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Review Article

Plant-Based Anti-Inflammatory Agents: A Scientific Review of Bioactive Compounds and Mechanisms

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ABSTRACT

Inflammation, caused by pathogens or damaged tissues, can lead to chronic diseases if left untreated. Although they provide relief, contemporary anti-inflammatory treatments-in particular, non-steroidal anti-inflammatory medicines, or NSAIDs-frequently have side effects. Because of their capacity to modify important inflammatory pathways like Cyclooxygenase (COX), Nitric Oxide Synthase (NOS), and Nuclear Factor kappa B (NF-κB), plant-derived chemicals have recently come to light as possible substitutes. Curcumin, resveratrol, and *Capsaicin* are examples of phytochemicals that have demonstrated strong anti-inflammatory properties by preventing oxidative stress and pro-inflammatory cytokines. Furthermore, green tea polyphenols and omega-3 fatty acids show great therapeutic promise in lowering inflammation and preventing chronic illnesses like cardiovascular disease and arthritis. Even though these plant-based treatments have potential, further research is needed to fully comprehend their molecular mechanisms and create clinically useful formulations. Inflammatory disorders may have safer, more sustainable therapy alternatives if medicinal plants are incorporated into traditional healthcare.

Keywords: Anti-inflammatory, Cyclooxygenase (COX), Nitric Oxide Synthase (NOS), Omega-3 fatty acids.

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INTRODUCTION

Overview of Inflammation and its Role in Chronic Diseases

Inflammation is a normal biological process that occurs when tissue injuries, microbial pathogen infection and chemical exposure occur. The innate and adaptive immune systems are also involved in this biological process. Immune cells that migrate from blood vessels and release mediators at a damaged region cause inflammation, which is necessary to eliminate invading pathogens, prevent infection, and repair injured tissues. Following this, there is an influx of inflammatory cells and the secretion of Reactive Oxygen Species (ROS), Reactive Nitrogen Species (RNS), and proinflammatory cytokines. As a result, the fundamental aim of inflammation is to strengthen the host's defense system. Typically, normal inflammation resolves promptly and independently; however, prolonged inflammation and inadequate resolution can give rise to several chronic health conditions.[1]

The body's initial response, known as acute inflammation, may trigger a cascade that results in tissue damage or infection. This phase is brief and occurs before the immune response develops. Acute inflammation also functions as a homeostatic mechanism that helps the body in the reparative process.[2]

The body sustains damage when there is persistent inflammation because the inflammatory response is out of control. The body is damaged by chronic inflammation because the inflammatory response gets out of control. Cyclooxygenase is the key enzymes that produce prostaglandins, prostacyclins, and thromboxanes, which are linked to inflammation, pain, and platelet aggregation (COX). Currently, the frequently common drugs for the treatment of acute inflammatory disorders are Non-steroidal and steroidal Anti-Inflammatory Drugs (NASIDs and SAIDs, respectively), despite their adverse effects on the kidneys and stomach. COX-1 and COX-2 enzyme activity is blocked by these medications. Prostaglandin synthesis is aided by COX enzymes. Since NSAIDs, or steroidal anti-inflammatory drugs, have been around for a while, prolonged use of them has resulted in negative side effects and damage to humans. [3,4]

The initiation of inflammation is a protective reaction to harmful external substances, like pathogens, viruses, dust particles, irritants, and damaged cells. This process involves several stages, beginning with an initiation phase, followed by a peak

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of inflammation, and concluding with a resolution phase. The initiation phase is crucial for effective defense by the host. It occurs due to both external and internal harmful stimuli, which can be mechanical, chemical, or biological in nature, resulting from the destruction of cells. The resolution phase is essential for diminishing inflammation and restoring normal cell function once the harmful stimuli are removed. Genetic factors, such as certain gene mutations, can sometimes prevent the body from effectively resolving inflammation.[5]

Signaling molecules and immune cells work together to promote inflammation. Cytokines play an important part in this process. They are classified into pro-inflammatory cytokines, including interleukin-1β, interleukin-6, and tumor necrosis factor-α, and anti-inflammatory cytokines, such as interleukin-1 receptor alpha, interleukin-4, interleukin-10, and transforming growth factor-β1. Pro-inflammatory cytokines stimulate systemic infection and kickstart an immune response against disease, while anti-inflammatory cytokines work to counteract these effects, reducing inflammation and aiding in healing. Inflammation promotes and regulates cellular processes such as apoptosis, necrosis, and autophagy, which are induced by oxidative stress. Oxidative stress and inflammation are closely linked, and the mechanisms behind this relationship are observed in various diseases, including irritable bowel syndrome, inflammatory bowel disease, and ulcerative colitis. Inflammation also leads to the modification of large molecules like proteins, lipids, DNA, and RNA, resulting in the production of numerous free radicals, including Reactive Oxygen Species (ROS). Pro-inflammatory cytokines, such as interleukin-1, interleukin-18, tumor necrosis factor-α, and p38 Mitogen-Activated Protein Kinases (MAPK), are primarily responsible for generating ROS, which in turn cause oxidative stress.[5]

