Anti inflammatory Potential of some Medicinal Plants

Muhammad Akhlaq[1], Asif Iqbal[1], Muhammad Khaleeq Alum[2], Sheraz Muhammad saddique[1], Muhammad Amjid Chishti[1], Neelum Shahzadi[1] ,Anum Aslam[1]

[1]Faculty of Eastern Medicine, Hamdard University, Karachi, Pakistan.
[2]Department of Zoology, govt. Emerson college, Multan, Punjab Pakistan.

Corresponding author: Muhammad Akhlaq
Email adress: muhammadakhlaq377@gmail.com
Cell:+923012028820

Abstract

Inflammation considered as a healthy phenomenon of the body immune system's reaction. Inflammation is characterised by four key symptoms: pain, redness, heat or warmth, and swelling. Herbal remedies are important therapies for a wide range of ailments all over the world. There are around 7500 species of medicinal plants, including representatives from over 17,000 flowering plant species. Even when synthetic chemistry has evolved out their expectations, the use of natural ingredients in the manufacture of drugs used in contemporary medicine is unparalleled. Several nonsteroidal antiinlammatory 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. Nonsteroidal antiinflammatory drugs (NSAIDs) have harmful effects. There are, however, medicinal herbs with antiinflammatory pharmacological properties that have few or no negative effects.This review contains data about medicinal herbs' having anti-inflammatory effects, and it will be helpful for new researchers and practitioners to find anti-inflammatory herbs.

Keywords

Herbs, Inflammation, Medicinal plants, NSAID,Potential.

1. INTRODUCTION

Inflammation is the body's extreme reaction to any type of injury. The four primary indicators of swelling are pain, warmth, rednessand swelling. At thesite of injury, the arterioles in the neighbouring tissue widens. This increases blood stream to the affected area, resulting in redness (Burke *et al.*, 2006). Inflammation is a ubiquitous process that occurs when homeostasis is disrupted, such as when there is damage, exposure to contaminating substances, or infection, and it is also triggered by innate immune system receptors for the removal of pathogens when they are identified (Campos, 2014). Inflammation is classified into two types:

Acute andchronic. Acute inflammation may be the system's initial reaction to hurtful stimuli. In chronic inflammation, the inflammatory reaction is out of proportion, causing harm to the tissues. Cyclooxygenase (COX) is a crucial enzyme in the synthesis of prostacyclins, prostaglandins, &thromboxane's, all of which are tangled in inflammation, platelet aggregation and pain (Pilotto *et al*., 2010). Vasoactive chemicals raise the permeability (pore size) of such arterioles, allowing blood cells, proteins, chemical substances and fluid to collect in that area. This fluid build-up causes swelling and can be painful because it compresses nerves in the site. Prostaglandins may also cause nerve irritation and contribute to pain(Grosser *et al*., 2011). Nonsteroidal antiinflammatory drugs (NSAIDs) are the most commonly prescribed medications worldwide (Virshette *et al*., 2019) and they are used to healthe acute & 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 (Pereira Leite *et al*., 2017) (Sostres & Lanas, 2016). The main pharmacology of NSAIDs is the central and peripheral inhibition of COX, affecting the translation of arachidonic acid into prostaglandins E2, thromboxane and prostacyclins. Both COX-1, COX-2, act in the body, are two enzymes 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 (Patel *et al*., 2016). NSAIDs, or nonsteroidal anti-inflammatory drugs, have long been used in humans. As a consequence, long-term use of these drugs results in negative effects and harms human normal systems such as the hepatic and gastric system. As anoutcome of adversative effects such as renal, cardiovascular, gastric lesions and gastrointestinal damage (Huerta *et al*., 2005) (Shih & Chang, 2007). Natural products (NPs) are biological compound/substance produced by analive entity (animals, microbes or plants) that possesses pharmacological activities and clinically beneficial in either raw or modified form (traditional remedies) (Goel *et al*., 2020). Traditional herbs and preparationsfor example, were regarded as drugs in the Ayurvedic medical system; the "Sushruta Samhita" (an Ayurvedic classic) contains approximately 700 plants for the treatment of 1100 ailments. A vast amount of information was provided by numerous traditional medical systems (Chinese materiamedica, Greek, Egyptian, Arab and Mesopotamian) as well as folk medicine (Ethnomedicine) and include Unani medicines as well. 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) derivedfrom cinchona, cocaine (1859), strychnine (1818), penicillin, tubocurarine (1935)and other bioactive isolated compounds (Goel *et al*., 2020). Over 80% of approved therapeutic medicines were derivateof naturally occurring chemicals or were inspired by natural substance. The NPs have been extensively studied, and 33 percent of the 1394 small molecule approved drugs introduced between 1981 and 2019 were natural items or its derivates and 35 percent were built around pharmacophore from an NP (Newman & Cragg, 2020). Plants may synthesise a wide range of phytochemical constituents as secondary metabolites. Several phytochemicals have been used successfully in treatment ofvariety of human disorders. The World Health Organization (WHO) has attempted to identify 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 (Verma, 2016). Plants have enormous potential in traditional medicine for the development of novel medications as well as the treatment of chronic and infectious diseases. By interfering with the biology of inflammation, anti inflammatory medications may assist to minimise tissue damaging and increase patient's comfort. The effective development of novel naturally taking place anti inflammatory drugs is mostly dependent on a multidisciplinary approach to discovering new chemicals (Thatoi & Dutta, 2009). The goal of this review is to look at the fundamental aspects of many medicinal herbs' anti-inflammatory properties.

