

Anti-inflammatory activity of plant-derived natural bio-organic ingredients: A review

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Abstract

Background: Inflammation is a natural process of defense that occurs in response to tissue injury, cell death, cancer, ischemia, and degeneration. It is also evoked after the invasion of body cells by various pathogens. If inflammation is not managed, it results in cancer or in an autoimmune disorder. Plant natural products possess the ability to neutralize inflammatory reactions. These are considered true healers and can be used for the treatment of tissue inflammation in the future. **Aim of the Review:** For writing the present review, the anti-inflammatory and immunomodulatory effects of plant extracts, bioorganic compounds, and herbal preparations from more than 200 plant species have been selected. **Materials and Methods:** An extensive literature search was done for anti-inflammatory and immunomodulatory activity of plant extracts, bioorganic compounds, plant essential oils, plant latex, gums, pigments, and herbal preparations published in English within the past 20 years through databases (PubMed, EMBASE, Scopus, and The Web of Science). **Results:** A total of 467 papers were found by searching, and 87 papers were screened after removing duplicates and reading article titles. Fifteen articles met the requirements to be included in this review. Among those selected, 17 articles reported *in vivo* research results, and 4 articles showed research results. **Conclusion:** Plant extracts, bioorganic compounds, plant essential oils, plant latex, gums, pigments, and herbal preparations can reduce inflammation by regulating the release of inflammatory cytokines involved in multiple signaling pathways. Plant natural products are expected to be developed as anti-inflammatory drugs.

Key words: Inflammation, mediators, plant natural products, pro-inflammatory cytokines, tissue injury

INTRODUCTION

Inflammation is a natural process of healing wounds caused by pathogens and parasites. It involves both systemic and local responses, activating both innate and adaptive immune defenses.^[1] In response to an injury, various cellular events and glandular secretions occur to heal the wound site. The innate immune response involves macrophages, mast cells, natural killer cells, and dendritic cells, while the adaptive immune system includes B and T cells, specialized cells, and inflammatory cells. Histamine can play a role in quick, touchy responses. Histamine applies H₂-receptor-mediated anti-inflammatory movement counting restraint of human neutrophil lysosomal chemical discharge, restraint of immunoglobulin (Ig)E-mediated histamine discharge from fringe leukocytes, and enactment of silencer T-lymphocytes. The main purpose of inflammation is the protection of body tissues from harmful substances and to respond to foreign antigens or tissue damage and to mitigate the impact of harmful

inflammatory substances. Throughout this process, various inflammatory mediators are produced and released during the body's different inflammatory responses.

More specifically, damaged body cells release specific substances such as vasoactive amines and peptides, eicosanoids, proinflammatory cytokines, and acute-phase proteins, which facilitate the inflammatory response. It helps to protect further tissue damage, ultimately leading to healing and recovery of tissue function. Inflammatory substances are divided into pro-inflammatory and anti-inflammatory mediators. Pro-inflammatory cytokines induce inflammation in the central nervous system (CNS), attracting immune cells and activating glial cells.^[2] Key mediators include interleukin

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(IL)-1, tumor necrosis factor- α (TNF- α), and thrombin, controlling processes in both healthy and diseased conditions. These crucial regulators significantly affect the blood vessels and result in heightened vascular permeability.^[3]

In addition, they modify morphogenic responses of blood vessels, promote adhesion and migration of leukocytes, enhance pro-coagulant activities, and increase the adhesion and aggregation of platelets. These small-molecule mediators control anti-inflammatory responses in both healthy and diseased conditions. Pro-inflammatory cytokines are produced and released as a reaction to oxidative stress and an overproduction of reactive oxygen species (ROS). Primary immune organs, such as IL-2, IL-1, and various cytokines, function as mediators to facilitate the healing process.^[4] More specifically, IL-12 exhibits both pro-inflammatory and anti-inflammatory characteristics.^[5] Inflammation contributes to conditions such as diabetes, Alzheimer's, Parkinson's, cardiovascular issues, respiratory disorders, renal problems, liver disease, and cancer^[2] [Figure 1].

Neuronal inflammation in the CNS can lead to neurological disorders due to the release of chemicals by endothelial cells, microglia, and astrocytes. Chronic inflammation, characterized by increased cytokine synthesis, ROS, and other mediators, is triggered by illness, injury, infection, or stress. Increased synthesis of cytokines (TNF and IL-1), ROS, and other inflammatory mediators (inducible nitric oxide synthase [iNOS]) is a hallmark of chronic, uncontrolled inflammation. Following CNS trauma, these markers are very noticeable and are accompanied by a notable recruitment and trafficking of peripheral neutrophils and macrophages to the site of

injury. More frequently, these neuroinflammatory reactions are mediated by microglia, which are innate immune cells of the CNS [Figure 2].

Non-steroidal pharmaceutical agents are commonly used to manage inflammatory conditions,^[6] but they can cause adverse effects.^[7] Phytochemical compounds extracted from plant species have been studied for their anti-inflammatory properties. These phytochemicals have been traditionally utilized throughout the globe for the treatment of inflammation.^[8] These compounds are superior to synthetic medications, which can have side effects and high costs. Therefore, the discovery and evaluation of new compounds with minimal side effects that exhibit strong anti-inflammatory properties may be derived from local medicinal plants. This review aims to highlight the anti-inflammatory capabilities of specific plant species for everyday use.

PROSTAGLANDIN (PG) E LEUKOTRIENES

Plants naturally produce anti-inflammatory substances that block cyclooxygenase (COX) enzymes that convert arachidonic acid to PGs. These substances, including PGs and leukotrienes, are eicosanoid lipid mediators involved in inflammation and homeostatic processes. Phospholipase-released arachidonic acid is the source of PGs and leukotrienes, which are strong eicosanoid lipid mediators implicated in inflammation and a variety of homeostatic biological processes. They function through G protein-coupled receptors and contribute to the inflammatory response.^[9] PGs and thromboxanes, a class of derivatives

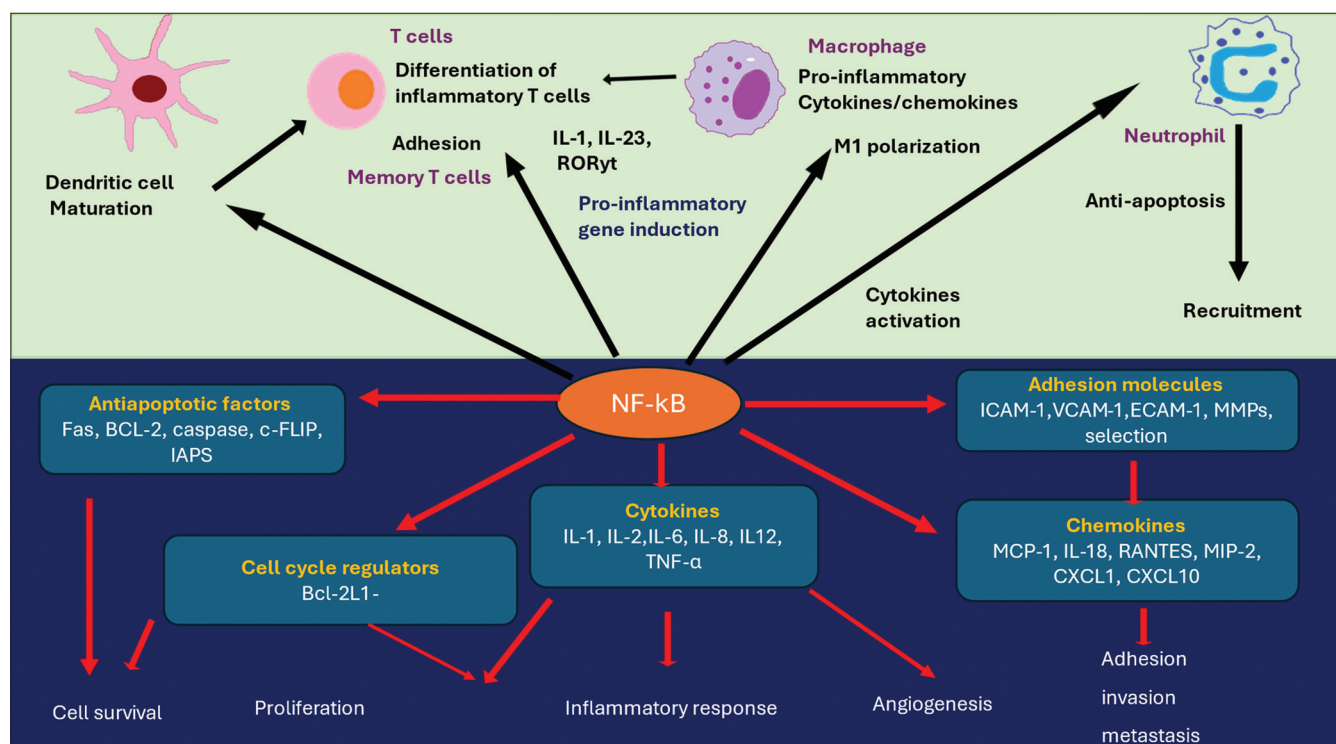


Figure 1: Role of various immune cells and molecules in the regulation of inflammatory response

of arachidonic acid, play a role in immune cell recruitment, vascular tone, and permeability modulation. Eicosanoids play a role in immune cell recruitment into the vascular wall, vascular tone and permeability modulation, and more.^[10] Histamine and bradykinin's effects on vascular permeability are amplified by vasodilator PGs at physiological quantities, and leukotrienes play a significant role in mediating leukocyte accumulation during acute inflammation. PG metabolites help resolve acute inflammation by preventing nuclear factor-kappa B (NF- κ B) activation. Thus, a range of activities that produce and reduce acute inflammation caused by bacterial infections are regulated by the oxygenation products of arachidonic acid.^[11]

THE TRANSCRIPTION FACTOR NF- κ B

The regulation of inflammatory responses is a prominent function of NF- κ B. In addition to modulating the expression of numerous pro-inflammatory genes in innate immune cells, NF- κ B also oversees the activation, differentiation, and effector functions of inflammatory T cells. NF- κ B is a crucial family of transcription factors involved in immunity, inflammation, cell division, proliferation, and survival. The activation of inducible NF- κ B requires the phosphorylation-induced proteasomal degradation of the inhibitor of NF- κ B proteins (I κ Bs), which maintain NF- κ B dimers in an inactive state within the cytosol of unstimulated cells. The I κ B kinase (IKK) complex, responsible for I κ B phosphorylation, serves as a convergence point for various signaling pathways that lead to NF- κ B activation.^[12] The core components of the NF- κ B signaling pathways undergo numerous post-translational modifications that further fine-tune NF- κ B activity. In addition to the cytosolic alterations of IKK and I κ B proteins, significant modifications also occur in the transcription factors involved. Over the last two decades, considerable progress has been made in understanding the intricate regulatory networks that control the NF- κ B response.

