



Ayurvedic Approach to Anti-inflammation: A Review on Polyherbal Asava Arishta.

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ABSTRACT-

Researching medicinal plants through traditional medical systems has gained international attention in recent years. Numerous medicinal plants found on our planet have been used for thousands of years and are valued globally as important sources of therapeutic substances for the prevention and treatment of a wide range of illnesses. Pain is a discomfort signal brought on by actual or potential bodily injury, and it frequently coexists with inflammation, which is a complex biological reaction of vascular tissue brought on by a variety of detrimental stimuli. Numerous illnesses, such as rheumatism, encephalitis, pneumonia, oesophagitis, cancer, heart problems, and fibrosis, are associated with the co-occurrence of inflammation and pain. Opioid analgesics and nonsteroidal anti-inflammatory medications are frequently used to treat pain and inflammation, but they can have a number of negative consequences. Herbal remedies could therefore be a good substitute. The potential anti-inflammatory and analgesic effects of many traditional medicine plants are assessed annually, but only a small number of these have been integrated into the healthcare system following clinical research. The purpose of this review is to gather data on promising phytochemicals from herbal plants that have been evaluated in inflammatory models using up-to-date scientific techniques.

Key words - Anti-inflammatory, Herbal plants, potential, mechanism of action.

Introduction –

The body's reaction to cellular damage is inflammation, which increases blood flow to the damaged tissue and serves as a defence mechanism to assist the body recognise and combat dangerous stimuli like poisons, bacterial infections, and cancer cells. Even though inflammation has a protective function, patients may still be at serious risk from it. It could make the condition worse by making the discomfort and complications worse. Tissue damage and inflammation-related pain are largely caused by the activation of local inflammatory mediators, including leukotrienes, prostaglandins, prostacyclin, thromboxane A₂, and platelet-activating factor, which are triggered by the arachidonic acid, cyclooxygenase, and lipoxygenase pathways [1,2]. Inflammation can cause symptoms like pain, cellular damage, and tissue swelling (oedema), even though it is an essential physiological defence mechanism to shield the body from dangerous stimuli. Repairing injured tissue and returning it to a healthy condition is inflammation's ultimate objective [3]. Inflammation mainly comes in two forms, which include the following:

1. 1.Acute inflammation

Increased vascular permeability, capillary leakage, and leukocyte migration are characteristics of this kind.

2. 2.Chronic inflammation

Fibrosis results from this kind of inflammation, which also includes the activation and multiplication of fibroblasts (angiogenesis) and the infiltration of mononuclear immune cells, including neutrophils, monocytes, and macrophages [4]. About 1% of people in affluent nations suffer from rheumatoid arthritis (RA), a chronic and crippling autoimmune illness, and inflammation is a common clinical problem [5]. Localised redness, swelling, discomfort, elevated body temperature, and loss of function are typical indicators of inflammation [6]. Changes in the production or activity of nitric oxide (NO), a short-lived gaseous free radical, are known to be important mediators of inflammation and to contribute to the development of experimental arthritis and acute inflammation [7, 8]. NO is created when the three isoforms of the enzyme Nitric Oxide Synthase (NOS) oxidise L-arginine. The third isoform, inducible NOS (iNOS), is activated by cytokines and is controlled at the gene level by inflammatory mediators, whereas constitutive NOS (cNOS) is dependent on calcium and calmodulin [9]. Elevated NOS activity or increased NO release has been observed in both acute and chronic inflammation models [10]. Moreover, administering L-arginine, a precursor for NO synthesis, has been linked to increased paw swelling in adjuvant arthritis models [9]. One of the most often prescribed drugs in the world, nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat fractures, soft-tissue injuries, and osteoarthritis. Ibuprofen and naproxen are examples of common NSAIDs [11]. Cortisone and prednisone are examples of glucocorticoids, which belong to another class of drugs. However, these medications are associated with significant concerns, such as high costs, severe side effects, and toxicity, particularly in patients being treated with biological response modifiers like tumor necrosis factor-alpha blockers [12]. Known side effects of these drugs

include gastrointestinal ulceration and bleeding, renal damage, hypertension, and hyperglycemia. A major drawback of these potent synthetic medications is their toxicity and the recurrence of symptoms after discontinuation. As a result, there is a growing need to screen and develop medications with anti-inflammatory properties, especially from naturally occurring sources. Numerous efforts are underway to identify anti-inflammatory compounds from locally grown medicinal plants [13]. Although most in vitro studies follow an initial in vivo assessment of plant extracts' anti-inflammatory effects, they provide valuable insight into the mechanisms through which herbal compounds exert their anti-inflammatory actions [14,15]. Herbal extracts' anti-inflammatory qualities have been assessed using a variety of experimental paradigms. The in vitro and in vivo methods frequently used to evaluate the anti-inflammatory properties of herbs and spices are compiled in this article.

Inflammatory Diseases –

Inflammatory abnormalities make constitute a broad, formally separate category of conditions that lead to a wide range of human illnesses. Inflammatory illnesses frequently involve the immune system. Common forms of inflammatory diseases include autoimmune diseases, allergic responses, and some myopathies. Inflammatory processes are the etiological cause of some prevalent non-immune diseases, including cancer, atherosclerosis, and ischemic heart disease [30].