Inflammation serves as a tissue response to injury, involving both systemic and localized reactions. Although modern medicine and advancements in synthetic pharmaceuticals have made significant strides, approximately 80% of the global population is unable to afford the offerings of the modern pharmaceutical sector. Consequently, a substantial number of individuals turn to traditional medicine, predominantly sourced from plants. This highlights the significance of natural anti-inflammatory agents.[6]

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is a major component found in hot peppers from the Capsicum species. Though it's often thought that *Capsaicin* worsens inflammation, research indicates that it can also reduce inflammation when its effects are intensified. Studies have suggested that *Capsaicin* could be utilized to mitigate inflammation and joint discomfort. *Capsaicin*, along with camphor oil and other natural topical solutions, is frequently used for alleviating muscle pain and for treating localized painful injuries.[7] Omega-3 fatty acids, also known as n-3 fatty acids or omega-3 oils, are a kind of polyunsaturated fatty acid with multiple double bonds on carbon atom 3.[8] They are considered essential nutrients for humans, but our bodies are unable to produce them. These fatty acids are mainly present in oily fish such as salmon, bluefish, tuna, and halibut. Additionally, they are found in canola, flaxseed, hemp, soybean, walnut, soy, tofu, green leafy vegetables, venison, buffalo, and others. Fish oil, specifically cod liver oil, a form of omega-3 EFA, is used for the treatment of muscular and skeletal.[9] Curcumin is a natural yellow pigment sourced from turmeric (*Curcuma longa*), a flowering plant in the ginger family. It has been traditionally employed as a spice for coloring and flavoring in food. Curcumin has a long history of use in Ayurvedic and Chinese medicine for its anti-inflammatory properties, treatment of digestive issues, and promotion of wound healing. Several clinical studies have confirmed curcumin's antioxidant, anti-inflammatory, and anticancer properties.[10] Green tea is well-known for its benefits to the heart and its role in cancer prevention, thanks to its antioxidant characteristics. Its role in reducing inflammation for the treatment of arthritis has gained recognition more recently. The active compounds in green tea, specifically polyphenols known as catechins, are particularly abundant in Epigallocatechin-3-Gallate (EGCG). Resveratrol is a compound found in plants of various sources, with the highest concentrations located in the skins of red wine grapes.[11,12]

PLANTS AS A SOURCE OF BIOACTIVE SUBSTANCES

Plants have been a crucial element in traditional medicine for centuries. To combat pathogens and environmental stress, plants produce a variety of substances with biological effects. These substances, derived from secondary metabolism, exhibit diverse biological activities. Among these, anti-inflammatory properties are particularly noteworthy.[13]

Herbs and medicinal plants have been utilized for their rich array of bioactive compounds for ages. The plant's raw material or its isolated compounds are widely used across generations of native healers to treat a broad range of conditions. Currently, these plants are the focus of extensive research but extracting their compounds for phytochemical and biological studies poses unique challenges that need to be overcome during the extraction process.[14]

Plants are of great importance due to their distinctive features as a major source of therapeutic phytochemicals, their effectiveness, safety, and minimal adverse effects. Bioactive compounds in plants encompass a variety of groups, including alkaloids, terpenoids, coumarins, flavonoids, nitrogen-containing compounds, organosulfur compounds, phenolics, and more. These compounds exhibit a wide range of biological activities, such as anti-inflammatory, immunostimulatory, anticancer, antioxidant, antimicrobial, and more.[14]

The categorization of bioactive compounds varies, often depending on the purpose of the classification. For instance, biosynthetic classifications aim for the simplicity of describing biosynthetic pathways, which may not align with the scope of pharmacological classifications. The bioactive compounds from plants are classified into three main groups: (a) terpenes and terpenoids (approximately 25,000 types), (b) alkaloids (approximately 12,000 types), and (c) phenolic compounds (approximately 8000 types).[15,16]

The majority of bioactive compounds belong to one of several families, each characterized by specific structural features due to their natural biosynthesis. There are four primary pathways for the biosynthesis of secondary metabolites or bioactive compounds: (1) Shikimic acid pathway, (2) malonic acid pathway, (3) Mevalonic acid pathway, and (4) non-Mevalonate (MEP) pathway.[17] Alkaloids are produced from aromatic amino acids (through the shikimic acid pathway) and aliphatic amino acids (through the tricarboxylic acid cycle). Phenolic compounds are synthesized via the shikimic acid pathway and malonic acid pathway.[18] Terpenes are produced through the shikimic acid pathway and malonic acid pathway. A simplified overview of the different pathways for the production of three major groups of plant bioactive compounds is presented in Figure 1.

