OVERVIEW OF ANTI- INFLAMMATORY DRUGS

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ABSTRACT

Anti-inflammatory treatment for this disease is difficult due to the diversity of pathogens and complex immune responses. However, antibiotics are often used to treat infections, reduce unpleasant symptoms, and modulate host responses. They can play a significant role in fighting hyper-inflammatory diseases such as COVID-19 by reducing systemic inflammation. However, their immune system can also cause serious infections. In addition, underestimating the patient's signs and symptoms can lead to a false sense of security, which can delay the diagnosis of the threat. NSAIDs are often used to treat pain, reduce inflammation, and reduce fever. These drugs work by blocking the body's production of prostaglandins.

Prostaglandins are chemicals that cause pain and discomfort. Aspirin, ibuprofen, and naproxen are examples of nonsteroidal anti-inflammatory drugs. These drugs are widely used. There are many over-the-counter medications. NSAIDs can cause side effects, but they are safe and effective when used as directed. Some people may experience nausea, vomiting, diarrhea, etc. Long-term use of NSAIDs increases the risk of stomach bleeding, kidney damage, and heart problems.

[Keywords] Inflammation, Antipyretic-Analgesics or NSAIDS, Prostaglandins, Anti-Inflammatory Drugs.

INTRODUCTION

Inflammation is a natural and necessary response of the body's immune system to infection, injury, or other harmful stimuli. It is a complex process that involves various cells, cytokines, and other mediators to eliminate the harmful agent, repair the damaged tissue, and restore the normal function of the affected area.
Inflammation can be regulated by various pharmacological and non-pharmacological approaches. Nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunomodulatory agents are commonly used to treat inflammation and its associated symptoms. Lifestyle changes, such as healthy diet, regular exercise, stress management, and smoking cessation, can also help to prevent and manage inflammation.

TYPES OF INFLAMMATION

There are two main types of inflammation: acute and chronic. Acute inflammation is a short-term, rapid response that occurs in response to injury, infection, or tissue damage. It is characterized by classic signs of redness, swelling, heat, pain, and loss of function. The purpose of acute inflammation is to eliminate the harmful agent, prevent its spread, and promote tissue repair.

Chronic inflammation is a long-term, low-grade response that persists for weeks, months, or years. It is associated with many chronic diseases, including cardiovascular disease, diabetes, obesity, cancer, and autoimmune diseases. Chronic inflammation can be caused by several factors, including persistent infections, exposure to environmental toxins, unhealthy diet, and lifestyle factors.