TYPES OF INFLAMMATORY DISEASE [16,17,18,19] -

DISEASE	EXPLANATION
Allergy	Inflammatory cytokines trigger autoimmune responses linked to inflammation.
Appendicitis	Inflammation of the vermiform appendix, or appendicitis, is linked to obstruction.
Arthritis	Bacterial and viral infections, along with immune complex formation, lead to inflammation of the joints, resulting in the destruction of joint cartilage and synovial fluid.
Asthma	Allergic respiratory diseases lead to smooth muscle hyperplasia, increased mucus production, and inflammation.
Bacillary angiomatosis	A skin condition in immunocompromised individuals is characterized by reddish, elevated lesions often surrounded by a scaly ring and accompanied by inflammation.
Cancer	Uncontrolled tissue growth linked to inflammation.
Cellulitis	Infection leads to subcutaneous inflammation of the connective tissue.
Colitis	Bacterial infections and ulcers cause inflammation in the colon.
Congestive heart failure, stroke, heart attack	Common heart diseases linked to inflammation include myocarditis, endocarditis, and atherosclerosis.
Cystitis	Cystitis is the term for bladder inflammation.
Dermatomyositis	When polymyositis affects the skin, it manifests as inflammation and reddish erythematous lesions.
Encephalitis	Inflammation in the brain can result from encephalitis caused by viral diseases.
Endocarditis	Endocarditis is the term used to describe inflammation of the heart valves and lining.
Fibrosis	The condition of fibrosisFibrosis is a disorder marked by an increase in intestinal fibrous tissue brought on by inflammation or direct toxic liver injury. In particular, when the liver is affected by cirrhosis, fibrous tissue may grow as a result of ongoing inflammation or injury.
Gastritis	Gastritis, an inflammation of the stomach's mucous membrane, can be brought on by alcohol misuse, <i>Helicobacter pylori</i> infection, and gastric acid reflux. The glomerular and alveolar basement membranes become inflamed and damaged in Goodpasture syndrome, a distinct autoimmune disease that mainly affects the kidneys and lungs.
Goodpasture syndrome	The Goodpasture SyndromeGoodpasture syndrome is an autoimmune disease that affects the basement membranes of the lung alveoli and kidney glomeruli.
Hepatitis	Viral hepatitis is the term for liver damage brought on by an inflow of acute or chronic inflammatory cells as a result of a viral infection.
Infectious rhinitis	Rhinitis that is contagiousThough other viruses like coronaviruses and adenoviruses can sometimes be to blame, rhinoviruses are usually the cause of the common cold, a viral infection of the respiratory system.
Insulinitis	Type 1 diabetes mellitus is an inflammatory or autoimmune condition that damages the islets of Langerhans and causes the pancreatic beta cells to be destroyed.

Leprosy	A chronic disease caused by <i>Mycobacterium leprae</i> , characterized by the formation of nodules on the body surface, is known as leprosy (also called Hansen's disease).
Mediterranean fever	A febrile disorder of unknown cause, characterized by recurrent episodes of fever and inflammation, commonly found in the Mediterranean region, is known as Familial Mediterranean Fever (FMF).
Meningitis	Inflammation of the meninges, particularly affecting the pia mater and arachnoid, due to bacterial or viral infections, is known as meningitis.
Esophagitis	Inflammation and pain in the esophagus due to gastric acid reflux or fungal infections is known as esophagitis. Gastric acid reflux-induced esophagitis is often referred to as gastroesophageal reflux disease (GERD), while fungal infections in the esophagus may lead to infectious esophagitis, commonly caused by <i>Candida</i> .
Thyroiditis	A diverse group of disorders characterized by inflammation and pain in the thyroid gland is known as thyroiditis. This group includes conditions like Hashimoto's thyroiditis, Graves' disease, and subacute thyroiditis, among others.
Tuberculosis	An infection of the lungs caused by <i>Mycobacterium tuberculosis</i> , characterized by fever, cough, inflammation, and difficulty in breathing, is known as tuberculosis (TB).
Urethritis	Inflammation in the uterus that develops as a component of urinary tract infections (UTIs) is known as endometritis. It can occur when a UTI ascends to affect the uterus, often in cases of untreated or severe infections.

ANALGESIC AND ANTI-INFLAMMATORY DRUGS AND THEIR ADVERSE EFFECT [16,20,19]-

DRUGS	Adverse effects
	Nonsteroidal anti-inflammatory drugs-
Acetaminophen	Skin rashes, gastrointestinal disturbances or bleeding, hives, hemolytic anemia, pancytopenia, jaundice, liver toxicity, and hepatic necrosis resulting from an overdose.
Aspirin	Nausea, vomiting, upper abdominal discomfort, peptic ulcers, tinnitus, allergic and anaphylactic reactions, an increased risk of Reye's syndrome in children, respiratory alkalosis, and hyperventilation.
Ibuprofen	Nausea, dizziness, drowsiness, indigestion, gastric or duodenal ulcers, gastrointestinal (GI) bleeding, headache, and tinnitus.
Indomethacin	Nausea, constipation, formation of gastric or duodenal ulcers, gastrointestinal (GI) bleeding, and hematologic changes.
Piroxicam	Nausea, vomiting, drowsiness, gastric or duodenal ulcers, and gastrointestinal (GI) bleeding.
Diclofenac sodium	Nausea, vomiting, gastric or duodenal ulcers, and GIT bleeding.
Ketoprofen	Dizziness, visual disturbances, nausea, constipation, vomiting, diarrhea, gastric or duodenal ulcer formation.
Ketorolac	Indigestion (dyspepsia), nausea, gastrointestinal pain, gastrointestinal bleeding and/or perforation of the stomach or intestines.
Mefenamic acid	Dizziness, fatigue, nausea, indigestion (dyspepsia), rash, constipation, bleeding.
Naproxen	Dizziness, visual disturbances, nausea, vomiting, gastric or duodenal ulcers, GIT bleeding.
Sulindac	Nausea, vomiting, diarrhea, gastric or duodenal ulcers, and gastrointestinal (GI) bleeding.
Valdecoxib	Headache, nausea, indigestion (dyspepsia)
Celecoxib and Rofecoxib	Headache, dizziness, drowsiness (somnolence), insomnia, indigestion (dyspepsia), rash, fatigue
	Opioid analgesic:
Fentanyl	Sedation, sweating, headache, vertigo, lethargy, confusion, light-headedness, nausea, vomiting.
Methadone	Light-headedness, dizziness, constipation.
Morphine sulfate	Sedation, hypotension, increased sweating, constipation, dizziness, drowsiness, nausea, vomiting, dry mouth.
Codeine	Sedation, sweating, headache, dizziness, lethargy.
Buprenorphine	Light-headedness, sedation, constipation, dizziness, nausea, vomiting.
Pentazocine	Light-headedness, sedation, constipation, dizziness, nausea, vomiting.