THE BIOLOGICAL PROCESSES INVOLVED IN THE ONSET OF INFLAMMATION

The Biological mechanisms associated with inflammation and the molecular targets for therapeutic interventions aimed at mitigating inflammation, as outlined in the provided text, encompass the following aspects:

1. **Vasodilation:** This phenomenon is mediated by Nitric Oxide (NO) and vasodilatory prostaglandins. Nitric oxide is synthesized by various isoforms of Nitric Oxide Synthase (NOS), while prostaglandins are derived from arachidonic acid through the action of Cyclo-Oxygenase (COX).[19]
2. **Fluid Leakage:** This result from an increase in vascular permeability, which is influenced by agents such as histamine, bradykinin, leukotrienes, complement components, substance P, and Platelet-Activating Factor (PAF).
3. **Leukocyte Movement:** This process includes several stages: margination, rolling, adhesion, diapedesis, and chemotaxis. Critical molecules involved are selectins, integrins, and their respective ligands (e.g., ICAM-1, PECAM-1).[20]
4. **Activation of the Coagulation Cascade:** This process is triggered by the expression of tissue factor, leading to thrombin formation and the subsequent generation of fibrin clots.
5. **Activation of the Complement System:** This can occur via three distinct pathways: classical, alternative, and lectin. The activation results in the generation of C3a and C5a.[21]
6. **Production of Cytokines:** Activated macrophages and other immune cells secrete pro-inflammatory cytokines (TNF-α, IL-1, IL-6) and chemokines (IL-8).
7. **T-Cell Differentiation:** The activation of TH1 and TH2 immune responses is modulated by specific cytokines and transcription factors.[22]
8. **Inhibition of Lipoxygenase:** Lipoxygenase plays a role in the synthesis of leukotrienes from arachidonic acid which are pro-inflammatory mediators. Inhibiting lipoxygenase can lead to a reduction in inflammation.[23]
9. **Inhibition of Nitric Oxide Production:** Numerous plant-derived flavonoids can impede the synthesis of nitric oxide, a free radical that contributes to inflammation through cytokine-activated macrophages, which are also recognized as pro-inflammatory mediators.[23]
10. Inhibition of Cyclooxygenase Numerous herbal compounds possess the ability to impede the production of prostaglandins through the action of two specific enzymes, cyclooxygenase 1 and 2.[23]
11. **Prostaglandins serve as mediators of inflammation and are classified into four types:** PGE2, PGI2, PGD2, and PGF2. These compounds play a significant role in the inflammatory response, manifesting the typical symptoms such as pain, redness, and swelling. The redness and swelling are attributed to increased blood flow, which enhances vascular permeability and induces vasodilation. Pain is a consequence of the interaction between prostaglandins and sensory neurons, as well as their influence on central nervous system sites.[24]
12. **Inhibition of Phospholipase:** Arachidonic acid is released from membrane lipid phospholipase and acts as a precursor for the synthesis of eicosanoids, including prostaglandins. The inhibition of phospholipase is essential for effectively managing inflammation.[25]
13. **Inhibition of Pro-Inflammatory:** Certain plant extracts can mitigate inflammation by suppressing the activity of pro-inflammatory cytokines. These cytokines are signaling molecules secreted by immune cells, predominantly T-cells and macrophages. Pro-inflammatory cytokines, such as IL-1beta and IL-6, are involved in the regulation of apoptosis, while TNF-alpha influences apoptosis through various signaling pathways.[26]

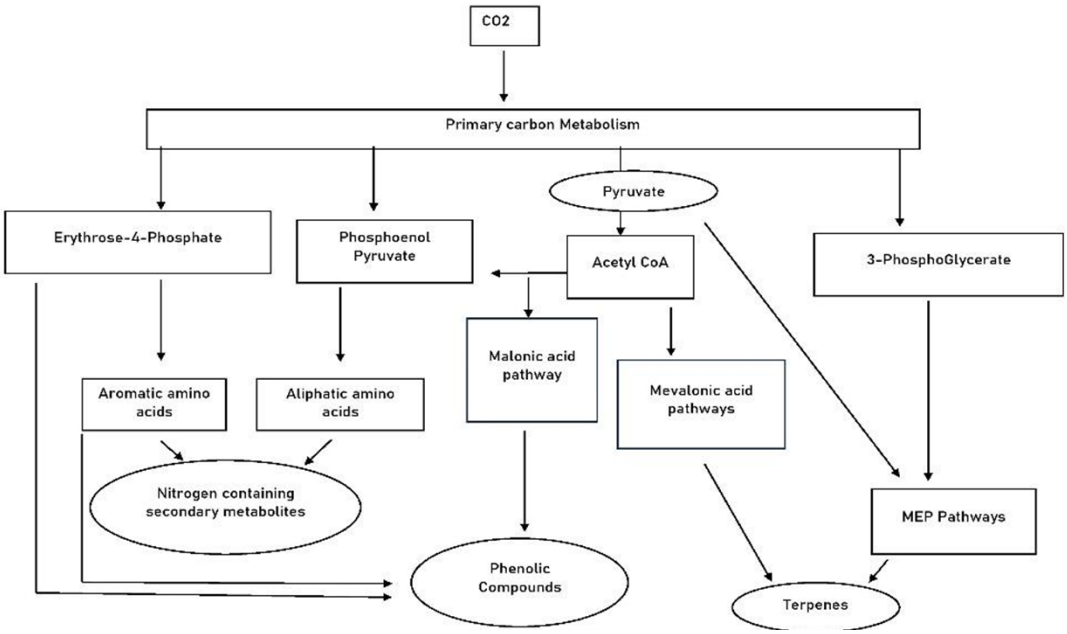

Figure 1: Biosynthesis of secondary metabolites.

