INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

An Overview of Pharmacological Models and Phytoconstituents for The Anti-Inflammatory and Analgesic Activity

Anjali Patil*, Vikas Dhole, Dr. Sanganna Burli, Prashant Kumbhar

Department of Pharmacology, Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, 416112, India.

ARTICLE INFO

Published: 31 Mar. 2025
Keywords:
Phytochemicals, bioactive compounds, CNS modulation, in-silico studies, therapeutic agents.
DOI:
10.5281/zenodo.15113192

ABSTRACT

Phytochemicals are bioactive compounds that are found in plants and are widely recognized as having analgesic along with anti-inflammatory properties. The most common phytochemicals include essential oils, flavonoids, and alkaloids, which are applied in medicine because of their different mechanisms of action. Essential oils reduce inflammation through decreasing the generation of pro-inflammatory mediators through cyclooxygenase (COX) as well as lipoxygenase (LOX). Flavonoids suppress the central pathways of inflammation, such as NF-kB, and also decrease oxidative stress. Alkaloids modulate the immune system and inhibit inflammatory enzymes. To test the pharmacological efficacy of these compounds, several in vivo models are used. Modulation of the CNS is tested by using methods such as the hot plate along with tail immersion tests, which measure a decrease in pain sensitivity. The acetic acid-induced writhing, carrageenan-induced paw edema, formalin-induced paw edema, along with egg albumin-induced paw edema procedures are used to evaluate the suppression of inflammation and pain at the site of damage in peripheral analgesia. Experimental methods have been augmented by in-silico methods like as similarity search analysis, molecular docking, and molecular dynamics simulations. All these approaches have been proved indispensable for the identification and prediction of the interaction of phytochemicals with the target proteins related to inflammation and pain. Computational tools help to evaluate the binding affinity, stability, and effectiveness of the interaction that guide new therapeutic agents' discovery. In totality, these in vitro and in silico models form a wholesome package to help move ahead the development of phytochemicals against inflammatory and pain-related conditions.

INTRODUCTION

***Corresponding Author:** Anjali Patil
Address: Department of Pharmacology, Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, 416112, India.
Email ✉: patilanjali9860@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Inflammation is a process that occurs in response to any sort of infection, stress, or injury to vascularized tissues. It transports hosts defense system cells and molecules through the circulation to where they are needed to fight the offending stimuli.[1] It is a defensive feedback mechanism that promotes tissue restoration. Inflammations are frequently marked by redness, heat, swelling, as well as discomfort, but they can also cause exudation and function loss. Prostaglandins, prostacyclins, leukotrienes, chemokines, and lymphokines like interleukin (IL)-1, interferon-α (IFN-α), γ, histamine, 5-hydroxytryptamine (5-HT), IL-8, along with tissue necrosis factor-α are among the powerful chemicals that are involved in the process of inflammation.[2] These mediators elicit a complementary reaction to environmental stimuli by generating multiple chemical pathways and events. According to studies, inflammations are acceptable in only a small percentage of cases, but in nearly all cases, they appear to have been severe as well as painful. If they are not appropriately cured using first aid, a good detection along with medication therapy, it could even be fatal. Inflammation can occasionally result in life-threatening conditions such rheumatoid arthritis, asthma, vasculitis, glomerulonephritis, and hay fever.[3,4] The pathologic reaction of living tissue to damage is inflammation, which causes a local buildup of blood cells and plasmatic fluid. Although the body uses inflammation as a defense mechanism to defend itself from infections, burns, poisonous substances, allergies, and other unpleasant stimuli, the intricate processes and mediators that go into an inflammatory reaction can cause, sustain, or worsen a number of illnesses.[5, 6]

One of the most significant adaptation and defense systems is pain. The International Association for the Study of Pain (IASP) describes it as a painful emotional as well as sensory encounter associated with potential or actual tissue injury.[7] A person's experience and perception of pain are subjective and impacted by their past experiences as well as their current physical and mental health. Such nociceptors have sensitivity to the unpleasant effects of heat, chemicals, and mechanical stimulation. Injured cells emit a large number of chemical mediators, which can activate or hypersensitive nociceptors to other substances. That describes the intense pain. The pain response is sent across the reflex arc via synapses between motor neurons in the anterior horn as well as sensory fibers in the dorsal horn of the spinal cord. Because of the fast mobility of both motor and sensory neurons produced by their anatomical layout, the brain transmits nerve impulses alerting the individual to move away from risky stimuli via efferent nerve fibers. Prostaglandins, histamine, along with bradykinin are key pain mediators.[4] Almost every civilization has relied on medicinal herbs for therapy. In India, ayurvedic medicine is very significant.[1] Many polyherbal formulations are prescribed for inflammatory conditions in traditional medical systems. Since ancient times, plant-based medications and formulations have been used. The pharmacological assessment of the traditional formulations for the purported activities in traditional medicine, however, has received relatively little attention.[8]

