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"A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drugs and Their Therapeutic Roles"

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Abstract

A wide range of chemicals known as anti-inflammatory drugs work to lessen inflammation, a biological reaction that causes pain, swelling, redness, and heat and is the root cause of many acute and chronic illnesses. These substances are crucial for the treatment of autoimmune diseases, arthritis, and other forms of pain. Corticosteroids and nonsteroidal anti-inflammatory medicines (NSAIDs) are the two main classes. Aspirin, ibuprofen, and naproxen are examples of NSAIDs that primarily function by blocking cyclooxygenase (COX) enzymes, which lowers the production of pro-inflammatory prostaglandins. NSAIDs are helpful, but because they affect both the COX-1 and COX-2 isoenzymes, they can have adverse effects on the kidneys, heart, and gastrointestinal tract. By altering gene expression and blocking pro-inflammatory cytokines, corticosteroids synthetic equivalents of cortisol reduce inflammation. However, they also come with dangers, including immunosuppression and metabolic abnormalities. More specificity and effectiveness in treating inflammatory and autoimmune illnesses have been made possible by recent developments in biological therapies that target particular cytokines or their receptors. These consist of receptor antagonists and monoclonal antibodies that target chemokines, interleukins, and tumor necrosis factor (TNF). Although some were removed because of cardiovascular concerns, the introduction of COX-2 selective inhibitors was intended to reduce gastrointestinal hazards. With continuous research aimed at enhancing their safety profiles and identifying methods to maximize treatment outcomes for patients with inflammatory diseases, anti-inflammatory drugs continue to play a crucial role in clinical practice.

Introduction

Infectious microorganisms like bacteria, viruses, or fungi typically cause inflammation when they enter the body, settle in specific tissues, or move through the bloodstream. Additionally, ischemia, degeneration, malignancy, cell death, and tissue damage can all cause inflammation. The development of inflammation is primarily influenced by both the innate and adaptive immune responses. The primary defense mechanism against invasive microbes and cancer cells is the innate immune system, which is mediated by a variety of cells such as mast cells, dendritic cells, and macrophages. By generating certain receptors and antibodies, more specialized cells like B and T cells, which are part of the adaptive immune systems, are in charge of eliminating cancer cells and invasive pathogens. **(Azab, A., Nassar, A., & Azab, A. N. (2016).)**

Based on how it manifests, inflammation is typically divided into two types: acute inflammation and chronic inflammation. Whether inflammation is acute or persistent is mostly determined by the immune system. Immune cells and biological substances have a tight relationship with the activation of inflammation. With their various immunological roles, innate lymphoid cells (LCs) in particular are crucial in inflammatory disorders. Acute inflammation is characterized by the infiltration of neutrophils and macrophages, while chronic inflammation is characterized by the infiltration of T lymphocytes and plasma cells. In the inflammatory response, these cells are crucial. **(Zuo, X., Gu, Y., Wang, C., Zhang, J., Zhang, J., Wang, G., & Wang, F. (2020).)**

Anti-inflammatory medications are frequently used to lessen inflammation, which is linked to a number of illnesses, including rheumatoid arthritis, asthma, Alzheimer's disease, Parkinson's disease, and infectious disorders such COVID-19 infections. Both acute and chronic illnesses are treated with these medications. Nonsteroidal anti-inflammatory drugs (NSAIDs), which include celecoxib, ibuprofen, naproxen, and diclofenac, are the most well-known anti-inflammatory medications on the market. Although steroids are also used as anti-inflammatory drugs, particularly for severe and chronic inflammation, prolonged use of steroids is linked to a number of adverse drug reactions (ADRs). In order to treat a variety of illnesses, safer and more effective anti-inflammatory medications are therefore required. **(Kumar, A., Chawla, P. A., & Kapoor, B. (2023))**

1.Alzheimer's disease (AD)