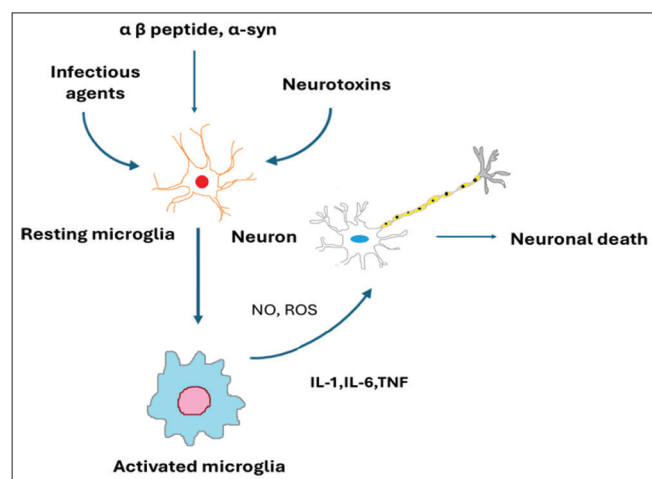


Figure 2: Role of microglia cells and secreted molecules in neural inflammation

Oral cavity inflammation is frequently a result of necrosis from chemical agents, traumatic injury from foreign objects, or gavage procedures. Chronic inflammatory lung disease is frequently characterized by an excess of mucus production and hypersecretion. Chronic inflammatory lung disease is frequently characterized by an excess of mucus production and hypersecretion. Excessive production of mucus in the airways is caused by the presence of neutrophil elastase, specific bacterial pathogens, and changed cytokine patterns. Airway blockage and impaired mucociliary clearance are consequent effects of this overproduction and hypersecretion of mucus [Figure 3].

Patients with various liver diseases, including alcoholic liver disease, cholestatic liver disease, autoimmune liver disease, non-alcoholic fatty liver disease, and chronic viral hepatitis, develop liver fibrosis. Hepatic inflammation plays a key role in these conditions, leading to progressive liver damage and fibrosis. Innate immune cells, activated by pathogen-derived products, produce mediators that initiate and sustain inflammation. Dendritic cells are vital for activating T-lymphocyte responses, while Kupffer cells and recruited macrophages produce cytokines and chemokines that contribute to prolonged inflammation and hepatocyte damage, despite the liver's tolerogenic environment for T-cells [Figure 4].

Patients with cardiovascular disorders, inflammatory bowel diseases, and other conditions show high levels of obesity-related adipose tissue inflammation, which leads to chronic systemic inflammation. This inflammation is driven by immune cell infiltration in enlarged adipose tissue, resulting in the production of inflammatory cytokines that harm target organs. In addition, various injuries can cause skeletal muscle inflammation, while kidney inflammation, or nephritis, can lead to protein leakage into urine, disrupting water absorption and causing tissue edema [Figure 5].

Nephritis, autoimmune diseases like lupus, and heart inflammation can lead to major health issues such as heart failure, coronary heart disease, and arrhythmias. Inflammation

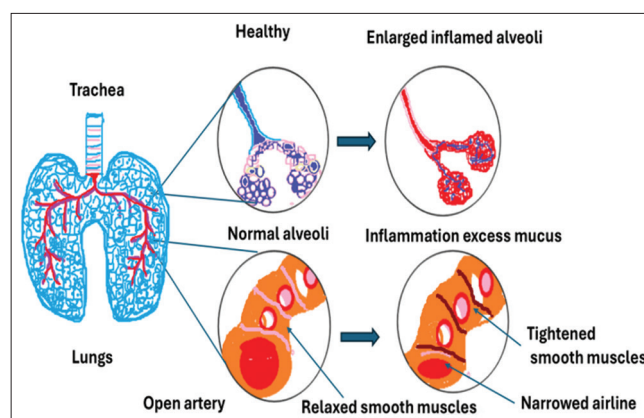


Figure 3: Alveolar inflammation and production of excess mucus during lung tissue inflammation

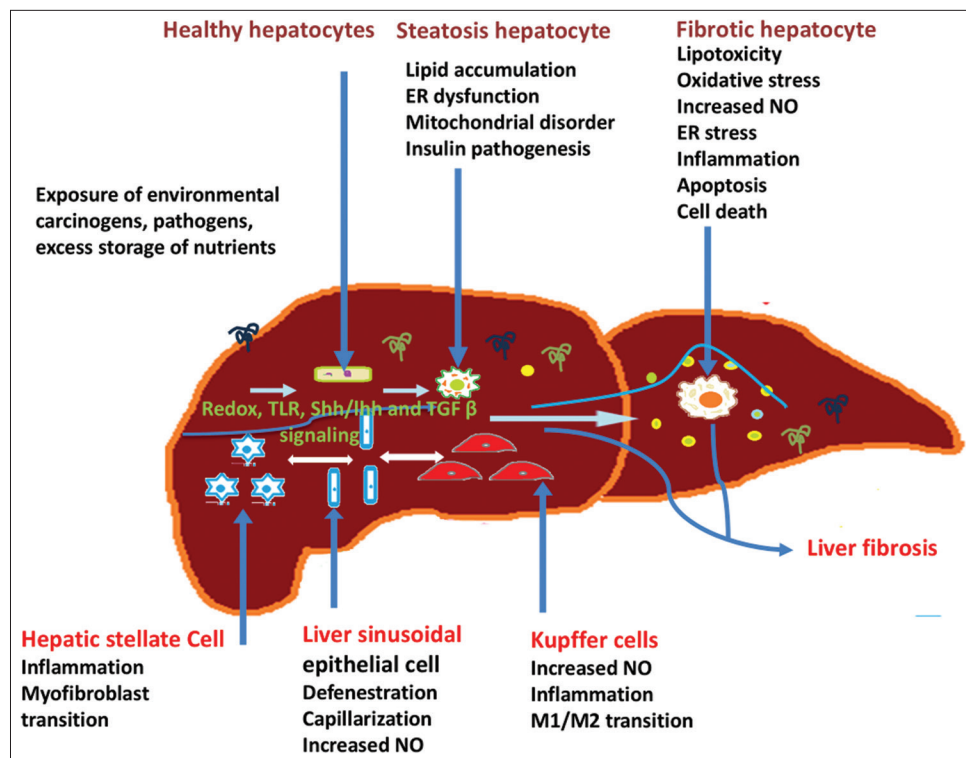


Figure 4: Effects of various carcinogens, pathogens, lipid accumulation, and other biological factors on hepatic tissue inflammation

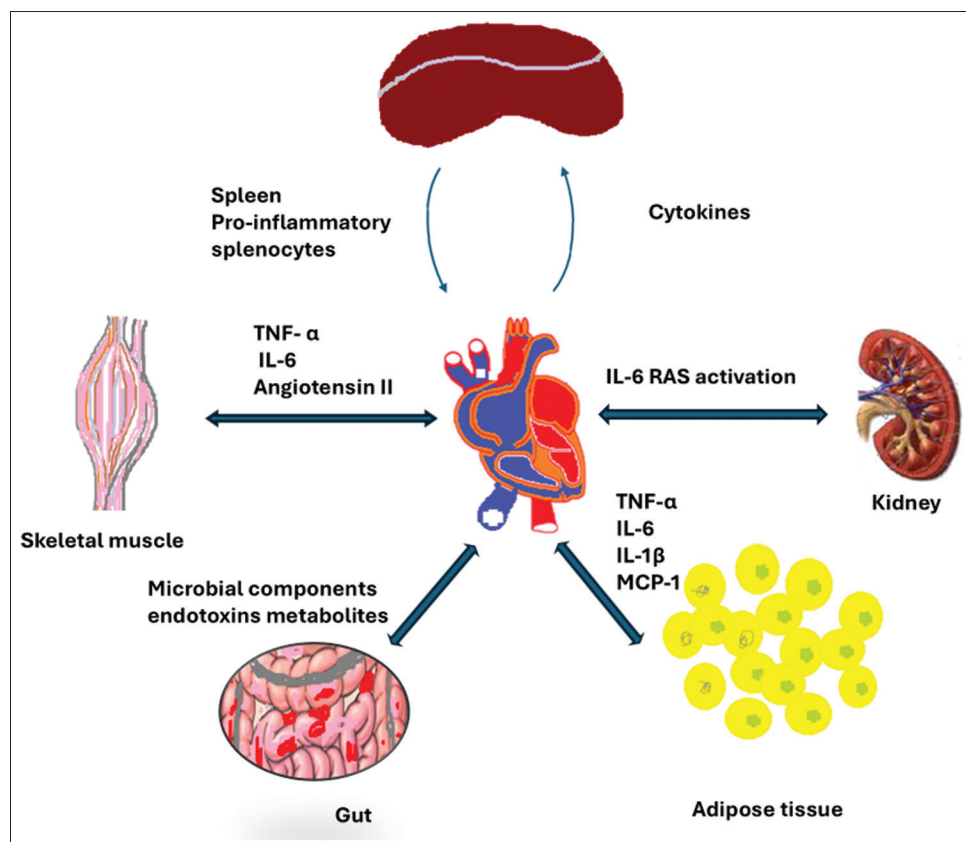


Figure 5: Role of various factors on inflammation of spleen, skeletal muscles, kidney, gut, adipose, and cardiovascular tissue

in the heart can cause atherosclerotic plaque formation and thrombogenicity, with cytokines like IL-1 β and IL-6 playing

a crucial role in the pathogenetic process of atherosclerosis. Cytokines such as TNF- α , IL-1 β , and IL-6 are crucial in

atherosclerosis pathogenesis, with infectious microbes linked to the disease through epidemiological studies [Figure 6].

