J. Kim, and M. J. Park. (2023). "Anti-Inflammatory Effects of Essential Oils from the Peels of Citrus Cultivars". *Pharmaceutics.* **15** (6): 1595. 10.3390/pharmaceutics15061595.

[90] C. Zhao, Y. Cao, Z. Zhang, D. Nie, and Y. Li. (2021). "Cinnamon and Eucalyptus Oils Suppress Lipopolysaccharide-Induced Inflammation In Vivo". *Molecules.* **26** (23): 7410. 10.3390/molecules26237410.

[91] L. F. Azevedo, A. Costa-Pereira, L. Mendonça, C. C. Dias, and J. M. Castro-Lopes. (2012). "Epidemiology of Chronic Pain: A Population-Based Nationwide Study on Its Prevalence, Characteristics, and Associated Disability in Portugal". *The Journal of Pain.* **13** (8): 773-783. 10.1016/j.jpain.2012.05.012.

[92] G. P. Caviglia, A. Garrone, C. Bertolino, R. Vanni, E. Bretto, A. Poshnjari, E. Tribocco, S. Frara, A. Armandi, M. Astegiano, G. M. Saracco, L. Bertolusso, and D. G. Ribaldone. (2023). "Epidemiology of Inflammatory Bowel Diseases: A Population Study in a Healthcare District of North-West Italy". *Journal of Clinical Medicine.* **12** (2): 641. 10.3390/jcm12020641.