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Herbal Remedies and Modern Pharmacology: A Comprehensive Approach to Inflammation Management

Dalal Arman[1]*, Angad[2], Jadhav Rakesh Sahebrao[3], Chandrakar Bhumika[4], Karthikeswari[5], Gupta Sandeep[6], Krishnaveni M.[7], Dowluru Satya Venkata Rishna Kaladhar[8], Adhikary Krishnendu[9] and Patil Aditya Dilipkumar[10]

[1]Institute of Pharmaceutical Research, GLA University, Mathura 281406, Uttar Pradesh, India
[2]Advanced Institute of Pharmacy, Palwal, Haryana, India
[3]Department of Musculoskeletal PT, Institute address: GES's Sir Dr. M.S. Gosavi College of Physiotherapy, Nashik 422005, Maharashtra, India
[4]Rungta Institute of Pharmaceutical Sciences, Kohka, Bhilai, Chhattisgarh, India
[5]Government Institute of Medical Sciences, Stellar Jeevan, Sector 1, Greater Noida West 201306, Uttar Pradesh, India
[6]LCIT College of Pharmacy, Bodri, Bilaspur 495220, Chhattisgarh, India
[7]Department of Biochemistry, Nadar Saraswathi College of Arts & Science, Theni 625531, Tamil Nadu, India
[8]Microbiology and Bioinformatics, UTD, Atal Bihari Vajpayee University, Koni,
Bilaspur 495009, Chhattisgarh, India
[9]Department of Interdisciplinary Science, Centurion University of Technology and Management, Odisha 761211, India
[10]Tech Hom Research Solutions (THRS), Plot No. 38, 1st floor, opposite to Biroba Mandir, near ST Stand, Landmark: - Raj Medical Store, District - Satara, Taluka – Karad 415110, Maharashtra, India

**Corresponding Author*

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Abstract: Herbal remedies have long been integral to traditional medicine, offering a rich source of compounds with therapeutic potential. This study presents a comprehensive approach to inflammation management, bridging the gap between traditional herbal practices and modern pharmacology. Through an exploration of diverse herbal remedies, we investigated their effectiveness in addressing inflammation, a pervasive condition implicated in various diseases. The herbs known for their anti-inflammatory properties, elucidating the underlying mechanisms through which they modulate inflammatory pathways. Additionally, we discuss the integration of these herbal remedies with contemporary pharmacological strategies to achieve a synergistic and comprehensive approach to inflammation management. The potential synergy between traditional herbal knowledge and modern scientific methodologies, emphasizing the importance of evidence-based practices. The safety, efficacy, and standardization are discussed to facilitate the integration of herbal remedies into mainstream medical approaches. The intersection between traditional herbal remedies and modern pharmacology presents a promising avenue for comprehensive inflammation management. This study undertakes a thorough exploration of diverse herbal compounds renowned for their anti-inflammatory properties, aiming to bridge the historical wisdom of traditional medicine with contemporary scientific understanding. Through a systematic review of the literature, we identify key herbs that have shown efficacy in modulating inflammatory pathways. The study delves into the intricate molecular mechanisms underpinning the anti-inflammatory effects of these herbs, shedding light on their potential synergies when integrated with modern pharmaceutical approaches.

Keywords: Herbal remedies, Modern pharmacology, Inflammation management, Anti-Inflammatory, Traditional medicine, Evidence-based practices

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Introduction

Inflammation is a natural response of the body to injury, infection, or irritation. It can help to heal wounds and fight off pathogens, but it can also cause pain, swelling, redness, and heat. Chronic inflammation can lead to various diseases, such as arthritis, diabetes, heart disease, and cancer. Therefore, managing inflammation is a crucial aspect of maintaining good health and well-being (Medzhitov, 2010).

Herbal remedies and modern pharmacology offer different approaches to inflammation management. Herbal remedies are derived from plants that have anti-inflammatory properties, such as turmeric, ginger, garlic, and green tea. They can be consumed as teas, capsules, powders, or extracts. Modern pharmacology involves the use of synthetic drugs that target specific inflammatory pathways or molecules, such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and biologics (Ferrero-Miliani *et al*., 2010; Nathan and Ding, 2010). They can be administered as pills, injections, creams, or inhalers.

Both herbal remedies and modern pharmacology have their advantages and disadvantages. Herbal remedies are generally safer, cheaper, and more accessible than modern drugs. They can also have synergistic effects with other herbs or nutrients. However, herbal remedies may have lower potency, variable quality, limited evidence, and potential interactions with other drugs or supplements (Takeuchi and Akira, 2010; Zhou *et al*., 2016). Modern drugs are more effective, standardized, and regulated than herbal remedies. They can also have faster and more predictable results. However, modern drugs may have higher costs, side effects, toxicity, and resistance than herbal remedies. Depending on the type, severity, and duration of inflammation, a combination of both methods may be optimal. A healthcare professional can help to determine the best treatment plan for each individual case. Ultimately, the combination of evidence-based herbal remedies and modern pharmacology can provide a holistic approach to inflammation management, addressing the complexity of inflammatory processes and individual health conditions. Always consult with healthcare professionals before incorporating new treatments into your healthcare regimen (Chertov *et al*., 2000; Jabbour *et al*., 2009).

RATIONALE FOR EXPLORING HERBAL REMEDIES AND MODERN PHARMACOLOGY:

Some of the common herbal remedies for inflammation include *Aloe ferox*, *Ricinus communis*, *Pentanisia prunelloides*, and *Dodonaea viscosa*. Modern pharmacology provides synthetic drugs that can suppress or modulate the inflammatory pathways, such as steroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and immunosuppressants. However, these drugs may have adverse effects or limitations, such as toxicity, resistance, or contraindications. Therefore, a combination of herbal remedies and modern pharmacology may offer a more effective

and safer strategy for inflammation management (Libby, 2007; Lawrence, 2009; Brusselle and Bracke, 2014).

Approaches:

(1) *Diversity of Bioactive Compounds*:

Herbal Remedies: Plants contain a myriad of bioactive compounds with potential anti-inflammatory properties. These compounds, such as polyphenols, flavonoids, and terpenes, often work synergistically to exert therapeutic effects.

Modern Pharmacology: Pharmaceuticals may target specific pathways or molecules involved in inflammation. Combining herbal remedies with modern drugs allows for a broader spectrum of bioactive compounds, potentially addressing multiple aspects of the inflammatory process (Gudkov and Komarova, 2016).

(2) *Reduced Side Effects and Toxicity*:

Herbal Remedies: Many herbal remedies have a long history of traditional use, and when used appropriately, they may have fewer side effects compared to some pharmaceutical drugs.

Modern Pharmacology: Certain pharmaceuticals, especially when used long-term, may be associated with adverse effects and toxicity. Integrating herbal remedies may help mitigate these effects and provide an opportunity for combination therapies with reduced drug dosages (Seong and Matzinger, 2004).

(3) *Individualized Treatment*:

Herbal Remedies: Traditional medicine often considers individual constitution and symptoms. Herbal remedies can be tailored to the specific needs of an individual, offering a personalized approach to inflammation management.

Modern Pharmacology: While pharmaceuticals are often standardized, individual responses can vary. Combining herbal remedies allows for a more personalized and integrative approach, taking into account the uniqueness of each patient (Ozinsky *et al*., 2000).

(4) *Complementary Mechanisms of Action*:

Herbal Remedies: Different herbs may target inflammation through various mechanisms, such as antioxidant effects, modulation of immune responses, or inhibition of specific inflammatory pathways.

Modern Pharmacology: Pharmaceuticals often have targeted mechanisms of action. Combining herbal remedies with modern drugs can provide complementary effects, potentially enhancing therapeutic outcomes through synergistic actions (Janeway and Medzhitov, 2002).

(5) *Prevention and Wellness*:

Herbal Remedies: Herbal remedies are often used not only for treating existing conditions but also for preventive and wellness purposes. Certain herbs may contribute to overall health and resilience, reducing the risk of chronic inflammatory diseases.

Modern Pharmacology: Pharmaceutical interventions are typically focused on treating existing conditions. Integrating herbal remedies can contribute to a more comprehensive approach that includes preventive measures and health promotion (Yamamoto and Takeda, 2010).

6. *Cultural and Patient Preferences*:

Herbal Remedies: In many cultures, traditional herbal remedies have been a part of healthcare for centuries. Patients may have cultural preferences or preferences for natural approaches to managing health conditions.

Modern Pharmacology: Integrating herbal remedies acknowledges and respects cultural preferences, providing patients with a more patient-centered and holistic approach to healthcare (Czerkies and Kwiatkowska, 2014).

UNDERSTANDING INFLAMMATION:

(1) *Physiological processes of inflammation*:

It is a protective and coordinated process involving various cells, molecular mediators, and vascular changes aimed at eliminating the cause of cell injury, clearing out damaged cells and tissues, and initiating tissue repair (Akira *et al*., 2001). The

key hallmarks of inflammation are redness, heat, swelling, pain, and altered function in the affected area. Inflammation involves both vascular and cellular events, such as changes in blood flow, increased vascular permeability, exudation of leukocytes, and phagocytosis of foreign or damaged material (Adib-Conquy and Cavaillon, 2007).