Sr. No.	Botanical Nomenclature	Family	Activity	Active Chemical Constituent	Extract type	Part
1.	Annona squamosa	Annonaceae	Both	Acetogenines, Cyclopeptides	Ethanol	Seeds [9]

2.	Commiphora Africana	Burseraceae	Both	Flavonoids, tannin, anthraquinone, cardiac glycosides, triterpenoids, saponins, alkaloids	Hydro-Ethanolic	Stem-bark[10]
3.	Mentha piperita	Labiatae	Both	menthol, menthone, 1,8-cineole	Methanol	Leaves [11]
4.	Plumbago zyelanicum	Plumbaginaceae	Both	Plumbagin, plumbagic acid, flavonoids, beta-sitosterol.	Methanol	Roots [12]
5.	Swertia chirata	Gnetaceae	Both	Secoiridoid bitters, alkaloids, xanthones and triterpenoids	Ethanol	Root [13]
6.	Zingiber officinalae	Zingiberaceae	Both	sequiterpene, gingerol and inoleoresin	Ethanol	Rhizome[14]
7.	Amaranthus Viridis (Green amaranth)	Amaranthaceae	A	steroids, alkaloids, glycolsides, flavanoids, phenolic compounds	Methanol	Whole plant [15]
8.	Emblica officinalis	Euphorbiaceae	I	phenolic compounds	methanol	Leaves and fruit [16]
9.	Ricinus communis	Euphorbiaceae	I	Steroids, saponins, alkaloids, flavonoids, glycosides.	Methanol, pet ether	Roots, leaves [17,18]
10.	Sesbania sesban (Hadga)	Leguminosae	I	Protein, sterol, saponin, flavonoid, Glycoside	Petroleum ether	Bark [19]

*A= Analgesic; I=Anti- inflammatory; Both= Analgesic and Anti- inflammatory [4]

Phytochemicals from medicinal herbs work in concert to produce the pharmacological effects that have been observed.[20] The present movement towards green products is responsible for the increased usage of phytochemicals in traditional medical systems.[21] Applications in medicine, nutraceuticals, cosmetics, and agriculture have long made use of natural products like isolated compounds, crude extracts, along with essential oils extracted out of different parts of medicinal plants. Treating inflammatory diseases in humans and creating contemporary medications are the main goals of the There is a strong scientific interest in natural products generated from plants with medicinal properties and extracts of them.[22] Even though medicinal plants are frequently used for biological purposes in both crude extract and isolated compound form, some research has shown that isolated compounds have greater anti-inflammatory disease activity than medicinal plant crude extracts. [23, 24] Phytochemicals from the polyphenol, terpenoids, flavonoids, saponin, and tannin families have been found to have the primary anti-inflammatory properties.[23,25,26] Biogenic MNPs may have anti-inflammatory

effects since they inhibit the production of proinflammatory cytokines (IL-6, TNF-alpha, and IL-1 beta) from lipopolysaccharide-treated macrophages.[27]

The mechanism of action of phytochemicals in anti-inflammatory activities

In order to resolve inflammatory responses and restore tissue coordination, phytochemicals are believed to work by lowering inflammatory stress by enhancing cytokine release, chemokines, and systematic regulators that cause cellular infiltration.[28] At the molecular and cellular levels, the mechanism behind the anti-inflammatory effect works similarly.[29] Phytochemicals can reduce prostanoid and leukotriene concentrations by blocking regulating enzymes like phospholipase A2, lipoxygenases, protein kinases, cyclooxygenases, phosphodiesterases, histamine synthesis, along with transcriptase activation. Research has demonstrated the anti-inflammatory qualities of flavonoids, polyphenols, alkaloids, tannins, saponins, along with terpenes.[30] Reports state that quercetin dramatically inhibits COX-2 and 5-LOX, two enzymes that convert arachidonic acid into ecosanoids. Resveratrol controls the inflammatory response by inhibiting activated immune cells, modifying eicosanoid synthesis, as wel as stopping the manufacture along with release of pro-inflammatory mediators.[31] Furthermore, it has been shown that flavonoids, tannins, and curcumins have anti-inflammatory qualities by scavenging free radicals and so blocking proinflammatory enzymes.[32]