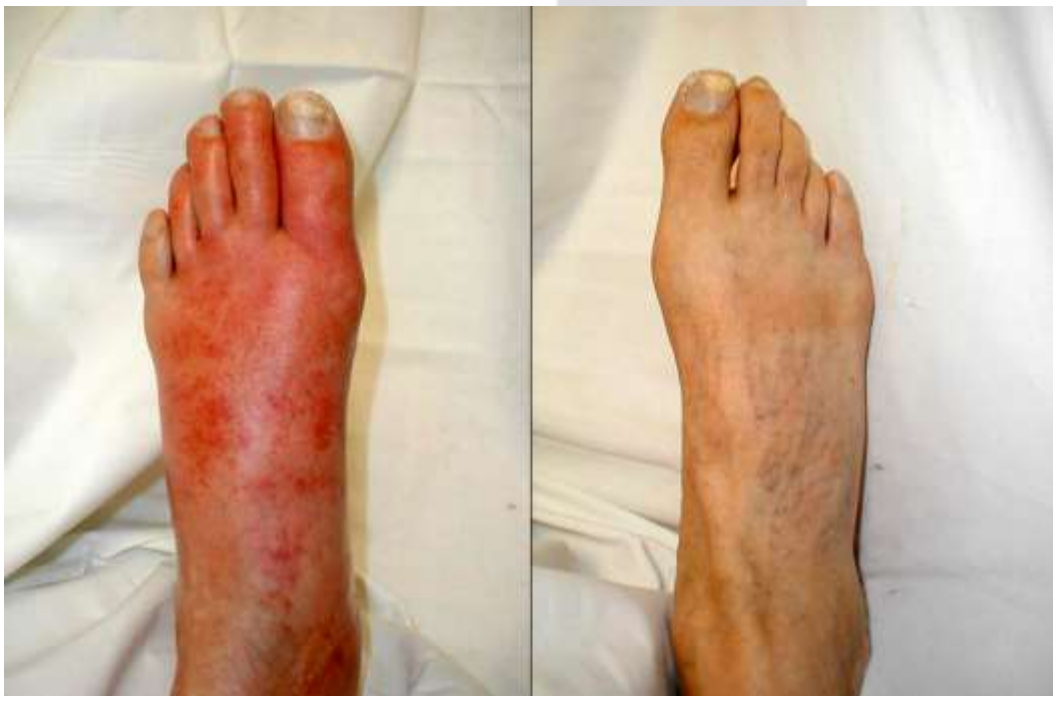
SIGNS OF INFLAMMATION

Four cardinal signs

1. Callor (heat)
2. Rubor (Redness)
3. Tumor (Swelling)
4. Dolor (Pain)

May also observe:

