RESEARCH PAPER

Targeting Inflammatory And Oxidative Stress Pathways Using Nature's Bioactive Compounds

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ABSTRACT

Body has many defences of mechanisms in which one of the crucial mechanisms is Inflammation that helps to maintain tissue homeostasis and benefits in inducing health and wellness of body. But when inflammation occurs for prolonged time, it generates a chronic inflammation which itself contributes in developing many pathophysiological diseases including rheumatoid arthritis, diabetes, neurodegeneration, cardiovascular disease etc. Allopathic therapies like NSAIDs, corticosteroids are meant to treat these diseases, but continuous use of these medications flourishes several toxicities including renal dysfunction, immune system suppression and gastrointestinal toxicities. Free radicals' generation occurs due to oxidative stress which is caused by various factors such as pollution, poor diet, and UV radiation. Prolonged oxidative stress may lead to various diseases like cancer, cardiovascular diseases, neurodegenerative, respiratory, autoimmune and kidney disorders. Although the body has an antioxidant defence system to combat oxidative stress, but it may fail under chronic conditions. In such cases antioxidants-both natural and synthetic are required.

As of today's scenario, medicinal plants came into the sight of significant scientific based interest which is safer and is holistic alternative medicine. This review is based on the comprehensive knowledge acknowledging anti-inflammatory and antioxidant potential of medicinal plants and different phytoconstituents namely flavonoids, polyphenols, terpenoids, alkaloids, and organosulfur compounds which acts through multiple molecular targets. Key inflammatory mediators like NF-kB, LOX, COX, iNOS and cytokines such as IL-1β, IL-6, and TNF-α exhibit strong antioxidant activity. They also exhibit strong radical-scavenging, metal-chelating, and lipid peroxidation inhibiting activities and modulates redox sensitive signalling pathways such as Keap1–Nrf2–ARE which enhances endogenous antioxidant enzyme expression. *In vitro* assays like DPPH, ABTS, FRAP, and ORAC evaluates radical scavenging and reducing power, while *in vivo* studies use markers like MDA, SOD, CAT, and GSH to reflect oxidative stress and antioxidant defense in biological systems. Few examples of herbal medicines include *Withania somnifera*, *Curcuma longa*, *Camellia sinensis*, *Zingiber officinale*, *Boswellia serrata* etc. which illustrate clinical and preclinical studies evidently. Furthermore, polyherbal formulations have synergistic effects by exhibiting activity through multiple pathways and promoting bioavailability. This review emphasizes on the potential of natural antioxidants and anti-inflammatory medicinal plants in promoting health and preventing oxidative stress induced diseases. Besides, there is always a need for standardization, extensive mechanistic research and large-scale clinical validation that will help in establishing their quality, efficacy, safety for the use of alternative medicine in various disease conditions.

KEYWORDS: Anti-inflammatory, phytoconstituents, polyherbal formulations, Antioxidant, Oxidative stress, Antioxidant assay.

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1.INTRODUCTION: Inflammation is primarily considered as the body's defence mechanism and is essential for healing but in excessive manner it can also cause potential harm to the body as well. It can lead to chronic inflammation which contributes to the pathogenesis of multiple disorders, including arthritis, cardiovascular disease, metabolic syndrome, and neurodegeneration (Aggarwal & Harikumar, 2009) which are associated with joint pain, heart issues, or even lifestyle diseases. In case of conventional management of inflammatory disorders, patients are largely relying on NSAIDs, corticosteroids, and biologics, which, despite their efficacy, possess many side effects like gastrointestinal irritation, renal dysfunction, immune suppression, rheumatoid arthritis, colitis, asthma, diabetes and neurodegeneration, when used for longer duration (Ammon, 2010). In context to this, medicinal plants have attracted a great degree of scientific interest as potential sources of novel anti-inflammatory agents. Traditional systems namely Ayurveda, Traditional Chinese Medicine, and Unani have long employed herbs like *Curcuma longa*, *Boswellia serrata*, and *Zingiber officinale* for curing inflammatory conditions, and modern pharmacological studies have managed to show their key mechanism of pathways (Grzanna et al., 2005; Russo & Borrelli, 2005). Medicinal plants have phytochemicals like polyphenols, flavonoids, terpenoids, and alkaloids which bespeaks antioxidant activity, by inhibition of MAPK pathways and NF-kB, and due to downregulation of these cytokines, they provide multi-target benefits (Cabrera et al., 2006). For centuries medicinal plants evidently demonstrate their abilities towards modulating pro- inflammatory mediators including NF-κB, iNOS, TNF-α, COX2, IL-6 and IL-1β (Aggarwal & Harikumar, 2009). Inflammation is designed throughout network of, mediators, immune cells and signalling pathways. IL-1β, IL-6 and TNF-α are the pro inflammatory cytokines which are key drivers of injuries in various tissues and chronic inflammation (Singh et al., 2011). NF-κof, h is a transcription factor which plays a vital part in managing the gene expression of inflammation, including cytokines, chemokines, COX-2, and iNOS. Enzymatic pathways that involve COX and LOX are expressed to regulate the biosynthesis of prostaglandins and leukotrienes, which bring about pain, fever, and oedema (Grzanna et al., 2005). Mitogen-Activated Protein Kinase (MAPKs) further disseminate inflammatory signals by initiating downstream transcription factors, while excessive ROS and nitric oxide production promote oxidative stress and tissue damage (Scartezzini & Speroni, 2000). Several phytochemicals harmonize these targets. For example, *Curcuma longa* which possesses curcumin evidently inhibits NF-κB and COX-2 expression (Aggarwal & Harikumar, 2009), *Boswellia serrata* which is known for containing boswellic acid that is orchestrated to block leukotriene biosynthesis via 5-LOX inhibition (Ammon, 2010), and *Camellia sinensis* and *Punica granatum* includes polyphenols in them which reduce oxidative stress and cytokine release (Larrosa et al., 2010). This ability to act at multiple nodes of the inflammatory region underlies the therapeutic benefits of plant-derived compounds.

Oxidative stress arises from an imbalance between the reactive oxygen species (ROS) and antioxidant defence system in the body. Inordinate accumulation of ROS leads to structural and functional damage of proteins, lipids, cell membranes and DNA (Ken-ichiro Sasaki et al 2022). This imbalance between ROS and antioxidants leads to the onset of various chronic diseases and plays significant role in aging process. Excessive ROS production induces lipid peroxidation, protein oxidation and DNA lesions like 8-oxo-2′-deoxyguanosine, resulting in cellular damage. These alterations lead to cancer, cardiovascular, neurodegenerative, respiratory, autoimmune, and kidney disorders. If left uncontrolled, oxidative stress leads to both disease progression and overall decline in health. (Pizzino G et al 2017).

The body has a defence system which is comprised of Enzymatic antioxidant defences (like glutathione peroxidase, superoxide dismutase, catalase etc.) and Non-enzymatic antioxidants (like glutathione, α-tocopherol, ascorbic acid, flavonoids, carotenoids, etc.) that protect against oxidative stress induced by free radicals. These defences include preventative mechanisms, repair mechanisms, antioxidant defences and physical defences (Shahin Sharif Ali et al 2008). Even though synthetic antioxidants like BHA, BHT, TBHQ, and PG have been used for a long time, their safety and effectiveness are still debated. This has led to a search for the natural alternatives. Natural antioxidants-derived from herbs have been the focus for both the scientific community and the industry for the past few years because of their nutritional value, curative potential and safety. Herbs are abundant in flavonoids, phenolic acids, terpenoids, alkaloids, and carotenoids, chemicals that neutralize ROS and also provide antimicrobial, anti-inflammatory and cytoprotective benefits (Ajila U et al., 2007; Sharifi-

Rad M et al., 2020). Among the most extensively researched are *Camellia sinensis* (green tea), *Rosmarinus officinalis* (rosemary), and *Curcuma longa* (turmeric), which not only give off strong antioxidant properties but also have the potential to modulate diseases (Xie J et al., 2017; Sheng Y et al., 2023).

2. TYPES & SYMPTOMS OF INFLAMMATION:

There is a general prevalence of two types of inflammation:

i) Acute inflammation: It can be explained as the body's rapid and short-term responses to any injury or infection. for e.g. reaction caused by allergies, infection triggered by chemical irritants, injury caused by trauma, burns, wounds, frostbite, laceration etc.

ii) Chronic inflammation: It is a prolonged low-grade response that can sustained for weeks, months or even for year. For e.g. cardiovascular disease, neurological, autoimmune, rheumatoid arthritis, cancer, lupus, chronic fatigue syndrome etc.

Celsus was Roman writer in the 1st century A.D and has coined the four cardinal signs of inflammation as:

a) Rubor which is redness
b) Tumor which is swelling
c) Calor which is heat
d) Dolor is pain

3. AGENTS RESPONSIBLE FOR CAUSING INFLAMMATION:

The following agents are considered to be the causative agents for Inflammation:

Infectious agents: These agents include toxins by bacteria and viruses, they also include moulds, parasites, fungi etc.

Immunogens: They include reactions via antigen - antibody reactions and cell mediated reactions.

Physical factors: They possess factors like cold, heat, mechanical trauma and radiation etc.

Chemical induced agents: includes poisons caused by organic and inorganic compounds.

Chemically inactive materials: includes foreign bodies.