KEY MOLECULAR TARGETS FOR ANTI-INFLAMMATORY INTERVENTIONS

The involvement of Mitogen-Activated Protein Kinases (MAPKs), with a particular emphasis on the p38 MAPK pathway, is significant in the modulation of inflammatory processes, as well as the potential application of MAPK inhibitors as therapeutic agents for inflammation. Excessive inflammation is a pivotal contributor to numerous human ailments, encompassing inflammatory and autoimmune diseases, neurodegenerative disorders, infections, cardiovascular conditions, and cancer. The p38 MAPK pathway is triggered by a range of inflammatory signals and is active in the synthesis and activation of inflammatory mediators, including cytokines, chemokines, and various enzymes. This pathway governs the expression of pro-inflammatory genes through both transcriptional and post-transcriptional mechanisms. Research has demonstrated that inhibitors targeting the p38 MAPK pathway exhibit anti-inflammatory properties in several preclinical models of chronic inflammatory conditions, such as rheumatoid arthritis, inflammatory bowel diseases, and neuroinflammation linked to stroke and Alzheimer's disease. The highest target genes identified were AKT1, CASP3, PTGS2, NOS3, and TP53, which were found to have the highest interactions with the plant compounds.[26-30]

AKT1 exhibited the highest interaction rate, comprising 20% of the connections within the compound-target network involving plant compounds. As a pivotal signaling center, AKT1 regulates numerous cellular functions, including metabolism, cell survival, growth, proliferation, and angiogenesis. It also demonstrates significant anti-inflammatory properties by inhibiting NF-κB-mediated transcription.[31] Following AKT1, CASP3 emerged as the second most enriched target, representing 9% of the interactions. CASP3 is essential in the activation cascade of caspases that facilitate the process of apoptosis. PTGS2 also ranked among the top enriched targets, accounting for 9% of the interactions. This enzyme is critical for the synthesis and production of inflammatory prostaglandins. NOS3, or endothelial nitric oxide synthase, was identified as one of the top 5 enriched targets, constituting 7% of the interactions. NOS3 is believed to have anti-apoptotic functions and is involved in downregulating genes associated with cell proliferation, as well as decreasing the expression of several pro-inflammatory cytokines, including IFN-γ, IL-1β, IL-6, and TNF-α. Additionally, TP53 was recognized as another highly enriched target, also representing 7% of the compound-target interactions. TP53 plays a role in identifying non-self-antigens, thereby initiating anti-tumor immunity through various mechanisms. The primary target genes with the most significant interactions with the plant compounds are likely to be central nodes in the compound-target network, playing vital roles in mediating the immunomodulatory effects of the plant extracts, including *Curcuma longa, Allium sativum, Olea europaea, Salvia officinalis, Glycyrrhiza glabra,* and *Silybum marianum*.[32-35]

The various mechanisms by which plant-derived compounds regulate inflammation across different cell types, including macrophages, cardiac myocytes, adipose tissue, and epithelial cells, are noteworthy. These mechanisms exhibit pleiotropy, often targeting multiple action sites within the TLR4 pathway. Certain mechanisms are shared among various phytochemicals, contributing significantly to their recognized anti-inflammatory

properties. In this regard, these phytocompounds collectively inhibit the expression of the TLR4 receptor and impede the activation of the NF-κB transcription factor. This action subsequently reduces the production of downstream pro-inflammatory cytokines, such as TNF-α, IL-6, and IL-1β, as well as free radicals like NO and ROS. Additionally, apart from their inhibitory effects on the TLR4/NF-κB pathway, these phytochemicals also activate the Nrf-2 signaling pathway, which plays a crucial role in mitigating oxidative stress. Furthermore, there exist specialized mechanisms that are particularly relevant to specific phytochemicals. At the epigenetic level, these compounds undergo significant modifications that enhance their anti-inflammatory capabilities. This review highlights that many of the discussed phytochemicals notably downregulate miR-155 and miR-21, both of which diminish NF-κB activity and suppress inflammatory factors such as TNF-α, IL-6, and MAPKs, thereby alleviating induced inflammation. In addition to regulating miRNA, these phytochemicals are instrumental in reducing the expression of pro-inflammatory genes and inhibiting NF-κB-dependent inflammation in various cells by targeting HATs (e.g., p300 HAT) and HDACs (e.g., HDAC I, II, and III).[36]

Additionally, certain phytochemicals, including CUR, API, tanshinone IIA, and SFN, have been shown to downregulate the expression of DNMTs (such as DNMT 1, 3a, and 3b) and inhibit DNA hypermethylation in the promoter regions of specific genes like Nrf2, thereby enhancing their expression. In contrast, RES is known to upregulate the expression of DNMT 3a and 3b, which leads to increased DNA hypermethylation of inflammatory genes, consequently reducing inflammation. Overall, these similarities and differences among phytochemicals contribute to their significant anti-inflammatory properties and highlight their varying therapeutic potential and effectiveness against particular inflammatory diseases across different cell types.[36]