DATA SEARCH

Source of Information

For writing this comprehensive research review on “Anti-inflammatory and immune-modulatory effects of plant natural products,” various databases were searched. For the collection of relevant information, specific terms such as medical subject headings (Mesh) and key text words, such as plant natural products, “their Anti-inflammatory and immune-modulatory effects,” and its use in wound healing management control,” published till 2024 were explored out in MEDLINE. There are more than 200 plant species that synthesize bio-organic constituents which exhibit anti-inflammatory and immune-modulatory effects were collected. Most especially for retrieving all articles pertaining to the traditional uses of plant natural products/extracts/compounds for inflammatory and immune-modulatory effects in animal models were searched in, electronic bibliographic databases and abstracts of published studies with relevant information on the inflammatory and immune-modulatory effects were

collected. Furthermore, references cited by the studies on the present topic were exhaustively searched. Relevant terms were used individually and in combination to ensure an extensive literature search. For updating the information about a subject and incorporation of recent knowledge, relevant research articles, books, conference proceedings, and public health organization survey reports were selected and collated based on the broader objective of the review. The present review aimed to systematically analyze published data on plant-origin contraceptives: Its use and side effects. This was achieved by searching databases, including SCOPUS, Web of Science, EMBASE, PubMed, Swiss-Prot, Google searches” and Cochrane library were searched. From this common methodology, discoveries and findings were identified and summarized in this final review.

Garlic

Garlic is composed of phenolic compounds, saponins, polysaccharides, and organosulfur compounds, among various other elements. It includes sulfur-containing substances such as alliin, thiosulfates, and allicin (diallyl thiosulfinate). These organosulfur compounds suppress the immune responses linked to cancer. They promote the growth of lymphocytes and macrophages, as well as the development

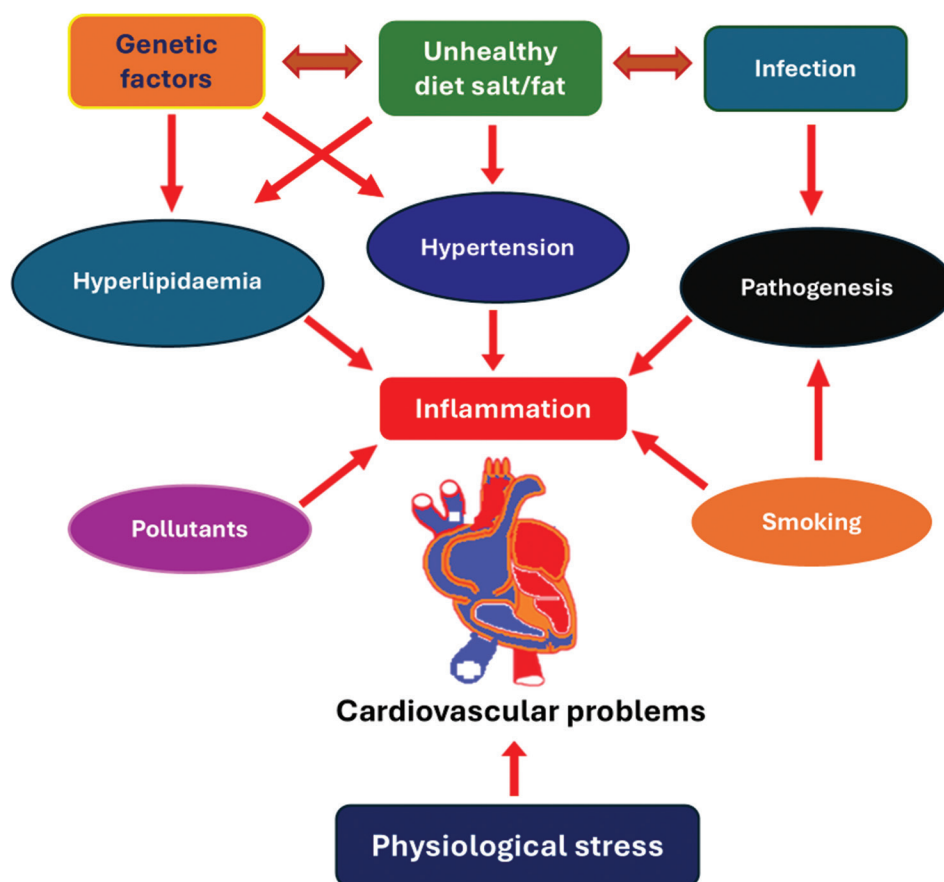


Figure 6: Effects of various pollutants, pathogens, lipid levels, and dietary nutrients on the initiation of inflammation-related cardiovascular problems

of natural killer cells. In addition, these compounds trigger phagocytosis and the release of IL-2, TNF- α , and interferon-gamma (IFN- γ). This leads to anti-inflammatory and antioxidant reactions while inhibiting the growth of emerging tumors.^[13] Garlic also contains garlicinins B (1), C (1), and D, which help regulate macrophage activation.^[14] Garlic (*Allium sativum* L.) contain garlicinins B(1), C(1), and D, which induce macrophage activation against disease pathogens.^[15] The organosulfur compounds from garlic help combat various physiological challenges, including oxidative stress, cardiovascular issues, cancer development, and immune dysfunction. Bio-organic organosulfur compounds derived from garlic have demonstrated chemotherapeutic properties against cancer and act as immune enhancers^[16,17] [Table 1]. A purified protein fraction from garlic influences cellular immune responses against transplanted tumors in a Balb/c mice model.^[18] Allicin is highly volatile and rapidly breaks down into diallyl sulfide, diallyl disulfide, diallyl trisulfide, and/or sulfur dioxide, among other substances. This group also contains methyl allyl disulfide and methyl allyl trisulfide. (c) Water-soluble organosulfur compounds are formed during the aqueous or alcoholic extraction of garlic through the breakdown of γ -glutamyl-S-allyl-L-cysteine into S-allyl-L-cysteine. The bioactive compounds in garlic, particularly flavonoids, may contribute to enhancing the body's defense system as immunostimulants [Table 1].

Ocimum sanctum (Tulsi)

Tulsi takes off contains various dynamic compounds, and the major compounds are linalool, eugenol, methylchavicol, methyl cinnamate, linolen, ocimene, pinene, cineol, anethol, estragole, thymol, citral, and camphor. Utilization of Tulsi takes off (*O. sanctum* Linn.) on purge stomach upgrades resistant control of the body.^[19] Sacred basil *O. sanctum* Linn: extracts and its phytochemical constituents show strong anti-inflammatory activity.^[20] Takes off have bio-organic compounds that appear immunomodulatory and anti-parasitic impacts.^[21] *O. sanctum* contains phenolic compound eugenol appears noteworthy anti-inflammatory action anti-inflammatory effects^[22] [Table 1]. These moreover appeared immune-modulatory impacts such as cytokine secretion accelerate histamine discharge, Ig discharge, lesson exchanging, cellular co-receptor expression, lymphocyte expression, and phagocytosis.^[21] Seeds of *O. sanctum* contain oil that has anti-inflammatory and immunomodulatory action due to the restraint of PG and arachidonate digestion system.^[23] Seed oils too appear hypotensive, anticoagulant, and immunomodulatory exercises. Lipoxygenase (LOX) inhibitory, histamine adversarial, and antisecretory exercises of the oil contribute toward antiulcer movement.^[23] The oil contains a-linolenic corrosive, an omega-3 greasy corrosive, which on digestion system produces eicosapentaenoic

Table 1: Plant extracts and their bioactive components and mechanisms of anti-inflammatory action

Plant species	Component	Anti-inflammatory effect	References
Garlic	Organosulfur compounds	Anti-inflammatory and anti-oxidative responses and inhibit the growth of an emerging tumor	[13]
	Garlicinins B (1), C (1), and D	Regulate macrophage activation	[14]
	Flavonoids	Acts as immunostimulants.	[16]
<i>Ocimum sanctum</i> Linn. (Tulsi)	linalool, eugenol, methylchavicol, methyl cinnamate, linolenic acid, ocimene, pinene, cineol,	Enhances the immune power of the body (Navin <i>et al.</i> , 2013)	[19]
<i>Ocimum sanctum</i>	High phenolic contents	Anti-inflammatory activity and cardioprotective effects	[26]
<i>Allium cepa</i> Linn.	Scale extract steroidal saponins	Shows anti-inflammatory and immunomodulatory effect	[28]
	Flavonoids	Hyaluronidase inhibiting activity and radical scavenging potential	[34]
	Quercetin-rich	Lowers down allergy and inflammation	[35]
<i>Allium</i> species	Typheramide and alfrutamide	Effect COXs and lipoxygenases activity	[37]
<i>Allium</i> species	Flavonoids tricin, apigenin, and quercetin	Did differential modulation of COX-mediated prostaglandin production by the putative cancer chemoprevention	[47,48]
<i>Allium</i> species	Ajoene	Anti-inflammatory properties	[49]
<i>Tinospora cordifolia</i>	Cordifolioside A	Activate the peritoneal macrophages and boost the non-specific host defenses.	[50]
	Cordifolioside A	Immune-stimulatory activity is due to the presence of and syringing in	[54]

(Contd...)