Plants with anti-inflammatory potential

Ajuga laxmannii (Lamiaceae)

Polymorphonuclear total leukocytes, leukocytes, oxidative stress& phagocytosis all decreased in response to the anti-inflammatory properties of *Ajuga laxmannii* 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 (Toiu et al., 2018).

Allium sativum (liliaceae)

Garlic oil has anti-inflammatory properties because it inhibits the formation and disassembly of the cytoskeleton.(Arreola *et al*., 2015).

Aloe ferox (Asphodelaceae)

The antiinflammatory properties of *Aloe ferox* extract are attributed to its gel, which contain 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 (Devaraj & Karpagam, 2011).

Aegle marmelos (Rutaceae):

In albino rats, the anti inflammatory effect of an aqueous extract of bealgri 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 inhibition has anti-inflammatory properties (Benni *et al*., 2011).

Anacardium occidentale (Anacardiaceae):

Anacardium occidentale leaf extract has anti-inflammatory properties, and oleamide has been identified as one of the most bioactive components linked to the plant's anti-inflammatory properties (Awakan *et al.*, 2018).

Cassia fistula (Caesalpiniaceae):

Cassia fistula bark extracts have a noteworthy antiinflammatory outcome in both acute and chronic antiinflammatory models of inflammation in rats. ROS, both 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* (Ilavarasan *et al.*, 2005).

Calamintha nepeta (Limiaceae):

Calamintha nepeta is antiinflammatory because it inhibits COX-2 synthesis by 40.10% (Galasso *et al.*, 2014).

Cassia occidentalis (Caesalpiniaceae):

The antiinflammatory properties of the *Cassia occidentalis* plant explored 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 antiinflammatory property. The results showed a note worthydrop in malondialdehyde heights in murine liverwort microsomes and a significant reduction in carrageenan induced inflammation at a dosage of 250 mg/kg in mice (Sreejith *et al*., 2010).

Citrus limetta (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-13acetate-induced ear weight, ear thickness, proinflammatory cytokine generation, lipid peroxidation, and improved histological damages in the ear tissues (Maurya *et al*., 2018).

Citrus limon (Rutaceae):

Citrus limon EOs administered orally at doses of 50mg, 100mg and 150 mg/kg significantly reduced the sum of writhes, while the maximum dose significantly reduced the sum of paw licking indicating an antiinflammatory effect (De Nunzio *et al*., 2020).

Cissampelos sympodialis (Menispermaceae):

The alkaloids total fraction and ethanolic extract derived from *Cissampelos sympodialis* aerial parts have antiinflammatory properties, as they reduced tumour necrosis factor- and interlukin-1 levels while increasing interlukin10 and glutathione–glutathione levels (Sami et al., 2021).

Coriandrum sativum (Apiaceous):

Coriander oil was found to have antiinflammatory properties in an in vivo ultraviolet erythema test (Reuter *et al*., 2008).