The primary cause of dementia, which is typified by a loss of thinking and independence in one's own everyday activities, is Alzheimer's disease (AD), a condition that results in the degradation of brain cells. The cholinergic and amyloid hypotheses are the two main theories put up as the causes of AD, which is thought to be a complex disease. The condition is also influenced by a number of risk factors, including aging, genetics, head trauma, vascular disorders, infections, and environmental variables. There are currently only two classes of approved medications to treat AD: cholinesterase enzyme inhibitors and N-methyl d-aspartate (NMDA) antagonists. These medications only work to treat the symptoms of AD; they neither prevent nor cure the condition. In order

to create effective treatments that can halt or alter the progression of AD, research is currently concentrating on understanding AD pathology by addressing a number of mechanisms, including aberrant tau protein metabolism, β-amyloid, inflammatory response, and cholinergic and free radical damage. Drugs that are currently on the market as well as potential future developments for AD therapy, including disease-modifying therapeutics (DMT), chaperones, and natural substances, are covered in this study. **(Breijyeh, Z., & Karaman, R. (2020).)**

2.Rheumatoid Arthritis

In addition to the clinical symptoms of pain, swelling, stiffness in several joints, fever, and malaise, rheumatoid arthritis is an autoimmune inflammatory disease that is mainly characterized by synovitis and extra-articular organ involvement, such as interstitial pneumonia. Soon after the outset, joint degradation advances, and irreversible physical impairment is observed after the afflicted joints are distorted. Therefore, from the very beginning of the disease, accurate diagnosis and therapy are necessary. While glucocorticoid and anti-inflammatory drug palliative therapy has been employed, disease-modifying antirheumatic medications (DMARDs) are now used to reduce immunological abnormalities and regulate disease activity. DMARDs are categorized into various classes, including biologic, targeted, and standard synthetic DMARDs. These medications have also been demonstrated to stop the long-term progression of joint degradation and physical disability by preserving remission. The development of molecular-targeted medicines has made it possible to employ therapeutic approaches that are based on pathogenic mechanisms. These approaches have also been used to treat a number of autoimmune inflammatory illnesses. **(Tanaka, Y. Rheumatoid arthritis. *Inflamm Regener* 40, 20 (2020).**

Pathophysiology of Rheumatoid Arthritis (RA)

Cytokines, especially interleukin-6 (IL-6), are involved in the pathophysiology of RA. IL-6 is essential for preserving homeostasis, controlling metabolism, and promoting the body's regenerative processes; when an infection or injury occurs, IL-6 levels locally increase, which sets off an inflammatory response. According to recent data, IL-6 may play a part in central sensitization linked to non-inflammatory pain as well as inflammation-induced pain. In the USA, EU, and Japan, sarilumab, an IL-6 inhibitor and human immunoglobulin (IgG1) monoclonal antibody, is authorized for use as a monotherapy or in conjunction with methotrexate (MTX) to treat adult patients with moderately to severely active RA who have not responded well to or become intolerant to one or more disease-modifying antirheumatic medications (DMARDs). **(Tanaka, Y., Takahashi, T., van Hoogstraten, H., Kato, N., & Kameda, H. (2025).**

Numerous medications are available to regulate and suppress inflammatory crises; immunosuppressants, steroids, and nonsteroid anti-inflammatory drugs are practical examples of these drugs that have side effects. In practice, however, we aim to apply the lowest effective dose with the most effectiveness and the fewest side

effects. Therefore, in order to achieve a greater pharmaceutical response and the least amount of undesirable side effects, we must incorporate natural anti-inflammatory elements into prescription therapy**. (Ghasemian, M., Owlia, S., & Owlia, M. B. (2016).**

Mediators and Biomarkers of Inflammation

Our knowledge of inflammation and its function in pathology has quickly expanded with the identification of cellular and molecular inflammatory mediators and the creation of sensitive biomarkers.

Key biomarkers include:

- Reactive oxygen species (ROS) and reactive nitrogen oxide species (RNOS)
- Formation of DNA adducts
- Cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha, and chemokines
- Acute-phase proteins, such as C-reactive protein or CRP
- Prostaglandins
- Cyclooxygenase (COX)-related metabolites
- Inflammation-related growth factors and transcription factors, such as NF-kappaB
- Major immune cell types **(Stone, W. L., Basit, H., Zubair, M., & Burns, B. (2024).**

Classification of anti-inflammatory agents

Worldwide, anti-inflammatory medications are widely used to treat both acute and chronic musculoskeletal pain. Three categories can be used to group the medications:

1.Non-steroidal anti-inflammatory drugs (NSAIDs)

2.Glucocorticoids

3.Disease modifying anti-rheumatic drugs (DMARDs).