PHYTOCHEMICALS WITH ANTI-INFLAMMATORY PROPERTIES

Phytochemicals with anti-inflammatory properties that reduce chronic pain may be therapeutic agents for many diseases. These phytochemicals work by modulating several important pathways including NF-κB, MAPK, STAT, and Nrf-2 signaling. Here we discuss the properties of phytochemicals with anti-inflammatory activity in various chronic diseases.[37]

Plants are among the most effective new anti-inflammatory medications for treating a variety of disorders in the body. Inflammation is an important defense against microbial infection, cell/tissue damage, and radiation. It is characterized by swelling, redness, heat, and pain in response to different infections (autoimmune and immune), Sclerosis (Heart).[38]

Consumption of fruits and vegetables containing phytochemicals in foods has been shown to have anti-inflammatory and antioxidant properties while reducing cancer and heart disease. Since many phytochemicals are considered to be plant-derived toxins, their anti-inflammatory properties have also been investigated. Therefore, there is high interest in research on these natural products, with many *in vitro* or animal model studies focusing on specific phytochemicals. Some studies suggest that the effects obtained with this drug may be significant at higher doses. However, the extraction and synthesis of phytochemicals can be laborious. In fact, preclinical research is necessary to isolate and focus on drugs that are clinically relevant and easy to extract or produce. Analyzing the composition of proven plant extracts or essential oils can reveal the phytochemicals present in them.[39]

SYNERGISTIC EFFECTS AND COMBINATION THERAPIES

Interaction with Conventional Anti-Inflammatory Drugs

Nonsteroidal Anti-Inflammatory Medicines (NSAIDs) are a significant class of medications used for anti-inflammatory, analgesic, and antipyretic effects. Their mechanism of action involves the inhibition of prostaglandin synthesis. NSAIDs can be categorized into two groups: non-selective agents that inhibit both COX-1 and COX-2, and selective COX-2 inhibitors. Although NSAIDs are effective in alleviating inflammation, they are associated with a variety of adverse effects, particularly impacting the gastrointestinal, cardiovascular, and renal systems.[46]

Protein Targets of NSAIDs

1. **COX Enzymes:** COX-1 and COX-2 serve as the primary targets for NSAIDs, facilitating the rate-limiting steps in the synthesis of prostaglandins. The binding site for drugs within COX enzymes consists of a hydrophobic channel, where both hydrophobic and polar interactions contribute to the stabilization of NSAID binding. Structural investigations have elucidated the binding configurations of various NSAIDs, including flurbiprofen, diclofenac, and celecoxib, within the active sites of COX.[40-43,46]
2. **Phospholipase A2 (PLA2):** PLA2 is another crucial enzyme that plays a role in the inflammatory cascade by releasing arachidonic acid from membrane phospholipids. NSAIDs have demonstrated the ability to bind to and inhibit PLA2 enzymes, typically through interactions with the catalytic residues His48 and Asp49.[46]
3. **Cytochrome P450 (CYP450) Enzymes:** CYP450 enzymes are integral to the oxidative metabolism of NSAIDs. The interaction of NSAIDs with CYP450s can result in drug-drug interactions and potential

toxicity. Structural studies have provided insights into the binding modes of NSAIDs such as diclofenac and flurbiprofen within the active sites of CYP450.[46,44]

4. **Lactoperoxidase (LPO):** LPO is a heme-containing peroxidase enzyme that can be inhibited by NSAIDs acting as competitive substrates. Structural analyses have demonstrated the binding of NSAIDs, including aspirin, indomethacin, and nimesulide, within the active site of LPO.[46]

5. **Transthyretin (TTR):** TTR is a transport protein involved in amyloid disorders. NSAIDs such as diclofenac, flufenamic acid, and flurbiprofen have been identified.[45,46]

6. **Lactoferrin (LF):** LF serves as an iron transport protein capable of non-selectively binding Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), which may mitigate their gastrointestinal toxicity. Human Serum Albumin (HSA): HSA functions as a principal drug transport protein, binding NSAIDs at various sites to enhance their distribution throughout the body. Peroxisome Proliferator-Activated Receptor γ (PPARγ): PPARγ is a nuclear receptor that can be activated by NSAIDs such as indomethacin, resulting in anti-inflammatory and metabolic benefits.[46]

MECHANISMS OF NSAID-INDUCED REACTIONS

The interaction of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with various protein targets, in addition to their inhibition of COX enzymes, plays a significant role in both their therapeutic and detrimental physiological outcomes. The non-selective binding of NSAIDs to enzymes such as CYP450, LPO, and PLA2 can result in drug-drug interactions, toxicity, and alterations in other signaling pathways. Therefore, the development of more selective NSAID inhibitors that specifically target the enzymes involved in eicosanoid production may mitigate the off-target adverse effects.[46]

FUTURE PROSPECTS IN THE DEVELOPMENT OF PLANT-BASED ANTI-INFLAMMATORY THERAPIES

1. **Identification of Innovative Bioactive Substances:** Progress in analytical methods, including mass spectrometry and metabolomics, may facilitate the identification of novel anti-inflammatory agents derived from lesser-known medicinal flora.