Alkaloids

Alkaloids, one of nature's most fascinating chemical groups, contain a wide range of structurally as well as functionally diverse compounds with innovative potential therapeutic and/or preventive applications in anti-inflammatory, NDDs, and AChE-inhibiting. According to the literature study as well as in silico ADMET analysis, alkaloids such as harmine, aloperine, berberine, sinomenine, oxymatrine, tetrahydropalmatine, tetrandrine, and galantamine may act as a lead drug against a range of anti-inflammatory and non-inflammatory disorders (NDDs). Many alkaloids are also poisonous; thus, it is critical to properly investigate their safety profiles. Collaborative study combining alkaloids with presently FDA-approved drugs might lead to more effective and long-lasting anti-inflammatory along with anti-AChE compositions.[33,34]

Flavonoids

Most research have found that flavonoids could have a therapeutic function in the treatment of cardiovascular problems, Parkinson's disease, colitis, neuropathic pain, arthritis, and cancer discomfort. Numerous studies have demonstrated the importance of flavonoids as a powerful family of molecules with analgesic, anti-inflammatory, as well as antioxidant properties, despite the fact that the specific mechanisms of action of these molecules are still unknown. Flavonoids can reduce pain and cellular inflammation by inhibiting the development and activation of various cellular regulatory proteins, including transcription factors and cytokines. The analgesic as well as anti-inflammatory actions of flavonoids, which are multi-target chemicals, have gotten more attention. 'The anti-inflammatory and analgesic properties are attributed to flavonoids such as Myricanol 5-laminaribioside, Rutin, Quercetin 3-sambubioside, Proanthocyanidin A2, Theaflavate A, Kaempferol 3-(2'',3''-diacetyl-4''-p-coumaroylrhamnoside), ent-Epicatechin-(4alpha->8)-ent-epicatechin 3-gallate, along with others. Flavonoids suppress the expression of VEGF and ICAM-1, inhibit the synthesis of inflammatory mediators like IL-1β, NO, TNF-α, along with COX-2, and activate the MAP kinase,

STAT3, NFkB, and NLRP3 inflammasome pathways.[33,34]

Polyphenols

Many natural substances, including flavonoids, alkaloids, tannins, saponins, steroids, and terpiniods, operate analogous to NSAIDs by inhibiting pathways that promote inflammation. They function to inhibit pathways that promote inflammation such as nuclear factor-kB (NF-kB) as well as the COX pathway. COX-2 inhibitors, such as flavonoids and phenols, block the cytokines that mediate inflammation. In cartilage explants, polyphenolic substances such catechins and epigallocatechin-3 galate prevent the release of proteoglycans and the breakdown of type 2 collagen caused by IL-1. Additionally, it reduces the activity associated with the transcription factor. NF-kB and inhibits IL-1b.[35,36]

Essential oils

Different plant sections generate essential oils with varying amounts and chemical compositions. Distillation remains the most straightforward and inexpensive means of isolating essential oils having a variety of biological activities, despite the fact that there are many different strategies for doing so.[37] Essential oils were volatile, oily, aromatic, and have a lower density than water. They are also known for their pungent odor, seldom colored liquids, as well as oxygenated functional groups.[38] They are a complex blend of numerous chemical compositions that are used as prospective anti-inflammatory drugs, including amines, benzene derivatives, terpene fatty acid derivatives, as well as phenylpropanoids.[39] This is due to the fact that essential oils include anywhere from a dozen to several hundred different phytochemical ingredients that have synergistic effect.[40]

Cytokines

There are now 18 cytokines having the name interleukin (IL). Other cytokines, like tumor necrosis factor (TNF), have maintained their original biological definition. Another approach to consider certain cytokines is their involvement in infection as well as inflammation. Some cytokines obviously enhance inflammation and are known as proinflammatory cytokines, whereas others inhibit the function of proinflammatory cytokines and are known as anti-inflammatory cytokines. For example, IL-4, IL-10, and IL-13 are powerful B lymphocyte activators. However, IL-4, IL-10, and IL-13 are all effective anti-inflammatory drugs. They're considered anti-inflammatory cytokines because they decrease the genes that produce proinflammatory cytokines including IL-1, TNF, and chemokines.[41] In contrast to the traditional medical system, complementary and alternative medicine (CAM) encompasses a broad range of practices, therapies, interventions, professions, applications, theories, and claims. A particular complementary and alternative medicine (CAM) treatment, like herbal medicine, may eventually be reclassified as a conventional medical practice with the help of supporting scientific evidence and clinical trials. Since herbal medicine is cSurrently viewed favorably by society, its use is becoming more and more common across all age groups.[42] In certain cases, traditional therapies such as opioids or nonsteroidal anti-inflammatory medicines (NSAIDs) must be discontinued due to adverse drug responses, ineffectiveness, or a high risk of catastrophic consequences. Patients like these, particularly the elderly, have little option but to endure through chronic pain or seek alternative types of treatment.[43] The World Health Organization (WHO) 1996 guidelines state that herbal medicine is defined as active end products that contain aerial or subterranean parts of plants, plant materials, or both. By blocking one or both