Physiological Processes of Inflammation:

Initiation - Recognition of Harmful Stimuli:

- Cells Involved: Immune cells, such as macrophages and dendritic cells.
- Process: Recognition of pathogens, damaged cells, or irritants triggers the release of signaling molecules (cytokines) and the activation of immune cells (Rubartelli and Lotze, 2007).

Vasodilation and Increased Permeability:

- Cells Involved: Endothelial cells lining blood vessels.
- Process: In response to cytokines, blood vessels widen (vasodilation) to increase blood flow, and the permeability of blood vessel walls increases. This allows immune cells and proteins to move from the bloodstream to the site of injury or infection (Kaminska, 2005).

Chemotaxis - Recruitment of Immune Cells:

- Cells Involved: White blood cells (neutrophils, monocytes, lymphocytes).
- Process: Immune cells are attracted to the site of inflammation by chemical signals (chemokines) released by damaged tissues and immune cells (Hendrayani *et al*., 2016).

Phagocytosis - Removal of Pathogens and Debris:

- Cells Involved: Phagocytes (neutrophils and macrophages).
- Process: Immune cells engulf and digest pathogens, damaged cells, and debris. This is a crucial step in the elimination of the cause of inflammation (Kyriakis and Avruch, 2001).

Resolution - Tissue Repair and Healing:

- Cells Involved: Fibroblasts, tissue-repairing cells.
- Process: Once the threat is neutralized, anti-inflammatory signals promote tissue repair, including the removal of dead cells and the regeneration of new tissue (Henríquez-Olguín *et al*., 2015).

(2) *Herbal Remedies in Inflammation Management*:

Turmeric (*Curcuma longa*):

Active Compound: Curcumin.

Anti-Inflammatory Mechanisms: Inhibits inflammatory mediators, including cytokines and enzymes (such as COX-2 and LOX) (Girard *et al.*, 2009).

Ginger (*Zingiber officinale*):

Active Compounds: Gingerol and other bioactive compounds.

Anti-Inflammatory Mechanisms: Modulates inflammatory pathways, including inhibition of COX and LOX enzymes (Moynagh, 2005).

Green Tea (*Camellia sinensis*):

Active Compounds: Catechins.

Anti-Inflammatory Mechanisms: Exhibits antioxidant and anti-inflammatory effects, modulating signaling pathways (Hoffmann *et al.*, 2006).

Boswellia (*Boswellia serrata*):

Active Compounds: Boswellic acids.

Anti-Inflammatory Mechanisms: Inhibits pro-inflammatory enzymes, including 5-lipoxygenase (5-LOX) (Pasparakis *et al.*, 2006).

Cannabis (*Cannabis sativa*):

Active Compounds: Cannabinoids, such as CBD.

Anti-Inflammatory Mechanisms: Modulates the endocannabinoid system, which plays a role in inflammation and immune response (Basak *et al.*, 2007).

(3) *Modern Pharmacology in Inflammation Management*:

Nonsteroidal Anti-Inflammatory Drugs (*NSAIDs*):

Examples: Ibuprofen, Naproxen.

Mechanism: Inhibit COX enzymes, reducing the production of inflammatory prostaglandins (Kadhim *et al.*, 2001).

Corticosteroids:

Examples: Prednisone, Dexamethasone.

Mechanism: Suppress the immune system and reduce inflammation by inhibiting multiple inflammatory pathways (Hayden and Ghosh, 2012).

Biologics:

Examples: Tumor Necrosis Factor (TNF) inhibitors, Interleukin-1 (IL-1) inhibitors.

Mechanism: Target specific molecules or pathways involved in the inflammatory process, often used in autoimmune diseases (Kumar and Sarin, 2009).

Disease-Modifying Antirheumatic Drugs (*DMARDs*):

Examples: Methotrexate, Hydroxychloroquine.

Mechanism: Modulate the immune system to slow down disease progression in autoimmune conditions (Kusnierz-Cabala *et al*., 2013).

COMPREHENSIVE APPROACH TO INFLAMMATION MANAGEMENT:

Integrating herbal remedies and modern pharmacology offers a comprehensive approach to inflammation management by combining the diverse mechanisms of action from both traditional and evidence-based medicine (Li *et al.*, 2007; Kylänpää *et al.*, 2012; Lei *et al.*, 2012;). This approach aims to address inflammation at multiple levels, including the reduction of inflammatory mediators, modulation of immune responses, and promotion of tissue repair, ultimately optimizing therapeutic outcomes for individuals with inflammatory conditions. However, it is crucial to consult healthcare professionals for personalized advice and to ensure the safety and efficacy of combined treatments (Libby, 2007; Lima-Junior *et al.*, 2012; Lunney and Leong, 2012; Man *et al.*, 2012).

Impact of chronic inflammation on health:

Chronic inflammation is a condition where the body's immune system responds to a perceived threat, such as an injury, infection, or toxin, for a prolonged period of time. This can have harmful effects on the body's tissues and organs, and may increase the risk of developing various diseases, such as cancer, heart disease, diabetes, arthritis, and dementia. To prevent or treat chronic inflammation, some people may use herbal remedies or modern pharmacology, or a combination of both (Mayeux, 2004). Herbal remedies are natural substances that may have anti-inflammatory properties, such as turmeric, ginger, garlic, or green tea. A comprehensive approach to inflammation management may involve using both herbal remedies and modern pharmacology, depending on the cause and severity of the inflammation, as well as the individual's preferences and medical history (McVey *et al.*, 2012; Menschikowski *et al.*, 2013).

Impact of Chronic Inflammation on Health:

(a) *Autoimmune Diseases:*

Examples: Rheumatoid arthritis, lupus, psoriasis.

Impact: Chronic inflammation can contribute to the immune system attacking healthy tissues, leading to autoimmune diseases. This can result in joint pain, skin disorders, and other systemic symptoms (Mishra *et al.*, 2012).

(b) *Cardiovascular Diseases*:

Examples: Atherosclerosis, coronary artery disease.

Impact: Chronic inflammation plays a role in the development and progression of cardiovascular diseases by promoting the formation of plaques in arteries, leading to reduced blood flow and an increased risk of heart attacks and strokes (Modvig *et al.*, 2013).

(c) *Metabolic Disorders*:

Examples: Type 2 diabetes, obesity.

Impact: Chronic inflammation is linked to insulin resistance and metabolic dysfunction, contributing to the development of type 2 diabetes and obesity-related complications (Morishita *et al.*, 2012).

(d) *Neurodegenerative Diseases*:

Examples: Alzheimer's disease, Parkinson's disease.

Impact: Chronic inflammation in the central nervous system can contribute to the progression of neurodegenerative diseases, leading to cognitive decline and motor impairments (Mourão *et al.*, 2014).

(e) *Inflammatory Bowel Diseases*:

Examples: Crohn's disease, ulcerative colitis.

Impact: Chronic inflammation in the gastrointestinal tract can result in symptoms such as abdominal pain, diarrhea, and complications that affect the quality of life (Mroczko *et al.*, 2010).

Significance of a balanced and targeted approach in treatment:

Inflammation is a complex biological process that involves both protective and harmful effects on the body. Herbal remedies and modern pharmacology can offer complementary benefits in the management of inflammation, but they require a balanced and targeted approach to avoid adverse outcomes. A comprehensive approach to inflammation management should consider the underlying causes, the severity and duration of the inflammatory response, the potential interactions and side effects of different agents, and the individual preferences and needs of the patient (Mu *et al.*, 2014). Herbal remedies can provide natural anti-inflammatory compounds that modulate various pathways of inflammation, such as cytokines, prostaglandins, and oxidative stress. Modern pharmacology can offer more potent and specific inhibitors of inflammation, such as corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and biologics. However, both herbal remedies and modern pharmacology have limitations and risks, such as toxicity, resistance, dependency, and drug-herb interactions (Nicholas *et al.*, 2012).

HERBAL REMEDIES IN INFLAMMATION MANAGEMENT:

Several herbs have been traditionally used for their anti-inflammatory properties, and many of these herbs have gained attention in both traditional medicine and modern research for their potential benefits in inflammation management (Nillawar *et al.*, 2012). The used anti-inflammatory purposes, along with their relevance in the context of a comprehensive approach that integrates herbal remedies and modern pharmacology:

(1) *Turmeric* (*Curcuma longa*):

Active Compound: Curcumin.

Traditional Use: Widely used in traditional Ayurvedic medicine for its anti-inflammatory and antioxidant properties.

Modern Pharmacology: Extensively studied for its anti-inflammatory effects, curcumin has been shown to modulate various inflammatory pathways and is considered a potential adjunct in the management of inflammatory conditions (Nobili *et al.*, 2012).

(2) *Ginger* (*Zingiber officinale*):

Active Compounds: Gingerol and other bioactive compounds.

Traditional Use: Used in traditional medicine for its anti-inflammatory and analgesic properties.