Table 1: (Continued)

Plant species	Component	Anti-inflammatory effect	References
	Cordifolioside A	Promising adjuvant activity	[53]
	Cordifolioside A	Enhance phagocytic activity and increase in nitric oxide and reactive oxygen species generation	[54]
<i>Cassia species</i>	Anthraquinones and flavonoids	Anti-inflammatory activity leaf extract of Cassia extract in RAW264.7 murine macrophage cell line.	[66-68]
<i>Taenia asiatica</i>	Alkaloids	Anti-inflammatory and analgesic effects	[72]
<i>Taenia asiatica</i>	Coumarins, alkaloids, terpenoids, 5 flavonoids, and lipids	Management of painful and inflammatory conditions	[74]
<i>Aloe vera</i>	Mucilaginous leaf gel	Anti-inflammatory and inhibits lipopolysaccharide-induced inflammatory responses in RAW264.7 macrophages.	[75]
<i>Aloe vera</i>	Polysaccharides	Hepatoprotective potential against chronic alcohol-induced hepatotoxicity in mice	[76]
<i>Aloe vera</i>	Pulp extract	Downregulates LPS-induced inflammatory cytokine production and expression of NLRP3 inflammasome in human macrophages	[82]
<i>Aloe vera</i>	Pulp extract	Abrocitinib shows prophylactic effect and assists in cancer prevention.	[93]
<i>Aegle marmelos</i>	Dried flower, root	Anti-inflammatory and leaf extracts of <i>A. marmelos</i> showed anti-inflammatory activity in Wistar rats.	[96,97]
<i>Aegle marmelos</i>	Leaf extract	Immunomodulatory effect	[103-105]
<i>Capparis spinosa</i>	Fruits contain two important flavonoids, i.e., isoginkgetin and ginkgetin, isocodoncarpine	Anti-inflammatory activity through strong NF- κ B inhibitor activity <i>in vivo</i> .	[109,110]
<i>Calotropis procera</i>	Milky white latex	Exhibits potent anti-inflammatory activity in various animal models that is comparable to standard anti-inflammatory drugs.	[115]
	Ethanol extract of the flowers	Anti-inflammatory activity while latex administration in animal models induces peritonitis, paw edema, hemorrhagic cystitis,	[123]
<i>Nerium oleander</i>	Oleander extract (NAE-8®)	Demonstrates antioxidant and anti-inflammatory properties without triggering immune cell activation or inflammatory cytokine release	[124]
<i>Nerium oleander</i>	Leaves contain triterpenes, specifically ursane-type triterpene 1, oleanane-type triterpene 2, and dammarane-type triterpene	Inhibit the production of ICAM-1	[126]
<i>Butea monosperma</i>	Butein	Anti-inflammatory effect	[127,128]
	Isobutrin	Possesses a natural sensitizer which belongs to the chalcone class	[132]
<i>Cinnamomum tamala</i>	Eugenol and total phenolic contents in its extracts.	Free radical (FR) scavenging, hypoglycemic potential on alloxan-induced hyperglycemia, and anti-inflammatory property in carrageenan-induced paw edema	[137]

(Contd...)

Table 1: (Continued)

Plant species	Component	Anti-inflammatory effect	References
<i>Cinnamomum tamala</i>	Cinnamaldehyde, which	Stimulates the secretion of anti-inflammatory molecules such as IL-1 β , TNF- α , IL-8, IL-6, and TLR4	[138]
	Curcumin	Mediated through its ability to inhibit cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS). COX-2, LOX, and iNOS	[139]
<i>Curcuma longa</i>	Curcumin	It suppresses tumor formation and exert chemopreventive effects on carcinogenesis	[140]
		Suppress inflammatory cytokines, including IFN- γ , IL-1 β , IL-6, IL-13, and IL-17a carrageenan-induced inflammatory model. NF- κ B/COX-2 pathway and iNOS inhibition	[141]
	Curcumin	Exerts anti-inflammatory activities by suppressing the activation of ERK 1/2 and p38 pathways and regulating innate immunity by regulating the activation of NK cells	[142]
	Curcumin	Inhibits lung cancer cell migration and invasion through the Rac1-dependent signaling pathway.	[143]
	Curcumin	Enhanced chemosensitivity of FDA-approved platinum (II)-based anti-cancer drugs involves downregulation of nuclear endonuclease G and NF- κ B as well as induction of apoptosis and G2/M arrest	[144]
<i>Curcuma longa</i>	Curcumin	Used to treat chronic inflammation caused during cancer, allergy, asthma, and autoimmune diseases.	[155]
	Curcumin	Enhances dual PI3K/Akt and mTOR inhibitor NVP-BEZ235-induced apoptosis in human renal carcinoma Caki Cells through down-regulation of p53-dependent Bcl-2 expression and inhibition of Mcl-1 protein stability	[152]
	Curcumin	Induces the apoptotic intrinsic pathway through upregulation of reactive oxygen species and JNKs in H9c2 cardiac myoblasts	[153]
Herbal preparations			
<i>Cinnamomum cassia</i>	Cinnamaldehyde is the main compound (69.15%), followed by methoxycinnamic acid (21.18%), benzyl alcohol (6.14%), and benzyl benzoate (3.53%)	Active against <i>Helicobacter pylori</i> and TNF- α stimulated IL-8 secretion, which displayed significant suppression of IL-8 in a concentration-dependent-manner.	[170]
(Triphala)	Fruits of <i>Terminalia chebula</i> , <i>Terminalia bellirica</i> , and <i>Emblica officinalis</i> .	Antioxidant and reactive oxygen species scavenging properties, and chemopreventive against benzo(a)pyrene induced forestomach tumorigenesis	164] 167]
	Sudarshanam oil has demonstrated	Significant efficacy against severe inflammation	[169]
<i>Emblica officinalis</i>	Fruit extract	Protective effect against myocardial necrosis in rats.	[166]

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Table 1: (Continued)

Plant species	Component	Anti-inflammatory effect	References
<i>Datura stramonium</i>	Leaves contain tropane alkaloids, Dinoxin B, a withanolide	Cytotoxic activities.	[171,176]
<i>Euphorbia hirta</i>	Solvent extract	Anti-inflammatory effect in an adjuvant-induced arthritic murine model and iNOS protein inhibition	[177-179]
<i>Syzygium cumini</i> (jambolana)	Anthocyanins, ellagic acid, glucoside, glycoside antimellin, jambosine, isoquercetin, kaempferol, and myricetin, jambolin	Anti-inflammatory and analgesic activities	[180]
	<i>Eugenia jambolana</i> (Jamun fruit)	Reduce liver inflammation, injury, and fibrosis during cholestasis	[182]
<i>Achyranthes aspera</i>	leaves	Topical application of anti-inflammatory activity	[187,188]
<i>Madhuca longifolia</i>	ethanol extract, saponin mixture, phenols in methanolic bark extract	Anti-inflammatory activity in acute (carrageenan-induced inflammation), sub-acute (formaldehyde-induced inflammation), and chronic (cotton pellet granuloma) models	[191,192]
<i>Madhuca indica</i>	Madhucosides A and B, protobassic acid glycosides	Inhibitory activity on free radical release from phagocytes	[193]
<i>Mentha longifolia</i>	Madhucosides A and B, protobassic acid glycosides	Anti-inflammatory effects in lipopolysaccharide-stimulated macrophages: reduction of nitric oxide production through inhibition of inducible nitric oxide synthase	[197]
<i>Mentha longifolia</i>	Myristicin, dehydrodiisoeugenol	Anti-inflammatory effect on RAW 264.7 macrophages stimulated with polyinosinic-polycytidylic acid, the compound	[198,199]
<i>Azima tetraacantha</i> Lam.	Leaves	Anti-inflammatory, analgesic, and antipyretic activities in Wistar rats and mice	[201]
<i>Terminalia arjuna</i>	Bark powder	Anti-inflammatory, immunomodulatory, and antinociceptive activity	[203]
<i>Terminalia arjuna</i>	Stem bark	Extract shows anti-oxidative properties	[209]
<i>Terminalia arjuna</i>	Tree-bark powder, Arjunolic acid, triterpenoid saponin,	Antioxidant and hypocholesterolaemic effects	[224,226]
<i>Terminalia arjuna</i>	Stem-bark extract	Attenuates human monocytic (THP-1) and does aortic endothelial cell activation	[213]
<i>Terminalia arjuna</i>	Leaf extract	Modulates circulatory antioxidants on 7,12-dimethylbenz(a) anthracene-induced Hamster Buccal Pouch Carcinogenesis.	[217]
<i>Terminalia arjuna</i>	Arjunic acid	Acts as a strong free radical scavenger. Arjunolic acid: shows multifunctional therapeutic uses	[211,210]
<i>Terminalia arjuna</i>	Contains 18,19-secooleanane-type triterpene glycosyl esters ursane triterpenoids and polyphenols, arjunic acid, and arjunolic	Antioxidant activity, Ameliorates arsenic-induced cytotoxicity in hepatocytes	[227]

corrosive and the same shown up to be capable of the organic action. *O. sanctum* fixed oil contains alpha-linolenic corrosive which appears anti-inflammatory action and does critical restraint of paw edema within the most noteworthy measurements (3 mL/kg). This movement changes the eicosanoid antecedent (i.e., polyunsaturated greasy acids: PUFA) accessibility through dietary control.^[24] *O. sanctum* is used in traditional/indigenous and ethnoveterinary medicines.^[25] Antioxidant property of the oil renders metabolic restraint, chemoprevention, and hypolipidemic movement.^[23] *O. sanctum* takes off appeared antioxidant, anti-inflammatory impact potential and cardioprotective impact which may be due to nearness of tall phenolic substance.^[26] The exercises of 5-LOX and cyclooxygenase-2 and levels of leukotriene B4 and thromboxane B2 found lifted in ISP-treated rats, which were altogether diminished ($P < 0.001$) in extricate pre-treated rats. Tulsi and turpentine oil upgrade infiltration potential of transdermal conveyance of flurbiprofen, a strong non-steroidal anti-inflammatory in pale-skinned person rats^[27] [Table 1].

