Review article

Anti-inflammatory potential of medicinal plants

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Abstract: Inflammation is said to be a healthy component of the body immune system's reaction. Inflammation is characterised by four key symptoms: pain, redness, heat or warmth and swelling. As secondary metabolites, plants may produce a wide range of phytochemical compounds, which possess anti-inflammatory characteristics. Herbal remedies are important therapies for a wide range of ailments all over the world. There are around 7 500 species of medicinal plants, including representatives from over 17 000 flowering plant species. Even when synthetic chemistry has developed out their expectations, the use of natural ingredients in the manufacture of drugs used in contemporary medicine is unparalleled. By interfering with the biology of inflammation, anti-inflammatory medications may assist to minimise tissue damaging and increase patient's comfort. Because of the bulky figure of species reachable for study, the effective development of novel naturally taking place anti-inflammatory drugs is mostly dependent on a multidisciplinary approach to discovering new chemicals. Despite the statistic that many review papers have been produced in this field, the conventional of them simply examined the issue from an area perspective. Several non-steroidal anti-inflammatory drugs have been shown to reduce inflammation and pain by decreasing the isoform of the cyclooxygenase enzyme's digestion of arachidonic acid, hence lowering prostaglandin production. Non-steroidal anti-inflammatory drugs have a host of harmful effects. There are, however, medicinal herbs with anti-inflammatory pharmacological properties that have few or no negative effects.

Keywords: Herbs, inflammation, medicinal plants, potential

Introduction

Inflammation is the body's extreme reaction to any type of injury. The four primary indicators of swelling are pain, warmth, redness and swelling. When a site of the human body is injured, the arterioles in the neighbouring tissue widen. This increases blood stream to the affected area, resulting in redness [1]. Inflammation is a ubiquitous process that occurs when homeostasis is disrupted such as when there is damage, exposure to contaminating substances, or infection. It is also triggered by innate immune system receptors for

the removal of pathogens when they are identified [2]. Inflammation is classified into two types: acute and chronic. Acute inflammation may be the system's initial reaction to cruel stimuli. In chronic inflammation, the inflammatory reaction is out of proportion causing harm to the tissues. Cyclooxygenase (COX) is a vital enzyme in the synthesis of prostacyclins, prostaglandins and thromboxanes, all of which are tangled in inflammation, platelet aggregation and pain [3]. Prostaglandins, thromboxane and prostacyclins are tangled in inflammation, platelet aggregation and pain [5]. Vaso-active chemicals rise the permeability of such arterioles, allowing blood cells, blood proteins, chemical substances and fluid to collect in that area. This fluid builds up causes swelling and can be painful because it compresses nerves in the site. Prostaglandins may also cause nerve irritation and contribute to pain [4]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed medications worldwide [5] and are used to treat acute and chronic pain caused by an inflammatory progression. NSAIDs are class of medications whose actions are all linked to COX inhibition in the release of prostaglandins and thromboxane [6, 7]. The main pharmacological mechanism of NSAIDs is the central and peripheral inhibition of COX, which affects with the translation of arachidonic acid into prostaglandins E_2, thromboxane and prostacyclins. Two different COX enzymes namely COX-1 and COX-2 involved in the action of NSAIDs. COX-1 is found in the majority of cells including foetal/amniotic fluid and is involved in physiological functions as regulation and protection. COX-2 is triggered by inflammation and pro-inflammatory cytokines [8]. NSAIDs have long been used in humans. As a result, long-term use of these drugs results in negative effects and harms human normal systems such as renal, cardiovascular, gastric lesions and gastrointestinal damage [9, 10].

Natural products (NPs) are any substance found in the universe. NP is a biological compound or substance produced by an alive entity (animals, microbes or plants) that has pharmacological activity and may be clinically beneficial in either raw or modified form [11]. Traditional herbs and preparations for example, were regarded as drugs in the Ayurvedic (a natural system of medicine) medical system; the "Sushruta Samhita" (an Ayurvedic classic) contains approximately 700 plants for the treatment of 1100 ailments. An enormous amount of information was provided by numerous traditional medical systems (Chinese materiamedica, Greek, Egyptian, Arab and Mesopotamian) as well as folk medicine (ethno-medicine). The separation of morphine from opium by Serturner (1804) marked the beginning of modern NP chemistry. Many of these discoveries resulted in the isolation of bioactive isolated chemicals as quinine (1820) isolated from cinchona, cocaine (1859), strychnine (1818), penicillin, tubocurarine (1935) and other bioactive isolated compounds [11]. Over 80% of the approved therapeutic medicines were derivate of naturally occurring chemicals or were inspired by natural substance. NPs have extensively been studied and it was discovered that 33% of the 1394 small molecule approved drugs introduced between 1981 and 2019 were natural items or its derivates and 35% were built around pharmacophore from a NP [12]. Plants may synthesise a wide range of phytochemical constituents as secondary metabolites. Several phytochemicals have successfully been used in treatment of variation of human disorders. The World Health Organization (WHO) has attempted to recognize all medical plants used around the world, resulting in a list of over 20 000 species. The majority of medicinal plant parts are used as raw pharmaceuticals and have a variety of clinical properties [13]. Plants have enormous potential in traditional medicine for the development of novel medications as well as in the treatment of chronic and infectious diseases [14]. The goal of this review is to look at the fundamental aspects of some medicinal herbs' anti-inflammatory properties to assist current and future