Figure 1 explains the pathways of acute and chronic inflammation; where it can be seen that IL-6 is the switch that turns a protective response into a persistent inflammatory loop.

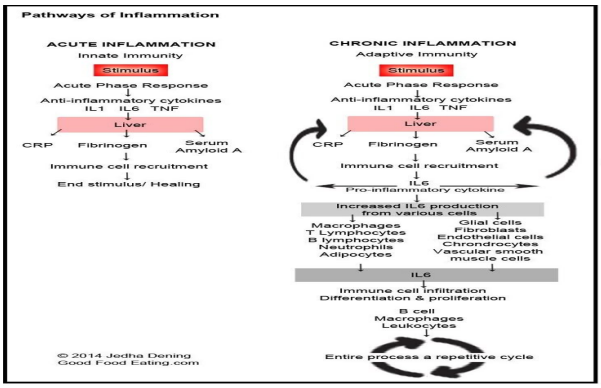

Fig. 1 Pathways of Acute and Chronic Inflammation (Nweze et al., 2022)

4. MECHANISM OF ACTION INVOLVED IN ANTI INFLAMMATION AND ANTI OXIDANT PROPERTIES:

i) Anti-inflammatory mechanisms of medicinal plants:

The principal molecular mechanisms by which the medicinal plants exert anti-inflammatory effects include:

a) **NF-κB Pathway Suppression**: In TNF-α, IL-1β and IL-6 are inflammatory cytokines which are responsible for the inflammation which are inhibited by many plants as they suppress NF-kB pathway. For e.g., *Curcuma longa*, *Allium sativum*, *Camellia sinensis* extracts suppress NF-κB activation thereby reducing downstream inflammatory signalling (Arreola et al., 2015; Biswas et al., 2002).

b) Pro-Inflammatory Cytokine's downregulation: IL-6, TNF-α and IL-1β are cytokines which are considered pro inflammatory cytokines which get suppressed by medicinal plants extracts like *Moringa oleifera*, *Nigella sativa*, *Phyllanthus amarus*, *Withania somnifera* etc., that tends to be helpful in contributing to reduce inflammation in various biological models (Salem, 2005; Harish and Shivanandappa, 2006; Singh et al., 2011).

c) Cyclooxygenase (COX) Inhibition: Many medicinal plants such as *Aloe vera*, *Salix alba* (white willow), *Hypericum perforatum* (St. John's Wort), and *Ocimum sanctum* (holy basil) have well established and well documented activity against the inflammation by inhibiting the COX-2 which further shows anti-inflammatory activity (Habeeb et al., 2007; Mahdi et al., 2006; Pattanayak et al., 2010).

d) Inducible Nitric Oxide Synthase (iNOS) Inhibition: iNOS oxygen mediated inhibition causes inflammation in wound and hepatic which are suppressed through plants such as *Calendula officinalis* and *Silybum marianum* (milk thistle) which

possesses the mechanism that are helpful in wound healing and hepatic inflammation, respectively (Preethi et al., 2009; Surai, 2015).

e) Lipoxygenase (LOX) and Leukotriene Inhibition: Diseases like arthritis, inflammation is due to leukotriene synthesis which gets inhibits by the inhibition of 5-LOX. *Boswellia serrata* and *Urtica dioica* are considered to be the dominant plants which are helpful in inhibition of 5-LOX which ultimately Inhibits leukotriene inhibition (Ammon, 2010; Haghi et al., 2015).

f) Antioxidant Activity-Mediated Effects: Inflammation caused by the oxidative stress are common in many diseases. Some plants having synergistic effect are often used such as *Emblica officinalis* possessing anti-oxidant activity and *Moringa oleifera* having anti-inflammatory activity are helpful in these kinds of cases (Scartezzini and Speroni, 2000; Jaja-Chimedza et al., 2017).

The figure 2 shows that inflammation can be reduced by blocking NF-κB activation, suppressing pro-inflammatory cytokines (especially IL-6, IL-1β, and TNF-α), and inhibiting COX-mediated prostaglandin production, thereby breaking the inflammatory cycle.

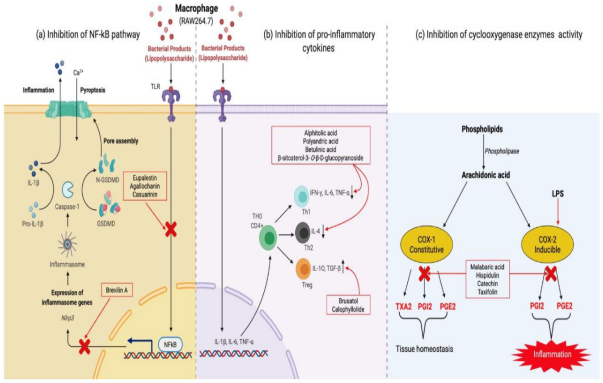

Fig. 2 Anti Inflammatory Mechanism of Action (Karma Yeshi, 2022)

ii) **Anti-oxidant molecular targets and pathways**

Antioxidant herbs provide protective benefits throughout a variety of different and complimentary mechanisms that neutralises free radicals and restore the redox equilibrium. These mechanisms are majorly categorised as Free radical scavenging, metal ion chelation, inhibition of lipid peroxidation, and upregulation of endogenous defence systems.

a) Free Radical Scavenging: Phenolic compounds demonstrate strong antioxidant properties because of their capacity to scavenge free radicals and ROS/RNS through the hydrogen atom transfer (HAT) mechanism. This process leads to the formation of peroxyl radicals (PCO•) and functions as a chain-breaking activity (Kruk, J. et al., 2022). The antioxidant role of flavonoids arises from their capacity to scavenge hydroxyl ('OH) and oxygen (O) radicals during both the initiation and termination phases of peroxyl radical reactions. The efficiency of flavonoids in scavenging hydroxyl radicals follows the sequence: myricetin > quercetin > rhamnetin > morin > diosmetin > naringenin > apigenin > catechin > 5,7-dihydroxy-3',4',5'-trimethoxyflavone > robinin > kaempferol > flavones (S. Rafat Husain et al., 1987).

b) Metal Ion Chelation: Transition metals ions, especially Fe^{2+} and Cu^{+} promote oxidative deterioration by catalyzing the breakdown of hydrogen peroxide into hydroxyl radicals and other ROS, as shown in the Fenton reaction:

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^- + \bullet OH$$

These radicals initiate and propagate oxidation due to their high reactivity. Chelating agents mitigate this process by forming stable complexes with metal ions, thus preventing their participation in redox reactions and reducing oxidation at metal-active sites (Chiara Mussio. Et al.,2025). Polyphenols (such as Rosmarinic acid) have the ability to chelate these metal ions, thereby sequestering them and inhibiting their role in the formation of harmful ROS (Kola, A. et al., 2023).

c) Inhibition of Lipid Peroxidation Lipid peroxidation refers to the process in which free radicals attack lipids containing carbon–carbon double bonds, particularly PUFAs (Polyunsaturated fatty acids) (Ayala A. et al., 2014). The capacity of antioxidants to inhibit lipid peroxidation was analysed by measuring MDA (malondialdehyde) level, which is a byproduct formed during membrane lipid peroxidation. Based on the type of lipid peroxidation inhibition, antioxidants can be categorized as: *Chain breaking antioxidants* (blocks chain propagation) which is shown by phenols and flavonoids, *Preventive* (Initiation process inhibition) and *Termination enhancers* (enhances chain termination, common in terpenes & terpenoids) (Valgimigli L, 2023).

d) Upregulation of endogenous enzymes via Nrf2–ARE pathway: The Keap1–Nrf2–ARE signaling pathway is a crucial defense system of antioxidants and act against oxidative stress thus protecting the cell from oxidative stress. The Keap1–Nrf2 protein–protein interaction (PPI) ‘s noncovalent inhibition has emerged as a key strategy to enhance the ARE-regulated cytoprotective enzymes expression, aiding the development of both therapeutic and preventive agents for various diseases and conditions. Natural

compounds, including curcumin, sulforaphane, and other isothiocyanates, have been extensively investigated for their potential to stimulate Nrf2-mediated gene expression (Dhulfiqar Ali Abed et al., 2015).

Figure 3 indicates the harm caused due to oxidative stress which leads to the onset of various diseases such as, Arthritis, Cancer, Cardiomyopathy, Neurodegeneration and Diabetes. (ROO: alkoxyl radical, ROO: peroxyl radical, ONOO−: perooxynitrite, NO2•: nitrogen dioxide radical, O2•−: superoxide radical, ROS: reactive oxygen species, SOD: superoxide dismutase, CAT: catalase, GPx: glutathione peroxidase, GSH: glutathione).

Figure 4 Indicates the action of antioxidant herbs in reducing mitochondria mediated oxidative stress in liver disease. (Alanine amino transferase (ALT) and aspartate amino transferase (AST), along with non-esterified fatty acids (NEFA), low-density lipoprotein cholesterol (LDLC), total cholesterol (TC), and tumor necrosis factor alpha (TNF-α) are key markers. The buildup of triglycerides (TG) and NEFA leads to changes in mitochondrial structure and the production of reactive oxygen species (ROS), causing damage to the liver and hepatocytes due to lipotoxicity and endoplasmic reticulum (ER) stress. Cinnamon enhances insulin sensitivity, which lowers both lipid levels and blood glucose. Resveratrol has been shown to decrease levels of low-density lipoprotein cholesterol (LDLC), total cholesterol (TC), and TNF-α. Curcumin has been effective in reducing levels of AST and ALT, as well as in decreasing liver fat accumulation. ↑ signifies up-regulation; ↓ signifies down-regulation.