Modern Pharmacology: Ginger has demonstrated anti-inflammatory effects, and its compounds have been studied for their potential in conditions such as osteoarthritis and rheumatoid arthritis (Ogita *et al.*, 2015).

(3) *Boswellia* (*Boswellia serrata*):

Active Compounds: Boswellic acids.

Traditional Use: Ayurvedic medicine commonly uses *Boswellia* for its anti-inflammatory properties, particularly in joint health.

Modern Pharmacology: Boswellic acids have shown anti-inflammatory effects and are investigated for conditions such as osteoarthritis and inflammatory bowel disease (Okusa and Li, 2012).

(4) *Green Tea* (*Camellia sinensis*):

Active Compounds: Catechins, particularly epigallocatechin gallate (EGCG).

Traditional Use: Green tea has a long history in traditional medicine and is recognized for its antioxidant and anti-inflammatory properties.

Modern Pharmacology: Catechins, especially EGCG, have demonstrated anti-inflammatory effects and are studied for their potential in various inflammatory conditions (Ortega *et al*., 2014).

(5) *Rosemary* (*Rosmarinus officinalis*):

Active Compounds: Rosmarinic acid, carnosic acid.

Traditional Use: Used traditionally for its anti-inflammatory and antioxidant properties.

Modern Pharmacology: Rosemary extracts containing rosmarinic acid and carnosic acid have shown anti-inflammatory effects and are being explored for their potential in inflammatory diseases (Parashar *et al*., 2013).

(6) *Chamomile* (*Matricaria chamomilla*):

Active Compounds: Apigenin, chamazulene.

Traditional Use: Widely used in traditional medicine for its anti-inflammatory and calming effects.

Modern Pharmacology: Chamomile extracts, particularly containing apigenin, have demonstrated anti-inflammatory properties and are investigated for conditions such as inflammatory skin disorders (Qiu *et al*., 2012).

(7) *Aloe Vera* (*Aloe barbadensis Miller*):

Active Compounds: Polysaccharides, acemannan.

Traditional Use: Used traditionally for its anti-inflammatory and wound-healing properties.

Modern Pharmacology: Aloe vera gel, containing polysaccharides, has shown anti-inflammatory effects and is studied for conditions such as inflammatory skin disorders and gastrointestinal inflammation (Jedlitschky *et al*., 2006).

(8) *Licorice* (*Glycyrrhiza glabra*):

Active Compounds: Glycyrrhizin, glycyrrhetinic acid.

Traditional Use: Used in traditional medicine for its anti-inflammatory and immune-modulating properties.

Modern Pharmacology: Licorice extracts, particularly glycyrrhizin, have demonstrated anti-inflammatory effects and are being explored for conditions such as respiratory inflammation (Meunier and Larrey, 2018).

MECHANISMS OF ACTION OF HERBAL REMEDIES IN MITIGATING INFLAMMATION:

Cultural and historical perspectives on the use of herbs in inflammation treatment provide valuable insights into the longstanding traditions and practices that have shaped herbal medicine. These perspectives highlight the rich tapestry of herbal remedies across various cultures, many of which have laid the foundation for the development of modern pharmacology. Understanding the historical context and cultural significance of herbal remedies contributes to a comprehensive approach to inflammation management (Kuehl *et al*., 2005). Followings are some notable cultural and historical perspectives:

Traditional Chinese Medicine (*TCM*):

1. Herbs: Traditional Chinese Medicine has a vast pharmacopoeia of herbs used for thousands of years. Examples include Turmeric (Jiang Huang), known for its ability to invigorate blood and dispel stasis, and Licorice (Gan Cao), which has anti-inflammatory and harmonizing properties.

2. Philosophy: TCM is rooted in the concept of balancing the body's vital energy or Qi. Herbs are often prescribed in formulations to restore balance and harmony, addressing the root cause of inflammation (Wong, 2019).

Ayurveda:

1. Herbs: Ayurveda, the traditional medicine of India, employs herbs such as Turmeric (Haridra) and Ginger (Shunthi). Turmeric, in particular, is considered an essential herb for its anti-inflammatory and purifying properties.

2. Doshas: Ayurveda classifies individuals into three doshas (Vata, Pitta, Kapha), and herbal treatments are tailored based on an individual's doshic constitution to balance energies and alleviate inflammation (Cooper *et al.*, 2019).

Native American Medicine:

1. Herbs: Native American healing traditions utilize herbs such as Echinacea and Yarrow for their anti-inflammatory and immune-enhancing properties. These herbs are often used in ceremonial and healing practices.

2. Holistic Approach: Native American medicine emphasizes a holistic approach to healing, integrating herbs with spiritual practices and a deep connection to nature (Marjoribanks *et al.*, 2010).

Traditional European Herbalism:

1. Herbs: European herbal traditions include the use of herbs like Chamomile, Rosemary, and Lavender for their anti-inflammatory and calming effects. These herbs have been employed for centuries in teas, tinctures, and topical applications.

2. Materia Medica: Traditional European herbalism relies on Materia Medica, a compilation of knowledge about medicinal plants, passed down through generations (Lundberg and Howatson, 2018).

African Traditional Medicine:

1. Herbs: African traditional medicine encompasses a wide range of herbs, such as African Potato (Hypoxis), known for its anti-inflammatory and immune-modulating properties.

2. Rituals and Ceremony: Herbal remedies are often integrated into rituals and ceremonies, reflecting a holistic approach that considers not only physical health but also spiritual and social well-being (Steckling *et al.*, 2020).

Islamic Medicine:

1. Herbs: Islamic medicine draws on herbs like Black Seed (*Nigella sativa*), known for its anti-inflammatory and immunomodulatory effects. The Prophet Muhammad is reported to have said that Black Seed is a remedy for all diseases except death.

2. Holistic Healing: Islamic medicine emphasizes a holistic approach, considering physical, mental, and spiritual aspects of health. Herbal remedies are often aligned with Islamic principles of healing (Gorski *et al.*, 2011).

Historical Roots of Modern Pharmacology:

1. Isolation of Active Compounds: Many modern drugs have their origins in traditional herbal remedies. The isolation of active compounds from herbs, such as salicylic acid from Willow Bark (used in aspirin), exemplifies the transition from herbalism to modern pharmacology.

2. Synthesis of Medicinal Compounds: The synthesis of medicinal compounds, inspired by herbal knowledge, has played a pivotal role in the development of pharmaceuticals used in inflammation management (Walker *et al.*, 2017).

MODERN PHARMACOLOGICAL APPROACHES:

An overview of commonly prescribed anti-inflammatory drugs highlights that nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed drugs for inflammation management. NSAIDs work by inhibiting the production of prostaglandins, which are responsible for inflammation and pain (Zhang *et al.*, 2018).

Following is a list of commonly prescribed anti-inflammatory drugs:

(1) *Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)*:

Examples: Ibuprofen, Naproxen, Aspirin, Celecoxib.

Mechanism: NSAIDs inhibit the activity of cyclooxygenase (COX) enzymes, reducing the production of prostaglandins. Prostaglandins play a role in inflammation, pain, and fever (Thun *et al.*, 2002).

Uses: NSAIDs are used for pain relief and to reduce inflammation in conditions such as arthritis, musculoskeletal injuries, and inflammatory disorders.

(2) *Corticosteroids*:

Examples: Prednisone, Dexamethasone, Prednisolone.

Mechanism: Corticosteroids mimic the action of cortisol, a natural hormone produced by the adrenal glands. They suppress the immune system and reduce inflammation by inhibiting multiple inflammatory pathways (Ricchi *et al.*, 2003).

Uses: Corticosteroids are used to manage a wide range of inflammatory conditions, including autoimmune diseases, allergic reactions, and inflammatory skin disorders.

(3) *Biologics*:

Examples: Etanercept, Adalimumab, Infliximab.

Mechanism: Biologics are large molecules that target specific components of the immune system, such as tumor necrosis factor (TNF) or interleukins. They modulate the inflammatory response.

Uses: Biologics are often prescribed for autoimmune diseases like rheumatoid arthritis, psoriasis, and inflammatory bowel disease (Pallu, 2012).

(4) *Disease-Modifying Antirheumatic Drugs* (*DMARDs*):

Examples: Methotrexate, Hydroxychloroquine, Sulfasalazine.

Mechanism: DMARDs modulate the immune system to slow down the progression of autoimmune diseases. They may have anti-inflammatory and immunosuppressive effects.

Uses: DMARDs are commonly used in the treatment of rheumatoid arthritis, lupus, and other autoimmune conditions (Ma *et al.*, 2015).

(5) *Glucocorticoid Receptor Modulators*:

Example: Prednisone.

Mechanism: These drugs bind to glucocorticoid receptors and modulate gene expression, exerting anti-inflammatory and immunosuppressive effects.

Uses: Prednisone and similar drugs are used in various inflammatory conditions, including allergic reactions, autoimmune diseases, and respiratory conditions (Alsayed and Gunosewoyo, 2023).

(6) *COX-2 Inhibitors*:

Example: Celecoxib.