2. **Understanding Mechanisms and Molecular Pathways:** Future research may aim to clarify the specific molecular mechanisms by which these bioactive substances exert their anti-inflammatory properties, potentially involving the modulation of particular cytokines, enzymes, or transcription factors such as NF-kB, COX-2, and IL-6.

3. **Synergistic Treatment Approaches:** The integration of plant-derived anti-inflammatory agents with standard pharmaceutical treatments may yield synergistic benefits, potentially allowing for reduced dosages of synthetic medications and a decrease in adverse effects. Investigating effective combinations could pave the way for new therapeutic strategies.

4. **Herbal Therapeutics:** With the advancements in genomics and bioinformatics, there is potential for the development of personalized medicine strategies utilizing medicinal plants. The efficacy of plant-based anti-inflammatory therapies may vary based on genetic predispositions, enabling tailored treatment plans.

5. **Nanotechnology for Improved Delivery:** The use of nanoparticle-based delivery systems has the potential to enhance the bioavailability and targeted administration of anti-inflammatory compounds derived from plants. This advancement may lead to increased treatment effectiveness while minimizing adverse effects.

6. **Clinical Trials and Standardization:** Future investigations should emphasize the necessity of extensive clinical trials to confirm the safety and effectiveness of medicinal plants in treating inflammation. Additionally, the standardization of extracts and dosages will be essential to achieve reliable therapeutic results.

7. **Sustainability and Conservation:** Given the rising demand for medicinal plants, it is imperative that future initiatives concentrate on sustainable harvesting practices and conservation measures to safeguard plant biodiversity, thereby ensuring a steady supply for medicinal applications without compromising ecosystems.

8. **Regulatory Framework and Integration into Healthcare:** The incorporation of medicinal plants with established anti-inflammatory properties into conventional healthcare could be bolstered by the development of regulatory frameworks that promote their integration into therapeutic practices.

CONCLUSION

Inflammation is a biological response triggered by adverse stimuli such as infections or tissue damage. While acute inflammation plays a crucial role in the healing process, chronic inflammation can result in tissue injury and contribute to various diseases, such as arthritis, cardiovascular conditions, and metabolic disorders. Existing treatments, including Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Steroidal Anti-Inflammatory Drugs

(SAIDs), often come with undesirable side effects, highlighting the need for safer alternatives. The mechanisms underlying inflammation involve a series of molecular events, such as vasodilation, the migration of leukocytes, the production of cytokines, and the activation of enzymes like Cyclooxygenase (COX) and phospholipase. Medicinal plants can influence these processes by inhibiting critical enzymes (e.g., COX, phospholipase, and nitric oxide synthase) and decreasing the synthesis of pro-inflammatory cytokines, including TNF-α and IL-6. Medicinal plants are rich in diverse bioactive compounds, such as alkaloids, terpenoids, and phenolics. These compounds can inhibit inflammatory pathways by interacting with specific receptors, mitigating oxidative stress, and modulating gene expression. Overall, medicinal plants represent a promising and sustainable source of anti-inflammatory agents.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

COX: Cyclooxygenase; **NOS:** Nitric Oxide Synthase; **NF-κB:** Nuclear Factor kappa B; **MAPKs:** Mitogen-Activated Protein Kinases; **SAID:** Steroidal Anti-Inflammatory Drugs; **NSAID:** Non- Steroidal Anti-Inflammatory Drugs; **PLA2:** Phospholipase A2; **CYP450:** Cytochrome P450; **LPO:** Lactoperoxidase.

SUMMARY

Inflammation is a vital biological response to injury, infection, or toxic stimuli, involving immune cells and mediators like cytokines, Reactive Oxygen Species (ROS), and enzymes such as Cyclooxygenase (COX). The acute inflammation helps tissue repair, chronic inflammation can lead to diseases like arthritis, cardiovascular disorders, and metabolic syndromes. Existing treatments, including NSAIDS and SAIDS, often have adverse effects, for safer replacements. Medicinal plants were rich in bioactive compounds like alkaloids, terpenoids, and phenolics, offer promising anti-inflammatory properties by targeting key pathways (e.g., NF-KB, MAPK) and reducing pro-inflammatory cytokines. Natural compounds such as curcumin, capsaicin, and omega-3 fatty acids demonstrate significant anti-inflammatory effects. Future research aims to identify novel plant-based therapies, optimize delivery systems (e.g., nanotechnology), and integrate them with conventional treatments for synergistic benefits. Sustainable practices and clinical validation are crucial for maximizing the benefits of plant-based anti-inflammatory substances in contemporary healthcare.