Cynodon dactylon (Poaceae):

Rat paw oedema was induced by serotonin, carrageenan,histamine,dextran and the cotton pellet technique were used to assess the antiinflammatory efficacy of an aqueous extract of *Cynodondactylon* at various dosage. The experiment was done at 3 different dose levels: 200mg, 400mg, and 600 mg/kg orally. The extract of Cynodon dactylon was safe when taken orally at all dosages tested, with no mortality up to 4g/kg of Aq. extract Cynodon dactylon exhibited strong antiinflammatory 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 & 5 hours (Garg & Paliwal, 2011).

Cyperus rotundus (Cyperaceae):

Cyperusrotundus EOs demonstrated a dose-dependent reduction in paw edoema 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 (Bandgar *et al*., 2010).

Cuminum cyminum (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 (Feng *et al*., 2016). Cumin EOs significantly suppressed the mRNA expressions of inducible nitric oxide synthase, cyclooxygenase-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 antiinflammatory effects (Yin *et al*., 2020).

Dendropanax morbifera (Araliaceae):

Methanolic extracts of *Dendropanax morbifera* inhibited the production of LPS induced pro inflammatory 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 highperformance liquid chromatography discovered compounds such as quercetin, myricetin, rutin, resveratrol, chlorogenic acid catechin and ferulic acid which are thought to be responsible for the antiinflammatory activity (Noh *et al*., 2015).

Glycyrrhiza glabra (Fabaceae):

The roots of Glycyrrhiza glabra (liquorice) were known to Roman medics as *Radixdulcis* and to Arab physicians as a cough remedy, and the plant has 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 (Kaur *et al*., 2013).

Ipomoea pescaprae (Convolvulaceae):

Ipomoea pescaprae leaf extracts were effective in treating dermatitis caused by jellyfish stings and edoema caused by ethyl phenyl propiolate in animals (Pongprayoon *et al*., 1991).

Emblica officinalis (Euphorbiaceae):

Emblica officinalis is a tree native to China, Indonesia, India and Malay Peninsula. It is used in these areas for its antiinflammatory and antipyretic properties. Recent research has revealed that the aquas 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 aquas fraction of methanol extract reduced human PMN migration (Asmawi *et al*., 1993).

Jasminum sambac (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. (Sengar *et al*., 2015).

Nicotiana tobacum (Solanaceae):

Nicotianatobacum 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, stigmasterol and trigonelline (Azab *et al*., 2016).

Leonotis ocymifolia (Lamiaceae):

In mouse models, the anti-inflammatory action of an 80 percent methanolic leaf extract of *Leonotis ocymifolia* reduced paw edoema by 75 percent after six hours of induction with carrageenan. Furthermore, it was discovered that all of the extract doses tested slowed granuloma synthesis significantly (Alemu *et al*., 2018).

Origanum ehrenbergii (Lamiaceae):

The antiinflammatory action of *Origanumehr enbergii* EOs in lipopolys accharide-induced inflammation in RAW264.7 cells was investigated and significant reduction in nitrous oxide generation was reported (Miguel, 2010).

Persicaria chinensis (Polygonaceae):

The molecular mechanism of the methanolic extract of *P.chinensis* against lipopolysaccharide-induced nitric oxide andPGE2 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 & mitogen-activated-protein kinase were reduced in both U937 cells and lipopolysaccharidestimulated RAW264.7 cells. As a result, these findings stalwartly suggested that a *P. chinensis* methanolic extract could be used as a treatment for mitogenactivated protein kinase/activator protein mediated-inflammation (Hossen *et al*., 2015).

Olea europaea (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 edoema (Fezai *et al.*, 2013).

Phyllanthus acidus (Phyllanthaceae):

For many years, *Phyllanthus acidus* has been used to treat respiratory problems, gastrointestinal problems, hepatitis, bronchitis, rheumatism, and asthma. Kim and colleagues discovered that a methanolic extract of P. acidus aerial parts inhibited prostaglandin-E2 and nitric oxide production while also preventing morphological changes in lipo-polysaccharide-treated RAW 264.7 cells (Kim *et al*., 2015). 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.(Kim *et al*., 2015).

Syzygium caryophyllatum (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 (Heendeniya *et al*., 2018).

Tephrosia purpurea (Fabaceae):

The antiinflammatory effect of different dosages of 50 percent alcoholic extract of T. purpurea root was studied using carrageenan and the produced paw oedema method.(Praveena *et al*., 2011).