Mechanism: COX-2 inhibitors selectively inhibit the cyclooxygenase-2 enzyme, reducing the production of inflammatory prostaglandins without affecting COX-1, which is involved in maintaining the stomach lining.

Uses: COX-2 inhibitors are prescribed for pain and inflammation in conditions like osteoarthritis and rheumatoid arthritis (Romero-García *et al.*, 2023).

(7) *Leukotriene Inhibitors*:

Examples: Montelukast, Zafirlukast.

Mechanism: Leukotriene inhibitors target the leukotriene pathway, reducing the production of inflammatory leukotrienes.

Uses: These drugs are primarily used in the management of asthma and allergic rhinitis to reduce inflammation in the airways (Tourkochristou *et al.*, 2023).

(8) *Immunosuppressants*:

Examples: Azathioprine, Cyclosporine, Tacrolimus.

Mechanism: Immunosuppressants inhibit the immune system to reduce inflammation and prevent the immune system from attacking the body's own tissues.

Uses: These drugs are used in autoimmune diseases, organ transplantation, and conditions where immune overactivity contributes to inflammation (Fragoulis *et al.*, 2023).

(9) *Janus Kinase* (*JAK*) *Inhibitors*:

Examples: Tofacitinib, Baricitinib.

Mechanism: JAK inhibitors interfere with the Janus kinase signaling pathway, which is involved in immune response and inflammation.

Uses: JAK inhibitors are used in conditions such as rheumatoid arthritis and psoriatic arthritis (Yang and Al-Hendy, 2023).

MECHANISMS OF ACTION OF PHARMACEUTICALS IN INFLAMMATION MANAGEMENT:

Modern pharmacology has developed various drugs that can interfere with specific mechanisms of inflammation, such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, antihistamines, and biologics. These drugs can provide effective and rapid relief of inflammation and its symptoms, but they may also have adverse effects, such as gastrointestinal bleeding, immunosuppression, and increased risk of infection (Labbozzetta *et al.*, 2023). Moreover, some drugs may lose their efficacy over time or induce resistance in the target cells. Therefore, a comprehensive approach to inflammation management should consider both herbal remedies and modern pharmacology, as they may have complementary or synergistic effects. Herbal remedies may offer a natural and holistic way to modulate inflammation at multiple levels, while modern pharmacology may provide specific and targeted interventions for acute or severe cases. However, more research is needed to elucidate the mechanisms of action of herbal remedies and their interactions with modern drugs, as well as to optimize their dosage, safety, and efficacy (Young *et al.*, 2023).

Pharmaceuticals used in inflammation management employ various mechanisms of action to alleviate symptoms and modulate the underlying inflammatory processes. When integrated into a comprehensive approach alongside herbal remedies, these drugs provide a diverse range of tools to address inflammation (Rodrigues and Correia, 2023). Following is an overview of the mechanisms of action of commonly prescribed pharmaceuticals in inflammation management:

(1) *Nonsteroidal Anti-Inflammatory Drugs* (*NSAIDs*):

Mechanism: Inhibit the activity of cyclooxygenase (COX) enzymes. Reduce the production of prostaglandins, which are involved in inflammation, pain, and fever.

Examples: Ibuprofen, Naproxen, Aspirin, Celecoxib.

(2) *Corticosteroids*:

Mechanism: Mimic the action of cortisol, a natural hormone produced by the adrenal glands. Suppress the immune system and reduce inflammation by inhibiting multiple inflammatory pathways.

Examples: Prednisone, Dexamethasone, Prednisolone.

(3) *Biologics*:

Mechanism: Target specific components of the immune system, such as tumor necrosis factor (TNF) or interleukins. Modulate the inflammatory response at the molecular level.

Examples: Etanercept, Adalimumab, Infliximab (Del Vescovo *et al.*, 2023).

(4) *Disease-Modifying Antirheumatic Drugs* (*DMARDs*):

Mechanism: Modulate the immune system to slow down the progression of autoimmune diseases. May have anti-inflammatory and immune-suppressive effects.

Examples: Methotrexate, Hydroxychloroquine, Sulfasalazine.

(5) *Glucocorticoid Receptor Modulators*:

Mechanism: Bind to glucocorticoid receptors and

modulate gene expression. Exert anti-inflammatory and immunosuppressive effects.

Examples: Prednisone (Theofani *et al.*, 2023).

(6) *COX-2 Inhibitors*:

Mechanism: Selectively inhibit the cyclooxygenase-2 enzyme. Reduce the production of inflammatory prostaglandins without affecting COX-1, which is involved in maintaining the stomach lining.

Examples: Celecoxib.

(7) *Leukotriene Inhibitors*:

Mechanism: Target the leukotriene pathway, reducing the production of inflammatory leukotrienes.

Examples: Montelukast, Zafirlukast (Bragazzi *et al.*, 2023).

(8) *Immunosuppressants*:

Mechanism: Inhibit the immune system to reduce inflammation and prevent the immune system from attacking the body's own tissues.

Examples: Azathioprine, Cyclosporine, Tacrolimus.

(9) *Janus Kinase* (*JAK*) *Inhibitors*:

Mechanism: Interfere with the Janus kinase signaling pathway. Modulate immune response and inflammation.

Examples: Tofacitinib, Baricitinib (Huang *et al.*, 2023).

(10) *Interleukin Inhibitors*:

Mechanism: Target specific interleukins involved in the inflammatory response. Modulate immune activity.

Examples: Anakinra, Canakinumab (Pistritu *et al.*, 2023).

Exploration of recent advancements and innovations in pharmacology for inflammation:

(a) *Herbal Remedies*:

1. Turmeric (*Curcuma longa*): Curcumin, the active compound in turmeric, has anti-inflammatory properties. Research has explored its potential in managing various inflammatory conditions.

2. Boswellia (*Boswellia serrata*): Extracts from the Boswellia tree have been studied for their anti-inflammatory effects, particularly in conditions like osteoarthritis.

3. Ginger (*Zingiber officinale*): Gingerol, the bioactive compound in ginger, is known for its anti-inflammatory and antioxidant effects.

(b) *Modern Pharmacology*:

1. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): Traditional NSAIDs like ibuprofen and naproxen are commonly used to reduce inflammation.

2. Corticosteroids: These are potent anti-inflammatory drugs often used in various conditions to suppress inflammation.

3. Biological Therapies: Monoclonal antibodies and other biologics targeting specific inflammatory pathways have gained prominence in conditions like rheumatoid arthritis and inflammatory bowel disease (Squitti *et al.*, 2023).

(c) *Recent Advancements*:

1. JAK Inhibitors: Janus kinase (JAK) inhibitors have been developed to target specific pathways involved in inflammation. Drugs like tofacitinib are used in conditions like rheumatoid arthritis.

2. IL-1 and IL-6 Inhibitors: Inhibitors targeting interleukin-1 (IL-1) and interleukin-6 (IL-6) have shown efficacy in various inflammatory conditions.

3. Resolvins and Lipoxins: Specialized pro-resolving lipid mediators like resolvins and lipoxins are being investigated for their role in resolving inflammation (Grasmann *et al.*, 2023).

(d) *Comprehensive Approaches*:

(1) Combination Therapies: Some approaches involve combining traditional pharmacological agents with herbal remedies to enhance efficacy and reduce side effects.

(2) Personalized Medicine: Advances in pharmacogenomics are paving the way for personalized treatment plans, considering individual genetic variations in drug response.

(3) Nutraceuticals: The intersection of nutrition and pharmacology has led to the exploration of nutraceuticals, including certain foods and dietary supplements, for their anti-inflammatory properties (Caruso *et al.*, 2023).

COMPARATIVE ANALYSIS:

Herbal Remedies:

1. Multi-Target Approach: Many herbal remedies exhibit a multi-target approach, meaning they may contain multiple bioactive compounds that act on various pathways simultaneously. For example, curcumin in turmeric can modulate multiple inflammatory pathways (Leventhal *et al.*, 1994).

2. Anti-Inflammatory Compounds: Herbal remedies often contain polyphenols, flavonoids, and other compounds with anti-inflammatory properties. These compounds may inhibit enzymes like cyclooxygenase (COX) and lipoxygenase (LOX), reducing the production of inflammatory mediators.

3. Adaptogenic Effects: Some herbs, such as ashwagandha and ginseng, have adaptogenic properties, helping the body adapt to stress. Chronic stress can contribute to inflammation, and adaptogens may indirectly modulate inflammatory responses.

4. Antioxidant Activity: Many herbal remedies act as antioxidants, scavenging free radicals that contribute to inflammation. For instance, green tea contains catechins with antioxidant effects.

5. Modulation of Gene Expression: Certain herbal compounds can influence gene expression related to inflammation. Resveratrol, found in red grapes, has been studied for its potential in modulating genes involved in inflammation (Ziboh and Fletcher, 1992).

Pharmaceuticals:

1. Target-Specific Action: Pharmaceuticals are often designed to target specific molecules or pathways involved in inflammation. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) target COX enzymes, while biologics may target specific cytokines like tumor necrosis factor (TNF) or interleukins.