REFERENCES

1. Min-Hsiung Pan 1, Ching-Shu Lai, Chi-Tang Ho. Anti-inflammatory activity of natural dietary flavonoids. Food & Function. 2010;1(1):15.
2. Frederick Ayertey, Ebenezer Ofori-Attah, Stephen Antwi, Michael Amoa-Bosompem, Georgina Djameh, Nathaniel Lartey Lartey, *et al.* Anti-inflammatory activity and mechanism of action of ethanolic leaf extract of *Morinda lucida* Benth, Journal of Traditional and Complementary Medicine. 2021;11:249-58.
3. Verma S. Medicinal plants with anti-inflammatory activity. J Phytopharmacol. 2016;5(4):157-9.
4. Burke, A., Smyth, E., and FitzGerald, G.A. Analgesicantipyretic agents; pharmacotherapy of gout. In L.B. Brunton, J.S. Lazo and K.L. Parker (Ed.)Goodman and Gilman's the Pharmacological Basis of Therapeutics New York: McGraw-Hill. 2005. p. 671-715.
5. Shrivastava AK, Keshari M, Neupane M, Chaudhary S, Dhakal PK, Shrestha L, *et al.* Evaluation of Antioxidant and Anti-Inflammatory Activities, and Metabolite Profiling of Selected Medicinal Plants of Nepal. J Trop Med. 2023;3.
6. Saleem TK, Azeem AK, Dilip C, Sankar C, Prasanth NV, Duraisami R. Anti-inflammatory activity of the leaf extracts of *Gendarussa vulgaris* Nees. Asian Pac J Trop Biomed. 2011;1(2):147-9.
7. Fattori V, Hohmann MS, Rossaneis AC, Pinho-Ribeiro FA, Verri WA. *Capsaicin*: current understanding of its mechanisms and therapy of pain and other pre-clinical and clinical uses. Molecules. 2016;21.844.
8. Molfino A, Amabile MI, Monti M, Muscaritoli M. Omega-3 polyunsaturated fatty acids in critical illness: Anti- Inflammatory, Proresolving, or Both? Oxid Med Cell Longev. 2017;5987082.
9. Kostoglou-Athanassiou I, Athanassiou L, Athanassiou P. The effect of omega-3 fatty acids on rheumatoid arthritis. Mediterr J Rheumatol. 2020;31:190-4.
10. Ghasemian M, Owlia S, Owlia MB. Review of Anti-Inflammatory Herbal Medicines. Adv Pharmacol Sci. 2016;9130979.
11. Ohishi T, Goto S, Monira P, Isemura M, Nakamura Y. Anti-inflammatory action of green tea. Antiinflamm Antiallergy Agents Med Chem. 2016;15:74-90.
12. Maroon JC, Bost JW, Maroon A. Natural anti-inflammatory agents for pain relief. Surg Neurol Int. 2010;13(1):80.
13. Yilma Hunde Gonfa, Fekade Beshah Tessema, Archana Bachheti, Nishant Rai, Mesfin Getachew Tadesse, A. Nasser Singab, *et al.* Anti-inflammatory activity of phytochemicals from medicinal plants and their nanoparticles: A review, Current Research in Biotechnology. 2023;6.
14. Fotsing Yannick Stéphane F, Kezetas Jean Jules B, El-Saber Batiha G, Ali I, Ndjakou Bruno L. Extraction of Bioactive Compounds from Medicinal Plants and Herbs [Internet]. Natural Medicinal Plants. IntechOpen; 2022.
15. Croteau R, Kutchan, TM, Lewis NG. Natural products (secondary metabolites). In Buchanan B, Gruissem W, Jones R (Eds.),Biochemistry and molecular biology of plants. Rockville, MD: American Society of Plant Physiologists. 2000;1250-318.
16. J. Azmir, I.S.M. Zaidul, M.M. Rahman, K.M. Sharif, A. Mohamed, F. Sahena, *et al.* Techniques for extraction of bioactive compounds from plant materials: A review, Journal of Food Engineering. 2013;4:426-36.
17. Jamwal, K.; Bhattacharya, S.; Puri, S. Plant growth regulator mediated consequences of secondary metabolites in medicinal plants. J. Appl. Res. Med. Aromat. Plants. 2018;9:26-38.
18. Ghasemzadeh, Ali and Jaafar, Hawa Ze. Effect of CO2 Enrichment on Synthesis of Some Primary and Secondary Metabolites in Ginger (*Zingiber officinale* Roscoe). International Journal of Molecular Sciences. 2011;12.
19. Salvemini D, Kim SF, Mollace V. Reciprocal regulation of the nitric oxide and cyclooxygenase pathway in pathophysiology: relevance and clinical implications. Am J Physiol Regul Integr Comp Physiol. 2013;304:473-87
20. Daniel, V. Anti-Inflammatory Activity. In: Hock, F. (eds) Drug Discovery and Evaluation: Pharmacological Assays. Springer, Cham. 2016.
21. Nesargikar PN, Spiller B, Chavez R. The complement system: history, pathways, cascade and inhibitors. Eur J Microbiol Immunol (Bp). 2012;2(2), 103-11.
22. Anne O'Garra, T-cell differentiation: Commitment factors for T helper cells, Current Biology. 2000;10(13), 492-4.
23. Botting, R., Botting, J. Cyclooxygenases. In: Offermanns, S., Rosenthal, W. (eds) Encyclopedia of Molecular Pharmacology. Springer, Berlin, Heidelberg. 2008.
24. Wang, B., Wu, L., Chen, J.*et al.* Metabolism pathways of arachidonic acids: mechanisms and potential therapeutic targets. Sig Transduct Target Ther. 2021;6:94.