1. Loss of function



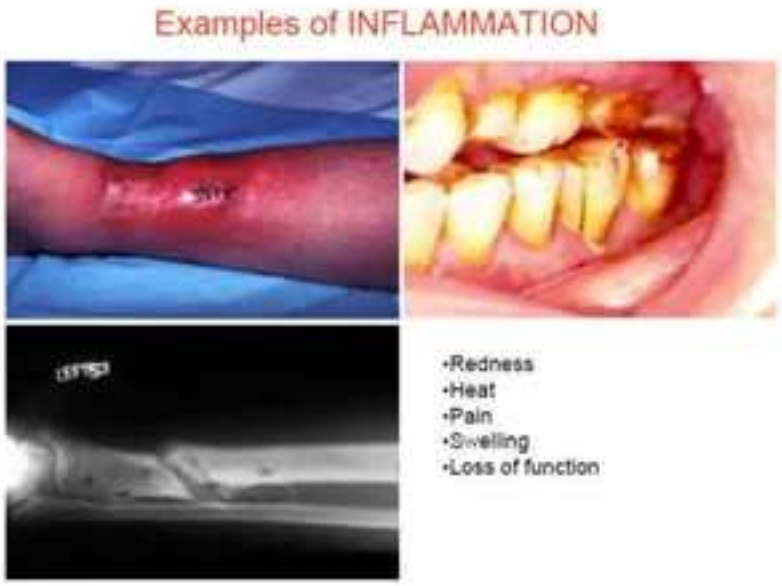


Fig. Examples of Inflammation

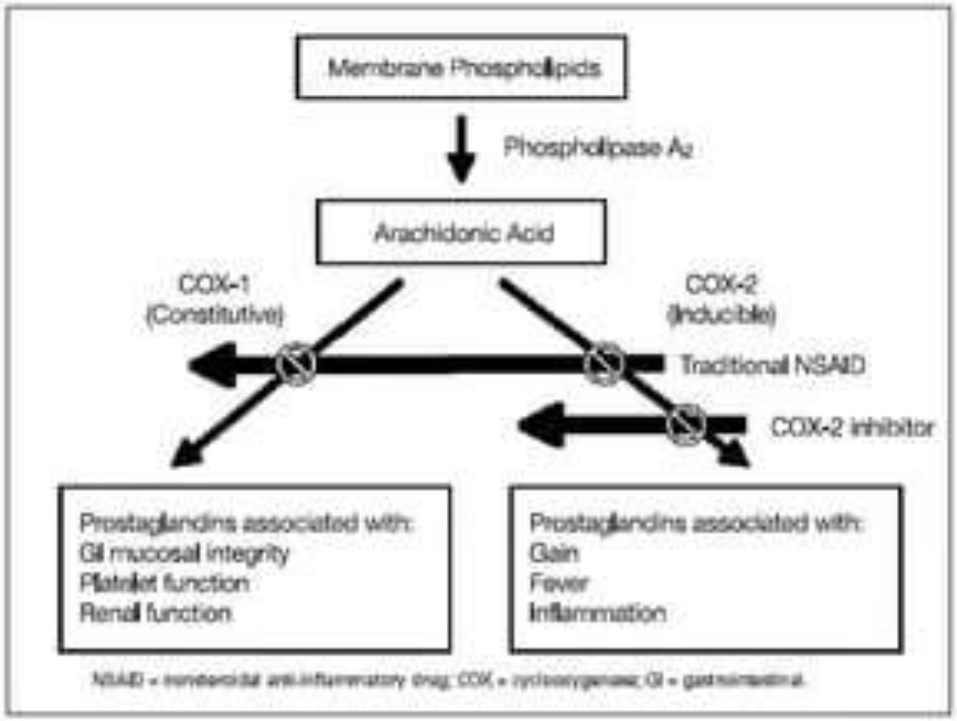
CLASSIFICATION

Anti Inflammatory Agents

1. Steroidal
2. Nonsteroidal

MECHANISM OF NSAIDS ACTION

COX -1and COX -2 inhibition There is overwhelming evidence pointing to the inhibition of cyclooxygenase enzyme as the main mechanism of NSAIDs' analgesic, antipyretic, and anti-inflammatory properties. Since the characterization of this mechanism by Vane for aspirin, other drugs in this class have proven consistent this mechanism. This is surprising considering the differences in structures of the individual drugs as described below.



Cyclooxygenase (COX) inhibition and the resulting inhibition of prostaglandin and other eicosanoid synthesis mitigate pain, fever, and inflammation. The cyclooxygenase (COX) enzyme also known as prostaglandin endoperoxide-ide H synthase (PGHS) exists in two isoforms: PGHS-1 or COX-1 and PGHS-2 or COX-2.There is a significant structural distinction between the two, with only 60% homology .Although encoded by different genes, both isoforms are membrane-bound glycoproteins autocatalyze the formation of prostanoid from arachidonic acid .COX-1 is expressed constitutively in most mammalian cells and tissues such as seminal vesicle, platelets, and endothelium.