of the cyclooxygenase (COX) and lipoxygenase pathways, the majority of herbal medications alter the metabolism of eicosanoid compounds. The best extract dosage and length of treatment for the majority of herbal medicines are still unknown, and their use is typically based on conventional techniques.[43,44]

Determination of CNS modulation in analgesic activity

Hot plate method

Mice were separated into groups of five and given treatments with vehicle, pentazocine (17.5 mg/kg, i.p.), along with a commercially available polyherbal preparation (30, 100, 300, as well as 500 mg/kg, p.o.). They were placed on a heated plate maintained at 55 ± 0.5ºC. Reaction time was determined as the time it took to leap off the hot plate or lick the paw. The reaction time was measured at intervals of 0, 15, 30, 45, 60, 90, and 120 minutes. 15 seconds was considered the cutoff time. The cutoff time is calculated as the average reaction time plus three times the standard deviation of the control mice's total latencies throughout all time periods. [45,46]

Tail immersion method

Pentazocine (17.5 mg/kg, i.p.), vehicle, and a commercially available polyherbal preparation (30, 100, 300, and 500 mg/kg) were ingested to mice in groups of five each. The mouse tail's distal 2–3 cm section was submerged in hot water that was kept at 55 ± 0.5ºC. The duration of the reaction was determined as the time it took the mouse to retrieve its tail from the hot water. [45,46]

Determination of peripheral analgesia

Acetic acid induced writhing method

In this procedure, mice were divided into groups of five and treated with vehicle or a polyherbal commercial formulation (30, 100, 300, and 500 mg/kg). The number of writhes produced by 0.6% acetic acid (10 ml/kg, i.p.) was used to assess the analgesic efficacy of marketed polyherbal formulations (30, 100, 300, and 500 mg/kg). During the following 20 minutes, the number of writhes per animal was recorded. The positive standard was aspirin (20 mg/kg, p.o.). One hour before the intraperitoneal injection of 0.6% acetic acid, aspirin and a polyherbal preparation were administered. The proportion of protection against writhing was used to assess analgesia. [45,46,47] It's computed as:

'Number of writhing in control group = Number of writhing in treated group/ Number of writhing in control group × 100'

Carrageenan induced rat paw edema

One hour before the carrageenan injection, rats in groups of five each received treatment with a vehicle, a polyherbal product (30, 100, 300, and 500 mg/kg, p.o.), and aspirin (20 mg/kg). Each rat's left hind paw's sub-plantar tissue received an injection of 0.1 ml of 1% carrageenan. Using a plethysmometer, the swelling of the foot that had been injected with carrageenan was measured at 0, 1, 2, 3, and 4 hours. 0.1 ml of the vehicle was injected into the right hind paw. [45,48,49]

Formalin induced rat paw edema

One hour before the formalin injection, rats in groups of five were given vehicle, a polyherbal compound that was marketed (30, 100, 300, and 500 mg/kg, p.o.), and aspirin (20 mg/kg). Each rat received a 0.05 ml injection of a 1%w/v formalin solution into the sub-plantar tissue of its left hind paw. Using a plethysmometer, the swelling of the foot that had received a formalin injection was

assessed at 0, 1, 2, 3, and 4 hours. 0.1 cc of the vehicle was injected into the right hind paw.[45,50,51] The % decrease in paw volume is calculated as:

'Change in volume in control group - Change in volume in treated group/Change in volume in control group × 100'

Egg albumin Induced Rat Paw Edema

Wistar rats were divided into three groups of five animals each, as follows:

Group 1- control (treated with I mL of NaCl (saline solution),
Group 2- standard (treated with Diclofenac Sodium injection 100 mg/kg, orally), while
Group 3- treated with 2% essential oil suspension of P. alliacea orally (using 10 mL/kg; dose volume to animal weight).