Solanum melongena (Solanaceae):

An aqueous extract of *Solanummelongena* L leaves was tried for antiinflammatory activity. In doses of 200 mg/kg & 400 mg/kg, the percentage of inhibition of the aqueous extract of S. melongena L was 42.62 percent, which was less than the 64.5 percent inhibition of the conventional pharmaceutical aspirin. Anti-inflammatory characteristics are possessed by chemical components such as ascorbic acid, alanine, arginine, and caffeic acid (Sharopov *et al*., 2015) (Im *et al*., 2016).(Silva *et al*., 2006).

Zingiber officinale (Zingiberaceae):

Shimoda and colleagues [55] investigated *Zingiberofficinale's* antiinflammatory effect by producing a 40% ethanolic extract from dried red ginger and testing its antiinflammatory efficacy in acute & chronic inflammation models. The results revealed a powerful suppressive result on acute & chronic inflammation, with macrophage activation inhibition appearing to play a role in this antiinflammatory action (Shimoda *et al*., 2010).

Sida cordifolia (Malvaceae):

Sida cordifolia 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 (Franzotti et al., 2000). It has been explored as an anti-inflammatory, a cell-proliferation inhibitor and a promoter of liver-growth

A- Zingiber officinale L. B-Aegle marmelos L. C-Ajuga laxmannii L.

D-Allium sativum L. E-Aloe ferox M. F-Anacardium occidentale L.

A-Calamintha nepeta L. B-Cassia fistula L. C-Cassia occidentalis L.

D-Citrus limetta R. E-Coriandrum sativum L. F-Cuminum cyminum L.

A-Cynodon dactylon L. B-Cyperus rotundus L. C-Emblica officinalis L.

D-Glycyrrhiza glabra L. E-Ipomoea pescaprae L. F-Jasminum sambac L.

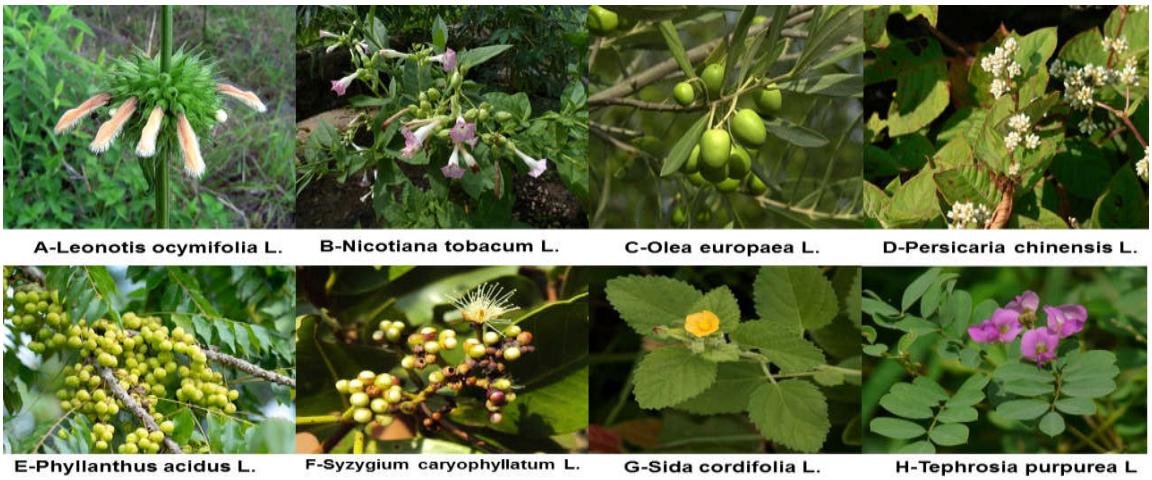

Fig.1: Plants with Antiinflammatory Potential

2. CONCLUSION

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, botulinic acid and oleanolic acid are among the plant-derived compounds being studied as potential anti-inflammatory medications. This review will assist current and future researchers in identifying anti-inflammatory medicinal plants, the active ingredients of which have been isolated using various separation procedures. However, a more in-depth investigation could be conducted to determine the actual mechanism(s) of action.