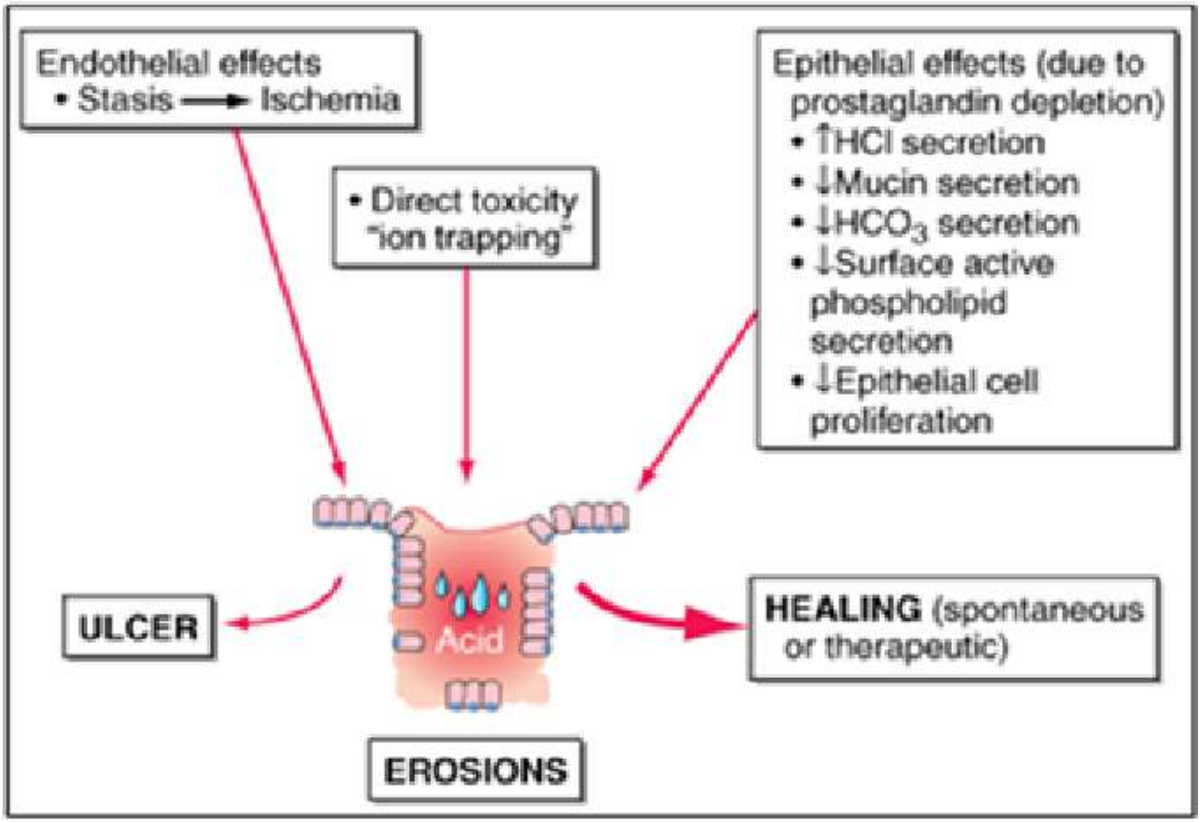


Fig. Mechanism by which NSAIDS may induce mucosal injury

In quiescent conditions, it performs ongoing regulatory functions referred to as "housekeeping duties." Prostaglandins produced by COX-1 activity perform functions such as gastro and renal protection, macrophage differentiation, platelet aggregation, and mucus production. In inflammatory conditions, molecular studies have demonstrated that COX-1 mRNA and protein expression do not change, confirming their limited role in the inflammatory process. COX-1, however, remains both experiment-tally and clinically relevant due to the adverse effects triggered by the nonselective inhibition of cyclooxygenase enzymes by some NSAIDs