On the second day of the trial, the identical treatments were administered again. Animals were fasted overnight before the third day of the experiment to enable adequate sample absorption into the bloodstream through the stomach cavity and to empty a portion of the gastrointestinal system. To fill the stomach, the medication was taken orally. A cannula needle was used to provide the appropriate dosages of medication. The right hind paw's subplantar area received a subcutaneous injection of 1.0 mL of 50% (v/v) fresh egg albumin thirty minutes later. Rat paw oedema was measured using the volume displacement technique (plethysmometer) at 1, 2, 3, and 4 hours before to and following the egg-albumin injection. After that, the paw size changes were assessed.[52,53] From the mean edema volume, the percent inhibition was calculated by using following formula:

% Inhibition of edema = 100 X (Vc-Vt/Vc)

Were,

Vc =Mean paw edema volume of control group

Vt =Mean paw edema volume of treated group

In-silico studies

Similarity search analysis

The recently created open-access program SIMSEARCH (https://github.com/ncordeirf-cup/SIMSEARCH), which determines the Tanimoto similarity between query and target compounds based on multiple fingerprints, was used to conduct the similarity search study. The involvement of phytoconstituents in the COX-2 enzyme was predicted using in silico techniques, although it is not easy to predict such qualities for a combination of phytochemicals. It should be noted that the anti-inflammatory properties revealed here may have been the consequence of the combined actions of phytochemicals with weak to moderate potencies against COX-2, and that synergistic effects may occur.[54]

Molecular docking analysis

The Protein Data Bank (PDB ID: 5IKR) provides the X-ray crystal structures of COX-2.55. Using Autodock Vina v1.2.0, the compounds were initially docked over the enzymes' catalytic sites, which were identified by the position of small molecules of inhibitors complexed via these proteins.[56] The bound ligands at the proteins' catalytic site were used to define a grid size of 40 Å × 40 Å × 40 Å. PoseView was used to obtain the 2D ligand-receptor interactions using the webserver ProteinsPlus .[57]

Molecular dynamics simulations

Using the AMBER forcefield along with output naming scheme, the PDB2PQR server (http://server.poissonboltzmann.org/pdb2pqr) fixed the protonation states of the amino acid

residues of the protein complexes at pH = 7.0.[58] Receptor-ligand as well as ligand-water interactions were described using the ff99SB and the general AMBER force field (GAFF), respectively.[59] The remaining techniques for trajectory analyses, 50 ns simulation, and binding free energies based on Molecular Mechanics Generalized Born Surface Area (MM-GBSA)[60,61] have already been explained.[62,63]

CONCLUSION

Overall, phytochemicals like essential oils, flavonoids, and alkaloids have some good therapeutic potential in reducing inflammation and pain. All of these mechanisms of action inhibition of the action of inflammatory enzymes, immune modulation, and free radicals scavenging capacity explain their efficacy as analgesics and anti-inflammatory agents. Pharmacological models of both central and peripheral actions may be used to evaluate such pharmacological effects. The studies involve in-silico work such as molecular docking as well as dynamics simulation for the discovery and optimization of novel phytochemical compounds by predicting their interactions with biological targets. The use of both experimental and computational approaches will improve the knowledge of the therapeutic mechanisms of phytochemicals to pave the way for developing effective plant-based treatments in inflammatory diseases and pain management.

REFERENCES

1. Pathak BK, Palandurkar KM, Singh M, Trigunayat A, Singh A, Giri R, et al. Evaluation of In vivo Analgesic and Anti-inflammatory Activity of Oroxyulum indicum, Baicalein, Chrysin with Phytochemical Analysis and Molecular Docking Study. Pharmacogn J. 2023;15(5): 811-822.
2. Serhan CN, Savill J. Resolution of inflammation: The beginning programs the end. Nat Immunol. 2005;6:1191–7.
3. Beg S, Swain S, Hasan H, Barkat MA, Hussain MS. Systematic review of herbals as potential anti-inflammatory agents: Recent advances, current clinical status and future perspectives. Pharmacogn Rev. 2011 Jul;5(10):120-37.
4. Sai Kiran A Dara, Sateesh Belamkar, A Review on Anti-Inflammatory and Analgesic activity of Herbal Origin, Asian Journal of Pharmaceutical Research and Development, Vol. 2 (3) May–June. 2014:45-53.
5. Sosa, S., Balick, M. J., Arvigo, R., Esposito, R. G., Pizza, C., Altinier, G., & Tubaro, A. (2002). Screening of the topical anti-inflammatory activity of some Central American plants. Journal of ethnopharmacology, 81(2), 211–215.
6. Vittalrao AM, Shanbhag T, Kumari KM, Bairy KL and Shenoy S, Evaluation of Anti-inflammatory and Analgesic Activities of Alcoholic Extract of Kaempferia Galanga in Rats, Indian J Physiol Pharmacol, 55 (1), 2011, 13–24.
7. Michel YB, Dubo is, Christopher G, Allen HL. Chronic pain management. In: Healy TEJ, Knight PR, eds. Wylie and Churchil - Davidson's A practice of Anaesthesia (7th edition). London, Hodder Arnold 2003:1235–1139.
8. M.S. Bagul, H. Srinivasa, N.S. Kanaki, M. Rajani. Anti-inflammatory activity of two Ayurvedic formulations containing guggul. Indian J Pharmacol, December 2005, Vol 37, 399-400.
9. Neha Pandey, Dushyant Barve, Phytochemical and Pharmacological Review on Annona squamosa Linn, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2(4), 2011, 1404-1412.