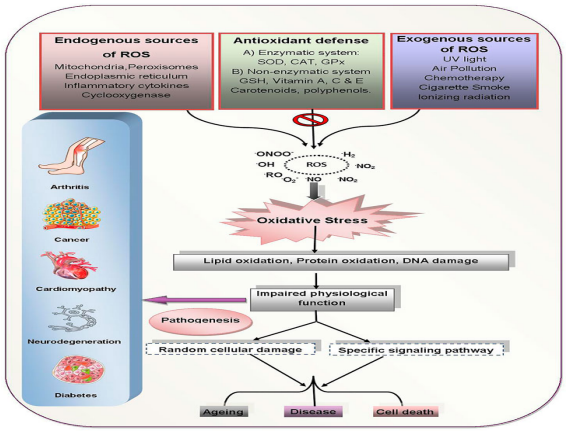

FIG 3 The damage of cells caused due to oxidative stress (Rudrapal et al., 2022)

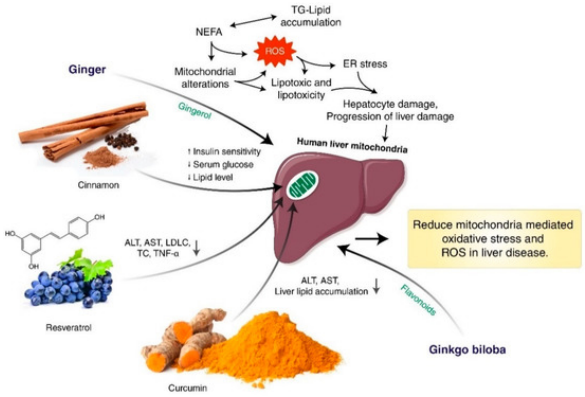

FIG 4: Action of antioxidant herbs in reducing mitochondria mediated oxidative stress in liver disease (Moon Nyeo Park 2022)

5. DETERMINATION OF ANTI-OXIDANT POTENTIAL OF MEDICINAL PLANTS

The antioxidant properties of herbal extracts are typically confirmed through various *in vitro* and *in vivo* tests, with each one measuring different aspects of the antioxidants' action. *In vitro* assays like DPPH (2,2-Diphenyl-1-picrylhydrazyl), FRAP (ferric reducing antioxidant power), ORAC (oxygen radical absorbance capacity) and ABTS radical scavenging evaluate radical scavenging and reducing power, while in vivo studies use markers like MDA, SOD, CAT, and GSH to reflect oxidative stress and antioxidant defense in biological systems. These standardized methods provide a solid and accurate foundation for the determination of the antioxidant potential of different herbs and phytochemicals and their use in medicine.

Table 1 represents the overview of Antioxidant Assays for Measuring Radical Scavenging and Reducing Capacity

TABLE 1 : *IN VITRO* ANTI OXIDANT ASSAYS AND THEIR PRINCIPLES:

Assay	Principle	Mechanism	Wavelength Range (nm)	Detection Method	Reference
DPPH	Measures antioxidant ability to scavenge DPPH radicals, causing color	Antioxidants donate electrons or H-atoms to reduce DPPH•, decreasing	500–550 nm (violet to yellow transition)	UV-Vis spectrophotometry	Kedare SB et al (2011)

	change.	absorbance.			
ABTS	Evaluates Antioxidant's ABTS•+ radical cation quenching ability	Antioxidants reduce the blue-green ABTS•+ radical to colorless, lowering absorbance	700–750 nm (blue-green region)	UV-Vis spectrophotometry	Bibi Sadeer N et al (2020)
FRAP	Measures the antioxidant potential via the reduction of ferric (Fe^{3+}) to ferrous (Fe^{2+}) ions.	Antioxidants reduce Fe^{3+}-TPTZ complex to Fe^{2+}-TPTZ, forming an intense blue color	540–600 nm (blue complex absorption)	UV-Vis spectrophotometry	Benzie IF & Strain JJ, (1996)
ORAC	Evaluates antioxidant capacity by scavenging peroxyl radical's oxidation	Antioxidants inhibit fluorescence decay of a probe (usually fluorescein) induced by AAPH-generated radical	Excitation: 485 ± 5 nm; Emission: 520 ± 5 nm	Fluorescence spectrometry	Cao G et al, (1993)

ii) *IN VIVO* ASSAYS

Animal *in vivo* antioxidant studies usually evaluate endogenous antioxidant enzyme activities like glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) as well as biomarkers like malondialdehyde (MDA), which is a sign of lipid peroxidation. Table 2 summarizes the assessment of Oxidative Stress Biomarkers and antioxidant defense enzymes

TABLE 2: IN VIVO ANTIOXIDANT ASSAYS WITH THEIR PRINCIPLES:

Assay	Principle	Assay Mechanism	Reference
MDA	Indicator of lipid peroxidation and oxidative stress.	Generated as a byproduct of free radical–induced lipid peroxidation.	Ayala et al., (2014); Surniyantoro HNE et al., (2023)
SOD	Primary enzymatic defense against superoxide radicals.	Catalyzes inhibition of superoxide-driven reduction reactions.	Alexander V. et al., (2017)
CAT	Enzyme protecting cells from hydrogen peroxide toxicity.	Decomposes hydrogen peroxide into water and oxygen.	Weydert CJ, Cullen JJ et al., (2010)
GSH	Major intracellular antioxidant maintaining redox balance.	Scavenges radicals via thiol conjugation and electron donation.	Khan Siraj et al., (2023)

6. MEDICINAL PLANTS SHOWING ANTI-INFLAMMATORY POTENTIAL:

A variety of medicinal plants have shown their anti-inflammatory potential and have been proven to be useful in modulation of diseases. For eg. *Curcuma longa* is known to inhibit NF-kB, COX, LOX pathways and has been very useful in the modulation of diseases like arthritis, IBD, diabetes, cancer & inflammation of neurons. *Zingiber officinale* is known to inhibit COX pathway as well as LOX pathway, reduces PGs which helps in modulating in diseases

like migraine, respiratory inflammation, gastritis etc. *Ocimum sativum* inhibits NF-kB and reduces COX-2 which helps in modulation of disease like liver inflammation, metabolic inflammation etc. *Camellia sinensis* inhibits NF-kB; modulate skin inflammation, cancer, obesity etc. Table 3 itemise about the most popular and active 50 medicinal plants showing anti-inflammatory potential, their common name, part used, method of preparation of extract, probable mechanism, assay method, active constituents and reported doses.

TABLE 3: PLANTS SHOWING ANTI INFLAMMATORY ACTIVITY:

Medicinal Plants	Common Name	Part's Used	Extract Preparation	Mechanism involved	Assay method	Species/ model/cell line	Active Constituent	Reported dose	Reference
Allium sativum	Garlic	Bulb	Aged garlic extract; ethanolic extract	Suppresses NF-kB; reduces TNF-α IL-1	Cytokine assays; paw edema	Rats ; macrophage cell lines	Allicin; S-allylcysteine; diallyl sulphides	200 mg/kg (rat, paw edema)	Arreola, R., et al. (2015)
Aloe vera	Aloe	Leaf gel	Gel extract; aqueous extract	Inhibits prostaglandins; reduces cytokines	TPA-induced ear edema; cytokine assays	Mice ; human keratinocytes	Aloin; acemannan	150 mg/kg (rat, carrageenan paw edema)	Habeeb, F., et al. (2007)
Andrographis paniculata	Kalmegh	Leaves, aerial parts	Standardized andrographolide extract	Andrographolide suppresses NF-kB, IL-6	Cytokine inhibition; ear edema models	Mice ; macrophage lines	Andrographolide; neoandrographolide	200 mg/kg (rat, paw edema)	Coon, J. T., & Ernst, E. (2004)
Artemisia annua	Sweet worm wood	Leaves	Ethanol, water	NF-kB, NLRP3	LPS macrophages; intestinal inflammation models	intestinal inflammation models	Artemisinin; artesunate; arteannuin B	NR	Li, R., et al. (2018)
Azadirachta indica	Neem	Leaves, bark, seeds	Ethanolic, aqueous extracts	Inhibits NF-kB, COX, , IL-6 TNF-α	Carrageenan-induced paw edema; LPS-stimulated macrophage assays	Rats ; RAW 264.7 macrophages	Azadirachtin; nimbidin; nimbolide	500 mg/kg (rat, carrageenan paw edema)	Biswas k, chattopadhyay I, Banerjee ,R.k and bandyopadhyay U. -2002