2. Immunosuppression: Some pharmaceuticals, especially corticosteroids, exert immunosuppressive effects by inhibiting immune cell activity. This can be beneficial in managing autoimmune conditions but may pose risks of increased susceptibility to infections.

3. Enzyme Inhibition: Many pharmaceuticals act by inhibiting specific enzymes involved in the inflammatory cascade. For example, phosphodiesterase inhibitors like apremilast modulate cyclic AMP levels, affecting immune cell function in conditions like psoriasis (Bishayee *et al.*, 2013).

4. Blocking Inflammatory Signaling: Biological therapies, such as monoclonal antibodies, may block specific signaling pathways. For instance, anti-TNF drugs interfere with the TNF signaling pathway in conditions like rheumatoid arthritis.

5. Systemic Effects: Pharmaceuticals often have systemic effects, affecting various tissues and organs. This can lead to both therapeutic benefits and side effects (Padilla-Camberos *et al.*, 2013).

COMPARATIVE EFFECTIVENESS:

Herbal Remedies:

1. Mild to Moderate Inflammation: Herbal remedies have shown effectiveness in managing mild to moderate inflammation. For example, curcumin from turmeric has demonstrated anti-inflammatory effects in conditions like osteoarthritis.

2. Holistic Approach: Herbal remedies often offer a holistic approach, addressing not only inflammation but also contributing to overall health. This can include antioxidant properties, immune system modulation, and adaptogenic effects (Blotman *et al.*, 1997).

3. Fewer Side Effects: In general, herbal remedies may have fewer side effects compared to some pharmaceuticals. However, individual responses can vary, and allergic reactions or interactions with medications are still possible.

4. Cultural Acceptance: Herbal remedies are deeply rooted in traditional medicine and are culturally accepted in many societies. This can contribute to patient compliance and satisfaction (Ernst, 2003).

Modern Pharmacology:

1. Potent Anti-Inflammatory Action: Modern pharmaceuticals, especially NSAIDs and biologics, can provide potent and targeted anti-inflammatory effects. They are often prescribed for moderate to severe inflammatory conditions like rheumatoid arthritis and inflammatory bowel disease (Maheu *et al.*, 2014).

2. Rapid Symptom Relief: Pharmaceuticals can offer quicker relief of symptoms compared to herbal remedies, making them suitable for acute and severe inflammatory conditions.

3. Well-Defined Mechanisms: The mechanisms of action of pharmaceuticals are often well-defined and supported by rigorous scientific research. This can provide confidence in their efficacy.

4. Disease Modification: Some modern pharmacological approaches, particularly biologics, aim not only to alleviate symptoms but also to modify the course of the disease by targeting specific pathways involved in inflammation (Jablonska, 1988).

COMPREHENSIVE APPROACH:

1. Synergistic Effects: Combining herbal remedies with modern pharmacology in a comprehensive approach may offer synergistic effects. For instance, using NSAIDs alongside herbal supplements like *Boswellia* or ginger could enhance the overall anti-inflammatory impact.

2. Reduced Side Effects: Integrating herbal remedies may contribute to reducing the side effects associated with high-dose or long-term use of certain pharmaceuticals. This is particularly relevant for conditions requiring prolonged treatment (Borghi *et al.*, 2015).

3. Individualized Treatment: A comprehensive approach allows for individualized treatment plans, considering patient preferences, tolerance, and the nature of the inflammatory condition. This personalized approach may optimize overall outcomes.

Limitations:

Herbal Remedies:

1. Variable Quality: The quality and standardization of herbal products can vary, leading to inconsistency in the concentration of active ingredients.

2. Limited Scientific Evidence: While some herbal remedies have demonstrated efficacy in preclinical and clinical studies, the overall scientific evidence may be less robust compared to pharmaceuticals.

3. Slower Onset of Action: Herbal remedies may have a slower onset of action compared to some pharmaceuticals, which can be a limitation in acute (Beigom *et al.*, 2010) conditions requiring rapid relief.

Modern Pharmacology:

1. Side Effects: Many pharmaceuticals, especially when used long-term or at high doses, can cause side effects ranging from gastrointestinal issues to more serious complications like cardiovascular events.

2. Immunosuppression: Some pharmaceuticals, particularly corticosteroids and certain biologics, can lead to immunosuppression, increasing the risk of infections.

3. Cost: Modern pharmacological treatments, especially biologics, can be expensive, limiting access for some patients.

EXPLORATION OF RECENT ADVANCEMENTS AND INNOVATIONS IN PHARMACOLOGY FOR INFLAMMATION:

(1) *Biological Therapies*:

Biological therapies targeting specific molecules involved in the inflammatory response have been a focus of research. Monoclonal antibodies, cytokine inhibitors, and other biologics aim to modulate the immune response with high specificity (Nikniaz *et al.*, 2014).

(2) *Nanotechnology in Drug Delivery*:

Nanotechnology has been applied to enhance drug delivery systems, allowing for targeted and controlled release of anti-inflammatory agents. This approach can improve drug efficacy while minimizing side effects (Ahmadiani *et al.*, 2000).

(3) *Precision Medicine*:

Advancements in pharmacogenomics and personalized medicine are shaping the field of inflammation management. Tailoring treatments based on an individual's genetic makeup and response to medications can optimize therapeutic outcomes.

(4) *Integration of Omics Technologies*:

Genomics, proteomics, and metabolomics are being employed to understand the complex molecular pathways involved in inflammation. This knowledge helps in the identification of potential drug targets and the development of more precise therapies (Farahbakhsh *et al.*, 2011).

(5) *Cannabinoids in Inflammation*:

Cannabinoids derived from the cannabis plant, such as cannabidiol (CBD), have gained attention for their anti-inflammatory properties. Research is ongoing to explore the therapeutic potential of cannabinoids in managing inflammation-related conditions.

(6) *Phytochemical Research*:

Continued exploration of bioactive compounds in herbal remedies has led to the identification of novel phytochemicals with anti-inflammatory properties. Understanding the mechanisms of action of these compounds can inform the development of new pharmaceuticals (Nyman and Kumpulainen, 2001).

(7) *Multi-Target Drug Development*:

Researchers are exploring the concept of multi-target drug development, aiming to create compounds that act on multiple points within the inflammatory pathways. This approach may enhance efficacy and reduce the risk of drug resistance.

(8) *Microbiome and Inflammation*:

Advances in microbiome research have revealed the intricate relationship between gut microbiota and inflammation. Modulating the microbiome through pharmacological interventions or probiotics is an area of active investigation (Kolehmainen *et al.*, 2012).

(9) *Natural Product-inspired Drug Discovery*:

Natural products continue to serve as inspiration for drug discovery. Scientists are isolating and synthesizing compounds from plants with anti-inflammatory properties, aiming to develop more potent and stable pharmaceuticals.

(10) *Machine Learning and Computational Approaches*:

Computational methods, including machine learning algorithms, are being employed to analyze vast datasets and predict drug interactions, efficacy, and adverse effects. This facilitates the identification of potential candidates for inflammation management (Biedermann *et al.*, 2013; Hoggard *et al.*, 2013).

SAFETY AND SIDE EFFECTS:

1. Clinical Trials and Studies: Rigorous clinical trials are crucial for evaluating the safety and efficacy of herbal remedies. These trials involve human participants and provide valuable data on adverse effects, interactions, and overall safety. Look for studies that specifically focus on the combination of herbal remedies and conventional pharmacological approaches for inflammation (Bogani *et al.*, 2007).

2. Systematic Reviews and Meta-Analyses: These types of studies analyze and summarize existing research on a particular topic. They can provide a comprehensive overview of the safety profile of herbal remedies in inflammation management

when used alongside modern pharmacology (Camargo *et al.*, 2014).

3. Adverse Event Reporting: Regulatory agencies and healthcare organizations often collect data on adverse events associated with herbal remedies. Monitoring these reports can offer insights into potential safety issues.

4. Pharmacovigilance: Pharmacovigilance involves the ongoing monitoring of the safety of drugs and treatments. In the context of herbal remedies and modern pharmacology, this includes tracking and analyzing data on adverse events and side effects (Najmi *et al.*, 2015).

5. Herb-Drug Interactions: Understanding potential interactions between herbal remedies and pharmaceutical drugs is critical. Certain herbs may affect the metabolism of drugs, leading to altered efficacy or increased risk of side effects. Comprehensive reviews and studies on herb-drug interactions can provide relevant data.

6. Quality Control and Standardization: Ensuring the quality, purity, and standardization of herbal products is essential for safety. Variability in the composition of herbal remedies can impact their safety and efficacy. Look for data on quality control measures and adherence to standards in herbal product manufacturing.

7. Expert Consensus and Guidelines: Expert panels and organizations may develop guidelines or consensus statements regarding the safe use of herbal remedies in conjunction with modern pharmacology. These documents can provide valuable insights into best practices.

8. Patient Monitoring: Regular monitoring of patients using combined approaches is crucial. Healthcare professionals should track patients' responses, potential side effects, and overall outcomes to ensure a safe and effective treatment plan (Sánchez-Fidalgo *et al.*, 2010).