researchers in identifying anti-inflammatory medicinal plants.

Plants with anti-inflammatory potential

Ajuga laxmannii (F. Lamiaceae): Polymorphonuclear total leukocytes, leukocytes, oxidative stress and phagocytosis all decreased in response to the anti-inflammatory properties of *Ajugalaxmannii* ethanolic extract. In terms of antioxidative stress and anti-inflammatory properties, A. *laxmannii* extract at 50 mg/ml outperformed diclofenac in tests. As a result of the findings, A. *laxmannii* is a valuable foundation of bioactive products that may be used as anti-inflammatory agents in a variety of herbal medicines [15].

Allium sativum (F.Amaryllidaceae): Garlic oil has anti-inflammatory properties because it inhibits the formation and disassembly of the cytoskeleton [16].

Aloe ferox (F. Asphodelaceae): The anti-inflammatory properties of *Aloe ferox* extract are attributed to its gel, which contains three malic acid acylated polysaccharides. Aloe resin, a plant-derived anti-inflammatory chemical, is also present. It also contains anti-inflammatory and anti-swelling enzymes carboxypeptidase and brady kinase [17].

Aegle marmelos (F. Rutaceae): In Wister rat, the anti-inflammatory effect of an aqueous extract of Bilwa root bark was considered using a carrageenan induced paw oedema model and a cotton pellet induced granuloma model, as well as the standard medicines indomethacin and Bilwa. The findings showed that the inhibition response was due to anti-inflammatory properties [18].

Anacardiumoccidentale (F. Anacardiaceae): The leaf extract has anti-inflammatory properties and oleamide was identified as one of the most bioactive components linked to the plant's anti-inflammatory properties [19].

Cassia fistula (F. Caesalpiniaceae): The bark extracts have a noteworthy anti-inflammatory outcome in acute and chronic anti-inflammatory models of inflammation in rats. ROS, endogenous and exogenous, have been linked to the pathophysiology of diseases as diabetes, atherosclerosis, cancer, arthritis and the ageing process. The presence of ROS complicates inflammatory disorders. Flavonoids and bioflavonoids are the main anti-inflammatory components of Cassia fistula [20].

Calamintha nepeta (F.Limiaceae): It is anti-inflammatory because it inhibits COX-2 synthesis by 40% [21].

Cassia occidentalis (F. Caesalpiniaceae): Sreejith and colleagues investigated the anti-inflammatory properties of the *Cassia occidentalis* plant as a whole using an ethanolic extract. In a carrageenan-induced paw oedema model, a dosage of 250 mg/kg was used to assess the anti-inflammatory property. The results showed a noteworthy drop in malondialdehyde heights in murine liverwort microsomes and a significant reduction in carrageenan induced inflammation at a dosage of 250 mg/kg in mice [22].

Citrus limetta (F. Rutaceae): The primary constituent of *Citrus limetta* essential oils (EOs) is limonene, a monoterpene hydrocarbon. When macrophages were pre-treated with C. limetta EOs, the amalgamation of proinflammatory cytokines as interlukin-6, tumour necrosis factor- and interlukin-1 was inhibited in lipopolysaccharide-induced inflammation, as was the amalgamation of ROS in H_2O_2-induced oxidative stress. An *in vivo* study, on the other hand, discovered that on the application of volatile oil topically, it reduced 12-O-tetradecanoylphorbol-13 acetate-induced ear weight, ear thickness, proinflammatory cytokine generation, lipid peroxidation and improved histological damages in the ear tissues [23].

Citrus limon (F. Rutaceae):Citrus limon EOs administered orally at doses of 50 mg/kg, 100 mg/kg and 150 mg/kg significantly reduced the sum of writhes, while the maximum dose significantly reduced the sum of paw licking indicating an anti-inflammatory effect [24].