Boswellia serrata	Indian frankincense	Resin	Boswellic acid standardized resin extract	Inhibits 5-LOX and leukotriene synthesis	Leukotriene inhibition assays; arthritis models	Human leukocytes; rats	Boswellic acids (AKBA; KBA)	240 mg/kg (rat, arthritis model)	Ammon, H. P. (2010)
Calendula officinalis	Marigold	Flowers	Ethanol, aqueous	COX2, iNOS, TNF-α	Topical models; carrageenan	carrageenan; clinical wound-healing	Triterpenoids; flavonoids; calenduloside	NR	Preethi K,C, Kuttan G and Kuttan R (2009)
Camellia sinensis	Green tea	Leaves	Polyphenol-rich extracts	EGCG inhibits NF-kB/MAPK pathways	LPS-induced inflammation; colitis models	Mice ; human cell lines	EGCG; epicatechin; catechins	300 mg/kg (mouse, carrageenan paw edema)	Cabrera, C., et al. (2006)
Capsicum annuum	Capsicum	Fruits	Ethanol	TRPV1, NF-kB	Inflammation and pain models; LPS macrophages	LPS macrophages	Capsaicin	NR	SurhY J, (2002)
Cassia fistula	Golden shower tree	Bark, fruit pulp	Ethanolic extract	Reduces cytokines; antioxidant-mediated	Carrageenan paw edema; cotton pellet granuloma	Rats	Flavonoids; anthraquinones	Not specified	Ilavarasan,R., Mallika, M and Venkataramam S., (2005)
Centella asiatica	Gotu kola	Leaves, whole plant	Aqueous, methanolic extracts	Downregulates TNF-α, IL-1; wound inflammation reduction	Wound inflammation models; cytokine assays	Rats ; human dermal cells	Asiaticoside; madecassoside	100 mg/kg (rat, paw edema)	James J.T and Dubery, (2009)
Cissus quadrangularis	Hadjod	Stem	Methanolic, aqueous extracts	Reduces prostaglandins and cytokines	Carrageenan paw edema; granuloma tests	Rats	Ketosteroids; quercetin	Not specified	Shirwaikar, A., et al. (2003)

Coptis chinensis / Berberis spp.	Berberine source	Roots, rhizome	Ethanol, water	NF-kB, NLRP3, MAPKs	Colitis; metabolic inflammation	metabolic inflammation ; LPS macrophages	Berberine	NR	Rios et al., (2019)
Coriandrum sativum	Coriander	Leaves/seeds	Ethanol, essential oil	NF-kB, COX2	In vitro; animal models	nan	Linalool; polyphenols	NR	Laribi, B., Kouki, K., M'Hamdi, M., &Bettaieb, T., (2015)
Cuminum cyminum	Cumin	Seeds	Essential oil	NF-kB, ERK/JNK	LPS-stimulated macrophages	nan	Cuminaldehyde; terpenes	NR	Gachkar, L., et al. (2007).
Curcuma longa	Turmeric	Rhizome	Curcumin standardized extract	Inhibits NF-kB, COX-2, iNOS; antioxidant	Carrageenan paw edema; LPS-induced inflammation	Rats ; RAW 264.7 cells	Curcumin; demethoxycurcumin; bisdemethoxycurcumin	100 mg/kg (rat, carrageenan-induced paw edema)	Aggarwal, B. B., & Harikumar, K. B. (2009)
Curcuma zedoaria	White turmeric	Rhizome	Ethanolic extract; essential oil	Suppresses COX-2; reduces edema and cytokines	Carrageenan-induced edema; cytokine assays	Rats ; macrophage cell lines	Zedoarone; curzerenone; curcuminoids	Not specified	Srinivasan, K., et al. (2010).
Echinacea purpurea	Purple Coneflower	Roots, aerial parts	Aqueous, ethanolic extracts	Suppresses TNF-α, IL-1; macrophage modulation	Cytokine assays; inflammation models	Mice ; human monocytes	Alkamides; caffeic acid derivatives	Not specified	Woelkart, K., & Bauer, R. (2008)

Emblica officinalis	Amla / Indian goose berry	Fruit	Aqueous, hydroalcoholic extracts	Reduces COX activity; antioxidant-mediated anti-inflammatory	Paw edema; oxidative stress-associated inflammation	Rats ; immune cells	Emblicanin; gallic acid; ellagic acid	250 mg/kg (rat, carrageenan paw edema)	Scartezzini, P., & Speroni, E. (2000)
Foeniculum vulgare	Fennel	Seeds, aerial parts	Methanol, essential oil	NF-kB, JNK/ERK	RAW 264.7 cells; neutrophil assays	neutrophil assays	Anethole; flavonoids	NR	Choi, E. M., & Hwang, J. K. (2004).
Garcinia mangostana	Mangosteen	Pericarp	Ethanol	NF-kB, MAPKs	Skin and systemic inflammation models	nan	Xanthones (Î±â_x0080__x0091_mangostin; garcinone)	NR	Pedraza-Chaverri, J., et al. (2008).
Ginkgo biloba	Ginkgo	Leaves	EGb 761 standardized extract	Inhibits platelet-activating factor; NF-kB modulation	Ischemia-reperfusion inflammation; cytokines	Rats ; human endothelial cells	Ginkgolides; bilobalide	Not specified	Smith, J. V., & Luo, Y. (2004)
Glycyrrhiza glabra	Licorice	Root	Aqueous, ethanolic extracts; deglycyrrhizinated	Glycyrrhizin modulates COX-2, NF-kB	Gastric inflammation models; cytokine assays	Rats ; gastric cell lines	Glycyrrhizin; liquiritin; isoliquiritigenin	75 mg/kg (rat, paw edema)	Fiore, C., et al. (2005)
Harpagophytum procumbens	Devil's claw	Tuber/root	Ethanol, aqueous	COX2, iNOS, TNF-α	Clinical and preclinical models of musculoskeletal pain/inflammation	nan	Harpagoside; harpagide	NR	Saha et al., 2021; Vlachojannis et al., (2008)
Hypericum perforatum	St. John's wart	Aerial parts	Ethanol	COX2, iNOS, NF-kB	Dermal/topical and in vitro models	nan	Hyperforin; hypericin; flavonoids	NR	Agostinis et al., 2005; Saddiqe et al., (2010)

Lavandula angustifolia	Lavender	Flowers/EO	Essential oil	NF-kB, COX2	Topical/oral models; pain/inflammation	pain/inflammation	Linalool; linalyl acetate	NR	Cavanagh & Wilkinson, 2002; recent updates (2023)
Matricaria chamomilla	Chamomile	Flowers	Ethanol, aqueous	COX2, iNOS, NF-kB	Topical/oral models; macrophages	macrophages	Apigenin; bisabolol; chamazulene	NR	McKay & Blumberg, 2006; Srivastava et al., (2010)
Mentha piperita	Peppermint	Leaves	Ethanol, essential oil	NF-kB, COX2	In vitro and animal models	nan	Menthol; menthone; rosmarinic acid	200 mg/kg (rat, paw edema)	Samojlik, I., et al. (2010).
Moringa oleifera	Moringa / Drumstick tree	Leaves	Aqueous, ethanolic extracts	Reduces IL-6, ; antioxidant-mediated	LPS-induced inflammation; paw edema	Rats ; macrophages	Quercetin; chlorogenic acid; isothiocyanates	400 mg/kg (rat, paw edema)	Jaja-Chimedza, A., et al. (2017)
Nigella sativa	Black seed / Kalonji	Seeds, oil	Seed oil; ethanolic extracts	Thymoquinone suppresses TNF-α ,IL-6, COX-2	Paw edema; cytokine assays	Rats ; macrophage cell lines	Thymoquinone; nigellone	400 mg/kg (rat, paw edema)	Salem, M. L. (2005)
Ocimum sanctum	Tulsi / Holy basil	Leaves	Aqueous, ethanolic extracts	Inhibits COX-2; reduces prostaglandins and cytokines	Carrageenan edema; stress-inflammation models	Rats ; macrophage assays	Eugenol; ursolic acid; rosmarinic acid	200 mg/kg (rat, paw edema)	Pattanayak, P., et al. (2010)
Olea europaea	Olive leaf	Leaves	Ethanol, aqueous	NF-kB, COX2, NLRP3	LPS macrophages; colitis	colitis ; neuroinflammation	Oleuropein; hydroxytyrosol	NR	Papadopoulou et al., (2024), Perles et al., (2023)

Origanum vulgare	Oregano	Leaves	Ethanol, methanol	NF-kB, COX2, iNOS	LPS macrophages; carrageenan paw edema	carrageenan paw edema	Carvacrol; thymol; rosmarinic acid	NR	Hotta et al., 2010; Vaziriann et al., (2015)
Paeonia lactiflora	White peony	Roots	Water, ethanol	NF-kB, TLR4, MAPKs	Colitis; arthritis	arthritis ; LPS macrophages	Paeoniflorin	NR	Zhao et al., (2019)
Phyllanthus amarus	Bhui amla	Whole plant	Aqueous, ethanolic extracts	Inhibits NO production and TNF-α	Macrophage NO assays; paw edema	Mice ; RAW 264.7 cells	Phyllanthin; hypophyllanthin	200 mg/kg (rat, paw edema)	Harish, R., &Shivanandappa, T. (2006).
Piper nigrum	Black pepper	Seeds	Piperine-rich extract	Piperine inhibits TNF-α, IL-1; NF-kB	Cytokine assays; paw edema	Rats ; RAW 264.7 macrophages	Piperine; chavicine	50 mg/kg (rat, paw edema)	Umar, S., et al. (2013)
Plantago major	Common plantain	Leaves	Hydroalcoholic	NF-kB, COX2	APAP hepatotoxicity; UC models	UC models ; wound models	Aucubin; acteoside	NR	Chiang, L. C., et al. (2002).
Punica granatum	Pomegranate	Fruit peel, juice	Polyphenol-rich extracts; juice concentrate	Polyphenols inhibit NF-kB; reduce IL-6, TNF-α	Colitis models; LPS-induced inflammation	Mice ; human colon cells	Punicalagin; ellagic acid	100 mg/kg (rat, paw edema)	Larrosa, M., et al. (2010)
Rosmarinus officinalis	Rosemary	Leaves	Ethanol, methanol	NF-kB, COX2, iNOS, TNF-α, IL6	LPS-stimulated macrophages; carrageenan-induced paw edema	carrageenan-induced paw edema	Carnosic acid; carnosol; rosmarinic acid	NR	Bahriâ Sahloul et al., (2023)