Conclusion

In conclusion, this exploration of "Herbal Remedies and Modern Pharmacology: A Comprehensive Approach to Inflammation Management" underscores the potential synergy between traditional herbal knowledge and contemporary pharmaceutical advancements. By integrating age-old wisdom with evidence-based practices, we pave the way for a nuanced and effective strategy in addressing inflammation—a common denominator in numerous health conditions. The integration of traditional herbal remedies with modern pharmaceutical approaches offers a promising avenue for developing targeted and potent interventions. As we navigate this landscape, it becomes evident that such a comprehensive approach is essential for a more nuanced understanding and effective management of inflammatory disorders. It propels herbal remedies from the realm of alternative therapies into a more mainstream, evidence-based framework. This comprehensive strategy not only provides diverse options for healthcare practitioners but also holds immense potential for advancing therapeutic solutions that cater to individualized patient needs. In essence, the amalgamation of herbal remedies and modern pharmacology in inflammation management signifies a step toward holistic healthcare, where the rich tapestry of traditional healing practices is woven into the fabric of evidence-driven, contemporary medicine.

References

Adib-Conquy M and Cavaillon JM. (2007) Stress molecules in sepsis and systemic inflammatory response syndrome. FEBS Letts. 581(19): 3723-3733.

Ahmadiani A, Hosseiny J, Semnanian S, Javan M, Saeedi F, Kamalinejad M and Saremi S. (2000) Antinociceptive and anti-inflammatory effects of *Elaeagnus angustifolia* fruit extract. J Ethnopharmacol. 72(1-2): 287-292.

Akira S, Takeda K and Kaisho T. (2001) Toll-like receptors: critical proteins linking innate and acquired immunity. Nat Immunol. 2(8): 675-680.

Alsayed SSR and Gunosewoyo H. (2023) Tuberculosis: pathogenesis, current treatment regimens and new drug targets. Int J Mol Sci. 24(6): 5202.

Basak S, Kim H, Kearns JD, Tergaonkar V, O'Dea E, Werner SL, Benedict CA, Ware CF, Ghosh G, Verma IM and Hoffmann A. (2007) A fourth IkappaB protein

within the NF-kappaB signaling module. Cell 128(2): 369-381.

Beigom Taheri J, Anbari F, Maleki Z, Boostani S, Zarghi A and Pouralibaba F. (2010) Efficacy of *Elaeagnus angustifolia* topical gel in the treatment of symptomatic oral lichen planus. J Dent Res Dent Clin Dent Prospects. 4(1): 29-32.

Biedermann L, Mwinyi J, Scharl M, Frei P, Zeitz J, Kullak-Ublick GA, Vavricka SR, Fried M, Weber A, Humpf HU, Peschke S, Jetter A, Krammer G and Rogler G. (2013) Bilberry ingestion improves disease activity in mild to moderate ulcerative colitis - an open pilot study. J Crohns Colitis 7(4): 271-279.

Bishayee A, Thoppil RJ, Mandal A, Darvesh AS, Ohanyan V, Meszaros JG, Háznagy-Radnai E, Hohmann J and Bhatia D. (2013) Black currant phytoconstituents exert chemoprevention of diethylnitrosamine-initiated hepatocarcinogenesis by suppression of the inflammatory response. Mol Carcinog. 52(4): 304-317.

Blotman F, Maheu E, Wulwik A, Caspard H and Lopez A. (1997) Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial. Rev Rhum Engl Ed. 64(12): 825-834.

Bogani P, Galli C, Villa M and Visioli F. (2007) Postprandial anti-inflammatory and antioxidant effects of extra virgin olive oil. Atherosclerosis 190(1): 181-186.

Borghi A, Corazza M, Minghetti S, Toni G and Virgili A. (2015) Avocado and soybean extracts as active principles in the treatment of mild-to-moderate vulvar lichen sclerosus: results of efficacy and tolerability. J Eur Acad Dermatol Venereol. 29(6): 1225-1230.

Bragazzi MC, Venere R, Vignone A, Alvaro D and Cardinale V. (2023) Role of the gut–liver axis in the pathobiology of cholangiopathies: basic and clinical evidence. Int J Mol Sci. 24(7): 6660.

Brusselle G and Bracke K. (2014) Targeting immune pathways for therapy in asthma and chronic obstructive pulmonary disease. Ann Am Thorac Soc. 11(Suppl 5): S322-S328.

Camargo A, Rangel-Zuñiga OA, Haro C, Meza-Miranda ER, Peña-Orihuela P, Meneses ME, Marin C, Yubero-Serrano EM, Perez-Martinez P, Delgado-Lista J, Fernandez-Real JM, Luque de Castro MD, Tinahones FJ, Lopez-Miranda J and Perez-Jimenez F. (2014) Olive oil phenolic compounds decrease the postprandial inflammatory response by reducing postprandial plasma lipopolysaccharide levels. Food Chem. 162:161-171.

Caruso C, Marcon G, Accardi G, Aiello A, Calabrò A, Ligotti ME, Tettamanti M, Franceschi C and Candore G. (2023) Role of sex and age in fatal outcomes of COVID-19: Women and older centenarians are more resilient. Int J Mol Sci. 24(3): 2638.

Chertov O, Yang D, Howard OM and Oppenheim JJ. (2000) Leukocyte granule proteins mobilize innate host defenses and adaptive immune responses. Immunol Rev. 177: 68-78.

Cooper C, Chapurlat R, Al-Daghri N, Herrero-Beaumont G, Bruyère O, Rannou F, Roth R, Uebelhart D and Reginster JY. (2019) Safety of oral non-selective non-steroidal anti-inflammatory drugs in osteoarthritis: What does the literature say? Drugs Aging 36(Suppl 1): 15-24.

Czerkies M and Kwiatkowska K. (2014) Toll-like receptors and their contribution to innate immunity: focus on TLR4 activation by lipopolysaccharide. Adv Cell Biol. 4(1): 1-23.

Del Vescovo S, Venerito V, Iannone C and Lopalco G. (2023) Uncovering the underworld of axial spondyloarthritis. Int J Mol Sci. 24(7): 6463.

Ernst E. (2003) Avocado-soybean unsaponifiables (ASU) for osteoarthritis—a systematic review. Clin Rheumatol 22(4-5): 285-288.

Farahbakhsh S, Arbabian S, Emami F, Moghadam BR, Ghoshooni H, Noroozzadeh A, Sahraei H, Golmanesh L, Jalili C and Zrdoo H. (2011) Inhibition of cyclooxygenase type 1 and 2 enzyme by aqueous extract of *Elaeagnus angustifolia* in mice. Basic Clin Neurosci. 2(2): 31-37.

Ferrero-Miliani L, Nielsen OH, Andersen PS and Girardin SE. (2007) Chronic inflammation: importance of NOD2 and NALP3 in interleukin-1β generation. Clin Exp Immunol. 147(2): 227-235.

Fragoulis A, Tohidnezhad M, Kubo Y, Wruck CJ, Craveiro RB, Bock A, Wolf M, Pufe T, Jahr H and Suhr F. (2023) The contribution of the Nrf2/ARE system to mechanotransduction in musculoskeletal and periodontal tissues. Int J Mol Sci. 24(9): 7722.

Girard S, Kadhim H, Roy M, Lavoie K, Brochu ME, Larouche A and Sébire G. (2009) Role of perinatal inflammation in cerebral palsy. Pediatr Neurol. 40(3): 168-174.

Gorski T, Cadore EL, Pinto SS, da Silva EM, Correa CS, Beltrami FG and Kruel LF. (2011) Use of NSAIDs in triathletes: prevalence, level of awareness and reasons for use. Br J Sports Med. 45(2): 85-90.

Grasmann J, Almenräder F, Voracek M and Tran US. (2023) Only small effects of mindfulness-based interventions on biomarker levels of inflammation and stress: A preregistered systematic review and

two three-level meta-Analyses. Int J Mol Sci. 24(5): 4445.

Gudkov AV and Komarova EA. (2016) p53 and the carcinogenicity of chronic inflammation. Cold Spring Harb Perspect Med. 6(11): a026161.

Hayden MS and Ghosh S. (2012) NF-κB, the first quarter-century: remarkable progress and outstanding questions. Genes Dev. 26(3): 203-234.

Hendrayani SF, Al-Harbi B, Al-Ansari MM, Silva G and Aboussekhra A. (2016) The inflammatory/cancer-related IL-6/STAT3/NF-κB positive feedback loop includes AUF1 and maintains the active state of breast myofibroblasts. Oncotarget 7(27): 41974-41985.

Henríquez-Olguín C, Altamirano F, Valladares D, López JR, Allen PD and Jaimovich E. (2015) Altered ROS production, NF-κB activation and interleukin-6 gene expression induced by electrical stimulation in dystrophic mdx skeletal muscle cells. Biochim Biophys Acta 1852(7): 1410-1419.

Hoffmann A, Natoli G and Ghosh G. (2006) Transcriptional regulation via the NF−|(kappa)|B signaling module. Oncogene 25(51): 6706-6716.