10. I. Ezekiel, 2M.A. Mabrouk and J.O. Ayo, Study of the Effect of Hydro-Ethanolic Extract of Commiphora africana (Stem-bark) on Inflammation and Pain in Rodents, Asian Journal of Medical Sciences 2(3),2010, 81-84.
11. Yousef A. Taher, Antinociceptive activity of Mentha piperita leaf aqueous extract in mice, Libyan Jouranal of Medicine, 7, 2012, 1-5.
12. Vineet Mittal, SK Sharma, Deepak Kaushik, Meenu Khatri and Kusum Tomar, A comparative study of analgesic activity of Plumbago zeylanica Linn. callus and root extracts in experimental mice, Research Journal of Pharmaceutical, Biological and Chemical Sciences, 1(4), 2010, 830-836.
13. Sreedam Chandra Das, Subrata Bhadra, Sumon Roy, Sajal Kumar Saha, Md. Saiful Islam and Sitesh Chandra Bachar, "Analgesic and Anti-inflammatory Activities of Ethanolic Root Extract of Swertia chirata", Jordan Journal of Biological Sciences, 5(1), 2012, 31-36.
14. Raji Y , Udoh U.S, Oluwadara O.O, Akinsomisoye O.S, Awobajo O, Adeshoga K, Anti-inflammatory and Analgesic Properties of the Rhizome Extract of Zingiber officinale, African Journal of Biomedical Research, 5, 2002, 121 – 124.
15. Bagepalli Srinivas Ashok Kumar, Kuruba Lakshman, Korala Konta Narsimha Jayaveera, Devangam Sheshadri Shekar, Chinna Swamy Vel Muragan, and Bachappa Manoj, Antinociceptive and Antipyretic Activities of Amaranthus Viridis Linn in Different Experimental Models, Avicenna J Med Biotechnol. 2009 Oct-Dec; 1(3): 167–171.
16. Manjeshwar Shrinath Baliga and Jason Jerome Dsouza, Amla (Emblica officinalis Gaertn), a wonder berry in the treatment and prevention of cancer, European Journal of Cancer Prevention, 20(3), 2011, 225-239.
17. Iiavarasan R1, Mallika M, Venkataraman S, Anti-inflammatory and free radical scavenging activity of Ricinus communis root extract, JEthnopharmacol. 2006 Feb 20;103(3):478-80.
18. Jitendra Jena, Ashish Kumar Gupta, Ricinus communis linn: A Phytopharmacological review, International Journal of Pharmacy and Pharmaceutical Sciences, 4(4), 2012, 25-29.
19. R. B. Patil, B. K. Nanjwade and F. V. Manvi, Effect of Sesbania Grandiflora and Sesbania Sesban Bark on Carrageenan Induced Acute Inflammation and Adjuvant Induced Arthritis in Rats, an International Journal of Pharmaceutical Sciences,1(1), 2010, 75-89.
20. Borquaye, L.S., Laryea, M.K., Gasu, E.N., Boateng, M.A., Baffour, P.K., Kyeremateng, A.,Doh, G., Anti-Inflammatory and Antioxidant Activities of Extracts of Reissantia Indica, Cissus cornifolia, and Grosseria vignei. Cogent. Biol. 6, 1–13.
21. Castro, J.P., Ocampo, Y.C., Franco, L.A., 2014. In Vivo and in Vitro Anti-Inflammatory Activity of Cryptostegia grandiflora Roxb. Ex r. Br. Leaves. Biol. Res. 47, 1–8.
22. Gemechu, W., Woldekidan, S., Teka, F., Mohammed, J., 2021. Ethnomedicinal Uses, Phytochemisty and Pharmacological Activities of Rumex nervosus. J. Anal. Pharm. Res. 10, 65–69.
23. Azab, A., Nassar, A., Azab, A.N., 2016. Anti-Inflammatory Activity of Natural Products. Molecules 21, 1–13.
24. Ribeiro, V.P., Arruda, C., El-Salam, M.A., Bastos, J.K., 2018. Brazilian Medicinal Plants with Corroborated Anti-Inflammatory Activities. Pharm. Biol. 56, 253–268.
25. Bunte, K., Hensel, A., Beikler, T., 2019. Polyphenols in the Prevention and Treatment of Periodontal Disease: A Systematic Review of in Vivo, Ex Vivo and in Vitro Studies. Fitoterapia 132, 30–39.