Salix alba	White willow	Bark	Aqueous bark extract; salicin	Salicin inhibits cyclooxygenase-derived prostaglandins	Carrageenan paw edema; COX activity assays	Rats ; human blood cells	Salicin; salicylic derivatives	Not specified	Mahdi, J. G., et al. (2006)
Salvia officinalis	Sage	Leaves	Ethanol	NF-kB, COX2, iNOS	LPS macrophages; models of colitis	models of colitis	Rosmarinic acid; carnosol	NR	Bozin et al., (2007); Farhat et al., (2022)
Scutellaria baicalensis	Chinese skullcap	Roots	Ethanol, water	NF-kB, MAPKs, NLRP3	LPS macrophages; DSS colitis	DSS colitis ; carrageenan	Baicalin; baicalein; wogonin	NR	Dinda et al., (2017); Zhao et al., (2016)
Silybum marianum	Milk thistle	Seeds	Ethanol	NF-kB, COX2, iNOS	LPS macrophages; hepatic inflammation models	hepatic inflammation models	Silymarin (silibinin)	NR	Surai, (2015); Abenavoli et al., (2018)
Terminalia chebula	Chebulic myrobalan	Fruits	Ethanol, aqueous	NF-kB, COX2	Colitis; arthritis	arthritis ; macrophage studies	Chebulagic/chebulinic acids; gallic acid	NR	Saleem, A., et al. (2002)
Thymus vulgaris	Thyme	Leaves	Ethanol	NF-kB, COX2	LPS macrophages; edema models	edema models	Thymol; carvacrol; rosmarinic acid	NR	Oca &Regleiro, (2012)
Tinospora cordifolia	Guduchi / Giloy	Stem, leaves	Aqueous, ethanolic extracts	Reduces TNF-α, IL-1; antioxidant	Paw edema; cytokine assays	Rats ; immune cell assays	Tinosporaside; cordifolioside	100 mg/kg (rat, formalin induced paw edema)	Singh, N., et al. (2003)
Urtica dioica	Stinging nettle	Leaves	Ethanol, aqueous	NF-kB, COX2, 5LOX	LPS macrophages; arthritis models	arthritis models	Flavonoids (kaempferol; quercetin); caffeic/ferulic acids	NR	Haghi et al., (2015); Chrubasik et al., (2007)

Withanias omnifera	Ashwagandha	Root, leaves	Hydroalcoholic, withanolide-standardized extract	Suppresses NF-kB; lowers TNF-α, IL-6	Paw edema; cytokine assays	Rats ; macrophages	Withanolides (withaferin A)	100 mg/kg (rat, arthritis model)	Singh, N., et al. (2011)
Zingiber officinale	Ginger	Rhizome	Aqueous, ethanolic extracts; gingerol-enriched	Inhibits COX and LOX; reduces prostaglandins	Carrageenan paw edema; cytokine inhibition assays	Rats ; macrophage cell lines	6-gingerol; 6-shogaol; zingerone	200 mg/kg (rat, formalin test)	Grzanna,R., et al.(2005)

7. KEY FUNCTIONAL GROUPS IN ACTIVE CONSTITUENT SHOWING ANTI INFLAMMATORY ACTIVITY:

i) **Phenolic and Polyphenolic groups:** These groups are mainly present in flavonoids such as quercetin, kaempferol, phenolic acids namely in gallic acid, rosmarinic acid, and tannins e.g., punicalagin**.** These functional groups contribute antioxidant properties as well and are helpful in the inhibition of NF-κB, COX, and cytokines which are considered to be inflammatory mediators. For example: EGCG (green tea), curcumin (turmeric).

ii) **Terpenoids and Triterpenoids:** These groups have carbon skeletons having multiple isoprene units, often possessing hydroxyl or carboxyl groups to improve activity.They inhibit enzymes such as COX, LOX as well as NF-κB signalling. Examples: Boswellic acids (Boswellia), andrographolide (Andrographis), withanolides (Ashwagandha).

iii) **Alkaloids and Nitrogen-containing compounds:** These contain nitrogen atoms in heterocyclic rings or amine groups, which often modulates production of cytokines and inflammatory enzyme activity. Examples: Berberine (*Coptis chinensis*), piperine (black pepper).

iv) **Organosulfur Compounds:** Groups which contains sulfur such as thiosulfinates and sulfides provide activity on the effect of immunomodulatory and anti-inflammatory through NF-kB inhibition. Examples: allicin and diallyl sulfides which are found in garlic

v) **Coumarins and Quinones:** They tends to have lactone rings or quinone structures that regulates inflammatory enzyme activity. Examples: Hyperforin (St. John's Wort), thymoquinone (*Nigella sativa*).

vi) **Miscellaneous Oxygen-containing groups:** Groups such hydroxyl, carbonyl, and methoxy are helpful in enhancing anti-inflammatory potential by flourishing parameters like solubility, antioxidant capacity, and enzyme binding. These are found in curcuminoids, flavonoids, and many phenolic compounds.

8. MEDICINAL PLANTS SHOWING ANTI-OXIDANT POTENTIAL:

Phytochemicals with antioxidant activities possess therapeutic potential to decrease oxidative stress and counteract various diseases that arises due to oxidative stress. For eg. Rosemary, rich in anti-oxidant compounds like flavonoids, carotenoids, and phenolic acids, have shown significant cardioprotective benefits (Aguayo-Morales H. et al., 2024). *Curcuma longa* containing Curcumin, genistein, resveratrol, luteolin, marine algae extracts, quercetin, apigenin and other plant-derived products have shown great potential for treating the various neurodegenerative diseases. (Gote S., Dubey S. et al., 2025). Thyme contains Polyphenols which are becoming significant therapeutic agents in the treatment of multiple sclerosis (MS), ulcerative colitis, vitiligo, and other autoimmune diseases. They work by triggering intracellular pathways that help control the host immune response, including the arachidonic acid-dependent pathway, mitogen-activated protein kinases (MAPKs) pathway, NF-κB signaling, phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt) signalling, and epigenetic modulation. Khan H, Sureda A et al 2019. Table 4 enumerate about the most popular and active 70 medicinal plants showing anti-oxidant potential, their part used, active

constituents, probable mechanism of action, *in-vitro* and *in-vivo* assay methods.

TABLE 4 : PLANTS SHOWING ANTIOXIDANT ACTIVITY:

Medicinal Plants	Parts Used	Active Constituents	Mechanism Of Action	Antioxidant Activity		Reference
				In Vitro assay	In Vivo Assay	
Syzygium aromaticum	Flower buds & essential oil	Eugenol, eugenyl acetate, β-caryophyllene, gallic acid, tannins	Free-radical scavenging via phenolic H-donation, lipid-peroxidation inhibition, metal chelation	DPPH $IC_{50} \approx 4.82 \times 10^{-2}$µg/mL Reducing power: $EC_{50} = 3.47 \times 10^{-2}$ µg/Ml	↓ Aldose reductase activity,↓ retinal sorbital activity, improved glycemia level	Selles SMA et al. (2020) Irahal IN et al. (2022)
Phyllanthus emblica	All parts , especially fruit	Ascorbic acid, gallic acid, ellagic acid, quercetin, tannins	Radical scavenging (Vit C + polyphenols), Fe^{3+} chelation, up-regulation of SOD/CAT/GPx	DPPH $IC_{50} \approx 39.7$ µg/mL;HRSA(Hydroxyl radical scavenging assay)≈0.42mg/ml ,lipid peroxidation≈84µg/mL	Rodent models: ↑ Catalase, SOD & GSH	Pranand a et al. (2023)
Ocimum sanctum L.	Leaves	eugenol, vanillin, rosmarinic acid, ursolic acid, gallic acid	Phenolic radical scavenging, metal chelation, inhibition of lipid peroxidation	DPPH EC_{50}: ≈ 3.91 ± 0.3 µg/ml, ABTS ≈ 1.6 ± 0.1 µg/ml; phosphomolybdate ≈ 2.31 ± 0.1 µg/ml (butanol extract)	N/A	Chaudhary A. et al., (2020).
Curcuma longa L.	Rhizomes	Curcuminoids (curcumin, demethoxycurcumin, bisdemethoxycurcumin) volatile oils (ar-turmerone, α-turmerone, curlone, zingiberene) polysaccharides (ukonan A–D); flavonoids	Direct ROS scavenging), metal chelation, inhibition of lipid peroxidation, , anti-inflammatory (NF-κB modulation)	DPPH scavenging activity of liposomal curcumin compared to free curcumin, purified curcumin shows stronger activity (lower IC_{50})	decreased MDA, increased SOD/CAT/ GPx	Shivkanya Fuloria et al (2022) Kirandeep Kaur et al (2024)
Camellia sinesis (L.)	Leaves	Polyphenols (catechins; flavonoids; anthocyanins; phenolic acids: gallic acid, chlorogenic acid); alkaloids (caffeine, theophylline, theobromine); amino acids (theanine, GABA); vitamins (C, E)	Radical scavenging, metal chelation, ↑SOD/GPx, ↓lipid peroxidation	DPPH IC_{50} = 69.5 µg/mL (methanolic extract)	↓MDA, ↑SOD ,GSH and GSH-Px in mice	Tiantian Zhao et al (2022) Hasan MR et al. (2024)