Non-steroidal anti-inflammatory drugs (NSAIDs)

The FDA has approved the use of nonsteroidal anti-inflammatory medicines (NSAIDs) as analgesics, antipyretics, and anti-inflammatory medications. Because of these side effects, NSAIDs can be used to treat a variety of illnesses, including migraines, gout, pyrexia, muscle pain, dysmenorrhea, arthritic conditions, and some acute trauma situations without using opioids. A family of medications known as nonsteroidal anti-

inflammatory medicines or analgesics has antipyretic (fever-lowering), analgesic, and, at higher dosages, anti-inflammatory properties. The word "nonsteroidal" sets these medications apart from steroids, which have a similar eicosanoid-depressing, anti-inflammatory activity among a variety of other effects. NSAIDs are unique among analgesics in that they are not narcotic. In the globe, nonsteroidal anti-inflammatory medicines are the most often prescribed medications. Although their antipyretic, anti-inflammatory, and analgesic properties may be advantageous, they are linked to serious adverse effects such peptic ulcers and gastrointestinal damage. The three most well-known medications in this class are naproxen, ibuprofen, and aspirin. NSAIDs are typically used to address illnesses including pain and inflammation, whether they are acute or chronic. (**Singh, S., Sharma, S., Singh, L., Goyal, S., & Gawad, J. B. (2013)**

Classification of NSAIDs based on structure

Salicylates, aryl and heteroaryl acetic acid derivatives, indole/indene acetic acid derivatives, anthranilates, and oxicams (enol acids) are the general categories into which NSAIDs may be categorized based on their chemical structure. An acidic moiety (carboxylic acid, enols) is joined to a planar aromatic functional group to form the overall structure of a typical NSAID. After salicylic acid was extracted from willow bark, salicylates were the first NSAIDs to be discovered [1]. Aryl or heteroaryl acetic acid derivatives are a significant family of NSAIDs, second only to salicylates. Among the most widely used NSAIDs are ibuprofen, fenoprofen, naproxen, and oxaprozin, which are structural derivatives of aryl or heteroaryl acetic acid. Indole or indene acetic acid, which comprises well-known pain relievers like sulindac and indomethacin, is the next class of NSAIDs. **(Bindu, S., Mazumder, S., & Bandyopadhyay, U. (2020)**

Mechanism of action

The cyclooxygenase (COX) enzyme is inhibited by NSAIDs, which is their primary mode of action. Arachidonic acid must be converted by cyclooxygenase in order to produce prostacyclins, prostaglandins, and thromboxanes. [9] The absence of these eicosanoids is thought to be the cause of NSAIDs' therapeutic effects. In particular, prostaglandins produce vasodilation, raise the hypothalamic temperature set-point, and contribute to anti-nociception, whereas thromboxanes aid in platelet adhesion.

COX-1 and COX-2 are the two cyclooxygenase isoenzymes. The body constitutively expresses COX-1, which contributes to renal function, platelet aggregation, and the preservation of the lining of the gastrointestinal tract. COX-2 is inducibly produced during an inflammatory reaction rather than constitutively expressed in the body. The majority of NSAIDs inhibit both COX-1 and COX-2 and are nonselective. However, because they solely target COX-2, COX-2 selective NSAIDs (such celecoxib) have a distinct profile of adverse effects. Crucially, COX-2 selective NSAIDs should offer anti-inflammatory treatment without endangering the gastric mucosa because COX-2 is primarily involved in inflammation and COX-1 is the primary mediator for maintaining the integrity of the gastric mucosa. **(Ghlichloo, I., & Gerriets, V. (2019).**

Pharmacodynamics and Pharmacokinetics of NSAIDs

The main way that NSAIDs work therapeutically is by inhibiting the cyclooxygenase enzymes (COX-1 and COX-2) that impede the formation of certain prostaglandins (PGs). Among other physiological processes, COX-1 generates prostaglandins and thromboxane A2, which regulate the mucosal barrier in the GI tract, renal balance, and platelet aggregation. PGs linked to fever, pain, and inflammation are produced by COX-2. Normal cells express COX-1, whereas inflammatory cells generate COX-2 [6–8]. The intended anti-inflammatory, antipyretic, and analgesic response of NSAIDs is probably represented by COX-2 inhibition, whereas COX-1 inhibition is mostly responsible for the undesirable side effects, such as GI and renal toxicities.