Cissampelos sympodialis (F. Menispermaceae): The alkaloids total fraction and ethanolic extract derived from *Cissampelos sympodialis* aerial parts have anti-inflammatory properties, as they reduced tumour necrosis factor- and interlukin-1 levels while increasing interleukin-1 and glutathione–glutathione levels [25].

Coriandrum sativum (F. Apiaceous): Coriander oil was found to have anti-inflammatory properties in an *in vivo* ultraviolet erythema test [26].

Cynodondactylon (F. Poaceae): Rat paw oedema was induced by serotonin, carrageenan, histamine, dextran and the cotton pellet technique were used to assess the anti-inflammatory efficacy of an aqueous extract of *Cynodon dactylon* at various dosage. The experiment was done at three different dose levels: 200 mg/kg, 400 mg/kg and 600 mg/kg, orally. The extract of *Cynodon dactylon* was safe when taken orally at all dosages tested, with no mortality up to 4 gm/kg of Aq. extract *Cynodon dactylon* exhibited strong anti-inflammatory properties in wholly of the models. The extract was recognised to significantly reduce ($p < 0.001$) the production of oedema caused by histamine, carrageenan, dextran and serotonin after 3 and 5 hours [27].

Cyperusrotundus (F. Cyperaceae): Cyperusrotundus EOs demonstrated a dose-dependent reduction in paw oedema rats from the second hour after carrageenan injection ($p < 0.01$). This EO inhibited pain due to inflammation ($p < 0.01$) at 500 mg/kg but pain caused by inflammation was meaningfully ($p < 0.05$) prevented at minimum doses [28].

Cuminum cyminum (F. Apiaceae): The anti-inflammatory ability of Cuminum cyminum volatile' oil in carrageenan-induced rat-paw oedema revealed that at a dose of 0.1 ml/kg, i.p., cumin volatile oil inhibited rat paw oedema in a dose responded manner when equated to the control group. Anti-inflammatory movement was also seen to be analogous to diclofenac sodium [29]. Cumin EOs significantly suppressed the mRNA expressions of inducible nitric oxide synthase, COX-2, interleukin-1 and IL-6 in lipopolysaccharide-stimulated RAW 264.7 cells, as determined by real-time polymerase chain reaction, PCR. Furthermore, western blotting studies revealed that cumin EOs inhibited the phosphorylation of ERK and c-Jun N-terminal kinase in response to LPS-induced transcriptional activation of nuclear factor kappa (NF-) (JNK). As a result, cumin EOs were found to inhibit the NF- and mitogen-activated protein kinases ERK and JNK signalling in LPS-stimulated RAW264.7 cells, resulting in anti-inflammatory effects [30].

Dendropanaxmorbifera (F. Araliaceae): Methanolic extracts of *Dendropanax morbifera* inhibited the production of LPS induced proinflammatory cytokines and mediators by defeating the expression of inducible nitric-oxide synthase and COX-2, as well as inhibiting the ERK1/2 signalling pathway. Furthermore, in leaf extracts phenolic compound analysis using high performance liquid chromatography (HPLC) discovered compounds such as quercetin, myricetin, rutin, resveratrol, chlorogenic acid, catechin and ferulic acid which are thought to be responsible for the anti-inflammatory activity [31].

Glycyrrhizaglabra (F. Fabaceae): The roots of Glycyrrhizaglabra (liquorice) were known to roman medics as *Radixdulcis* and to Arab physicians as a cough remedy and the plant have been grown in Europe since the 18th century for its distinctive taste. Glycyrrhiza glabra contains the anti-inflammatory triterpenes glycyrrhizin (6 - 13%) and glycyrrhizic acid [32].

Ipomoea pescaprae (F. Convolvulaceae): Ipomoea pescaprae leaf extracts were effective in treating dermatitis caused by jellyfish stings and edoema caused by ethyl phenyl propiolate in animals [33].

Emblica officinalis (F. Euphorbiaceae): It is a tree native to China, Indonesia, India and Malay Peninsula. It is used in these areas for its anti-inflammatory and antipyretic properties. Recent research has revealed that the aqueous fraction of methanol extract of leaves has anti-inflammatory properties. The effect of fraction on the releases of inflammatory mediators as leukotriene B4,

thromboxane and platelet activating factor was studied. At low doses, the aqueous fraction of methanol extract reduced human PMN migration [34].

Linn, Jasminum sambac (F. Oleaceae): Jasminum sambac L is widely grown throughout India, and its roots and leaves have long been used to treat fever, discomfort, and inflammation. Its leaves have anti-inflammatory properties that have been demonstrated. [35].