Allium sativum L.	Bulb	Organosulfur compounds :allicin, alliin, ajoenes, vinyldithiins, sulfides	ROS scavenging, thiol-based redox activity, ↑SOD/GPx, ↓lipid peroxidation	DPPH IC_{50} =31 µg/ml,	↓MDA in serum and ↑SOD activity after garlic extract supplementation .	Gaber El-Saber Batiha et al (2020) Pârvu M et al (2019)
Zingiber officinale	Rhizomes	Gingerol, shogaols, paradols, flavonoids, phenolic acids	Radical scavenging (phenolics/gingerols/shogaols), reducing power, inhibition of lipid peroxidation, up-regulation of antioxidant enzymes	DPPH IC_{50}: Lowest IC50 = 15.23 µg/ml when sundried ABTS/FRAP: dried ginger vs fresh showed ~95% DPPH radical inhibition and FRAP ~15.35-fold higher in sun-dried vs fresh.	↑ TAC,GPx & CAT↓MDA	Mustafa I. & Chin N. L. (2023) Morvaridzadeh M et al (2021)
Gingko biloba	Leaves	Flavonol glycosides (quercetin, kaempferol, isorhamnetin), terpene lactones (ginkgolides, bilobalide)	Strong radical scavenging (flavonoids), metal-ion chelation, inhibition of lipid peroxidation, mitochondrial ROS suppression	DPPH IC_{50}: ~24.25 µg/mL (leaf extract)	Rat brain model: ↓MDA, ↑SOD and GPx	Zhang L. et al., (2022). Zhao J. et al., (2011)
Rosmarinus officinalis	Leaves	Carnosic acid, carnosol, rosmarinic acid, cafffeic acid	Radical scavenging by phenolics/diterpenes, reducing power, lipid-peroxidation inhibition	DPPH IC_{50} ≈ 221.6 µg/mL (hexane extract) ABTS ≈ 310.5 mM TE/g dry extract FRAP ≈ 394.7 mM TE/g dry extract	Human trial (9 healthy volunteers): after 5 days 250 mL aqueous extract/day → ↑ serum TAS by ~18%, ↑ erythrocyte GSH ~72%, ↑ SOD ~21%, ↓ erythrocyte MDA ~17%	Ibrahim N. et al., (2022) Bilto Y.Y. & Alabdallat N.G., (2015)
Clitoria ternatea	Flowers & leaves	Anthocyanins (ternatins), flavonols (quercetin, kaempferol), phenolic acids	Potent radical scavenging via anthocyanins; inhibition of lipid peroxidation; ferric-reducing activity	DPPH IC_{50}: ~ 195.5 µg/mL ABTS: ~42.9 µg/mL	In oxidative-stress rat models: ↓ MDA, ↑ SOD, CAT, GSH	Wang, Y.et al(2025)

Mentha spicata	Leaves	Carvone,trans-Carveol ,β-Caryophyllene , 1,8-Cineole, Germacrene D ,Menthone ,α-Pinene	Free-radical scavenging via phenolic H-donation, metal-ion reduction, inhibition of lipid peroxidation	DPPH $IC_{50} \approx 87.9$ µg/mL (leaf ethanolic extract) ABTS $IC_{50} \approx$ 173.8 µg/mL	↓ MDA,↑CAT, SOD, and GPX	El Menyiy N et al (2022)
Melissa officinalis	Leaves (aerial parts)	Rosmarinic acid, caffeic acid, protocatechuic acid, cinnamic acid, chlorogenic acid, gallic acid, ferulic acid, ellagic acid, p- coumaric acid, and salvianolic acid	free-radical scavenging, lipid peroxidation inhibition, and endogenous antioxidant system protection	DPPH $IC_{50} \approx$ 4.76–9.95 µg/mL , FRAP ≈ 329–342 mg AAE/g dry extract	In vivo (rat carrageenan paw-edema model): extracts improved systemic antioxidant status (↑ GSH, ↓ TBARS) after oral administration	Draginic N. et al., (2022)
Nigella sativa (Black cumin)	Seeds/ oil	Thymoquinone, tocopherols, vitamin A and C, β-carotene	Radical scavenging by phenolics and thymoquinone, reducing power, metal-ion chelation, inhibition of lipid peroxidation	DPPH $IC_{50} \approx$ 9.895 ± 0.817 µM TE ; TAA ≈11.273 ± 0.935 µM TE (seed oil extract)	↓ MDA/TBARS; ↑ SOD, CAT, GSH; protection in liver/renal/oxidative-stress models	Bordoni L. et al., (2019).
Pimenta dioica	leaves, berries	Eugenol, galloyl- and di-galloyl derivatives, phenolic acids	Phenolic radical-scavenging (H-donation), inhibition of lipid peroxidation, metal ion reduction	DPPH $IC_{50} \approx 390$ µg/mL for aqueous extract (leaves) In methanol extract ORAC ~ 44.1 µmol TE/100 g; FRAP ~ 4.5 mmol Fe^{2+}/g for methanol extract	N/A	Miyajima Y. et al., (2004)
Origanum vulgare	Leaves, flowering tops, essential oil	Phenolic acid, flavonoids , kaempferol , luteolin, apigenin	H-atom donation by phenolics, metal-ion reduction, lipid chain-breaking by carvacrol/thymol	DPPH ≈ 108.6 mg TE/g; ABTS ≈ 115.2 mg TE/g; FRAP ≈ 13.7 mg TE/g; CUPRAC ≈ 1.2 mg TE/g; TPC ≈ 362 mg GAE/g	N/A	Michalaki A et al. (2023)
Salvia officinalis	Leaves , flowers	camphor, 1,8-cineole, α-thujone, borneol, β-thujone, and viridifloro	Phenolic radical scavenging, lipid peroxidation inhibition, ROS-enzyme inhibition	DPPH $IC_{50} \approx 10.4$ µg/mL; ABTS ≈ 0.9- 1.2µg/mL; FRAP ≈ 94-98 µM Fe^{2+}/g	N/A	Brindisi, M et al (2021)

Petroselinum crispum	Leaves, seed	Apigenin, alpha-pinene, apiol, myristicin	Radical scavenging (flavones), metal chelating, enzyme up-regulation of SOD & CAT	DPPH EC_{50} ≈ 15.5 mg/mL; FRAP ≈ 189.8 mM Fe^{2+}/mg; TPC ≈ 12.49 mg GAE/g	↓MDA, ↑ GSH	Epifanio et al. (2020)
Elettaria cardamomum	Seeds, pods; essential oil	1, 8-cineole α-terpineol, sabinene nerol and α-pinene	Free-radical scavenging via monoterpenes and phenolic donation; inhibition of lipid peroxidation	DPPH IC_{50} ≈ IC_{50} ~ 423 µg/mL (ethanolic extract) ; FRAP ≈ 95.0 mg AAE/g	Rats (CCl_4 hepatotoxicity): ↓ MDA, ↑ SOD, CAT, GPx; improved hepatic histology; lipid stabilization	Tarfaoui, K et al. (2022) Elguindy, N. M et al (2016)
Glycrrhiza glabra	Roots	Glycyrrhizin, triterpene saponins, flavonoids, isoflavonoids and chalcones	Phenolic radical scavenging, metal-chelating, Nrf2 activation, inhibition of ROS-producing enzymes	DPPH IC_{50} ≈ 43.6 µg/mL; ABTS IC_{50} ≈ 77.3	Rats: hepatoprotection & reduced lipid peroxidation	Asl & Hossein (2008) Lim TK. (2015)
Withania somnifera	Roots, leaves	alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins	Free-radical scavenging, Nrf2-dependent antioxidant enzyme induction, mitochondrial protecting DPPH	DPPH IC_{50} ≈ 37.8 µg/mL; ABTS IC_{50} ≈ 34.4 µg/mL	Rodents: ↓ MDA, ↑ SOD, CAT, GPx; prevented stress-induced oxidative damage; neuroprotective in PD model	Narayanaswamy, C.et al (2025) Suganya K et al(2020)
Silybum marianum	seeds	flavonolignans (silybin A and silybin B, isosilybin A, isosilybin B, silychristin and silydianin),flavonoids, fatty acids	Radical scavenging by flavonolignans, membrane stabilization, GSH regeneration, Nrf2 activation	DPPH IC_{50}: 19.2 ± 2.3 µg/mL;ABTS IC_{50}: 7.2 ± 1.7 µg/mL;FRAP IC_{50}: 24.1 ± 1.2 µg/mL ;CUPRAC IC_{50}: 22.2 ± 1.2 µg/mL	CCl_4-treated rats: ↓ MDA by ~60%, ↑ GSH, SOD, CAT; protection against hepatic oxidative stress	Lekmine S et al (2015) Vargas-Mendoza et al. (2014)
Panax ginseng	Root	Ginsenosides (Rb1, Rg1, Rg3, Re), polysaccharides, phenolics	Direct radical scavenging, mitochondrial protection, up-regulation of antioxidant genes (Nrf2, HO-1)	DPPH IC_{50} ≈ 0.893 mg/mL; ABTS ≈ 0.210 mg/Ml	N/A	Zhang P et al. (2024)
Nigella sativa	seeds	thymoquinone, thymol, nigellidine, carvacrol, α-pinene, p-cymene, and α-hederin	Free-radical scavenging via thymoquinone; lipid-peroxidation inhibition; upregulates antioxidant enzymes	DPPH IC_{50} ≈ 12.4±0.5 µg/mL; FRAP: 520±15 µM Fe(II) equivalents),	Rats (CCl_4, diabetic): ↓ MDA, ↑ SOD/CAT/GPx; hepatoprotective & nephroprotective	Khan, I., & Shaikh(2025) & İlhan, N., & Seçkin, D. (2005)