Plants as natural Anti-inflammatory Agents –

Unlike contemporary allopathic drugs, which usually rely on a single active ingredient that targets a single pathway, herbal medicines work holistically. On the other hand, a variety of substances found in plants interact to influence various facets of intricate biological processes [21]. For centuries, medicinal plants have offered a wide variety of biologically active compounds, which are commonly used as either pure or crude materials to treat various ailments [22]. Over 1.5 million people follow traditional medical systems that use medicinal plants for therapeutic, preventive, and health-promoting purposes [23]. With the world's largest collection of medicinal plants, India is well-positioned to continue playing a major role in producing raw materials for crude drugs as well as bioactive ingredients for pharmaceuticals, cosmetics, and other products [24]. The use of herbal remedies has been steadily increasing due to the toxicity and side effects of various allopathic drugs.

Herbal anti-inflammatory agents -

Herbal remedies are the culmination of centuries of traditional medical practices and restorative expertise. The management of numerous severe illnesses, such as pain and inflammation, remains challenging despite the enormous advancements in medical science over the past few decades [25]. The creation of strong analgesic and anti-inflammatory medications with fewer adverse effects is necessary because the currently prescribed medications have some serious side effects [26]. Herbal medicine proved to be safer, more effective, more culturally acceptable, and less harmful than synthetic drugs. The kingdom of plants contains a wide variety of chemical substances that are considered to be more compatible with the human body and are part of the physiological processes of live plants [29]. Effective analgesics and anti-inflammatory agents have also been demonstrated for alkaloids, flavonoids, xanthone, coumarin, sterols, withaferin-A, andrographolide, and other phytoconstituents [30, 31]. Thus, there is a pressing need for study on herbal medicine and its uses in everyday life.

Herbal Plant Use and the Development of Drugs [32-36]:

Botanical Name	Family	Parts Used	Constituent Compounds
<i>Acacia catechu</i>	Mimosaceae	Bark, wood, flowering tops, gum.	Tannin, gum, catechuic acid
<i>Azadirachta indica</i>	Meliaceae	Leaf, root, oil, seed, gum, fruit, flower.	Margosine, bitter oil, azadirachtin.
<i>Caesalpinia crista</i>	Caesalpinaceae	Seeds, root, leaf, root bark.	Oleic, linoleic, palmitic, stearic acid, phytosterols.
<i>Cassia angustifolia</i>	Caesalpinaceae	Pods, dried leaves.	Emodin, cathartin, mucilage, senna-picrin, oleanic acid.
<i>Coriandrum sativum</i>	Umbelliferaeapiaceae	Leaf, bark, flower	Tannin, cathartin, malic acid, cathartin, albuminoids.
<i>Cuscuta reflexa</i>	Convolvulaceae	Plant, seed, fruit, stem.	Cuscutine, flavonoid, glucoside, bergenin, coumarin.
<i>Enicostema littorale</i>	Gentianaceae	Whole plant.	Alkaloids, gentiocrucine
<i>Erythrina variegata</i>	Papilionaceae	Leaves, bark, roots, flower.	2-Hydroxygenistein, genistein.
<i>Euphorbia hirta</i>	Euphorbiaceae	Plant, roots, leaves	Ascorbic acid, β -amyirin, choline, inositol, linoleic acid, β -sitosterol.
<i>Euphorbia tirucalli</i>	Euphorbiaceae	Root, plant (milk, juice).	β -sitosterol, ellagic acid, citric acid, malic acid, eupholglucose.
<i>Fagonia cretica</i>	Zygophyllaceae	Leaves, twigs, bark.	Betulin
<i>Ficus benghalensis</i>	Moraceae	Aerial roots, bark, seeds, leaves, buds, fruits, latex.	Skin, fruits contain 10% tannin.
<i>Ficus carica</i>	Moraceae	Fruit, root.	Alkaloids, ascorbic acid, caffeic acid, niacin, linoleic acid, lutein, β -carotene, pantothenic acid, β -amyirin.
<i>Ficus religiosa</i>	Moraceae	Bark, leaves, fruits, tender shoots, seeds.	The bark contains tannins, rubber, wax.

<i>Foeniculum vulgare</i>	Apiaceae	Fruit, root, seeds, leaves.	Ascorbic acid, estragole, coumaric acid, caffeic acid, α -terpinene, scoparone, scopoletin, cynarin, D-limonene, α -phellandrene.
<i>Gentiana kuroo</i>	Gentianaceae	Rhizomes (roots)	Gentiopicrosine, gentianic acid
<i>Gloriosa superba</i>	Liliaceae	Rhizome, tuber, leaves, flower	Choline, colchicine, stigmaterol, salicylic acid, 2-methylcolchicine.
<i>Glycyrrhiza glabra</i>	Papilionaceae	Roots, leaves.	Genistein, eugenol, bergapten, glycyrrhizin, acetophenone, estragole, camphor, ascorbic acid, apigenin, anethole.
<i>Gmelina arborea</i> Roxb	Verbenaceae	Whole plant.	Betulin
<i>Grewia asiatica</i>	Tiliaceae	Leaves, roots, fruits, bark.	Betulin
<i>Hibiscus rosa-Sinensis</i>	Malvaceae	Buds, roots, leaves, flower	Quercetin, ascorbic acid.
<i>Hygrophila auriculata</i>	Acanthaceae	Roots, leaves, seeds.	Oleic and linoleic acids in seed oil, palmitic acid, stearic acid.
<i>Manihot esculenta</i>	Euphorbiaceae	Tuberous roots.	Ascorbic acid, palmitic acid, lauric acid, stearic acid, oleic acid.
<i>Martynia annua</i>	Pedaliaceae	Fruits, leaves.	Pelargonidin-3,5-diglucoside, cyanidin-3-galactoside, semi-drying oil.
<i>Momordica charantia</i>	Cucurbitaceae	Whole plant	5-Hydroxytryptamine, alkaloids, ascorbic acid, β -carotene, cholesterol, lutein, diosgenin, lanosterol, lycopene, momordicin, charantin niacin, momordicoside.
<i>Moringa oleifera</i>	Moringaceae	Roots, bark, leaves, seeds.	Choline, moringinine, myristic, ascorbic acid, β -carotene, niacin, oleic acid, spirochin, stearic acid, tocopherol, vanillin.
<i>Nelumbo nucifera</i>	Nymphaeaceae	Whole plant.	Anonaine, ascorbic acid, β -carotene, copper, erucic acid, glutathione, hyperoside, myristic acid, nuciferine, oxoushinsunine, rutin, stearic acid, trigonelline, kaempferol, D-catechin.
<i>Nicotiana tobacum</i>	Solanaceae	Leaves.	1,8-Cineole, 4-vinylguaiaicol, acetaldehyde, acetophenone, alkaloids, anabasine, nicotinic acid