Allium cepa Linn.

The red onion *A. cepa* Linn. scale extricate appears anti-inflammatory and immunomodulatory impact on tentatively actuated atypical prostatic hyperplasia in Wistar rats. Elberry *et al.* 2014.^[28] In addition, green onion takes off contains apigenin which appeared anti-inflammatory impacts in mice. Onion apigenin decreases UV-B-induced skin irritation.^[29] Apigenin is utilized for cancer anticipation.^[30,31] *Allium ampeloprasum* var. porrum. bulbs contain a unused steroidal saponin with anti-inflammatory and anti-ulcerogenic properties.^[32] A comparable defensive impact was seen in rutin against intense gastric mucosal injuries initiated by ischemia reperfusion.^[33] Red onion contains flavonols which inhibit hyaluronidase action and radical scavenging potential.^[34] Quercetin-rich onion peel extricates impact adipokine expression within the visceral fat tissue of rats^[35] Quercetin brings down hypersensitivity and irritation^[36] whereas typheramide and alfrutamide found in *Allium* species impact COXs and LOXs action.^[37] Quercetin ensures against swimming stress-induced changes in oxidative biomarkers within the hypothalamus of rats^[37] whereas dimethyl sulfone may be a dietary biomarker for onion admissions.^[38] In spite of the fact that quercetin appears *in vivo* genotoxicity^[39,40] but its lower concentration play critical part avoidance of hypersensitivity and inflammation.^[41] The steam distillate from freeze-dried onion grows appears antioxidant/anti-inflammatory exercises (*A. cepa* L.).^[42] Onion peel hydroalcoholic extricate appears vasorelaxant and hypotensive impacts in rodent.^[43] Onion hinders chemotaxis of human polymorphonuclear leukocytes by thiosulfates and cepaenes.^[43,44] Onions appear antiasthmatic^[45] and are utilized for joint pain treatment.^[46] Flavonoids tricetin, apigenin, and quercetin had differential balance of COX-mediated PG generation by the putative cancer chemoprevention.^[47,48]

Peroxidase dynamic cell-free extricate from onion strong squanders appeared biocatalytic properties and putative pathway of ferulic corrosive oxidation.^[48] Ajoene, a common item disconnected from Allium, appears anti-inflammatory properties^[49] [Table 1].

Tinospora cordifolia

T. cordifolia stem parts contain major bioactive compounds and actuate the peritoneal macrophages and boost the non-specific have guards.^[50] These extricates appeared immune-stimulating movement and upgrade the levels of IFN- γ , TNF- α , and IL-1 β .^[51] Tc too appears immunomodulatory impacts.^[52] Its fluid and methanolic extricates appeared immunomodulatory and resistant stimulatory movement against *Salmonella* Typhimurium. This immune-stimulatory movement is due to nearness of cordifolioside A and syringing in Tc.^[53] It extricates appeared noteworthy improvement in phagocytic movement and increment in nitric oxide (NO) and receptive oxygen species era at concentration 0.1–2.5 $\mu\text{g/mL}$.^[54] *Tinospora crispa* has imperative phytochemicals, that is, cordioside, quercetin, eicosenoic corrosive (paullinic corrosive), and boldine^[55] polysaccharides, terpenoids, flavonoids, alkaloids, glycosides, and lactones which are capable of immunomodulation action.^[56] This movement is additionally detailed in fluid extricates of the stem and root of Tc.^[57,58] A mediate (1,4)-alpha-D-glucan (alpha-DG), from Tc, appeared novel resistant stimulatory impacts and actuated the level of professional- and anti-inflammatory cytokines (IL-1 β , IL-6, TNF- α , IFN- γ , and IL-10) within the lung and spleen of endotoxin-stimulated adolescent rats^[59] [Table 1].

Advance, a polysaccharide (G1-4A) disconnected from guduchi, has appeared promising adjuvant movement.^[60] More particularly, Neem-guduchi has more immunomodulatory potential.^[61] Guduchi Ghana arranged by classically was found to have critical immunostimulatory activity on the safe framework^[61] [Table 1]. Immunomodulatory impact of a separated division from *T. crispa* on intracellular expression of INF- γ , IL-6, and IL-8.^[55] *Alpinia galanga* and *T. cordifolia* were found active against H37Rv INH-sensitive and resistant INH strains of *Mycobacterium tuberculosis*.^[56] *T. crispa* (L.) is used for the treatment of hypertension, diabetes, rheumatism, jaundice, inflammation, fever, fractures, scabies, and urinary disorders.^[62] Protective effects of *T. crispa* extracts on H₂O₂-induced oxidative stress and TNF- α -induced inflammation on human umbilical vein endothelial cells^[63] [Table 1].

Cassia fistula

Aqueous and alcoholic extracts of *C. fistula* bark show anti-inflammatory activity in sub-acute models of inflammation in Wistar albino rats.^[64,65] This anti-inflammatory activity is due to the presence of anthraquinones^[66] and flavonoids in *Cassia* species.^[67] Similar anti-inflammatory activities have been reported in the leaf extract of *Cassia* extract in

RAW264.7 murine macrophage cell line.^[68] Similar anti-inflammatory activity is also reported in *Cassia tora*^[64] and *Cassia occidentalis* L.^[69] in ovalbumin-induced airways inflammation in a mouse model of allergic asthma^[70] [Table 1]. *C. fistula* is a potential candidate in health management.^[70] *C. fistula* shows a significant stimulation of the cell-mediated immunity and no effects on the humoral immunity^[71] [Table 1].

Taenia asiatica

T. asiatica plant contains coumarins, alkaloids, terpenoids, 5 flavonoids and lipids, alcohols, phenolic acids, lignans, steroids, and greasy acids. Among them, the foremost characteristic compounds for *T. asiatica* are coumarins and alkaloids. These bio-organic compounds basically alkaloids appeared anti-inflammatory and pain-relieving impacts.^[72] These surprisingly decrease paw and joint swelling and diminish the spleen files. These viably ensured the bone and cartilage of the knee joint from disintegration, injury, and mishappening versus those from the control bunch.^[72] This anti-inflammatory action is kept up by the discharges of cytokines such as TNF- α , IL-1 β , and IL-6. These were found altogether lower than the ones from the control bunch separately, whereas cytokines like IL-10 were surprisingly higher compared with the control bunch.^[73] *T. asiatica* appears antinociceptive and anti-inflammatory impacts in the formalin-induced torment test and the carrageenan-induced edema paw. A decrease in carrageenan actuated intense aggravation paw edema was noteworthy ($P < 0.01$) taking after organization of 100 mg/kg measurements. *T. asiatica* appears critical antinociceptive and anti-inflammatory impacts utilizing the carrageenan-induced paw edema and formalin-induced torment tests and underpins the recounted utilize for excruciating and provocative conditions^[74] [Table 1]. Plant extract is utilized within the administration of excruciating and provocative conditions^[74] [Table 1].

Aloe vera

Mucilaginous leaf gel of *A. vera* is utilized to treat inflammatory-based disorders. Aloe emodin from rhubarb (*Rheum rhabarbarum*) restrains lipopolysaccharide (LPS)-induced incendiary reactions in RAW264.7 macrophages.^[75] It contains anti-inflammatory fixings^[75] which too appear antioxidant impacts in rats.^[76] *A. vera* adventitious root extracts appear upgrade anti-inflammatory action through the modification of essential and auxiliary metabolites through salicylic corrosive elicitation.^[77,78] A watery extricate of *Aloe arborescens* (*A. arborescens* Process.) contains lectins (glycoproteins) and mannans (polysaccharides) which appear immunomodulatory, anti-inflammatory, antiviral, and antibacterial exercises.^[79] *A. vera* polysaccharides appeared antitumor, antioxidant, anticoagulant, antidiabetic, and radioprotective exercises. These too appeared antiviral, hypolipidemic, and immunomodulatory exercises.^[80] *A. vera*

polysaccharides appeared hepatoprotective potential against unremitting alcohol-induced hepatotoxicity in mice.^[81] *A. vera* downregulates LPS-induced incendiary cytokine generation and expression of NLRP3 inflammasome in human macrophages.^[82] *A. vera* represses the COX pathway and decreases PG E2 generation from arachidonic corrosive. C-glucosyl chromone was separated from *A. vera* gel extricates which appeared anti-inflammatory action^[83] [Table 1].