Centella asiatica	Leaves, aerial parts	asiaticosides, brahmoside, asiatic acid, and brahmic acid	Radical scavenging, Nrf2 activation, enhanced SOD/CAT expression, neuroprotective	DPPH IC_{50} ≈ 9.62 ± 0.88 µg/mL;ABTSIC50 ≈27.21 µg/mL	Rats ($AlCl_3$, diabetic, aging): ↓ MDA, ↑ SOD, GSH, TBARS, and NO	Kumari S et al. (2016)
Echinacea purpurea	Root	Cichoric acid, caftaric acid, echinacoside, polysaccharides	Radical scavenging, metal chelation	DPPH(EC50) ≈ 6.6 µM	N/A	Lim, T. K. (2014)
Artemisia annua	Leaves	Polyphenols, flavonoids	Radical scavenging; reduces oxidative damage	DPPH IC_{50} ≈ 5.17 µg/mL; OH• IC_{50} ≈ 17.83 µg/mL; NO• IC_{50} ≈ 79.94 µg/mL; Lipid peroxidation IC_{50} ≈ 41.56 µg/Ml	N/A	Gavarić N et al (2025)
Hypericum perforatum	Aerial parts	Hypericin, hyperforin, flavonoids	Free radical scavenging; electron donation	DPPH IC_{50} ~9.82 µg/mL and ABTS IC_{50} ~7.01 µg/mL (ethanol extract)	Rodents (stress/depression): ↑ SOD/CAT in brain, ↓ MDA; neuroprotective effect	Ağar, O. T et al. (2025)
Coriandrum sativum	Leaves, seeds	Phenols, flavonoids, linalool	Free radical scavenging, ferric reducing power, lipid peroxidation inhibition	DPPH IC_{50} ~222 µg/mL (ABTS); metal chelation ~368 µg/mL; lipid peroxidation IC_{50} ~590 µg/mL	N/A	Harsha SN et al (2014)
Moringa oleifera	Leaves	Phenolics (quercetin, chlorogenic acid, gallic acid), flavonoids	Radical scavenging; reduces oxidative damage; ferric-reducing activity	DPPH IC_{50} ≈ 49.30 µg/mL (methanol extract); ABTS IC_{50} ≈ 11.73 µg/mL (methanol extract) — leaves	N/A	Fitriana WD et al(2016)
Curcuma zedoaria	Rhizome	Curcuminoids, sesquiterpenes (zedoalactone), phenolics	Phenolic H-donation, radical scavenging, some metal chelation; EO fractions show lipophilic antioxidant activity	DPPH IC_{50} ≈ 153–186 µg/mL for EtOAc	In rodent/food-model studies: ↓ MDA/TBARS, ↑ SOD/CAT with methanolic/ EtOAc fractions; fraction-dependent effects.	Budiansyah A et al. (2023)

Mentha spicata	Leaves	Rosmarinic acid, eriocitrin, flavonoids, menthone, pulegone (EO)	Hydrophilic phenolic scavenging (rosmarinic acid/eriocitrin), EO terpenes contribute to lipophilic antioxidant action	DPPH IC_{50} (extracts) ≈ 20–60 µg/mL; ABTS ≈ 50–120 µmol TE/g; FRAP moderate (several mmol Fe^{2+}/g); TPC ≈ 80–220 mg GAE/g	In vivo/biological: improved antioxidant enzymes (SOD/CAT), lowered lipid peroxidation in stress models; EO shows moderate activity in food systems.	Henao-Rojas JC et al. (2022) Bardawel, S.K.et al. (2018)
Crocus sativus	Stigmas	Crocin, safranal, picrocrocin	Strong carotenoid/diapocarotenoid radical quenching (crocin/crocetin), protects lipids and proteins, upregulates endogenous enzymes	DPPH IC_{50} (ethanolic extracts) ≈ 299.44 µg/mL	Animal/cell studies: ↓ MDA, ↑ SOD/GPx	Hatziagapiou K et al (2019)
Matricaria chamomilla (syn. Chamomilla recutita)	Flowers	apigenin, apigenin-7-glucoside, luteolin, quercetin, chamazulene, bisabolol — flavonoids	Flavone radical scavenging (apigenin), membrane protection	DPPH EC_{50} ≈ 26.7 µg/mL in ethanol extract	↓ MDA, ↑ SOD/GSH	Al-Dabbagh B et al. (2019)
Allium cepa	Bulb, skins	Quercetin, kaempferol, catechin, anthocyanins	Radical scavenging, lipid peroxidation inhibition	DPPH IC_{50} ≈ 43.24 µg/mL; ABTS ≈ 560.61 µg/mL (Polyphenols)	↓ MDA , ↑ SOD/CAT/GPx; ameliorated hepatic oxidative stress	Marefati N et al. (2021)
Bacopa monnieri	Leaves, aerial parts	Bacosides A/B, flavonoids, saponins	Radical scavenging, Nrf2 activation, mitochondrial protection	DPPH, ABTS, TPC	↓ MDA ↑ SOD and GPx	Simpson T et al. (2015)
Mangifera indica	Leaves	phenolic acids, flavonoids, benzophenone derivatives, and mangiferin	Strong phenolic radical scavenging, metal chelation, lipid-peroxidation inhibition	DPPH: IC_{50} ≈ 26.866 µg/ml; ABTS: ≈ 14.653 µg/ml FRAP: ≈ 820 µmol Fe^{2+}/g extract	N/A	Işık M et al.,(2025)
Momordica charantia	Fruit (extracts)	Ascorbic acid, flavonoids, cucurbitane triterpenoids	Radical scavenging (phenolics/triterpenoids), reducing power, inhibition of lipid peroxidation	DPPH IC_{50} ≈ 111.87 µg/mL (ethanol extract) Superoxide scavenging IC_{50} ≈ 331.26 µg/mL (ethyl acetate extract)	N/A	Talukder M.E.U. et al. (2013)

Santalum album	Heartwood	α- and β-santalol, cedrol, esters, aldehydes, phytosterols	Radical scavenging, phenolic reducing power, lipid-peroxidation inhibition	FRAP: ≈1.0 µmol Fe^{2+}/mL	N/A	Shivashankara, A. R.et al(2021)
Andrographis paniculata	Leaves / whole plant	Andrographolide, flavonoids, phenolics	Radical scavenging by phenolics/diterpenoids, reducing power, inhibition of lipid peroxidation	DPPH IC_{50} ≈ 3.2 µg/mL	Improved antioxidant enzyme levels (SOD, CAT), increased GSH, reduced lipid-peroxidation markers in oxidative stress models	Mussard E. et al., (2019).
Picrorhiza kurroa	Leaves	Iridoid glycosides (picroside I/II), phenolic acids, flavonoids	Radical scavenging (phenolic/flavonoid H-donation), reducing power, metal-ion chelation, inhibition of lipid peroxidation	DPPH IC_{50} ≈ 39.58 µg/mL (ethyl-acetate extract) & ~67.48µg/mL (ethanol extract) ABTS ≈ 48.36 µg/ml(ethanol extra reduced	Reduced TBARS/MDA, improved antioxidant enzyme activities (SOD, CAT, GSH)	Kant K. et al. (2013)
Psoralea corylifolia	Seeds	flavonoids, coumarins, meroterpenes, and benzofurans	Radical-scavenging via phenolics, reducing power, inhibition of lipid peroxidation	DPPH IC_{50} ≈ 61.5 ± 2.9 µg/mL; ABTS IC_{50} ≈ 56.05 ± 0.6 µg/mL; FRAP ≈ 18.8 ± 0.5 mmol TE/g; ORAC ≈ 18.94 ± 0.07 µmol TE/g	Seed extract improved antioxidant status (↓ MDA, ↑ GSH)	Shah AB,et al 2025 Kamboj, J.et al (2011)
Semecarpus anacardium	Nuts, stem bark	Phenolic compounds (e.g., butein), flavonoids, tannins	Radical scavenging via phenolics, metal chelation, inhibition of lipid peroxidation, up-regulation of antioxidant enzyme systems	DPPH IC_{50} ≈ 43.28 ± 4.34 µg/mL (stem bark ethyl acetate extract)	improved antioxidant status	Sahoo A. K et al (2008)
Terminalia chebula	Fruit (also bark/leaves)	Chebulinic acid, gallic acid, ellagic acid, tannins	Phenolic/tannin radical scavenging, lipid-peroxidation inhibition	DPPH IC_{50} ≈ 22.16 µg/mL (variety dependent) FRAP ≈ 113.4 mmol Fe^{2+}/g extract (one variety)	N/A	Khalil E et al. (2023)

Uncaria tomentosa	Leaves (also bark)	Proanthocyanidins (e.g., propelargonidin dimers), flavan-3-ols, hydroxycinnamic acids, alkaloids	Radical scavenging via phenolics, metal-ion reduction, proanthocyanidin-driven antioxidant effects	DPPH $IC_{50} \approx 5.23$ µg/mL (aqueous leaf extract) and ORAC ≈ ~12.06 µmol TE/mg	N/A	Navarro-Hoyos M. et al., (2018).