3. REFERENCES

1. Alemu, A., Tamiru, W., Nedi, T., & Shibeshi, W. (2-018). Analgesic and anti-inflammatory effects of 80 % methanol extract of Leonotis ocymifolia (burm. F.) iwarsson leaves in rodent models.Evidence-Based C-omplementary and Alternative Medicine, 2018.
2. Arreola, R., Quintero-Fabián, S., López-Roa, R. I., Flores-Gutiérrez, E. O., Reyes-Grajeda, J. P., Carrera-Quintanar, L., & Ortuño-Sahagún, D. (2015). Immun-omodulation and anti-inflammatory effects of garlic of garlic compounds. Journal of Immunology Research 2015.
3. Asmawi, M. Z., Kankaanranta, H., Moilanen, E., & Vapaatalo, H. (1993). Anti-inflammatory activities of Emblica officinalis Gaertn leaf extracts. Journal of Pharmacy and Pharmacology, 45(6), 581–584.
4. Awakan, O. J., Malomo, S. O., Adejare, A. A.,Igunnu A., Atolani, O., Adebayo, A. H., & Owoyele, B.V. (2018). Anti-inflammatory and bronchodilatory constituents of leaf extracts of Anacardium occidentale L.in animal models. Journal of Integrative Medicine, 16 (1), 62–70.
5. Azab, A., Nassar, A., & Azab, A. N. (2016). Anti-inflammatory activity of natural products. Molecules, 21(10), 1321.
6. Bandgar, B. P., Patil, S. A., Korbad, B. L., Biradar, S.C., Nile, S. N., & Khobragade, C. N. (2010). Synthesis and biological evaluation of a novel series of 2, 2- bisaminomethylated aurone analogues as antiinflammatory and antimicrobial agents. European Journal of Medicinal Chemistry, 45(7), 3223–3227.
7. Benni, J. M., Jayanthi, M. K., & Suresha, R. N. (20-11). Evaluation of the antiinflammatory activity of Aegle marmelos (Bilwa) root. Indian Journal of Pharmacology, 43(4), 393.
8. Burke, A., Smyth, E., & FitzGerald, G. A. (2006). Analgesic-antipyretic agents; pharmacotherapy of gout. The Pharmacological Basis of Therapeutics.

New York: McGraw Hill Medical Publishing Division.