A. vera with transemulgel and nimesulide decreases irritation.^[84] *A. vera* appears immunomodulatory properties and its divisions on the reaction of macrophages against *Candida albicans*.^[85] *A. vera* gel appears immunostimulatory and immunomodulatory properties.^[86] *A. barbadensis* process. extricate (AVH200[®]) appears potential to diminish the actuation, multiplication, and cytokine discharge of sound human blood T-cells. AVH200[®] appears a suppressive impact on human blood T cells *in vitro*.^[86] *A. vera* components act as cancer prevention agents or immunostimulants and appear immunomodulatory impacts on phorbol myristate acetate-stimulated leukocytes in a dose-dependent way ($P \leq 0.05$).^[87] *A. vera* (*A. barbadensis* Miller) supplemented probiotic lassi anticipates Shigella penetration from epithelial obstruction into the systemic bloodstream in mice.^[88] Aloe emodin applies a strong anticancer and immunomodulatory movement on BRAF-mutated human melanoma cells.^[89] Aloe polysaccharide is utilized as adjuvants as they have immunity-enhancing capacities. These can be utilized within the definition for the improvement of poultry antibodies.^[90] *A. vera* downregulates LPS-induced provocative cytokine generation and expression of NLRP3 inflammasomes in human macrophages.^[82] *A. vera* is utilized to treat visual infections, conjunctivitis, dry eye, dacryocystitis, or degenerative infections. *A. vera* (*A. barbadensis* Mill operator [Liliaceae]) has wound-healing properties. It moreover appears immunomodulatory, anti-inflammatory, or antioxidant exercises [Table 1].^[91]

A. vera extricate is utilized to reestablish the work of human corneal cells.^[92] *A. vera* ethanol and ethyl acetic acid derivation extricates are moreover utilized in eye drops to treat inflammations and other afflictions of the outside parts of the eye such as the cornea. Aloctin I found in *A. vera* leaf mash extricate appears prophylactic impact and helps in cancer prevention.^[93] *A. vera* leaf mash extricate diminishes serum sialic corrosive and tumor rot calculate alpha levels which is a critical tumor marker. Aloctin I appeared immunomodulatory and mitogenic impacts of lectins *A. vera* which may well be proposed as a prophylactic. *A. vera* leaf mash lectin (Aloctin I) appears tumor preventive impacts on Ehrlich ascites tumors in mice. Aloe gel appears antidiabetic, anticancer, and anti-microbial exercises in case its fixings are utilized in disable quantities/limits.^[94] Plant contains polysaccharides which comprise of a few monosaccharides of which mannose is prevailing. Polysaccharides hinder the opsonization of zymosan HPS and show adjuvant movement

in counteracting agent generation and the acceptance of delayed-type touchiness in mice^[95] [Table 1].

Aegle marmelos

A. marmelos root extract showed anti-inflammatory activity in Wistar rats.^[96,97] In addition, nickel nanoparticles phytofabricated from watery leaf extricates of *A. marmelos* Correa appeared *in vitro* anti-inflammatory movement.^[98] Fluid extricate of *A. marmelos* unripe natural product appears anti-inflammatory impact^[99] against bowel malady.^[100] Beta caryophyllene and caryophyllene oxide, separated from *A. marmelos*, work as strong anti-inflammatory operators against lymphoma and neuroblastoma cells.^[101] These did not appear tweak of expression of IL-8 quality in bronchial epithelial cells by 5-methoxypsoralen.^[102] Comparable immunomodulatory impact of *A. marmelos* leaf extricate was observed in freshwater angle *Cyprinus carpio*, *Catla catla*,^[103] and other exploratory animals^[104] contaminated by bacterial pathogen *Aeromonas hydrophila*.^[103] Comparative immunomodulatory action of methanolic natural product extricate of *A. marmelos* was found in exploratory creatures.^[105] Ethanolic extricate of clears out of *A. marmelos* (Linn.) appeared lipid bringing down action in hyperlipidemic models of Wistar pale skinned person rats.^[106] Bel clears out appeared chemomodulatory impacts against DMBA-induced skin tumorigenesis in Swiss pale-skinned person mice.^[107] *A. marmelos* natural product watery extricate fluid methanolic division (AMF) anticipated incendiary changes and β -cell harm in conjunction with a decrease in mitochondrial and endoplasmic reticulum swelling. Plant appears a protective impact of AMF in Sort 2 diabetic rats that are due to the conservation of β -cell function and insulin-sensitivity through expanded PPAR γ [Table 1].

Capparis spinosa

Ethanolic extract of *Capparis decidua* fruit ameliorates methotrexate-induced hepatotoxicity by suppressing oxidative stress and inflammation by modulating NF- κ B signaling pathway. Three extracts, namely aqueous extract, alcoholic extract, and hydro-alcoholic extract of the stem (at a dose of 500 mg/kg), were studied for anti-inflammatory activity using the carrageenan-induced rat paw edema model. The percentage inhibition of edema was calculated and compared with indomethacin as a standard drug. Results revealed that all the extracts show significant inhibition of carrageenan-induced rat paw edema, the aqueous extract exhibiting the highest anti-inflammatory activity as compared to other extracts.^[108]

Caper plant (*C. spinosa* L.) fruits are used in folk medicine for the treatment of inflammatory disorders, such as rheumatism. There are two important flavonoids,^[109] which showed anti-inflammatory activity at a low concentration

of 20 mM and 7.5 mM, respectively. Both compounds have also shown strong NF-B inhibitor activity *in vivo*. Caper (*Capparis spinosa* L.) is a drought-tolerant plant; its leaves and fruits contain bioflavonoids which inhibit NF-kappa B activation. These also showed anti-inflammatory activity.^[110-112] *C. spinosa* aqueous extract contains 13 compounds (1–13), mainly flavonoids, indoles, and phenolic acids, and most of them have shown anti-inflammatory effects^[113] and inhibited the carrageenan-induced paw edema in mice.^[114]

Similar activity was also reported in the ethanolic and aqueous extracts of *C. decidua*. More particularly, *C. decidua* was found to possess significant antipyretic effects but was devoid of analgesic activity. More particularly, *C. decidua* was found to possess significant antipyretic effects but was devoid of analgesic activity. Flavonols (kaempferol and quercetin derivatives) and hydroxycinnamic acids (caffeic acid, ferulic acid, p-cumaric acid, and cinnamic acid) isolated from *C. spinosa* showed anti-inflammatory activity [Table 1].

Calotropis procera

The milky white latex derived from the plant demonstrates significant anti-inflammatory properties in various animal models, comparable to conventional anti-inflammatory medications.^[115] It exhibits a protective effect against inflammatory hyperalgesia and mitigates oxidative stress in rats with Freund's complete adjuvant-induced monoarthritis.^[116] The ethanol extract of *C. procera* flowers has also been reported to possess anti-inflammatory effects, while the administration of latex in animal models can lead to conditions such as peritonitis, paw edema, and hemorrhagic cystitis, as well as immunological and allergic responses, which can be managed using various anti-inflammatory drugs.^[117] Similar effects have been observed with the use of aspirin, ibuprofen, and other non-steroidal anti-inflammatory drugs, which may also contribute to cancer prevention.^[118] The protein fraction of *C. procera* latex has been shown to inhibit the growth of sarcoma, a specific type of cancer.^[119] Furthermore, *C. procera* latex exhibits anti-inflammatory activity in experimental murine models, as noted by Rathee *et al.*,^[120] and reduces the activity of various inflammatory mediators.^[117] Likewise, the leaves of *Calotropis gigantea* have been reported to demonstrate anti-inflammatory effects across different biological systems.^[121] Similarly, *C. gigantea* leaves^[121] show anti-inflammatory activity in various biological systems.^[122] Anti-inflammatory effect of the latex from *C. procera* in three different experimental models: Peritonitis, paw edema, and hemorrhagic cystitis^[123] [Table 1].

Nerium oleander

Oleander extract (NAE-8®) has been shown to possess antioxidant and anti-inflammatory properties in both

laboratory and animal research. It provides antioxidant benefits without activating immune cells or causing the release of inflammatory cytokines. It shows unique biological efficacy.^[124] Extracts from both the leaves and flowers of *N. oleander* L. result in a reduction of glutathione levels, attributed to the presence of glycosides and alkaloids, according to Page C. The anti-inflammatory effects of *Nerium indicum* are characterized by the inhibition of PGE2 in murine splenic lymphocytes.^[125] The bioactive fraction derived from *N. indicum* leaves (NILE) enhances the levels of IL-2, IL-10, and IFN- γ , while simultaneously reducing IL-4, TNF- α , NO, COX-1, and COX-2 activities. The ethanolic extract from *N. oleander* flowers exhibited a highly significant anti-inflammatory effect ($P < 0.005$) in models utilizing cotton pellets and carrageenan. In addition, it decreased the expression of genes associated with iNOS, TNF- α , IL-1 beta, and COX-2 mRNA. Furthermore, it resulted in a substantial reduction in leukocyte count (73.09%) and C-reactive protein levels (54.60%), while effectively inhibiting the activities of COX-1, COX-2, 5-LO, and 12-LO enzymes. However, at elevated doses (2000 mg/kg), hepatotoxic effects were observed. The leaves of *N. oleander* also contain triterpenes, including ursane-type triterpene 1, oleanane-type triterpene 2, and dammarane-type triterpene, which have demonstrated the capacity to inhibit ICAM-1 production^[126] [Table 1].