Herbal plants used to treat skin inflammation [37-45]:

Plant's botanical name	Part used	Mode of preparation	Mode action	Chemical constituents
<i>Chromolaena odorata</i>	Leaves	Extraction	Modulation of Nrf2	Chromomoric acid
<i>Clematis viticella</i>	Aerial	Alcoholic extraction	Inhibition of the release of NO, TNF- α	Curcumin
<i>Curcuma longa</i>	Rhizome	–	Modulation of skin disruption	Curcumin
<i>Glycyrrhiza uralensis</i>	Root	Lipophilic oil/water emulsion	Reduction of skin dryness	Triterpenoids, glycyrrhizin, and glycyrrhetinic acid
<i>Matricaria recutita</i>	Flowers	Aqueous extraction	Inhibition of prostaglandins and leukotriene synthesis	α -Bisabolol, matricin, luteolin apigenin, and apigenin-7-glucoside
<i>Phyllanthus acidus</i>	Leaves	Methanol extraction	Inhibition of granuloma formation	Phenols and flavonoids
<i>Rutaceae citrus</i>	Fruit	Water juice preparation	Reduce skin irritation	Citric acid
<i>Salvia officinalis</i>	Leaves	–	Inhibits growth of infectious bacteria	–
<i>Solanum incanum</i>	Root	Methanol extraction	Inhibition of phospholipase A2, protein kinase C, and	flavonoids

			tyrosine kinases production	
<i>Symphytum officinale</i>	Root	–	Inhibits synthesis of prostaglandins, and glycopeptides	Rosmarinic acid and glycopeptide

Herbal plants used to treat liver inflammation [46-51]:

Plant's botanical name	Part used	Mode of preparation	Mode of action	Chemical constituents
<i>Berberis vulgaris</i>	Aerial	Methanol extraction	Inhibit and decline the effect of stress in the liver	Flavonoids,
<i>Gardenia jasminoides</i>	Fruit	–	Inhibits liver fibrosis and suppresses expression of CYP2E1	Geniposide
<i>Glycyrrhiza glabra</i>	Root twigs and Root intercept	Hydroethanolic extraction	Inhibiting NO production in cells	Glycyrrhetic acid, liquiritin, glabridin, and liquiritigenin

Herbal Plants used to treat Cardiovascular Inflammation [52-56]:

Plant's botanical name	Part used	Mode of preparation	Mode of action	Chemical constituents
<i>Cimicifuga racemosa</i>	Rhizome	Aqueous extraction	Inhibition of TNF- α production by downregulation of ERK and NF- κ B activities	Cimiracemate A
<i>Ginkgo biloba</i>	Leaves	Aqueous extraction	Inhibit angiotensin-converting enzyme	Quercetin, ferulic acid, allicin, gensenosides, myricetin, and kaempferol
<i>Ocimum sanctum</i>	Whole part	Aqueous extraction	Blocking cyclooxygenase and lipooxygenase pathways	Linolenic acid
<i>Ocimum basilium</i>	Leaves	Supercritical fluid extraction	Decrease in pro-inflammatory cytokines secretion	Linalool, eugenol, and α -bergamatone
<i>Salvia miltiorrhiza</i>	Rhizome	Aqueous extraction	Blocking activation of the NF- κ B and MAPK pathways	Diterpene chinone

Herbal plants to treat joint inflammation [37,57-62]:

Plant's botanical name	Part used	Mode of preparation	Mode of action	Chemical constituents
<i>Annona squamosa</i>	Stems	Extraction	Inhibition of neutrophils degranulation	11 Ent-kaurenes
<i>Artemisia absinthium</i>	Aerial	Extraction	Inhibition of COX-2 expression and synthesis of cytokines	6,7-Dimethoxy coumarin
<i>Berberis vulgaris</i>	Root	Solvent extraction	Reduce chronic joint inflammation	Berberine and oxyacanthine
<i>Ficus sycomorus</i>	Bark	Hot water Infusion	Inhibition of skeletal muscle contraction	Gallic tannins, saponins, alkaloids, and flavone aglycones
<i>Salix</i> spp.	Bark	Aqueous extraction	Blocking the activity of pro-inflammatory mediators, cytokines, and enzymes	Polyphenols, flavonoids, and salicin
<i>Sinomenium acutum</i>	Stem	Aqueous extraction	Inhibits angiogenesis	Sinomenine

Herbal plants used to gastrointestinal inflammation [63-67]:

Plant's botanical name	Part used	Mode of preparation	Mode of action	Chemical constituents
<i>Angelica sylvestris</i>	Roots	Dichloromethane extraction	Inhibition of IL-8 production	Coumarins
<i>Ocimum basilicum</i>	Leaves	Hydrodistillation	Reduction of myeloperoxidase activity	1,8-cineole
<i>Persicaria chinensis</i>	Aerial part	Methanol extraction	Blockage of LPS-induced NO production	Caffeic acid, kaempferol, and quercetin

<i>Sanicula europaea</i>	Roots	Methanol and DCM extractions	Reduction of IL-8 and E-selectin secretion	Saponins
<i>Vitis vinifera</i>	Leaves	Aqueous extraction	Inhibition of IL-8 secretion	Polyphenols and quercetin glycoside

Herbal plants used to treat lung inflammation [68-71]:

Plant's botanical name	Part used	Mode of preparation	Mode of action	Chemical constituents
<i>Allium sativum</i>	Bulb	Cold decoction	–	–
<i>Caragana tangutica</i>	Heartwood	Ethyl acetate extraction	Decrease the expression of cyclooxygenase-2	Flavonoids, phenolics, anthraquinones, and saponins
<i>Eriobotrya japonica</i>	Leaves	Hot water infusion	Inhibits heme oxygenase-1(HO-1) expression	Triterpenes
<i>Paonia lactiflora</i>	Root	Hydroethanolic extraction	Inhibits pro-inflammatory cytokines	Paeoniflorin albiflorin, paeonin, and lactiflorin
<i>Lonicera japonica</i>	Leaves and flowers	Ethanol extraction	Reduces pro-inflammatory cytokine production	Iridoids and flavonoids