The majority of NSAIDs have a high bioavailability and are easily absorbed in the digestive system. Diclofenac is one medication that experiences hepatic first-pass metabolism, which lowers its bioavailability. However, certain medications, including paracecoxib and sulindac sulfide, are prodrugs that require hepatic metabolism to generate their active metabolites. NSAIDs have a strong affinity for plasma proteins. NSAIDs are typically eliminated in the urine after being digested in the liver. The half-life of common NSAIDs varies; aspirin, for example, might last 0.25–0.3 hours, whereas piroxicam can last 45–50 hours. Due to their lower body water content than adults, all of these pharmacokinetic characteristics might alter as people age. Volumes of distribution may change and protein binding may be decreased. (**Wongrakpanich, S., Wongrakpanich, A., Melhado, K., & Rangaswami, J. (2018)**

Drug interaction of NSAIDs

One of the most frequent reasons for bad medication responses is NSAID drug interactions. Elderly patients should be provided NSAIDs with care as their ages and drug regimens grow. When used with certain medications, NSAIDs can change the risk of bleeding and/or gastrointestinal ulcers. These medications include angiotensin converting enzyme, beta blockers, calcium antagonists, digitalis glycosides, diuretics, corticosteroids, selective serotonin reuptake inhibitors (SSRIs), warfarin, clopidogrel, aspirin, and other anticoagulants. Methotrexate, a popular drug for rheumatoid arthritis, has been shown to have decreased renal clearance when used with certain NSAIDs. Kasturi, J., Palla, P. R., Bakshi, V., & Bogg, N. (2019).

Common adverse effect

Gastrointestinal toxicity	. Dyspepsia . Gastroduodenal ulcers . Gi bleeding and perforation
Cardiovascular adverse effects	. Edema . Hypertension . Congestive heart failure . Myocardial infarction . Stroke and other Thrombotic events
Nephrotoxicity	. Electrolyte imbalance . Sodium retention . Edema . Reduce glomerular filtration rate . Nephrotic syndrome . Acute interstitial nephritis . Renal papillary necrosis . Chronic kidney disease

2. Corticosteroids/ Glucocorticoids

The adrenal cortex releases a type of steroid hormones called corticosteroids, which includes mineralocorticoids and glucocorticoids1. Nonetheless, glucocorticoids are typically referred to as "corticosteroids." Glucocorticoids, so named because of their impact on the metabolism of carbohydrates, control a variety of cellular processes, including as inflammation, development, homeostasis, metabolism, and cognition2. The global market for glucocorticoids is projected to be worth over USD 10 billion annually, and they are one of the

most prescribed medications in the world due to their substantial immune-modulatory effects. Many inflammatory and autoimmune conditions, including multiple sclerosis, septic shock rheumatoid arthritis, asthma, allergies, and inflammatory bowel disease, are now clinically treated with glucocorticoids. Unfortunately, the negative side effects linked to high dosages (used to treat SLE and systemic vasculitis) and prolonged usage restrict the therapeutic advantages of glucocorticoids. Osteoporosis, skin atrophy, diabetes, obesity of the abdomen, glaucoma, cataracts, avascular necrosis and infection, growth retardation, and hypertension are some of these adverse effects. Ramamoorthy, S., & Cidlowski, J. A. (2016).