Butea monosperma

Butein, extracted from the flowers of *B. monosperma*, exhibits significant anti-inflammatory properties.^[127] According to Gao *et al.*,^[128] butein is particularly beneficial for health maintenance and the treatment of inflammatory conditions^[129]. It effectively inhibits the IL-1 β -induced inflammatory response in human osteoarthritis^[130] and its derivatives also demonstrate a reduction in inflammatory responses associated with lymphedema.^[131] Isobutrin, derived from *B. monosperma*, acts as a natural sensitizer belonging to the chalcone class.^[132] In addition, it exhibits anti-inflammatory effects^[133] and shows inhibitory activity against metalloproteinases, contributing to its anti-aging properties.^[133]

B. monosperma is characterized by a variety of chemical constituents, including sterol- β -D-glucopyranoside, nonacosanoic acid, and 3-Z-hydroxyeuph-25-ene. The stem bark contains kino-tannic acid, gallic acid, and pyrocatechin. Its leaves are abundant in glucosides and kino-oil, while the flowers contain monospermoside (butein 3-e-D-glucoside), isomonospermoside, and various flavonoids such as palestine and prunetin, along with steroids, triterpenes, butein, butin, isobutrin, coreopsin, and isocoreopsin (butin 7-glucoside), as well as sulfurein. The gum of the plant includes pyrocatechin, and the sap contains isomeric flavanones and their glucosides, butrin, and chalcones. The seeds are noted for containing galactose-specific lectin and palasonin. Furthermore, the plant is rich in metabolically significant flavonoids, including

rhamnetin, quercetin, kaempferol, and catechin most of which have demonstrated strong anti-inflammatory activity [Table 1].

Prosopis cineraria

Members of the *Prosopis* genus, *Prosopis africana*, *Prosopis alba*, *Prosopis cineraria*, *Prosopis farcta*, *Prosopis glandulosa*, *Prosopis juliflora*, *Prosopis nigra*, *Prosopis ruscifolia*, and *Prosopis spicigera*, leaves, branches, and stems contain flavonoids, tannins, alkaloids, quinones, or phenolic compounds that showed anti-inflammatory activity^[134-136] [Table 1].

Cinnamomum tamala

C. tamala is known to possess eugenol and a significant amount of total phenolic compounds in its extracts.^[137] These extracts have demonstrated the ability to scavenge free radicals across various species, exhibit hypoglycemic effects in alloxan-induced hyperglycemia, and possess anti-inflammatory properties in models of carrageenan-induced paw edema and LPS-induced NO production in rat peritoneal macrophage cultures. In addition, *C. tamala* contains cinnamaldehyde, which stimulates the secretion of anti-inflammatory molecules such as IL-1 β , TNF- α , IL-8, IL-6, and TLR4^[138] [Table 1].

Curcuma longa

C. longa, commonly known as turmeric, is utilized in the management of chronic inflammation associated with conditions such as cancer, allergies, asthma, and autoimmune diseases. This plant contains curcumin, a yellow pigment that serves as a significant spice and food coloring agent.^[139] Curcumin has been shown to inhibit tumor development and provide chemopreventive effects against carcinogenesis.^[140] It reduces the levels of inflammatory cytokines, including IFN- γ , IL-1 β , IL-6, IL-13, and IL-17a, in carrageenan-induced inflammation models. In addition, it induces morphological changes related to inflammation in the skin. The anti-inflammatory properties of curcumin are believed to be mediated through the NF- κ B/COX-2 pathway and the inhibition of iNOS.^[141] Furthermore, curcumin demonstrates anti-inflammatory effects by inhibiting the activation of the ERK 1/2 and p38 pathways, while also modulating innate immunity through the regulation of NK cell activation.^[142] The anti-inflammatory action of curcumin is likely attributed to its capacity to inhibit COX-2, LOX, and iNOS. These enzymes play crucial roles in mediating inflammatory processes, and their improper upregulation has been linked to the pathophysiology of various human cancers and inflammatory disorders^[139] [Table 1].

Curcumin is recognized as one of the most effective natural plant compounds, demonstrating significant healing properties along with a range of activities including antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer effects. Research indicates that curcumin inhibits the migration and invasion of lung cancer cells through the Rac1-dependent signaling pathway.^[143] Furthermore, it enhances the chemosensitivity of FDA-approved platinum (II)-based anticancer agents by downregulating nuclear endonuclease G and NF- κ B, while also promoting apoptosis and G2/M cell cycle arrest.^[144] In addition, curcumin improves the chemopreventive efficacy of phospho-sulindac in lung cancer by enhancing its pharmacokinetics.^[145] It has also been shown to exert antiproliferative effects on human pancreatic cancer by upregulating the extrinsic apoptotic pathway.^[146] A novel 4-arylidene curcumin analog, T63, has been identified as a contributor to cell cycle arrest and apoptosis in lung cancer cells.^[147] Moreover, the curcumin analog h-4073 has been found to enhance the therapeutic effectiveness of cisplatin in treating head-and-neck cancer.^[148] A pilot study demonstrated that the topical application of a cream containing sandalwood oil and turmeric can prevent radiodermatitis in head-and-neck cancer patients receiving external beam radiotherapy.^[149] In addition, curcumin has been shown to influence ion channels and transporters^[150] [Table 1].

Turmeric, devoid of curcumin, demonstrates both anti-inflammatory and anticancer properties.^[151] Curcumin has been shown to enhance apoptosis in human renal carcinoma Caki cells induced by the dual PI3K/Akt and mTOR inhibitor NVP-BEZ235, primarily through the downregulation of p53-dependent Bcl-2 expression and the inhibition of Mcl-1 protein stability.^[152] In addition, curcumin triggers the intrinsic apoptotic pathway by increasing levels of ROS and JNKs in H9c2 cardiac myoblasts.^[153] Furthermore, demethoxycurcumin derived from the rhizome of *C. longa* effectively suppresses the induction of iNOS in an *in vitro* model of inflamed human intestinal mucosa.^[154] Both the extract of *C. longa* L. and curcumin have been found to inhibit the activity of 12/15-LOX^[155] [Table 1].

Curcumin nanoformulations and microcells containing curcumin have demonstrated anticancer efficacy against hepatocellular carcinoma (HCC) in animal models.^[156] Likewise, polymeric nanocurcumin and curcumin nanospheres have exhibited significant anticancer properties.^[157,158] In addition, curcumin has been shown to inhibit the vasculogenic mimicry capacity of HCC cells through the suppression of STAT3 and PI3K/AKT pathways.^[159] Both curcumin nanoparticles and free curcumin have also been found to inhibit the expression of the human telomerase reverse transcriptase gene in breast cancer.^[160] Furthermore, curcumin displays activities akin to those of recently identified TNF blockers, vascular endothelial growth factor blockers, human epidermal growth factor receptor blockers, and HER2 blockers^[155] [Table 1].

HERBAL PREPARATIONS

Triphala, an Ayurvedic formulation composed of *Embolia officinalis*, *Terminalia bellirica*, and *Terminalia chebula*, is recognized for its potent anti-inflammatory properties.^[161] Research indicates that Triphala provides chemoprotective effects against carcinogenic damage to the liver induced by 1,2-dimethylhydrazine dihydrochloride in mice.^[162] In addition, it possesses antioxidant capabilities and can scavenge ROS.^[163,164] Triphala significantly reduces oxidative stress and offers protective benefits against myocardial necrosis in rat models.^[165] Furthermore, it effectively elicits a cell-mediated immune response in rats subjected to noise stress^[166] and demonstrates immunomodulatory effects by enhancing neutrophil functions.^[166] Moreover, it exhibits hemopreventive potential against benzo(a)pyrene-induced forestomach tumorigenesis in murine models.^[167]

In addition, various Ayurvedic plants such as Tamala (*C. tamala*), Daruhlad (*Berberis aristata*), and Ativisha (*Aconitum heterophyllum*) have been shown to reduce inflammation associated with prostatic hyperplasia in rats. Tamala specifically inhibits androgen mechanisms in the prostate and modulates inflammatory mediators, with its formulations effectively slowing down prostate enlargement and inflammation.^[168] Similarly, a polyherbal preparation utilizing Sudarshanam oil has demonstrated significant efficacy against severe inflammation.^[169] Furthermore, extracts from *Coriandrum sativum*, *Foeniculum vulgare*, *Matricaria chamomilla*, and *Prunus domestica* have been found to significantly suppress ROS from *Helicobacter pylori*-infected cells ($P < 0.01$).^[170] In addition, plant extracts from *A. galanga*, *Cinnamomum cassia*, *C. tamala*, *Mentha arvensis*, *Myrtus communis*, *Oligochaeta ramosa*, *Polygonum bistorta*, *Rosa damascena*, *Ruta graveolens*, *Syzygium aromaticum*, *Tamarix dioica*, and *T. chebula* have exhibited strong inhibitory activity against IL-8 secretion. *Berberis aristata* shows anti-inflammatory and cytoprotective effects. *C. cassia* causes TNF- α stimulation and causes suppression of IL-8 secretion in a concentration-dependent manner. Plants *T. cordifolia*, *C. longa*, *T. chebula*, *E. officinalis*, *Andrographis paniculata*, and *T. bellirica* contain so many phytochemicals such as tannins, glycosides, flavonoids, and triterpenoids which also cut down tissue inflammation [Table 1].

Datura stramonium

Antioxidants play a crucial role in safeguarding body tissues by neutralizing highly ROS, as noted by Batool *et al.*, 2017.^[171] Various phytochemicals derived from medicinal plants are recognized for their substantial antioxidant capabilities. Key antioxidant phytochemicals encompass phenolics, flavonoids, terpenoids, vitamins, alkaloids, saponins, minerals, and specific pigments. These diverse compounds assist the body in countering numerous diseases

associated with oxidative stress, as highlighted by Govind, 2014; Memariani *et al.*, 2021.^[172,173] In addition to their antioxidant properties, the mechanisms through which these plants provide protection against liver damage may involve anti-inflammatory effects, prevention of necrosis, regulation of lipid metabolism, and antiapoptotic actions, as discussed by Meng *et al.*, 2018.^[174] Liver fibrosis poses a significant health risk, and if not addressed in a timely manner, it can progress to serious liver conditions such as cirrhosis and HCC, according to Aydın *et al.*, 2018.^[175] The leaf extract of *D. stramonium* has demonstrated anti-inflammatory properties in models of CCL4-induced hepatic injury^[176] [Table 1].