Mechanism of action of phytochemicals in anti-inflammatory activities-

By increasing the release of systemic mediators, cytokines, and chemokines, which encourage cellular infiltration to resolve inflammatory reactions and restore tissue coordination, phytochemicals are thought to reduce inflammatory stress [72]. Phytochemicals have well-established anti-inflammatory properties at the cellular and molecular levels [73]. These substances function by blocking important inflammatory enzymes, including phospholipase A2, lipoxygenases, cyclooxygenases, histamine synthesis, protein kinases, phosphodiesterase, and transcriptase activation. Leukotriene and proteinoid concentrations are lowered as a result of this inhibition. Flavonoids, polyphenols, alkaloids, saponins, tannins, and terpenes have all been demonstrated to have anti-inflammatory qualities in vitro [74]. For example, quercetin has been found to significantly inhibit enzymes responsible for producing eicosanoids from arachidonic acid, including COX-2 and 5-LOX. Resveratrol, by modulating eicosanoid synthesis, suppressing activated immune cells, and preventing the production and release of pro-inflammatory mediators, plays a role in regulating the inflammatory response [75]. Additionally, flavonoids, curcumin, and tannins demonstrate anti-inflammatory effects by inhibiting pro-inflammatory enzymes and scavenging free radicals [76]. Although the precise mechanism of action of metal-based nanoparticles (M/MONPs) against diseases is still not fully understood, several studies suggest possible mechanisms. Some researchers propose that M/MONPs bind to proteins and DNA containing phosphorus and sulfur, leading to the breakdown of disease-causing substances. Others suggest that the antimicrobial effects of M/MONPs are due to metallic ions released into the cell walls of bacteria or viruses, which disrupt their integrity and function [76].

Conclusion –

Since the beginning of animal life, plants have been used as food and medicine. . Plants include a vast array of pharmacologically active compounds, and each herb has its own unique combination and set of properties. Depending on the constituents of each herb and the patient's perceived needs, a number of plants have been described for the treatment of different ailments in Ayurveda and other traditional medical systems. Inflammatory and painful diseases are common and need greater attention. Reviewing the herbal remedies utilized by various medical systems and tribal/ethnic cultures to alleviate pain and inflammation is fundamentally crucial. Nowadays, a lot of individuals are searching for herbal cures and ways to alleviate their illnesses. The search for a safe and natural method of treating illness is the root cause of this. In order to achieve therapeutic relevance, our efforts should be focused on reviewing medicinal plants, screening for activity, isolating and characterizing the active components, and clarifying the connection between structure and activity. Since anti-inflammatory medicinal plant extracts typically contain numerous components, it is probable that they influence the intricate balance of entire immune cell cellular networks by acting on a variety of targets. Since modifying inflammatory disease processes may need complementary activities on multiple genes, this may be more advantageous than medicines that act on a single target. Stated differently, the effectiveness of herbal remedies and anti-inflammatory substances derived from herbs may rely on the disruption of many targets.

REFERENCE –

1. Umar MI, Altaf R, Iqbal MA, Sadiq MB. *In vivo* experimental models to investigate the anti-inflammatory activity of herbal extracts (review). *Sci Int* 2010; 22:199-203.
2. Graham JE, Robles TF, Kiecolt-Glaser JK, Malarkey WB, Bissell MG, Glaser R, *et al.* Hostility and pain are related to inflammation in older adults. *Brain Behav Immune* 2006; 20:389-400.
3. C. H. Lee and E. Y. Choi, "Macrophages and inflammation," *Journal of Rheumatic Diseases*, vol. 25, no. 1, pp. 11–18, 2018.
4. Nadkarni AK. *Indian Materia Medica*. Popular Press Bldg. 2000.
5. Cardinali PD and Esquifino IA. Circadian disorganization in experimental arthritis. *Neuro Signals*. 2003; 12:267-282.
6. Pervical M. Understanding the natural management of pain and inflammation, *Clinical Nutrition insights*. 1999;4:1-5