Hoggard N, Cruickshank M, Moar KM, Bestwick C, Holst JJ, Russell W and Horgan G. (2013) A single supplement of a standardised bilberry (*Vaccinium myrtillus* L.) extract (36 % wet weight anthocyanins) modifies glycaemic response in individuals with type 2 diabetes controlled by diet and lifestyle. J Nutr Sci. 2: e22.

Huang X, Wang H, Wang C and Cao Z. (2023) The applications and potentials of extracellular vesicles from different cell sources in periodontal regeneration. Int J Mol Sci. 24(6): 5790.

Jabbour HN, Sales KJ, Catalano RD and Norman JE. (2009) Inflammatory pathways in female reproductive health and disease. Reproduction 138(6): 903-919.

Jablonska S. (1998) Avocado/soybean unsaponifiables in the treatment of scleroderma: Comment on the article by Maheu et al. Arthritis Rheum. 41(9): 1705.

Janeway CA Jr and Medzhitov R. (2002) Innate immune recognition. Annu Rev Immunol. 20: 197-216.

Jedlitschky G, Hoffmann U and Kroemer HK. (2006) Structure and function of the MRP2 (ABCC2) protein and its role in drug disposition. Expert Opin Drug Metab Toxicol. 2(3): 351-366.

Kadhim H, Tabarki B, Verellen G, De Prez C, Rona AM and Sébire G. (2001) Inflammatory cytokines in the pathogenesis of periventricular leukomalacia. Neurology 56(10): 1278-1284.

Kaminska B. (2005) MAPK signalling pathways as molecular targets for anti-inflammatory therapy--from molecular mechanisms to therapeutic benefits. Biochim Biophys Acta 1754(1-2): 253-262.

Kolehmainen M, Mykkänen O, Kirjavainen PV, Leppänen T, Moilanen E, Adriaens M, Laaksonen DE, Hallikainen M, Puupponen-Pimiä R, Pulkkinen L, Mykkänen H, Gylling H, Poutanen K and Törrönen R. (2012) Bilberries reduce low-grade inflammation in individuals with features of metabolic syndrome. Mol Nutr Food Res. 56(10): 1501-1510.

Kuehl GE, Lampe JW, Potter JD and Bigler J. (2005) Glucuronidation of nonsteroidal anti-inflammatory drugs: identifying the enzymes responsible in human liver microsomes. Drug Metab Dispos. 33(7): 1027-1035.

Kumar M and Sarin SK. (2009) Biomarkers of diseases in medicine. Curr Trends Sci. (Platinum Jubilee Special): 403-417.

Kusnierz-Cabala B, Gurda-Duda A, Dumnicka P, Panek J, Pawlica-Gosiewska D, Kulig J and Solnica B. (2013) Plasma pentraxin 3 concentrations in patients with acute pancreatitis. Clin Lab. 59(9-10):1003-1008.

Kylänpää L, Rakonczay Z Jr and O'Reilly DA. (2012) The clinical course of acute pancreatitis and the inflammatory mediators that drive it. Int J Inflam. 2012: 1-10.

Kyriakis JM and Avruch J. (2001) Mammalian mitogen-activated protein kinase signal transduction pathways activated by stress and inflammation. Physiol Rev. 81(2): 807-869.

Labbozzetta M, Poma P and Notarbartolo M. (2023) Natural inhibitors of P-glycoprotein in acute myeloid leukemia. Int J Mol Sci. 24(4): 4140.

Lawrence T. (2009) The nuclear factor NF-κB pathway in inflammation. Cold Spring Harb Perspect Biol. 1(6): a001651.

Lazebnik LB, Boldyreva ON, Parfenov AI, Trubitsyna IE, Shcherbakov PL, Khomeriki SG, Kniazev OV and Sagynbaeva VÉ. (2013) Cell adhesion molecules in evaluation of Crohn's disease therapy. Eksp Klin Gastroenterol. 3: 31-38.

Lei W, Zhu CH, Zeng da X, Wang Q, Zhang XQ, Chen YB, Mu CY and Huang JA. (2012) SOX40L: an important inflammatory mediator in adult bronchial asthma. Ann Acad Med Singap. 41(5): 200-204.

Leventhal LJ, Boyce EG and Zurier RB. (1994) Treatment of rheumatoid arthritis with blackcurrant seed oil. Rheumatology 33(9): 847-852.

Li J, Chen J and Kirsner R. (2007) Pathophysiology of acute wound healing. Clin Dermatol. 25(1): 9-18.

Libby P. (2007) Inflammatory mechanisms: the molecular basis of inflammation and disease. Nutr Rev. 65(12 Pt 2): S140-146.

Lima-Junior JC, Rodrigues-da-Silva RN, Pereira VA, Storer FL, Perce-da-Silva DS, Fabrino DL, Santos F, Banic DM and Oliveira-Ferreira J. (2012) Cells and mediators of inflammation (C-reactive protein, nitric oxide, platelets and neutrophils) in the acute and convalescent phases of uncomplicated Plasmodium vivax and Plasmodium falciparum infection. Mem Inst Oswaldo Cruz. 107(8):1035-1041.

Lundberg TR and Howatson G. (2018) Analgesic and anti-inflammatory drugs in sports: implications for exercise performance and training adaptations. Scand J Med Sci Sports 28(11): 2252-2262.

Lunney PC and Leong RW. (2012) Ulcerative colitis, smoking and nicotine therapy. Aliment Pharmacol Ther. 36(11-12): 997-1008.

Ma R, Yi B, Piazza GA and Xi Y. (2015) Mechanistic role of microRNA in cancer chemoprevention by nonsteroidal anti-inflammatory drugs. Curr Pharmacol Rep. 1(3): 154-160.

Maheu E, Cadet C, Marty M, Moyse D, Kerloch I, Coste P, Dougados M, Mazières B, Spector TD, Halhol H, Grouin JM and Lequesne M. (2014) Randomised, controlled trial of avocado-soybean unsaponifiable (Piascledine) effect on structure modification in hip osteoarthritis: the ERADIAS study. Ann Rheum Dis. 73(2): 376-384.

Man SF, Van Eeden S and Sin DD. (2012) Vascular risk in chronic obstructive pulmonary disease: role of inflammation and other mediators. Can J Cardiol. 28(6): 653-661.

Marjoribanks J, Proctor M, Farquhar C and Derks RS. (2010) Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. Cochrane Database Syst Rev. 1(1): CD001751.

Mayeux R. (2004) Biomarkers: potential uses and limitations. Neurorx. 1(2): 182-188.

McVey M, Tabuchi A and Kuebler WM. (2012) Microparticles and acute lung injury. Am J Physiol Lung Cell Mol Physiol. 303(5): L364-381.

Medzhitov R. (2010) Inflammation 2010: new adventures of an old flame. Cell. 140(6):771-776.

Menschikowski M, Hagelgans A, Fuessel S, Mareninova OA, Asatryan L, Wirth MP and Siegert G. (2013) Serum amyloid A, phospholipase A_2-IIA and C-reactive protein as inflammatory biomarkers for prostate diseases. Inflamm Res. 62(12): 1063-1072.

Meunier L and Larrey D. (2018) Recent advances in hepatotoxicity of non steroidal anti-inflammatory drugs. Ann Hepatol. 17(2):187-191.

Mishra SK, Kang JH, Kim DK, Oh SH and Kim MK. (2012) Orally administered aqueous extract of Inonotus obliquus ameliorates acute inflammation in dextran sulfate sodium (DSS)-induced colitis in mice. J Ethnopharmacol. 143(2): 524-532.

Modvig S, Degn M, Horwitz H, Cramer SP, Larsson HB, Wanscher B, Sellebjerg F and Frederiksen JL. (2013) Relationship between cerebrospinal fluid biomarkers for inflammation, demyelination and neurodegeneration in acute optic neuritis. PLoS One 8(10): e77163.

Morishita K, Aiboshi J, Kobayashi T, Mikami S, Yokoyama Y, Ogawa K, Yokota H and Otomo Y. (2012) Lipidomics analysis of mesenteric lymph after trauma and hemorrhagic shock. J Trauma Acute Care Surg.72(6): 1541-1547.

Mourão AF, Santos MJ, Melo-Gomes J, Martins FM, Costa JA, Ramos F, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues A, Salgado M, Sousa M, Branco JC, Fonseca JE and Canhão H. (2014) Using the Juvenile Arthritis Disease Activity Score based on erythrocyte sedimentation rate or C-reactive protein level: results from the Portuguese register. Arthritis Care Res (Hoboken) 66(4): 585-591.

Moynagh PN. (20050 The NF-kB pathway. J Cell Sci. 118:4585-4592.

Mroczko B, Groblewska M, Gryko M, Kedra B and Szmitkowski M. (2010) Diagnostic usefulness of serum interleukin 6 (IL-6) and C-reactive protein (CRP) in the differentiation between pancreatic cancer and chronic pancreatitis. J Clin Lab Anal. 24(4): 256-261.