Mechanism of action

The majority of autoimmune illnesses are treated with glucocorticoids on a long-term basis. Gout is treated with short-term glucocorticoid therapy, while tendonitis and painful osteoarthritic joints are frequently treated with intra-articular glucocorticoid injections. One important way that glucocorticoids suppress inflammation is by lowering the expression of genes that are triggered by cytokines. All cells contain glucocorticoids, which attach to the cytoplasmic steroid receptor before moving to the nucleus, where certain DNA sequences identify the complex. By blocking the activation of the transcription factors AP-1 and NF-κB, binding to DNA mostly suppresses transcription. Gene expression for almost all proinflammatory cytokines is induced by AP-1 and NF-κB. Additionally, inflammatory genes that encode T cell development factors including IL-2, IL-4, IL-15, and IL-17 as well as interferon-γ (IFN-γ) are suppressed by glucocorticoids. Furthermore, glucocorticoids decrease the expression of genes that code for intracellular adhesion molecule-1 (ICAM-1), inducible nitric oxide synthase, and COX-2, all of which are often triggered by the cytokines TNF-α and IL-1β. Genes encoding anti-inflammatory chemicals, including the cytokine IL-10 and the IL-1 type 2 decoy receptor, are expressed more when glucocorticoids are present. Dinarello, C. A. (2010)

Drug Interaction of Glucocorticoids

A review is conducted of the several ways that glucocorticoids interact with other medications. The most notable and significant of these interactions are those that occur between the glucocorticoid metabolism and liver microsomal enzyme-inducing drugs, such as rifampicin and anticonvulsants (phenytoin and barbiturates). We described a polymyositis patient receiving prednisolone treatment who experienced a recurrence following concurrent rifampicin usage. Patients receiving rifampicin treatment showed notable variations in the levels of accelerated metabolism among glucocorticoids, with dexamethasone, prednisolone, and hydrocortisone being the most common. In clinical treatment, it is necessary to pay close attention to the interactions between glucocorticoids and other medications. **Kawai, S., & Ichikawa, Y. (1994).**

Common adverse effect

Both short-term and long-term (chronic) illnesses can be safely and effectively managed with corticosteroids. They may have adverse effects, just like any other medicine. Among the most typical adverse effects of corticosteroids are:

	Side effects
Glucocorticoids	. An increased appetite. . Unexpected weight gain. . Skin changes, including bruising more easily than usual and increased acne. . Retaining water, which makes your skin and face look swollen or puffy. . Stomach irritation. . Muscle weakness. . Mood swings, including increased anxiety, restlessness or trouble sleeping. . Increased body hair.

3. Disease modifying anti-rheumatic drugs (DMARDs)

Drugs known as disease-modifying anti-rheumatic medications (DMARDs) are used or being researched for various inflammatory disorders. They reduce inflammation, halt joint deterioration, and lessen the systemic symptoms of rheumatoid arthritis. Biological DMARDs (bDMARDs), targeted synthetic DMARDs (tsDMARDs), and conventional synthetic DMARDs (csDMARDs) are the three main categories.

• The csDMARDs consist of the older, lower molecular mass medications, such as leflunomide, sulfasalazine, and antimalarial methotrexate. Because of their gradual onset of action, members of this category are sometimes referred to as slow-acting antirheumatic medications (SAARDs).

• The low molecular mass, synthetic medications known as phosphodiesterase 4 inhibitors and Janus kinase inhibitors, which were developed to target certain processes, are the most recent agents and are hence referred to as DMARDs. Pile, K. D., Graham, G. G., & Mahler, S. M. (2016)

Mechanism of action

The manner that each DMARD works is different, yet they all eventually disrupt important inflammatory cascade pathways. For instance, methotrexate suppresses cell-mediated immunity, decreases neutrophil adhesion, inhibits neutrophil leukotriene B4 synthesis, suppresses fibroblast adenosine release, inhibits local IL-1 production, lowers IL-6 and IL-8 levels, and inhibits the expression of the synovial collagenase gene. Other drugs in this family work by preventing lymphocytes from proliferating or by causing them to malfunction. Leflunomide prevents lymphocyte proliferation by inhibiting dihydroorotate dehydrogenase, which in turn prevents pyrimidine production. By inhibiting oxidative, nitrative, and nitrosative damage, sulfasalazine exerts its anti-inflammatory actions. Conversely, hydroxychloroquine inhibits intracellular toll-like receptor TLR9 and is a relatively modest immunomodulatory drug.