Nicotianatobacum (F. Solanaceae): *Nicotianatobacu*m leaf extract is used as an anti-inflammatory. Chemical elements that are mostly effective include 4-vinylguaiacol, 1, 8-cineole, acetaldehyde, alkaloids, anabasine, nicotinic acid, acetophenone, nicotine, sorbitol,scopoletin, quercitrin, tocopherol, trigonelline, stigmasteroland trigonelline [36].

Leonotis ocymifolia (F. Lamiaceae): In mouse models, the anti-inflammatory action of 80% methanolic leaf extract of *Leonotis ocymifolia* reduced paw edoema by 75% after six hours of induction with carrageenan. Furthermore, it was discovered that all of the extract doses tested slowed granuloma synthesis significantly [37].

Origanumehrenbergii (F. Lamiaceae): The anti-inflammatory action of *Origanumehrenbergii* EOs in lipopolysaccharide-induced inflammation in RAW264.7 cells was investigated and significant reduction in nitrous oxide generation was reported [38].

Persicariachinensis (F. Polygonaceae): The molecular mechanism of the methanolic extract of *P. chinensis* against lipopolysaccharide-induced nitric oxide and PGE2 in RAW264.7, macrophages discovered that it significantly reduced the expression of lipo-polysaccharide-induced proinflammatory cytokines. The activation and phosphorylation of activator protein-1 and mitogen-activated-protein kinase were reduced in both U937 cells and lipopolysaccharide stimulated RAW264.7 cells. As a result, these findings stalwartly suggested that a *P. chinensis* methanolic extract could be used as a treatment for mitogen activated protein kinase/activator protein mediated-inflammation [39].

Olea europaea (F. Oleaceae): Extra virgin olive oil from *Olive tree* was found to have anti-inflammatory activity comparable to dexamethasone treatment in rats with carrageenan-induced paw oedema [40].

Phyllanthus acidus (F. Phyllanthaceae): For many years, *Phyllanthusacidus* has been used to treat respiratory problems, gastrointestinal problems, hepatitis, bronchitis, rheumatism, and asthma. Kim and colleagues discovered that methanolic extract of P. acidus aerial parts inhibited prostaglandin E_2 and nitric oxide production while also preventing morphological changes in lipo-polysaccharide-treated RAW 264.7 cells [41]. Furthermore, this extract inhibited the expression of inducible nitric oxide synthase and COX-2, as well as lowering NF- nuclear levels. Among the flavonoids discovered in the methanolic extract of *P. acidus* aerial parts, kaempferol and quercetin were found to be somewhat active anti-inflammatory substances. As a result, it was discovered that the methanol extract of *P. acidus* aerial parts inhibited downstream transcription NF gene in vivo and *in vitro* [41].

Syzygium caryophyllatum (F. Myrtaceae): The *in vitro* capacity of various doses of *Syzygium caryophyllatum* aqueous root extract to prevent inflammation has also been demonstrated using a heat-induced egg albumin denaturation bio assay technique [42].

Tephrosia purpurea (F. Fabaceae): The anti-inflammatory effect of different dosages of 50% alcoholic extract of T. purpurea root was studied using carrageenan and the produced paw oedema method [43].