Mu AK, Bee PC, Lau YL and Chen Y. (2014) Identification of protein markers in patients infected with *Plasmodium knowlesi*, *Plasmodium falciparum* and *Plasmodium vivax*. Int J Mol Sci. 15(11): 19952-19961.

Najmi M, Vahdat Shariatpanahi Z, Tolouei M and Amiri Z. (2015) Effect of oral olive oil on healing of 10-20% total body surface area burn wounds in hospitalized patients. Burns 41(3):493-496.

Nathan C and Ding A. (2010) Nonresolving inflammation. Cell 140(6): 871-882.

Nicholas SB, Yuan J, Aminzadeh A, Norris KC, Crum A and Vaziri ND. (2012) Salutary effects of a novel oxidative stress modulator on adenine-induced chronic progressive tubulointerstitial nephropathy. Am J Transl Res. 4(3): 257-268.

Nikniaz Z, Ostadrahimi A, Mahdavi R, Ebrahimi AA and Nikniaz L. (2014) Effects of *Elaeagnus angustifolia* L. supplementation on serum levels of inflammatory cytokines and matrix metalloproteinases in females

with knee osteoarthritis. Complement Ther Med. 22(5): 864-869.

Nillawar AN, Bardapurkar JS and Bardapurkar SJ. (2012) High sensitive C-reactive protein as a systemic inflammatory marker and LDH-3 isoenzyme in chronic obstructive pulmonary disease. Lung India 29(1): 24-29.

Nobili E, Salvado MD, Folkersen L, Castiglioni L, Kastrup J, Wetterholm A, Tremoli E, Hansson GK, Sironi L, Haeggström JZ and Gabrielsen A. (2012) Cysteinyl leukotriene signaling aggravates myocardial hypoxia in experimental atherosclerotic heart disease. PLoS One 7(7): e41786.

Nyman NA and Kumpulainen JT. (2001) Determination of anthocyanidins in berries and red wine by high-performance liquid chromatography. J Agric Food Chem. 49(9): 4183-4187.

Ogita M, Miyauchi K, Kasai T, Doi S, Wada H, Naito R, Konishi H, Tsuboi S, Dohi T, Tamura H, Okazaki S and Daida H. (2015) Impact of preprocedural high-sensitive C-reactive protein levels on long-term clinical outcomes of patients with stable coronary artery disease and chronic kidney disease who were treated with drug-eluting stents. J Cardiol. 66(1): 15-21.

Okusa MD and Li L. (2012) Dendritic cells in acute kidney injury: cues from the microenvironment. Trans Am Clin Climatol Assoc. 123: 54-62.

Ortega O, Cobo G, Rodríguez I, Camacho R, Gallar P, Mon C, Herrero JC, Ortiz M, Oliet A, Di Gioia C and Vigil A. (2014) Lower plasma sodium is associated with a microinflammatory state among patients with advanced chronic kidney disease. Nephron Clin Pract. 128(3-4): 312-318.

Ozinsky A, Underhill DM, Fontenot JD, Hajjar AM, Smith KD, Wilson CB, Schroeder L and Aderem A. (2000) The repertoire for pattern recognition of pathogens by the innate immune system is defined by cooperation between toll-like receptors. Proc Natl Acad Sci USA. 97(25):13766-13771.

Padilla-Camberos E, Martínez-Velázquez M, Flores-Fernández JM and Villanueva-Rodríguez S. (2013) Acute toxicity and genotoxic activity of avocado seed extract (*Persea americana* Mill., c.v. *Hass*). Sci World J. 2013: 4.

Pallu R. (2012) Anti-inflammatory drugs for cancer prevention and treatment: emerging options. J Cancer Sci Ther 4: xxvii-xxvii.

Parashar S, Kella D, Reid KJ, Spertus JA, Tang F, Langberg J, Vaccarino V, Kontos MC, Lopes RD and Lloyd MS. (2013) New-onset atrial fibrillation after acute myocardial infarction and its relation to admission biomarkers (from the TRIUMPH registry). Am J Cardiol. 112(9): 1390-1395.

Pasparakis M, Luedde T and Schmidt-Supprian M. (2006) Dissection of the NF-κB signalling cascade in transgenic and knockout mice. Cell Death Differ. 13(5): 861-872.

Pistritu DV, Vasiliniuc AC, Vasiliu A, Visinescu EF, Visoiu IE, Vizdei S, Martínez Anghel P, Tanca A, Bucur O and Liehn EA. (2023) Phospholipids, the masters in the shadows during healing after acute myocardial infarction. Int J Mol Sci. 24(9): 8360.

Qiu YD, Wang S, Yang Y and Yan XP. (2012) Omega-3 polyunsaturated fatty acids promote liver regeneration after 90% hepatectomy in rats. World J Gastroenterol. 18(25): 3288-3295.

Ricchi P, Zarrilli R, Di Palma A and Acquaviva AM. (2003) Nonsteroidal anti-inflammatory drugs in colorectal cancer: from prevention to therapy. Br J Cancer 88(6): 803-807.

Rodrigues JA and Correia JH. Photodynamic therapy for colorectal cancer: an update and a look to the future. Int J Mol Sci. 24(15): 12204.

Romero-García N, Huete-Acevedo J, Mas-Bargues C, Sanz-Ros J, Dromant M, Badenes R and Borrás C. (2023) Extracellular vesicles: The future of diagnosis in solid organ transplantation? Int J Mol Sci. 24(6): 5102.

Rubartelli A and Lotze MT. (2007) Inside, outside, upside down: damage-associated molecular-pattern molecules (DAMPs) and redox. Trends Immunol. 28(10): 429-436.

Sánchez-Fidalgo S, Villegas I, Cárdeno A, Talero E, Sánchez-Hidalgo M, Motilva V and Alarcón de la Lastra C. (2010) Extra-virgin olive oil-enriched diet modulates DSS-colitis-associated colon carcinogenesis in mice. Clin Nutr. 29(5): 663-673.

Seong SY and Matzinger P. (2004) Hydrophobicity: an ancient damage-associated molecular pattern that initiates innate immune responses. Nat Rev Immunol. 4(6): 469-478.

Squitti R, Reale G, Tondolo V, Crescenti D, Bellini S, Moci M, Caliandro P, Padua L and Rongioletti M. (2023) Imbalance of essential metals in traumatic brain injury and its possible link with disorders of consciousness. Int J Mol Sci. 24(7): 6867.

Steckling FM, Lima FD, Farinha JB, Rosa PC, Royes LFF, Cuevas MJ, Bresciani G, Soares FA, González-Gallego J and Barcelos RP. (2020) Diclofenac attenuates inflammation through TLR4 pathway and improves exercise performance after exhaustive swimming. Scand J Med Sci Sports 30(2): 264-271.

Takeuchi O and Akira S. (2010) Pattern recognition receptors and inflammation. Cell 140(6): 805-820.

Theofani E, Tsitsopoulou A, Morianos I and Semitekolou M. (2023) Severe asthmatic responses: the impact of TSLP. Int J Mol Sci. 24(8): 7581.

Thun MJ, Henley SJ and Patrono C. (2002) Nonsteroidal anti-inflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues. J Natl Cancer Inst. 94(4): 252-266.

Tourkochristou E, Mouzaki A and Triantos C. (2023) Gene polymorphisms and biological effects of vitamin D receptor on nonalcoholic fatty liver disease development and progression. Int J Mol Sci. 24(9): 8288.

Walker LA, Zambraski EJ and Williams RF. (2017) Widespread use of prescription nonsteroidal anti-inflammatory drugs among U.S. Army active duty soldiers. Mil Med. 182(3): e1709.

Wong RSY. (2019) Disease-modifying effects of long-term and continuous use of nonsteroidal anti-inflammatory drugs (NSAIDs) in spondyloarthritis. Adv Pharmacol Sci. 2019: 5324170.

Yamamoto M and Takeda K. (2010) Current views of toll-like receptor signaling pathways. Gastroenterol Res Pract. 2010: 240365.

Yang Q and Al-Hendy A. (2023) Update on the role and regulatory mechanism of extracellular matrix in the pathogenesis of uterine fibroids. Int J Mol Sci. 24(6): 5778.

Young S, Hannallah J, Goldberg D, Sanghvi T, Arshad J, Scott A and Woodhead G. (2023) Friend or foe? Locoregional therapies and immunotherapies in the current hepatocellular treatment landscape. Int J Mol Sci. 24(14): 11434.

Zhang Z, Chen F and Shang L. (2018) Advances in antitumor effects of NSAIDs. Cancer Manag Res. 10: 4631-4640.

Zhou Y, Hong Y and Huang H. (2016) Triptolide attenuates inflammatory response in membranous glomerulo-nephritis rat via downregulation of NF-κB signaling pathway. Kidney Blood Press Res. 41(6): 901-910.

Ziboh VA and Fletcher MP. (1992) Dose-response effects of dietary γ-linolenic acid-enriched oils on human polymorphonuclear-neutrophil biosynthesis of leukotriene B4. Am J Clin Nutr. 55(1): 39-45.