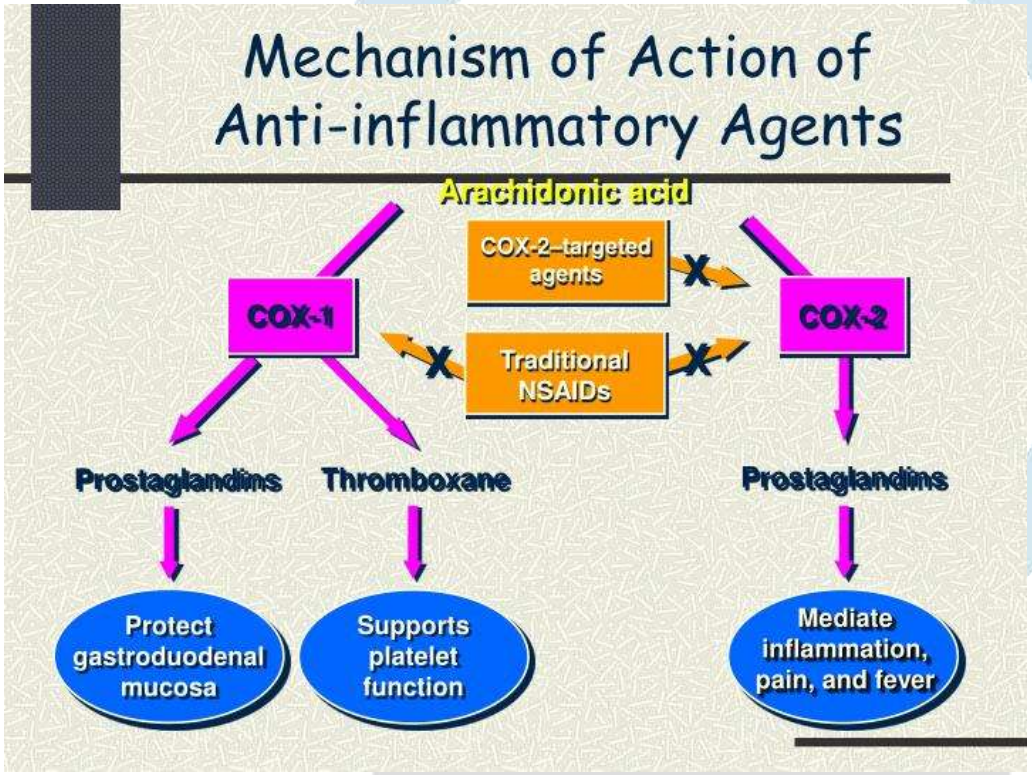


Fig. Mechanism of Action of Nonsteroidal Anti-Inflammatory Drugs

ANTI INFLAMMATORY DRUGS

Pharmacokinetics

- All= weak acids except Nebutomone (ketone)
- Racemic, single (naproxen), non (diclofenac)
- Biotransformation= phase 1 & 2 reactions
- CYT P450 2C, CYT P450 3A
- Enterohepatic circulation
- Excretion = rena

Pharmacodynamics

Inhibition of prostaglandins = cycloxygenase Reversible acetylation (aspirin= irreversible) Minor mechanisms

- Inhibition of chemotaxis
- IL 1 down regulation

- Decreased free radicals & superoxides
- Interference with intracellular calcium

Adverse Effects

- CNS= headache, tinnitus, dizziness
- CVS= edema, hypertension, CCF
- GIT= Dyspepsia, bleeding, nausea, vomiting
- Hematological= thrombocytopenia, aplastic anemia(rare), neutropenia
- Renal= Hyperkalemia, proteinuria, azotemia
- Hepatitis, asthma, rashes, SJ syndrome

Aspirin (ASA)

- ASA = Pka, 3.5 vs 3.0 (salicylic acid)
- Esterases = 15 minutes ---acetic acid and salicylates--- stomach, upper GIT
- Avoid = concomitant ibuprofen, probenecid
- Can use acetaminophen
- Albumin bound, Elimination t1/2 = 3-5 hours
- Salicylism, respiratory alkalosis, metabolic acidosis--- urinary alkalization, dialysis

Fig. Symptoms of Aspirin Overdose

Indomethacin & Others

- MEFANAMIC ACID
- Inhibits both cycloxygenase and phospholipase A
- DICLOFENAC SODIUM
- Avoid with Aspirin
- Hepatotoxic: like Sulindac

USES

Most NSAIDS Are Effective In

- Rheumatoid arthritis/Rheumatic heart disease
- Ischemic heart disease
- Inflammatory bowel disease/reactive arthritis ϖ Ankylosing spondylitis, Psoriatic arthritis, Gout
- Trauma, post operative, dental diseases
- Menstrual disorders/ dysmenorrhoea
- Patent ductus arteriosus, carcinoma colon

The main purposes of NSAIDs are to treat pain, lessen inflammation, and lower fever. They are used to treat a number of conditions.

- migraines and headaches
- Arthritis (includes osteoarthritis and rheumatoid arthritis)
- Period cramps
- joint and muscle ache
- tooth ache
- pain following surgery
- fever and other cold or flu-related symptoms

CONCLUSIONS

Anti-inflammatory medications are frequently used in infections to mitigate accompanying symptoms. They also act as host immune response modifiers and play an essential role in treating infections in selected groups of patients, e.g., with mucoviscidosis or COVID-19.

However, anti-inflammatory agents generally impair the immune system. NSAIDs inhibit granulocytes functions and enhance cytokines production, including TNF, and may contribute to the emergence of bacterial soft tissue infections or promote the development of the life-threatening disease from a minor infection, usually well-controlled by an immune system. Reducing infected patient's symptoms and signs of inflammation may provide a false sense of security and delay diagnosis of serious infections.