7. Daniel SF. Therapeutic Administration of a selective inhibitor of nitric oxide synthase Does not ameliorate the chronic inflammation and tissue damage associated with adjuvant-Induced arthritis in rats, *J Pharmacol Expt Ther.*1998;32:714-721.
8. Zumora RA and Billar TR. Inducible nitric oxide synthase and inflammatory disease. *Mol Med* 2000; 6:347-356.
9. Corbett JA. Interleukin-1 β -induced formation of EPR-detectable iron-nitrosyl complexes in islets of Langerhans. *J Biol Chem.*1991; 266:21351-21354.
10. Mederos M, Effect of chronic nitric oxide synthesis inhibition on the inflammatory response induced by carrageenan in rats, *Eur J Pharmacol.*1995; 285:109.
11. Malizos KN. Do steroids, conventional non-steroidal anti-inflammatory drugs and selective Cox-2 inhibitors adversely affect fracture healing. *J Musculoskelet Neuronal Interact.* 2009; 9:44-52.
12. Barnes PM. Complementary and alternative medicine use among adults, United states. *Adv Data.* 2002; 343:1-19.
13. Srinivasan K, Muruganandan S, Lal J, Chandra S, Tandan SK and Ravi Prakash V. Evaluation of anti-inflammatory activity of *Pongamia pinnata* in rats, *J Ethnopharmacol.* 2011; 78:151-157.
14. An HJ, Jeong HJ, Lee EH, Kim YK, Hwang WJ, Yoo SJ, *et al.* Xanthii fructus inhibits inflammatory responses in LPS-stimulated mouse peritoneal macrophages. *Inflammation* 2004; 28:263-70.
15. Jang SI, Kim BH, Lee WY, An SJ, Choi HG, Jeon BH, *et al.* Stylopine from *Chelidonium majus* inhibits LPS-induced inflammatory mediator in RAW 264.7 cells. *Arch Pharm Res* 2004; 27:923-9
16. Richard F, Michelle AC, Luigi XC: Lippincott's Illustrated Reviews: Pharmacology. Lippincott Williams & Wilkins, Philadelphia, Fourth edition 2008.
17. Burke A, Smyth E, Fitz-Gerald GA: Analgesic-antipyretic agents; pharmacotherapy of gout. In: Brunton LL, Lazo JS, Parker KL (eds.): Goodman & Gilman's The Pharmacological Basis of Therapeutics. McGraw-Hill, New York, Eleventh edition 2006.
18. Tripathi KD: Essentials of Medical Pharmacology. Jaypee Brothers Medical Publisher, New Delhi, Sixth edition 2008.
19. Grover JK: Adverse Drug Reactions. CBS Publishers & Distributors, New Delhi, First edition, 2006.
20. Craig CR, Stitzel RE: Modern Pharmacology with Clinical Applications. Lippincott Williams & Wilkins, Philadelphia, Fifth edition 2003.
21. Durmowicz AG and Stenmak KR. Mechanisms of structural remodeling in chronic pulmonary, Hypertension. *Pediatr Rev.* 1999; 20:91-101
22. Arif T, Bhosale JD, Kumar N, Mandal TK, Bendre RS, Lavekar GS and Dabur R. Natural Products antifungal agents derived from plants. *Journal of Asian Natural Products Research.* 2009; 7:621-638.
23. Dasilva EJ. Medicinal plants: a reemerging health aid, *Electronic Journal of Biotechnology.* 1999; 2:57-70.
24. Tiwari S. Plants: a rich source of herbal medicines. *Journal of Natural Products.* 2008; 1:27-35.
25. Adedapo AA, Sofidiya MO, Afolayan AJ: Anti-inflammatory and analgesic activities of the aqueous extracts of *Margaritaria discoidea* (Euphorbiaceae) stem bark in experimental animal models. *Revista de Biologia Tropical* 2009; 57: 1193-1200.
26. Saha A, Ahmed M: The analgesic and anti-inflammatory activities of the extract of *Albizia lebbek* in animal model. *Pakistan Journal of Pharmaceutical Science* 2009; 22: 74-77.
27. Chavan MJ, Wakte PS, Shinde DB: Analgesic and antiinflammatory activity of Caryophyllene oxide from *Annona squamosa* L. bark. *Phytomedicine* 2010; 17: 149-51.
28. Kamboj VP: Herbal medicine. *Current Science* 2000; 78: 35- 39.
29. Shah BS, Nayak BS, Seth AK, Jalalpure SS, Patel KN, Patel MA, Mishra AD: Search for medicinal plants as a source of anti-inflammatory and anti-arthritis agents- a review. *Pharmacognosy Magazine* 2006; 2: 77-86.
30. Singh A, Malhotra S, Subban R: Anti-inflammatory and analgesic agents from Indian medicinal plants. *International Journal of Integrative Biology* 2008; 3: 57-72.
31. Virshette, S.J.; Patil, M.K.; Somkuwar, A.P. A review on medicinal plants used as anti-inflammatory agents. *J. Pharmacogn. Phytochem.* 2019, 8, 1641–1646.
32. Oguntibeju, O.O. Hypoglycaemic and anti-diabetic activity of selected African medicinal plants. *Int J. Physiol. Pathophysiol. Pharmacol.* 2019, 11, 224–237.
33. Azab, A.N.; Nassar, A.; Azab, A.N. Anti-Inflammatory Activity of Natural Products. *Molecules* 2016, 21, 1321.
34. Sharopov, F.; Braun, M.S.; Gulmurodov, I.; Khalifaev, D.; Isupov, S.; Wink, M. Antimicrobial, antioxidant, and anti-inflammatory activities of essential oils of selected aromatic plants from Tajikistan. *Foods* 2015, 4, 645–653.
35. Bauri, R.K.; Tigga, M.N.; Saleebkullu, S. A review on use of medicinal plants to control parasites. *J. Nat. Prod. Resour.* 2015, 6, 268–277.
36. Maione, F., Russo, R., Khan, H., Mascolo, N., 2016. Medicinal Plants with Anti- Inflammatory Activities. *Nat. Prod. Res.* 6419, 1–10.
37. Kirmizibekmez, H., Inan, Y., Reis, R., Sipahi, H., Goren, A.C., Yesilada, E., 2019. Phenolic Compounds from the Aerial Parts of *Clematis viticella* L. and Their *in Vitro* Anti- Inflammatory Activities. *Nat. Prod. Res.* 33, 2541–2544. <https://doi.org/10.1080/14786419.2018.1448815>.
38. Seiwerth, J., Tasiopoulou, G., Hoffmann, J., Wölflle, U., Schwabe, K., Quirin, K.W., Schempp, C.M., 2019. Anti-Inflammatory Effect of a Novel Topical Herbal Composition (VEL-091604) Consisting of Gentian Root, Licorice Root and Willow Bark Extract. *Planta Med.* 85, 608–614. <https://doi.org/10.1055/a-0835-6806>.
39. Dawid-Pa'c, R., 2013. Medicinal Plants Used in Treatment of Inflammatory Skin Diseases. *Postep. Dermatologii Alergol.* 30, 170–177. <https://doi.org/10.5114/pdia.2013.35620>.
40. Chakraborty, R., Biplab, D., Devanna, N., Sen, S., 2012. Antiinflammatory, Antinociceptive and Antioxidant Activities of *Phyllanthus acidus* L. Extracts. *Asian Pac. J. Trop. Biomed.* 2 [https://doi.org/10.1016/S2221-1691\(12\)60343-8](https://doi.org/10.1016/S2221-1691(12)60343-8). S953–S961.