9. Campos, J. F. (2014). BP; Paredes-Gamero, EJ; Cardoso, CAL;Souza, KP; dos Santos, EL Antimicrobial, antioxidant and cytotoxic activities of propolis from Melipona orbignyi (Hymenoptera, Apidae). Food and Chemical Toxicology, 65, 374–380.
10. De Nunzio, C., Salonia, A., Gacci, M., & Ficarra, V. (2020). Inflammation is a target of medical treatment for lower urinary tract symptoms associated with benign prostatic hyperplasia. World J. of Urology, 38(11), 2771–2779.
11. Devaraj, A., & Karpagam, T. (2011). Evaluation of anti-inflammatory activity and analgesic effect of Aloe vera leaf extract in rats. Int Res J Pharm, 2(3), 103–110.
12. Feng, Y., Yu, Y.-H., Wang, S.-T., Ren, J., Camer, D., Hua, Y.-Z., Zhang, Q., Huang, J., Xue, D.-L., & Zhang, X.-F. (2016). Chlorogenic acid protects D-galactose-induced liver and kidney injury via antioxidation and anti-inflammation effects in mice. Pharmaceutical Biology, 54(6), 1027–1034.
13. Fezai, M., Senovilla, L., Jemaà, M., & Ben-Attia, M. (2013). Analgesic, anti-inflammatory and anticancer activities of extra virgin olive oil. Journal of Lipids, 2013.
14. Franzotti, E. M., Santos, C. V. F., Rodrigues, H., Mourao, R. H. V, Andrade, M. R., & Antoniolli, A. R. (2000). Anti-inflammatory, analgesic activity and acute toxicity of Sida cordifolia L.(Malva branca). Journal of Ethnopharmacology, 72(1–2), 273-277.
15. Galasso, S., Pacifico, S., Kretschmer, N., Pan, S.-P., Marciano, S., Piccolella, S., Monaco, P., & Bauer, R. (2014). Influence of seasonal variation on Thymus longicaulis C. Presl chemical composition and its antioxidant and antiinflammatory properties. Phytochemistry, 107, 80–90.
16. Garg, V. K., & Paliwal, S. K. (2011). Antiinflammatory activity of aqueous extract of Cynodon dactylon. International Journal of Pharmacology, 7(3), 370–375.
17. Goel, B., Sahu, B., & Jain, S. K. (2020). Plant-Derived Drug Discovery: Introduction to Recent Approaches. In Botanical Leads for Drug Discovery (pp. 1–27). Springer.
18. Grosser, T., Smyth, E., & FitzGerald, G. A. (2011). Anti-inflammatory, antipyretic, and analgesic agents pharmacotherapy of gout. Goodman and Gilman's the Pharmacological Basis of Therapeutics, 12, 959–1004.
19. Heendeniya, S., Ratnasooriya, W. D., & Pathirana, R. N. (2018). In vitro investigation of antiinflammatory activity and evaluation of phytochemical profile of Syzygium caryophyllatum.
20. Hossen, M. J., Baek, K.-S., Kim, E., Yang, W. S., Jeong, D., Kim, J. H., Kweon, D.-H., Yoon, D. H., Kim, T. W., & Kim, J.-H. (2015). In vivo and in vitro anti-inflammatory activities of Persicaria chinensis methanolic extract targeting Src/Syk/NF-êB. Journal of Ethnopharmacology, 159, 9–16.
21. Huerta, C., Castellsague, J., Varas-Lorenzo, C., & Rodríguez, L. A. G. (2005). Nonsteroidal antiinflammatory drugs and risk of ARF in the general population. American Journal of Kidney Diseases, 45(3), 531–539.
22. Ilavarasan, R., Malika, M., & Venkataraman, S. (2005). Antiinflammatory and antioxidant activities of Cassia fistula Linn bark extracts. African Journal of Traditional, Complementary and Alternative M-Medicines, 2(1), 70–85.
23. Im, K., Lee, J. Y., Byeon, H., Hwang, K.W., Kang W., Whang, W. K., & Min, H. (2016). InVitro ant Vitro antioxidative and anti-inflammatory activities of the ethanol extract of eggplant (Solanum melongena) stalks in macrophage RAW 264.7 cells.The *Food and Agricultural Immunology*, *27*(6), 758–771.
24. Kaur, R., Kaur, H., & Dhindsa, A. S. (2013). Glycyrrhiza glabra: a phytopharmacological review. International Journal of Pharmaceutical Sciences and Research, 4(7), 2470.
25. Kim, S. H., Park, J. G., Lee, J., Yang, W. S., Park, G. W., Kim, H. G., Yi, Y.-S., Baek, K.-S., Sung, N. Y., & Hossen, M. J. (2015). The dietary flavonoid Kaempferol mediates anti-inflammatory responses and via the Src, Syk, IRAK1, and IRAK4 molecular targets. Mediators of Inflammation, 2015.
26. Maurya, A. K., Mohanty, S., Pal, A., Chanotiya, C. S., & Bawankule, D. U. (2018). The essential oil from Citrus limetta Risso peels alleviates skin inflammation: In-vitro and in-vivo study. Journal of Ethnopharmacology, 212, 86–94.
27. Miguel, M. G. (2010). Antioxidant and antiinflammatory activities of essential oils: a short review. Molecules, 15(12), 9252–9287.
28. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly

four decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803.

29. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803.
30. Noh, H. J., Hwang, D., Lee, E. S., Hyun, J. W., Yi, P. H., Kim, G. S., Lee, S. E., Pang, C., Park, Y. J., & Chung, K. H. (2015). Anti-inflammatory activity of a new cyclic peptide, citrusin XI, isolated from the fruits of Citrus unshiu. Journal of Ethnopharmacology, 163, 106–112.
31. Patel, D. P., Schenk, J. M., Darke, A., Myers, J. B., Brant, W. O., & Hotaling, J. M. (2016). Nonsteroidal anti-inflammatory drug use not associated with erectile dysfunction risk: results from the Prostate Cancer Prevention Trial. BJU International, 117(3), 500.
32. Pereira Leite, C., Nunes, C., Jamal, S. K., Cuccovia, I. M., & Reis, S. (2017). Nonsteroidal antiinflammatory therapy: a journey toward safety. Medicinal Research Reviews, 37(4), 802–859.
33. Pilotto, A., Sancarlo, D., Addante, F., Scarcelli, C., & Franceschi, M. (2010). Non-steroidal antiinflammatory drug use in the elderly. Surgical Oncology, 19(3), 167–172.
34. Pongprayoon, U., Baeckstrom, P., Jacobsson, U., Lindström, M., & Bohlin, L. (1991). Compounds inhibiting prostaglandin synthesis isolated from Ipomoea pes-caprae. Planta Medica, 57(06), 515–518.
35. Praveena, R., Amarnath, S., & Jegadeesan, M. (2011). Anti inflammatory activity of Tephrosia purpurea root. International Journal of Pharmacognosy and Phytochemical Research, 3(4), 93–94.
36. Reuter, J., Huyke, C., Casetti, F., Theek, C., Frank, U., Augustin, M., & Schempp, C. (2008). Anti inflammatory potential of a lipolotion containing coriander oil in the ultraviolet erythema test. JDDG Journal Der Deutschen Dermatologischen Gesellschaft, 6(10), 847–851.
37. Sami, A., Usama, M., Saeed, M. M., & Akram, M. (2021). Medicinal plants with non-steroidal anti-inflammatory-like activity.
38. Sengar, N., Joshi, A., Prasad, S. K., & Hemalatha, S. (2015). Anti-inflammatory, analgesic and antipyretic activities of standardized root extract of Jasminum sambac. Journal of Ethnopharmacology, 160, 140–148.
39. Sharopov, F., Braun, M. S., Gulmurodov, I., Khalifaev, D., Isupov, S., & Wink, M. (2015). Antimicrrobial, antioxidant and antiinflammatory activity of essential oils of selected aromatic plants from Tajikistan. Foods, 4(4), 645–653.
40. Shih, S.-C., & Chang, C.-W. (2007). Nonsteroidal anti-inflammatory drug-related gastrointestinal bleeding in the elderly. International Journal of Gerontology, 1(1), 40–45.
41. Shimoda, H., Shan, S.-J., Tanaka, J., Seki, A., Seo, J.-W., Kasajima, N., Tamura, S., Ke, Y., & Murakami, N. (2010). Antiinflammatory properties of red ginger (Zingiber officinale var.Rubra) extract & and suppression of nitric oxideproduction by its constituents. Journal of Medicinal Food, 13(1), 1-56–162.
42. Silva, R. L., Melo, G. B. de, Melo, V. A. de, Antoniolli, Â. R., Michellone, P. R. T., Zucoloto, S., Picinato, M. A. N. C., Franco, C. F. F., Mota, G. de A., & Castro e Silva, O. de. (2006). Effect of of the aqueous extract of Sida cordifolia on liver regeneration after partial hepatectomy. Acta Cirurgica Brasileira, 21, 37–39.
43. Sostres, C., & Lanas, Á. (2016). Appropriate prescription, adherence and safety of non-steroidal anti-inflammatory drugs. Medicina Clínica (English Edition), 146(6), 267–272.
44. Sreejith, G., Latha, P. G., Shine, V. J., Anuja, G. I., Suja, S. R., Sini, S., Shyamal, S., Pradeep, S., Shikha, P., & Rajasekharan, S. (2010). Anti-allergic, anti-inflammatory and anti-lipidperoxidant effects of Cassia occidentalis Linn.
45. Thatoi, H. N., & Dutta, S. K. (2009). Antibacterial activity and phytochemical screening of leaf and bark extracts of Vitex negundo l. from similipal biosphere reserve, Orissa. Journal of Medicinal Plants Research, 3(4), 294–300.
46. Toiu, A., Mocan, A., Vlase, L., Pârvu, A. E., Vodnar, D. C., Gheldiu, A.-M., Moldovan, C., & Oniga, I. (2018). Phytochemical composition, antioxidant, antimicrobial and in vivo antiinflammatory activity of traditionally used Romanian Ajuga laxmannii (Murray) Benth.("Nobleman's Beard"–Barba Împaratului).Frontiers in Pharmacology, 9, 7.
47. Verma, S. (2016). Medicinal plants with antiinflammatory activity. J Phytopharmacol, 5(4),157–159.
48. Virshette, S. J., Patil, M. K., & Somkuwar, A. P. (2019). A review on medicinal plants used as anti inflammatory agents. J. Pharmacogn. Phytochem, 8, 1641–1646

49. Yin, S., Yang, H., Tao, Y., Wei, S., Li, L., Liu, M., & Li, J. (2020). Artesunate ameliorates DSS-induced ulcerative colitis by protecting intestinal barrier and inhibiting inflammatory response Inflammation, 43(2), 765–776.