REFERENCES:

1. Bhatia H, Sidhu M, Sharma Y, Kumar A. Anti-inflammatory and anti-arthritic activity of flavonoids from Grewia asiatica Linn. J Ethnopharmacol. 2021 Feb 10;266:113428.
2. Kumar R, Sharma A, Bhatnagar S, Srivastava A. Anti-inflammatory and analgesic potential of methanol extract of stem bark of Ficus religiosa. J Ethnopharmacol. 2021 Feb 10;266:113453.
3. Mahajan SG, Mehta AA. Suppression of ovalbumin-induced Th2-driven airway inflammation by betulinicacid. Int Immunopharmacol. 2021 Mar;93:107395.
4. Wang J, Wang L, Liu Y, Li Z, Li Y, Zhou Y, et al. Anti-inflammatory and antioxidant activities of phenolic compounds from the flowers of Sedum sarmentosumBunge. J Ethnopharmacol. 2021 Mar 1;267:113622.
5. Pradhan P, Tudu B, Thangavel S, Nayak D, Santra S, Roy S. In vitro and in vivo anti-inflammatory activity of Cissampelos pareira Linn. leaves. J Ethnopharmacol. 2021 Apr 24;271:113835.
6. Ahmad R, Ahmad N, Naqvi AA, Rasheed N, SiddiquiZS. Antioxidant and anti-inflammatory potential of Terminalia chebula Retz. against carbon tetrachloride-induced liver injury in rats. J Ethnopharmacol. 2021 May 12;274:114063.
7. Xie J, Wang Y, Huang Y, Fang C, Zhu J, Wang Z, et al. Anti-inflammatory activity of flavonoids from the leaves of Diospyros kaki in LPS-stimulated RAW264.7 cells. J Ethnopharmacol. 2021 May 15;274:114031.
8. Kim YJ, Kim HH, Cho SH, Shin HM, Hong SP, Choi YW, et al. Anti-inflammatory activity of Angelica decursiva root extract in lipopolysaccharide-stimulated RAW264.7 cells and mouse models of inflammation. J Ethnopharmacol. 2021 Jun 2;275:114190.
9. Singh A, Yadav A, Prasad AK, Tiwari R, Agarwal H, Mishra BB, et al. Immunomodulatory and anti-inflammatory potential of Cordia rothii Roem. & Schult. leaf extract. J Ethnopharmacol. 2021 Jun 24;275:114205.
10. Lee JY, Lee S, Kim JW, Hong S, Park YJ, Hwang JS, et al. Anti-inflammatory effects of a mixture of Inulabritannica and Paeonia lactiflora extracts in LPS-induced RAW264.7 cells and a mouse model of sepsis. J Ethnopharmacol. 2021 Aug 30;277:114277.
11. Hwang YP, Jeong HG. Kaempferol inhibits LPS-induced inflammatory responses in RAW264.7 cells and zebrafish. J Ethnopharmacol. 2021 Sep 2;277:114303.
12. Shi J, Zhu H, Sun J, Ye Q, Huang J, Xia J, et al. Antioxidant and anti-inflammatory activities of total flavonoids from Sargassum fusiforme. J Ethnopharmacol. 2012 Jan 6;139(1):198-203.
13. Lee JH, Lee DU, Jeong CS. Effects of Ecklonia cava ethanolic extracts on airway hyperresponsiveness and inflammation in a murine asthma model: role of suppressions of IL-4 and IL-5. Phytomedicine. 2012 Mar 15;19(5):446-53.
14. Gao X, Deeb D, Liu YB, Gautam SC. Role of epigallocatechin-3-gallate in cell cycle progression and apoptosis signaling in SKOV-3 cell line. BiochemPharmacol. 2010 Mar 15;79(6):745-52.
15. Al-Oqail MM, El-Shaibany A, Al-Sheddi ES, Al-Massarani SM, Farshori NN, Al-Khedhairy AA. Anti-inflammatory and antinociceptive activities of Stachysschimperi essential oil in experimental animal models. BMC Complement Altern Med. 2015 Feb 22;15:85.
16. Wang T, Feng Y, Sun X, Ikuyo Y, Hirayama K, Hirose A, et al. Anti-inflammatory and anti-allergic activities of Pentaherbs formula, Moutan Cortex (root bark of Paeonia suffruticosa