42. 42. Malik, K., Ahmad, M., Zafar, M., Ullah, R., Mahmood, H.M., Parveen, B., Rashid, N., Sultana, S., Shah, S.N.L., 2019. An Ethnobotanical Study of Medicinal Plants Used to Treat Skin Diseases in Northern Pakistan. *BMC Complement. Altern. Med.* 19, 1–38. <https://doi.org/10.1186/s12906-019-2605-6>.
43. 43. Tresch, M., Mevissen, M., Ayrlé, H., Melzig, M., Roosje, P., Walkenhorst, M., 2019. Medicinal Plants as Therapeutic Options for Topical Treatment in Canine Dermatology. *BMC Vet. Res.* 15, 1–19. <https://doi.org/10.1186/s12917-019-1854-4>.
44. 44. August, J., Enoc, W.N., Daisy, M.G.N., Wilbroda, O.A., Alphonse, W.W., Ngeranwa, J.N., 2018. Antinociceptive and Anti-Inflammatory Effects of Flavonoids Rich Fraction of *Solanum incanum* (Lin) Root Extracts in Mice. *J. Phytopharm.* 7, 399–403.
45. 45. Dawid-Pa'c, R., 2013. Medicinal Plants Used in Treatment of Inflammatory Skin Diseases. *Postep. Dermatologii Alergol.* 30, 170–177. <https://doi.org/10.5114/pdia.2013.35620>.
46. 46. Asadi-Samani, M., Kafash-Farkhad, N., Azimi, N., Fasihi, A., Alinia-Ahandani, E., Rafieian-Kopaei, M., 2015. Medicinal Plants with Hepatoprotective Activity in Iranian Folk Medicine. *Asian Pac. J. Trop. Biomed.* 5, 146–157. [https://doi.org/10.1016/S2221-1691\(15\)30159-3](https://doi.org/10.1016/S2221-1691(15)30159-3).
47. 47. Zhang, A., Sun, H., Wang, X., 2013. Recent Advances in Natural Products from Plants for Treatment of Liver Diseases. *Eur. J. Med. Chem.* 63, 570–577.
48. 48. Lam, P., Cheung, F., Tan, H.Y., Wang, N., Yuen, M.F., Feng, Y., 2016. Hepatoprotective Effects of Chinese Medicinal Herbs: A Focus on Anti-Inflammatory and Anti-Oxidative Activities. *Int. J. Mol. Sci.* 17, 1–37. <https://doi.org/10.3390/ijms17040465>.
49. 49. Yu, J.Y., Ha, J.Y., Kim, K.M., Jung, Y.S., Jung, J.C., Oh, S., 2015. Anti-Inflammatory Activities of Licorice Extract and Its Active Compounds, Glycyrrhizic Acid, Liquiritin and Liquiritigenin, in BV2 Cells and Mice Liver. *Molecules* 20, 13041–13054. <https://doi.org/10.3390/molecules200713041>.
50. 50. Jung, J.C., Lee, Y.H., Kim, S.H., Kim, K.J., Kim, K.M., Oh, S., Jung, Y.S., 2016. Hepatoprotective Effect of Licorice, the Root of *Glycyrrhiza uralensis* Fischer, in Alcohol-Induced Fatty Liver Disease. *BMC Complement. Altern. Med.* 16, 1–10. <https://doi.org/10.1186/s12906-016-0997-0>.
51. 51. Eldalawy, R., Al-Ani, W.M.K., AbdulKareem, W., 2021. Phenotypic, Anatomical and Phytochemical Investigation of Iraqi *Silybum marianum*. *J. Phys. Conf. Ser.* 1879, 1–11. <https://doi.org/10.1088/1742-6596/1879/2/022029>.
52. 52. Maione, F., Russo, R., Khan, H., Mascolo, N., 2016. Medicinal Plants with Anti-Inflammatory Activities. *Nat. Prod. Res.* 6419, 1–10.
53. 53. Liperoti, R., Vetrano, D.L., Bernabei, R., Onder, G., 2017. Herbal Medications in Cardiovascular Medicine. *J. Am. Coll. Cardiol.* 69, 1188–1199. <https://doi.org/10.1016/j.jacc.2016.11.078>.
54. 54. Adegbola, P., Aderibigbe, I., Hammed, W., Omotayo, T., 2017. Antioxidant and Anti-Inflammatory Medicinal Plants Have Potential Role in the Treatment of Cardiovascular Disease. *Am. J. Cardiovasc. Dis.* 7, 19–32.
55. 55. Arranz, E., Jaime, L., López de las Hazas, M.C., Reglero, G., Santoyo, S., 2015. Supercritical Fluid Extraction as an Alternative Process to Obtain Essential Oils with Anti-Inflammatory Properties from Marjoram and Sweet Basil. *Ind. Crops Prod.* 67, 121–129. <https://doi.org/10.1016/j.indcrop.2015.01.012>.
56. 56. Li, Z.M., Xu, S.W., Liu, P.Q., 2018. *Salvia miltiorrhiza* Burge (Danshen): A Golden Herbal Medicine in Cardiovascular Therapeutics. *Acta Pharmacol. Sin.* 39, 802–824. <https://doi.org/10.1038/aps.2017.193>.
57. 57. Kadhim, M.J., Kaizal, A.F., Hameed, I.H., 2016. Medicinal Plants Used for Treatment of Rheumatoid arthritis. *Int. J. Pharm. Clin. Res.* 8, 1685–1694.
58. 58. Murugananthan, G., Sudheer, K.G., Sathya, C.P., Mohan, S., 2013. Anti-Arthritic and Anti-Inflammatory Constituents from Medicinal Plants. *J. Appl. Pharm. Sci.* 3, 161–164. <https://doi.org/10.7324/JAPS.2013.3429>.
59. 59. Wambugu, S.N., Mathiu, P.M., Gakuya, D.W., Kanui, T.I., Kabasa, J.D., Kiama, S.G., 2011. Medicinal Plants Used in the Management of Chronic Joint Pains in Machakos and Makueni Counties. Kenya. *J. Ethnopharmacol.* 137, 945–955. <https://doi.org/10.1016/j.jep.2011.06.038>.
60. 60. Dragos, D., Gilca, M., Gaman, L., Vlad, A., Iosif, L., Stoian, I., Lupescu, O., 2017. Phytomedicine in Joint Disorders. *Nutrients* 9, 1–18. <https://doi.org/10.3390/nu9010070>.
61. 61. Xia, X., May, B.H., Zhang, A.L., Guo, X., Lu, C., Xue, C.C., Huang, Q., 2020. Chinese Herbal Medicines for Rheumatoid Arthritis: Text-Mining the Classical Literature for Potentially Effective Natural Products. *Evidence-Based Complement. Altern. Med.* 2020, 1–14. <https://doi.org/10.1155/2020/7531967>.
62. 62. Kadhim, M.J., Kaizal, A.F., Hameed, I.H., 2016. Medicinal Plants Used for Treatment of Rheumatoid arthritis. *Int. J. Pharm. Clin. Res.* 8, 1685–1694.
63. 63. Vogl, S., Picker, P., Mihaly-Bison, J., Fakhrudin, N., Atanasov, A.G., Heiss, E.H., Wawrosch, C., Reznicek, G., Dirsch, V.M., Saukel, J., Kopp, B., 2013. Ethnopharmacological *in Vitro* Studies on Austria's Folk Medicine-An Unexplored Lore *in Vitro* Anti-Inflammatory Activities of 71 Austrian Traditional Herbal Drugs. *J. Ethnopharmacol.* 149, 750–771. <https://doi.org/10.1016/j.jep.2013.06.007>.
64. 64. Da Silva, E., S'a, R.D.C., Andrade, L.N., De Oliveira, R.D.R.B., De Sousa, D.P., 2014. A Review on Anti-Inflammatory Activity of Phenylpropanoids Found in Essential Oils. *Molecules* 19, 1459–1480. <https://doi.org/10.3390/molecules19021459>.
65. 65. Hossen, M.J., Jeon, S.H., Kim, S.C., Kim, J.H., Jeong, D., Sung, N.Y., Yang, S., Baek, K.S., Kim, J.H., Yoon, D.H., 2015. *In Vitro* and *in Vivo* Anti-Inflammatory Activity of *Phyllanthus acidus* Methanolic Extract. *J. Ethnopharmacol.* 168, 217–228. <https://doi.org/10.1016/j.jep.2015.03.043>.
66. 66. Vogl, S., Picker, P., Mihaly-Bison, J., Fakhrudin, N., Atanasov, A.G., Heiss, E.H., Wawrosch, C., Reznicek, G., Dirsch, V.M., Saukel, J., Kopp, B., 2013. Ethnopharmacological *in Vitro* Studies on Austria's Folk Medicine-An Unexplored Lore *in Vitro* Anti-Inflammatory Activities of 71 Austrian Traditional Herbal Drugs. *J. Ethnopharmacol.* 149, 750–771. <https://doi.org/10.1016/j.jep.2013.06.007>.