25. Jean-Marc Zingg, Modulation of signal transduction by vitamin E, Molecular Aspects of Medicine. 2007;28:481-506.
26. Zhang JM, An J. Cytokines, inflammation, and pain. Int Anesthesiol Clin. Springer. 2007;45(2):27-37.
27. Moens U, Kostenko S, Sveinbjørnsson B. The Role of Mitogen-Activated Protein Kinase-Activated Protein Kinases (MAPKAPKs) in Inflammation. Genes (Basel). 2013;4(2):101-33.
28. Cargnello M, Roux PP. Activation and function of the MAPKs and their substrates, the MAPK-activated protein kinases. Microbiol Mol Biol Rev. 2011;75(1):50-83.
29. Qinwen Zheng, Shutong Li, Aoxue Wang, Man Zhe, Panpan Yang, Yongya Wu, *et al*. p38 mitogen-activated protein kinase: Functions and targeted therapy in diseases, Oncology, 2023.
30. Bozena Kaminska, MAPK signalling pathways as molecular targets for anti-inflammatory therapy-from molecular mechanisms to therapeutic benefits, Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics. 2005; 1754:53-62.
31. Weichhart, T. and Säemann, M. The PI3K/Akt/mTOR pathway in innate immune cells: Emerging therapeutic applications. Ann. Rheumatic Dis. 2008;67:70-74.
32. Ha, Y. M.*et al*. β1-adrenergic receptor-mediated HO-1 induction, via PI3K and p38 MAPK, by isoproterenol in RAW 264.7 cells leads to inhibition of HMGB1 release in LPS-activated RAW 264.7 cells and increases in survival rate of CLP-induced septic mice. Biochem. Pharmacol. 2011;82(7):769-77.
33. Guo, G.*et al*. Trp53 inactivation in the tumor microenvironment promotes tumor progression by expanding the immunosuppressive lymphoid-like stromal Networkp53null promotes stroma expansion and tumor progression. Can. Res. 2013;73(6):1668-75.
34. He, X.-Y.*et al*. p53 in the myeloid lineage modulates an inflammatory microenvironment limiting initiation and invasion of intestinal tumors. Cell Rep. 2015;13(5):888-97.
35. Khairy, A., Ghareeb, D.A., Celik, I, *et al.* Forecasting of potential anti-inflammatory targets of some immunomodulatory plants and their constituents using*in vitro*, molecular docking and network pharmacology-based analysis. Sci Rep. 2023;13:9539.
36. HA, Yousef MH and Abdelnaser A, The Anti-Inflammatory Properties of Phytochemicals and Their Effects on Epigenetic Mechanisms Involved in TLR4/NF-κB-Mediated Inflammation. Front. Immunol. 2021.
37. Shin, S. A., Joo, B. J., Lee, J. S., Ryu, G., Han, M., Kim, *et al.* Phytochemicals as Anti-Inflammatory Agents in Animal Models of Prevalent Inflammatory Diseases. Molecules. 2020;25(24):5932.
38. Chen L., Deng H., Cui H., Fang J., Zuo Z., Deng J., *et al.* Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018;9:7204-18.
39. Pantalos, G.; Vaou, N.; Papachristidou, S.; Stavropoulou, E.; Tsigalou, C.; Voidarou, C.; *et al.* Antioxidant and Anti-Inflammatory Phytochemicals for the Treatment of Inflammatory Bowel Disease: A Systematic Review. Appl. Sci. 2024;14:2177.
40. Gudis, K. and Sakamoto, C. The role of cyclooxygenase in gastric mucosal protection. Dig. Dis. Sci. 2005;50:16-23
41. Mattia, C. and Coluzzi, F. COX-2 inhibitors: pharmacological data and adverse effects. Minerva Anestesiol. 2005;71:461-70.
42. P J Loll, R M Garavito, The X-ray crystal structure of the membrane protein prostaglandin H2 synthase-1. Nature. 1994;367:243-9
43. K Gupta, C T Sharkey, P J Loll, Structural analysis of NSAID binding by prostaglandin H2 synthase: time-dependent and time-independent inhibitors elicit identical enzyme conformations. Biochemistry. 2001;40:5172-80.
44. Guengerich, F.P.Cytochrome p450 and chemical toxicology. Chem. Res. Toxicol. 2008;21:70-83
45. Jacobson, D.R. *et al.* Variant-sequence transthyretin (isoleucine 122) in late-onset cardiac amyloidosis in black Americans. N. Engl. J. Med. 1997;336:466-73
46. Avaneesh K. Dwivedi, Vaishali Gurjar, Sanjit Kumar, Nagendra Singh, Molecular basis for nonspecificity of nonsteroidal anti-inflammatory drugs (NSAIDs), Drug Discovery Today. 2015;20(7):863-73.

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