In contrast, the mode of action of biologics is highly selective. Biologics' main purposes are to: (1) disrupt the synthesis or function of cytokines; (2) block the "second signal" necessary for T-cell activation; or (3) reduce the number of B-cells or block the substances that stimulate B-cells. The protein tyrosine kinase JAK, which mediates cytokine signaling, is inhibited by the small drug tofacitinib. **(Aletaha D, Smolen JS. Diagnosis and Management of Rheumatoid Arthritis: A Review. JAMA. 2018 and Wang W, Zhou H, Liu L. Side effects of methotrexate therapy for rheumatoid arthritis: A systematic review. Eur J Med Chem. 2018)**

Drug Interaction of DMARDs

A number of drugs, including proton pump inhibitors, sulfasalazine, amoxicillin, and non-steroidal anti-inflammatory drugs (NSAIDs), can prevent methotrexate from being excreted by the kidneys, which increases its effectiveness and raises the possibility of side effects.
Although using multiple conventional DMARDS and combining a biologic DMARD with a conventional DMARD is thought to be safe, using a combination of different biologic DMARDs is not advised because of the higher risk of severe immunosuppression that could result in infections that are serious and possibly fatal. Benjamin, O., Goyal, A., & Lappin, S. L. (2018).

Common adverse effect

	Side Effects
Potential DMARDs	. An increased risk of infection (biologics have a higher risk of this) . Low white blood cell count (leukopenia) . Low red blood cell count (anemia) . Low platelet count (thrombocytopenia) . Elevated liver enzymes
Traditional DMARDs	. Loss of appetite . Nausea and vomiting . Diarrhea . Abdominal pain . Skin rash
Biologic DMARDs	. Tuberculosis herpes or hepatitis . Elevated cholesterol . Increased risk of blood clots . Infusion or injection site reactions

Anti-inflammatory drugs as potential antimicrobial agents

Public health, therapy, and prevention are significantly impacted by the link and causative involvement of infectious pathogens in chronic inflammatory disorders. Antibiotics and anti-inflammatory medications are among the many medications that must be administered in order to pharmacologically treat combination infection and inflammatory illnesses. Dual-action medications must be created because this can have negative effects. Promising options seem to be anti-inflammatory medications that have already demonstrated antibacterial qualities. NSAIDs, namely aceclofenac, diclofenac, and ibuprofen, were evaluated in clinical

studies including patients with cellulitis and uncomplicated UTIs. Patients with UTIs experienced a reduction in symptoms when ibuprofen, a medication that has been studied in the most research, was administered. As attractive candidates for dual-action medication development, non-steroidal anti-inflammatory medications (NSAIDs) may be used to treat a variety of inflammatory and infectious conditions, including TB, musculoskeletal infections, and urinary tract infections. However, before these NSAIDs are used in practice, more clinical research is needed to determine their bactericidal efficacy. **(Okpala, O. E., Rondevaldova, J., & Kokoska, L. (2025)**

Plant-based phytochemicals as a sources of anti-inflammatory agents

It is well recognized that phytochemicals derived from plants may include anti-inflammatory properties. Numerous research have documented the potential ability of medicinal plants' pure chemicals, crude extracts, and metal/metal oxide nanoparticles (M/MONPs) to reduce inflammation and treat illness. About 50 medicinal plants were found to have phytochemicals that were used to treat inflammatory illnesses. These phytochemicals included flavonoids, terpenoids, polyphenols, saponins, tannins, alkaloids, anthraquinones, and some of its M/MONPs. These plants' natural compounds showed encouraging anti-inflammatory properties to treat inflammation-related conditions of the skin, liver, heart, joints, gastrointestinal tract, nervous system, and lungs. Numerous investigations into the phytochemistry, M/MONPs, and anti-inflammatory properties of phytochemicals derived from medicinal plants have produced new, safe medication with fewer adverse effects. the study of medicinal plant natural ingredients and their nanoparticles for the treatment of various illnesses. **(Gonfa, Y. H., Tessema, F. B., Bachheti, A., Rai, N., Tadesse, M. G., Singab, A. N., & Bachheti, R. K. (2023).**