26. N'guessan, B.B., Asiamah, A.D., Arthur, N.K., Frimpong-Manso, S., Amoateng, P., Amponsah, S.K., Kukuia, K.E., Sarkodie, J.A., Opuni, K.F.M., Asiedu-Gyekye, I.J., 2021. Ethanolic Extract of Nymphaea lotus L. (Nymphaeaceae) Leaves Exhibits in Vitro Antioxidant, in Vivo Anti-Inflammatory and Cytotoxic Activities on Jurkat and MCF-7 Cancer Cell Lines. BMC Complement. Med. Ther. 21, 1–13.
27. Tyavambiza, C., Elbagory, A.M., Madiehe, A.M., Meyer, M., Meyer, S., 2021. The Antimicrobial and Anti-Inflammatory Effects of Silver Nanoparticles Synthesised from Cotyledon orbiculata Aqueous Extract. Nanomaterials 11, 1–19.
28. Dragos, D., Gilca, M., Gaman, L., Vlad, A., Iosif, L., Stoian, I., Lupescu, O., 2017. Phytomedicine in Joint Disorders. Nutrients 9, 1–18.
29. 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.
30. 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.
31. 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.
32. 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.
33. Ferraz CR, Carvalho TT, Manchope MF, Artero NA, Rasquel-Oliveira FS, Fattori V, Casagrande R, Verri WA Jr. Therapeutic Potential of Flavonoids in Pain and Inflammation: Mechanisms of Action, Pre-Clinical and Clinical Data, and Pharmaceutical Development. Molecules. 2020 Feb 10;25(3):762.
34. Babita Aryal, Bimal Kumar Raut, Salyan Bhattarai, Sobika Bhandari, Parbati Tandan, Kabita Gyawali, Kabita Sharma, Deepa Ranabhat, Ranjita Thapa, Dipa Aryal, Atul Ojha, Hari Prasad Devkota, Niranjan Parajuli, Potential Therapeutic Applications of Plant-Derived Alkaloids against Inflammatory and Neurodegenerative Diseases. Hindawi Evidence-Based Complementary and Alternative Medicine Volume 2022, Article ID 7299778.
35. Roksana Rahman, Ummul Khayer Fatema and Israt Jahan Bulbul, Preliminary Phytochemical Screening, Analgesic and Anti-Inflammatory Activity of Ficus glomerata Fruit Extract, European Journal of Medicinal Plants 14(3): 1-10, 2016, Article no.EJMP.25322.
36. Ghosh S, May MJ, Kopp EB. NF-k B and Rel proteins. Evolutionarily conserved mediators of immune responses. Annu Rev Immunol. 1998;16:225–60.
37. Sepahvand, R., Delfan, B., Ghanbarzadeh, S., Rashidipour, M., Veiskarami, G.H., Ghasemian-Yadegari, J., 2014. Chemical Composition, Antioxidant Activity and Antibacterial Effect of Essential Oil of the Aerial Parts of Salvia sclareoides. Asian Pac. J. Trop. Med. 7, 491–496.
38. Miguel, M.G., 2010. Antioxidant and Anti-Inflammatory Activities of Essential Oils. Molecules 15, 9252–9287.
39. Da Silveira, 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.