9. KEY FUNCTIONAL GROUPS IN ACTIVE CONSTITUENT SHOWING ANTI-OXIDANT ACTIVITY:

i) **Flavonoids**- Derivatives of benzo-γ-pyrone with pyrene and phenolic rings are called flavonoids. The ability of flavonoids to lower alpha-tocopherol radicals, activate antioxidant enzymes, chelate metal catalysts, transfer electrons from free radicals, and inhibit oxidases is responsible for their protective mechanism in physiological systems. The flavonoid heterocycle (i) facilitates conjugation between the aromatic rings and (ii) has a free 3-OH, both of which increase antioxidant activity. In order for flavonoids to scavenge free radicals, a free 3-OH must be present (KE Heim et al 2002).

ii) **Phenolic Acids-** Compounds containing both a phenolic structure and a carboxylic acid group are classified as "phenolic acids." Polyphenols are present in various plant-based diets, although they are most abundant in fruit skins, seeds, and vegetable leaves. Because of the phenol moiety's (hydroxyl substituent) reactivity, phenolic acids shows antioxidant activity. The primary mechanism for their antioxidant activity is radical scavenging by H- atom donation. Phenolic acids' aromatic ring substituents have an impact on the structure's stability and, in turn, their capacity to quench radicals. (Kumar N, Goel N.et al 2019).

iii) **Tannins**- Tannins are important secondary metabolites in plants, crucial in determining sensory characteristics and nutritional value of various fruits, vegetables, beverages, and other plant-based meals. Plant-based foods, including legume seeds, fruits, vegetables, nuts, cereals, chocolate, as well as drinks like wine, cider, tea, and cocoa, are rich in these compounds. Tannins are considered as strong antioxidants because of their high polyphenolic content, which efficiently scavenges free radicals, lowers oxidative stress, and prevents lipid peroxidation. They also interact with dietary proteins, which impacts the digestion and bioavailability of nutrients. Furthermore, iron, copper, and other metal ions that catalyse oxidative processes can be chelated by tannins. Tannins lessen oxidative damage by decreasing the availability of these metals. (Cosme, F.et al 2025).

iv) **Carotenoids**- Carotenoids are associated with reduced risk of several diseases, such as heart diseases, cancer, diabetes, obesity, and neurological diseases, since they have cytoprotective, photoprotective, antioxidant, and many other qualities. Carotenoids are tetraterpenes that are typically made up of polyene chains and are mainly made up of isoprene units (8) with a 40-carbon skeleton. By activating nuclear hormone receptor pathways like retinoic acid receptors (RAR), peroxisome proliferator-activated receptors (PPARs), or retinoid X receptors (RXR), carotenoid metabolites may influence health benefits through direct or indirect mechanisms, including antioxidant actions and regulation of transcription factors like Nrf2 and NF-κB. (T Bohn, 2019).

v) **Terpenoids** -Triterpenoids are isopentenyl pyrophosphate oligomer metabolites. Their main sources include a variety of plants, including seaweeds, and the waxy coverings of medicinal herbs and fruits, such as figs, mistletoe, cranberries, apples, olives, lavender, thyme, oregano and rosemary. Because of their analgesic, anti-inflammatory, antipyretic, cardiotonic hepatoprotective, sedative, and tonic properties, triterpenoids are utilised medicinally in many Asian nations (Bishayee A et al 2011). Through a variety of processes, such as metal ion chelation, direct scavenging of free radicals, and modification of antioxidant enzyme activity, terpenoids demonstrate their antioxidant qualities. They may enter into cell membranes due to their lipophilic nature, which interferes with oxidative processes and strengthens defence

mechanisms. Additionally, several terpenoids upregulate endogenous antioxidant enzymes by activating redox-sensitive signalling pathways, such as the Nrf2/ARE pathway (Gutiérrez-Del-Río et al 2021).

vi) **Alkaloids**- Alkaloids are a class of naturally occurring bioactive chemicals that have a nitrogen atom in their ring structure. These molecules are typically found inside heterocyclic rings and are responsible for a variety of related compounds that have neutral and slightly acidic properties *(*Atpadkar PP et al 2023). Because of their antioxidant qualities, alkaloids have the potential to treat neurodegenerative illnesses by focussing on oxidative stress processes. By modulating antioxidant enzymes and scavenging free radicals, they can lessen oxidative damage.

10. ACTIVE CONSTITUENTS AND THEIR CHEMICAL STRUCTURE:

i) ANTI INFLAMMATORY COMPOUNDS:

Figure 5 represents examples of active chemical compounds with anti-inflammatory actions and their chemical structure

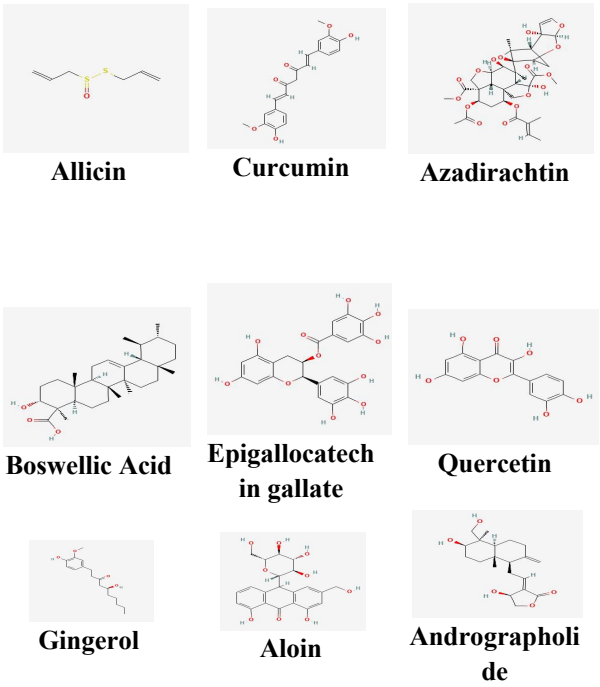

Fig 5 Active chemical compounds with anti-inflammatory actions and their chemical structure

ii)ANTI OXIDANT COMPOUNDS:

Figure 6 represents examples of active chemical compounds with anti-oxidant actions and their chemical structure.

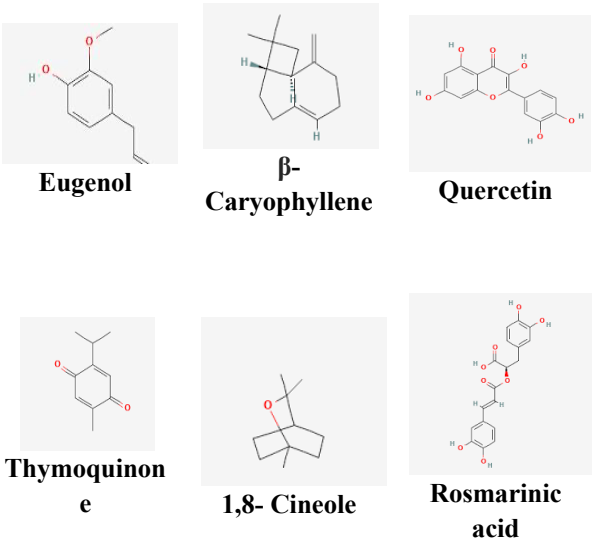

Fig 6 Active chemical compounds with anti-oxidant actions and their chemical structure

11. CONCLUSION

This review highlights the role of anti-inflammatory and antioxidant agents, which are derived from plants, in managing inflammation, oxidative stress and diseases associated with them. Key phytochemicals, particularly phenolic acids, flavonoids, carotenoids, terpenoids, tannins, and alkaloids, demonstrate strong radical-scavenging, metal-chelating, and lipid peroxidation–inhibiting activities. And many other constituents like quercetin, nitrogen containing compound, organosulfur compound, coumarins etc acts as an anti-inflammatory agent by inhibiting NF-κB, LOX, COX, iNOS pathways. Various in vitro and in vivo assays are used to determine the antioxidant and anti-inflammatory potential of these compounds. Although significant research has been done on these herbs, there are several challenges faced by researchers, such as the standardisation of extracts and variation in plant part used, geographic origin, harvest time and extraction solvent. Moreover, in vitro antioxidant assays are not much correlated with in vivo effects, as many phytochemicals show strong in vitro antioxidant activity but show limited in vivo effects. In vivo studies require robust animal models and human clinical trials, both of which are still very limited. Many compounds also demonstrate herb-drug interaction, causing major safety issues. Future research should be focused on developing methods which ensure reproducible and comparable results. Advanced methods like nanoencapsulation or controlled release systems should be included for

improving. Thorough in vivo studies and human clinical trials are required for validating therapeutic efficacy and safety. Deeper insights into mechanisms can be obtained through some modern analytical tools, like metabolomics and molecular pathway studies. For enhancing the safety and effectiveness of herbs, a thorough evaluation of herb-drug interactions and strict regulations must be done.

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