67. Sangiovanni, E., Lorenzo, C.D., Colombo, E., Colombo, F., Fumagalli, M., Frigerio, G., Restani, P., Agli, M.D., 2015. The Effect of in Vitro Gastrointestinal Digestion on the Anti-Inflammatory Activity of *Vitis vinifera*. Food Funct. 2015, 1–11. <https://doi.org/10.1039/c5fo00410a>.
68. Suroowan, S., Mahomoodally, M.F., 2016. A Comparative Ethnopharmacological Analysis of Traditional Medicine Used against Respiratory Tract Diseases in Mauritius. J. Ethnopharmacol. 177, 61–80. <https://doi.org/10.1016/j.jep.2015.11.029>.
69. Niu, X., Li, Y., Li, W., Hu, H., Yao, H., Li, H., Mu, Q., 2014. The Anti-Inflammatory Effects of *Caragana tangutica* Ethyl Acetate Extract. J. Ethnopharmacol. 152, 99–105. <https://doi.org/10.1016/j.jep.2013.12.026>.
70. Santana, F.P.R., Pinheiro, N.M., Mernak, M.I.B., Righetti, R.F., Martins, M.A., Lago, J.H., Lopes, F.D., Tibério, I.F., Prado, C.M., 2016. Evidences of herbal medicine-derived natural products effects in inflammatory lung diseases. Mediators Inflamm. 2016 <https://doi.org/10.1155/2016/2348968>.
71. Kim, H.P., Lim, H., Kwon, Y.S., 2017. Therapeutic Potential of Medicinal Plants and Their Constituents on Lung Inflammatory Disorders. Biomol. Ther. 25, 91–104.
72. Dragos, D., Gilca, M., Gaman, L., Vlad, A., Iosif, L., Stoian, I., Lupescu, O., 2017. Phytomedicine in Joint Disorders. Nutrients 9, 1–18. <https://doi.org/10.3390/nu9010070>.
73. Hossen, M.J., Jeon, S.H., Kim, S.C., Kim, J.H., Jeong, D., Sung, N.Y., Yang, S., Baek, K.S., Kim, J.H., Yoon, D.H., 2015. In Vitro and in Vivo Anti-Inflammatory Activity of *Phyllanthus acidus* Methanolic Extract. J. Ethnopharmacol. 168, 217–228. <https://doi.org/10.1016/j.jep.2015.03.043>.
74. Nunes, C.R., Arantes, M.B., de Faria, P.S.M., da Cruz, L.L., de Souza, P.M., de Moraes, L. P., Vieira, I.J.C., de Oliveira, D.B., 2020. Plants as Sources of Anti-Inflammatory Agents. Molecules 25, 1–22. <https://doi.org/10.3390/molecules25163726>.
75. Arifin, Y.F., Hamidah, S., Panjaitan, S., Suhartono, E., 2015. In Vitro Anti-Inflammatory Activities of Red Gemor (*Nothaphoebe Cf Umbelliflora*). J. Med. Bioeng. 4, 312–317. <https://doi.org/10.12720/jomb.4.4.312-317>.
76. Adebayo, S.A., Dzoyem, J.P., Shai, L.J., Eloff, J.N., 2015. The Anti-Inflammatory and Antioxidant Activity of 25 Plant Species Used Traditionally to Treat Pain in Southern African. BMC Complement. Altern. Med. 15, 1–10. <https://doi.org/10.1186/s12906-015-0669-5>.
77. Mutuma, G.G., Ngeranwa, J., Kin, G.M.A., Kiruki, S., 2020. Phytochemical and Anti-Inflammatory Analysis of *Prunus Africana* Bark Extract. Res. J. Pharmacogn. 7, 31–38. <https://doi.org/10.22127/rjp.2020.229941.1583>.