40. Kusuma, H., Altway, A., Mahfud, M., 2019. An Optimization of Microwave Hydrodistillation Extraction of Vetiver Oil Using a Face-Centered Central Composite Design. J. Chem. Technol. Metall. 54, 803–809.
41. Charles A. Dinarello, MD. Proinflammatory Cytokines, CHEST 2000; 118:503–508.
42. Eisenberg, D.M.; Davis, R.B.; Ettner, S.L.; Appel, S.; Wilkey, S.; van Rompay, M.; Kessler, R.C. Trends in Alternative Medicine Use in the United States, 1990–1997: Results of a Follow-up National Survey. JAMA 1998, 280, 1569–1575.
43. Jahromi, B.; Pirvulescu, I.; Candido, K.D.; Knezevic, N.N. Herbal Medicine for Pain Management: Efficacy and Drug Interactions. Pharmaceutics 2021, 13, 251.
44. Weiner, D.K.; Ernst, E. Complementary and Alternative Approaches to the Treatment of Persistent Musculoskeletal Pain. Clin. J. Pain 2004, 20, 244–255.
45. M Mohan, VS Gulecha, VM Aurangabadkar, R Balaraman, A Austin and S Thirugnanasampathan, Analgesic and anti-inflammatory activity of a polyherbal formulation (PHF-AROGH). Oriental Pharmacy and Experimental Medicine 2009 9(3), 232-237.
46. Turner RA. (1971) Screening Methods in Pharmacology, Academic Press. 100-113.
47. Koster R, Anderson M, Beer EJ. (1959) Acetic acid for analgesic screening. Proc. Soc. Exp. Biol. 18, 412-415.
48. Winter CA, Risley EA, Nuss GW. (1962) Carrageenin induced edema in hind paw of the rat as assay for anti-inflammatory drugs. Proceed of the soc for Exp Biol and Med. 11, 544-547.
49. Vogel HG. (2002) Drug discovery and evaluation, pharmacological Assay. Springer. 2, 670.
50. Roy A, Gupta JK, Lahiri SC. (1982) Further studies on anti-inflammatory activity of two potent indan-1-acetic acids. Indian J. Physiol. Pharmacol. 26, 206-214.
51. Dimo T, Agathe L, Fotio T, Nguelefack B, Asongalem EA, Kamtchouing P. (2006) Anti-inflammatory activity of leaf extracts of Kalanchoe crenata A. Indian J. Pharmacol. 38, 115-119.
52. Marsik P, Kokoska L, Landa P, Nepovin A, Soduek P, Vanek. In vitro inhibitory effects of thymol and quinones of Nigella sativa seeds on cyclooxygenase-1- and -2- catalyzed prostaglandin E2 biosyntheses. Planta Med. 2005;71(8):739-42.
53. Aderoju A. Oluwa, Opeyemi N. Avoseh, O. Omikorede, Isiaka A. Ogunwande and Oladipupo A. Lawal. Study on the Chemical Constituents and Anti-inflammatory Activity of Essential Oil of Petiveria alliacea L. British Journal of Pharmaceutical Research 15(1): 1-8, 2017.
54. S.Gupta et al. Analgesic and Anti-inflammatory Activities of Trayodashang Guggulu, an Ayurvedic Formulation, Phytomedicine Plus 2 (2022) 100281.
55. Orlando, BJ, Malkowski, MG., 2016. Substrate-selective inhibition of cyclooxygeanse-2 by fenamic acid derivatives is dependent on peroxide tone. J. Biol. Chem. 291 (29), 15069–15081.
56. Trott, O, Olson, AJ., 2009. AutoDockVina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J. Comput. Chem. 31 (2), 455–461.
57. Stierand, K., Maaß, P., Rarey, M., 2006. Molecular complexes at a glance: Automated

generation of two-dimensional complex diagrams. Bioinformatics 22, 1710–1716.

58. Dolinsky, TJ, Czodrowski, P, Li, H, Nielsen, JE, Jensen, JH, Klebe, G, Baker, NA, 2007. PDB2PQR: expanding and upgrading automated preparation of biomolecular structures for molecular simulations. Nucleic Acids Res 35 (Web Server), W522-W525.
59. Wang, J, Wolf, RM, Caldwell, JW, Kollman, PA., Case, D.A., 2004. Development and testing of a general amber force field. J. Comput. Chem. 25 (9), 1157–1174.
60. Srinivasan, J, Miller, J, Kollman, PA, Case, DA, 1998. Continuum solvent studies of the stability of RNA hairpin loops and helices. J. Biomol. Struct. Dyn. 16 (3), 671–682.
61. Ylilauri, M, Pentik¨ainen, OT., 2013. MMGBSA As a tool to understand the binding affinities of filamin–peptide interactions. J. Chem. Inform. Model. 53 (10), 2626–2633.
62. Halder, AK, Honarparvar, B., 2019. Molecular alteration in drug susceptibility against subtype B and C-SA HIV-1 proteases: MD study. Struc. Chem. 30 (5), 1715–1727.
63. Halder, AK, Cordeiro, MNDS., 2021. Multi-target in silico prediction of inhibitors for mitogen-activated protein kinase-interacting kinases. Biomolecules 11 (11), 1670.

HOW TO CITE: Anjali Patil*, Vikas Dhole, Dr. Sanganna Burli, Prashant Kumbhar, An Overview of Pharmacological Models and Phytoconstituents for The Anti-Inflammatory and Analgesic Activity, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 3, 3367-3378 https://doi.org/10.5281/zenodo.15113192