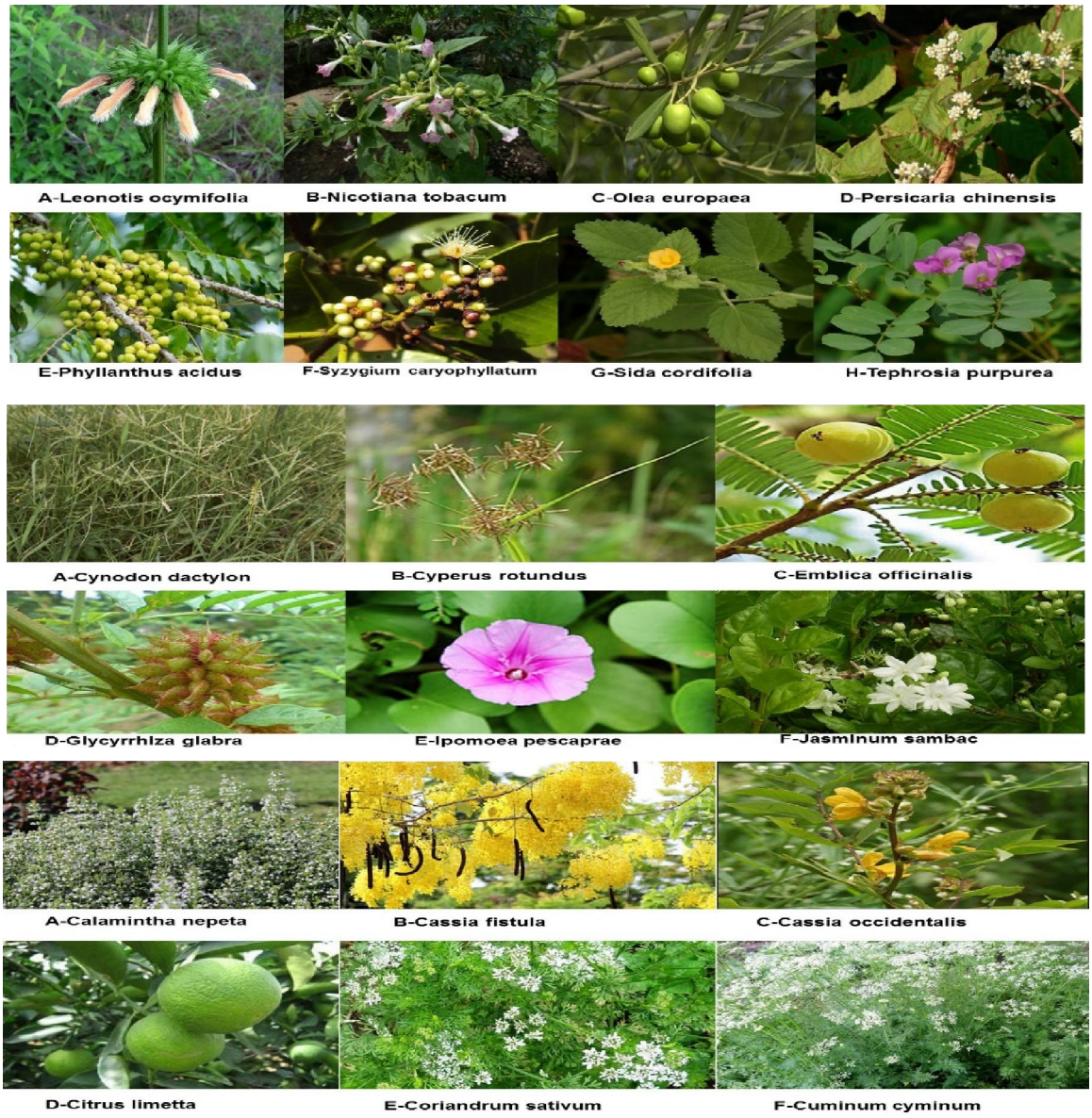
Solanum melongena (F. Solanaceae): An aqueous extract of *Solanum melongena* L leaves was tried for anti-inflammatory activity. In doses of 200 mg/kg and 400 mg/kg, the percentage of inhibition of the aqueous extract of S. melongena L was 42%, which was less than the 64.5% inhibition of the

conventional pharmaceutical aspirin. Anti-inflammatory characteristics are possessed by chemical components such as ascorbic acid, alanine, arginine and caffeic acid [44, 45].

Zingiber officinale (F. Zingiberaceae): Shimoda and colleagues [55] investigated *Zingiber officinale's* anti-inflammatory effect by producing 40% ethanolic extract from dried red ginger and testing its anti-inflammatory efficacy in acute and chronic inflammation models. The results revealed a powerful suppressive result on acute and chronic inflammation, with macrophage activation inhibition appearing to play a role in this anti-inflammatory action [46].

Sida cordifolia Linn (F. Malvaceae): It is a Malvaceae family perennial mallow subshrub. *Sida cordifolia* is practised in traditional systems of medicine to treat oral mucosa inflammation, blennorrhoea, nasalcongestion and asthmatic bronchitis [47]. It has been explored as an anti-inflammatory, a cell-proliferation inhibitor and a promoter of liver-growth [48].

Figure 1: Some common medicinal plants with anti-inflammatory activity



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Conclusion: In recent years, anti-inflammatory plants have been the focus of research. Inflammatory disorders are common in the ageing societies of both developed as well developing countries, but the treatments used to treat them can have serious side effects. Curcumin, boswellic acid, resveratrol, baicalein, ursolic acid, betulinic acid and oleanolic acid are among the plant-derived compounds being studied as potential anti-inflammatory medications. The active ingredients of which can be isolated using various separation procedures. These kinds of studies may direct to the discovery of new compounds that can aid in the treatment of inflammatory diseases.

Author contributions: MA: Design the study and writing - review and editing the manuscript. MKA: collecting and analyses of the data. MMA: Contribute data analysis. All the authors approved the final version of the manuscript.

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