Euphorbia

Antioxidants play a crucial role in safeguarding body tissues by neutralizing highly ROS. *Euphorbia hirta* has demonstrated anti-inflammatory properties in a murine model of adjuvant-induced arthritis.^[177,178] The mechanism of these anti-inflammatory effects was observed in LPS-induced RAW 264.7 cells, where selective inhibition of the iNOS protein was noted^[179] [Table 1].

Eugenia jambolana

E. jambolana, commonly known as jambolan, along with *Syzygium cumini* seeds, is rich in significant bio-organic compounds such as anthocyanins, ellagic acid, jambosine, isoquercetin, kaempferol, and myricetin, as well as glycoside antimellin or jambolin.^[180] This plant has a long-standing tradition in the preparation of various Ayurvedic medicines. The ethanolic extract of *E. jambolana* seeds has been utilized for treating gastric ulceration and secretion in rat models.^[181] Furthermore, *E. jambolana* (Jamun fruit) has been shown to reduce liver inflammation, injury, and fibrosis during cholestasis,^[182] while the stem bark extract exhibits both anti-inflammatory and analgesic properties.^[183] The extract of *E. jambolana* has also demonstrated protective effects against cisplatin-induced damage in rat testis when compared to N-acetyl cysteine.^[184] In addition, the crude extract of *E. jambolana* interacts with human cytochrome P450 enzymes.^[185] Inhibition of dipeptidyl peptidase-4 by *Pterocarpus marsupium* and *E. jambolana* has been found to improve conditions in streptozotocin-induced Alzheimer's disease^[186] [Table 1].

Achyranthes aspera

A. aspera has shown anti-inflammatory effects when applied topically, as evidenced by studies.^[187,188] It effectively suppresses the release of various mediators during both the early and late phases of inflammation. The ethanolic fraction of this plant also reduced mediator release in the early phase; however, its impact on chronic inflammation

was less pronounced.^[189] *A. aspera* roots also showed anti-inflammatory activity^[190] [Table 1].

Madhuca indica

Madhuca longifolia ethanol extract and the mixture of *M. longifolia* saponins (MLSM) have been shown to significantly reduce acute (carrageenan-induced), sub-acute (formaldehyde-induced), and chronic (cotton pellet granuloma) inflammation in rat models.^[191] In addition, the bark extract of this species contains phenolic compounds that exhibit antioxidant properties.^[192] *M. indica* is known to contain Madhucosides A and B, as well as protobassic acid glycosides, which have demonstrated inhibitory effects on free radical release from phagocytes.^[193] Furthermore, oleanolic and ursolic triterpenoids have been identified as effective in inhibiting croton oil-induced ear edema in mice, as well as in carrageenan and TPA-induced edemas.^[194] The triterpenoids derived from oleanane and ursane compounds in *M. indica* have also shown activity against formaldehyde-induced edema and arthritis in rat models.^[195] *M. indica* appears to inhibit both the synthesis of PGs and their mediators, potentially by reducing the expression of intercellular adhesion molecule-1 through TNF- α .^[196] Traditionally, *M. longifolia* has been utilized in Chinese medicine for the treatment of kidney stones^[196] [Table 1].

Mentha longifolia

M. longifolia exhibits anti-inflammatory properties in macrophages stimulated by LPS, leading to a decrease in NO production through the inhibition of iNOS.^[197] In addition, Myristicin demonstrates an anti-inflammatory effect on RAW 264.7 macrophages activated by polyinosinic-polycytidylic acid.^[198] The compound dehydrodiisoeugenol and its metabolites also possess anti-inflammatory characteristics.^[199] Furthermore, ZnO/CuO/Ag nanocomposites combined with secondary metabolites from *M. longifolia* have been shown to create an effective synergy that may enhance various stages of wound healing by modulating cytokines and growth factors throughout the healing process^[200] [Table 1].

Azima tetracantha

This plant is commonly known as “Yashankala” in Ayurveda. Friedelin found in *A. tetracantha* Lam. leaves shows anti-inflammatory, analgesic, and antipyretic activities in Wistar rats and mice.^[201] Treatment with friedelin reduced the inflammation caused by carrageenan-induced hind paw edema, croton oil-induced ear edema, acetic acid-induced vascular permeability, cotton pellet-induced granuloma, and adjuvant-induced arthritis. Similarly, methanol extract of *A. tetracantha* leaves acts as a chain-breaking antioxidant molecule and is capable of inhibiting inflammatory enzymes

and the proliferative potential of breast cancer cells^[202] [Table 1].

Terminalia arjuna

T. arjuna (Combretaceae) is known to possess a wide array of bio-organic compounds that exhibit various biological activities, including anti-inflammatory, antioxidant, immunomodulatory, and antinociceptive effects in experimental animal models.^[203] The stem bark extract of *T. arjuna* is rich in 18,19-secooleanane-type triterpene glycosyl esters,^[204] ursane triterpenoids,^[205] and polyphenols.^[206] In addition, a novel cardenolide has been identified from the roots of *T. arjuna* along with triterpene glycosides.^[207,208] The plant also contains arjunic acid and arjunolic acid,^[208] which have demonstrated antioxidant properties.^[209] Arjunic acid acts as a potent free radical scavenger^[210] and is associated with various therapeutic applications.^[211] Furthermore, pentacyclic triterpenes derived from *T. arjuna* offer multiple benefits for aged and dry skin.^[212] The stem bark extract has been shown to reduce activation in human monocytic (THP-1) and aortic endothelial cells^[213] while its aqueous extract mitigates tert-butyl hydroperoxide-induced oxidative stress in the HepG2 cell model.^[214] The aqueous extract also provides protective effects against dehydration-induced oxidative stress and uremia in male rats.^[215] Moreover, arjunolic acid has been found to protect against arsenic-induced testicular oxidative stress.^[216] *T. arjuna* (Roxb.) has been shown to modulate circulatory antioxidants in the context of 7,12-dimethylbenz(a)anthracene-induced carcinogenesis in the hamster buccal pouch^[217] [Table 1].

T. arjuna leaf extract exhibits anti-tumor properties against Ehrlich ascites carcinoma in murine models^[218] and demonstrates antimutagenic effects.^[219] In addition, the bark extract of *T. arjuna* induces apoptosis in the human hepatoma cell line HepG2.^[220] Its tannin fraction has been shown to modulate the genotoxicity of mutagens in *Salmonella* Typhimurium^[221] [Table 1].

The seeds of *T. arjuna* contain cardenolides,^[207] which have been found to enhance myocardial function in streptozotocin-induced diabetic rats.^[222] Triterpenoids derived from two species of *Terminalia*^[204] improve baroreflex sensitivity and myocardial function in rats with isoproterenol-induced chronic heart failure.^[223] The ethanolic fraction of *T. arjuna* bark exhibits anti-atherogenic activity in hypercholesterolemic rabbits.^[224] Furthermore, the bark of *T. arjuna* reduces cardiotoxicity induced by Doxorubicin^[225] and demonstrates antioxidant and hypocholesterolemic effects in a randomized placebo-controlled trial.^[226] The bark extract also provides cardioprotective effects in rats with isoproterenol-induced chronic heart failure and protects the heart from ischemic-reperfusion injury^[223] [Table 1].

The ethanolic extract of *T. arjuna* bark exhibits anti-atherogenic properties in hypercholesterolemic rabbits.^[224] Arjunolic acid, a triterpenoid saponin, has been shown to mitigate arsenic-induced cytotoxicity in hepatocytes.^[227] In addition, *T. arjuna* demonstrates phytomedicinal effects against cardiac oxidative stress induced by carbon tetrachloride.^[227] The bark also provides ulcer protection by enhancing the gastric mucosal defense mechanisms in experimental rats.^[228] Furthermore, the aqueous extract of *T. arjuna* is effective in preventing hepatic and renal disorders caused by carbon tetrachloride.^[229] The plant contains naphthalene glycosides, which possess antioxidant and NO inhibitory activities.^[230] Moreover, *T. arjuna* has been found to restore impaired endothelial function in chronic smokers^[231] and exhibits protective effects against DLA tumor cells^[232] [Table 1].

CONCLUSION

This review article explores the anti-inflammatory activity of plant-derived natural bio-organic ingredients from over 200 species. These plants contain flavonoids, tannins, alkaloids, quinones, and phenolic compounds that can neutralize inflammatory reactions. *C. tamala* contains cinnamaldehyde, which stimulates the secretion of anti-inflammatory molecules. Curcumin has been shown to inhibit tumor development and provide chemopreventive effects against carcinogenesis. Triphala, an Ayurvedic formulation, is recognized for its potent anti-inflammatory properties and antioxidant capabilities. Other plants such as *T. cordifolia*, *C. longa*, *T. chebula*, *E. officinalis*, *A. paniculata*, and *T. bellirica* contain phytochemicals that reduce tissue inflammation. Antioxidants play a crucial role in safeguarding body tissues by neutralizing highly ROS. *E. hirta*, *E. jambolana*, *A. aspera* roots, *M. longifolia* ethanol extract, *Mentha longifolia*, and *A. tetraantha* Lam. leaves have shown anti-inflammatory, analgesic, and antipyretic activities. *T. arjuna*'s stem bark extract is rich in triterpene glycosides and a novel cardenolide.

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