Mechanism of action of phytochemicals in anti-inflammatory activities

The mechanism of action of phytochemicals is thought to be the reduction of inflammation stress through the enhancement of the release of systematic mediators, cytokines, and chemokines to induce cellular infiltration for the resolution of inflammatory responses and the restoration of tissue coordination **(Dragos et al., 2017).** At the cellular and molecular levels, the anti-inflammatory activity mechanism is widely used **(Hossen et al., 2015).** By inhibiting regulating enzymes such lipoxygenases, cyclooxygenases, phospholipase A2, histamine production, protein kinases, phosphodiesterase's, and transcriptase activation, phytochemicals can lower proteinoid and leukotriene concentrations. In vitro studies have demonstrated the anti-inflammatory properties of flavonoids, polyphenols, alkaloids, saponins, tannins, and terpenes **(Nunes et al., 2020).** According to reports, quercetin significantly inhibits the enzymes that produce eicosanoids from arachidonic acid, including COX-2 and 5-LOX. By altering eicosanoid synthesis, suppressing activated immune cells, and preventing the production and release of pro-inflammatory mediators, resveratrol regulates the inflammatory response **(Arifin et al., 2015).** Additionally, flavonoids, curcumins, and tannins have been shown to have anti-inflammatory properties via inhibiting proinflammatory enzymes through their ability to scavenge free radicals **(Adebayo et**

al., 2015). Although the exact method of action of M/MONPs against illnesses is yet unknown, several data have been reported that suggest potential possibilities. Various viewpoints were presented by certain academics to explain the tenable mechanisms of action of M/MONPs. According to some research, M/MONPs attach to proteins and DNA that contain phosphorus and sulfur, which ultimately breaks down disease-causing substances. Others assert that the death of bacteria or viruses is caused by metallic ions released from M/MONPs into their cell walls **(Mutuma et al., 2020; Al-Otibi et al., 2021).**

Therapeutic Applications

Flavonoids, terpenoids, and coumarins are among the several components of the plant that give it its therapeutic qualities. Recent advancements that support its use as a therapeutic agent in a number of fields—including anti-inflammatory, antioxidant, analgesic, antimicrobial, hepatoprotective, anti-allergic, anticancer, and anti-hypertensive—are included in the review. Its significance in treating metabolic syndromes and CNS illnesses is not well understood. The chemical components that give it its therapeutic impact and the corresponding mechanism of action are also explained. (**Sah, A., Naseef, P. P., Kuruniyan, M. S., Jain, G. K., Zakir, F., & Aggarwal, G. (2022).**

Biological medications and small molecule inhibitors that target immune cells, inflammatory cytokines, and intracellular kinases have emerged as the gold standard for treating autoimmune illnesses in recent decades. TNF, IL-6, IL-17, and IL-23 inhibition has transformed the management of autoimmune conditions such psoriasis, ankylosing spondylitis, and rheumatoid arthritis.

Anti-CD20 mAb-based B cell depletion therapy has demonstrated encouraging outcomes in patients with neuroinflammatory disorders, and systemic lupus erythematosus can be treated by blocking B cell survival factors. By altering T cell activity, targeting co-stimulatory molecules expressed on Ag-presenting cells and T cells is also anticipated to have therapeutic promise in autoimmune disorders. In the realm of autoimmune and hematologic disorders, small molecule kinase inhibitors that target the JAK family—which is in charge of signal transduction from several receptors—have recently attracted a lot of attention. In terms of therapeutic effectiveness and safety profiles, there are still unmet medical demands, nonetheless. New treatments use sophisticated molecular engineering methods to create immunological tolerance without impairing immune function. **(Jung, S. M., & Kim, W. U. (2022).**

Conclusion

NSAIDs remain essential for treating inflammation, pain, and fever due to their proven effectiveness and accessibility. Advances in drug design, especially selective COX-2 inhibitors, have improved safety profiles, though risks like gastrointestinal and cardiovascular effects persist. Careful use, particularly in at-risk patients, is vital. Continued research into safer formulations and personalized therapies will enhance their future role in clinical practice.

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