Andr.), and its constituents. EvidBased Complement Alternat Med. 2013;2013:127919.
17. Wang J, Cao B, Zhao H, Feng J. Emerging roles of Ganoderma lucidum in anti-aging. Aging Dis. 2017 Apr;8(2):691-707.
18. Yoshino S, Kim M, Awa R, Kuwahara T, Miura T. Anti-inflammatory effects of clove bud extracts on rat dermal fibroblasts. Int J Mol Sci. 2017 Dec 7;18(12):2633.
19. Kim JS, Kim YJ, Cho KH, Woo JS, Kim JW. Anti-inflammatory effect of aqueous extract from the root of Brassica rapa L. in murine macrophage RAW 264.7 cells. Nutr Res Pract. 2011 Apr;5(2):156-61.
20. Piao XL, Park JH, Cui JG, Ryu JH, Park YM, Kim SH, et al. Antioxidant and anti-inflammatory effects of Quercetin 7-O-β-D-glucopyranoside from the leaves of Brasenia schreberi in cultured RAW264.7 cells. BiolPharm Bull. 2011;34(8):1173-7.
21. Kwon YS, Kim J, Lim JW, Kim MS, Kim JS, Kim YJ, et al. Anti-inflammatory effects of Scutellaria baicalensisextract via suppression of immune modulators and MAP kinase signaling molecules. J Ethnopharmacol. 2013 Jun 3;148(2):647-56.
22. Kuo YC, Chen CC, Lin YL, Chou CH, Chen YJ, Chung JG, et al. Induction of apoptosis in the Hep G2 cell line by extracts from the medicinal mushroom Antrodiacinnamomea. Biosci Biotechnol Biochem. 2006 Apr;70(4):781-9.
23. Rajput MS, Sarkar S, Pandey AK, Gupta A. In-vitro and in-vivo anti-inflammatory activity of Terminaliachebula fruit. J Ethnopharmacol. 2011 Jun 14;136(1):236-41.
24. Saravanan R, Pari L. Antihyperglycemic and anti-inflammatory effects of Aloe vera leaf extract in experimental type 2 diabetic rats. Phytother Res. 2014;28(3):438-450.
25. Chakraborty D, Debnath S, Mitra A, Sahu PK, GhoshD. Anti-inflammatory, antioxidant and antimicrobial activity of the root extract of Mukia maderaspatana Linn. J Ethnopharmacol. 2012;141(1):397-401.
26. Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. Ethnopharmacological approaches to wound healing—exploring medicinal plants of India. J Ethnopharmacol. 2007;114(2):103-113.
27. Sahoo S, Ghosh G, Das D, Nayak S, Das N. Anti-inflammatory activity of the root extract of Trichosanthesdioica Roxb.(Cucurbitaceae) in albino rats. J Ethnopharmacol. 2012;141(3):1056-1061.
28. Kumari M, Sharma V, Sardana S, Jain S. Antioxidant and anti-inflammatory activity of methanol extract of Terminalia chebula Retz.(Combretaceae). Afr J TraditComplement Altern Med. 2011;8(5):544-551.
29. Kalaivani P, Saranya M, Renuka Devi R, Srivastava A, Suganya N. Evaluation of anti-inflammatory activity of the leaves of Euphorbia hirta Linn. on carrageenan-induced paw edema in rats. Asian Pac J Trop Biomed. 2012;2(11):876-878.
30. Rangari VD, Kashyap RS, Telang AG, Moharil RB, Patil MB. Anti-inflammatory activity of Sesbaniagrandiflora (Linn.) Pers. leaf extract in acute and chronic inflammation in rats. Asian Pac J Trop Med. 2011;4(10):799-802.
31. Arifuddin M, Das S, Saudagar RB, Asad M. Anti-inflammatory activity of crude extract of Plumbagozeylanica leaves against carrageenan-induced paw edemain rats. Pharmacogn Mag. 2011;7(27):324.

32. Subramanian S, Rajapandian S, Sivasubramanian A, Perumal P. Antioxidant and anti-inflammatory activities of Lippia nodiflora L. extracts. Int J Curr Microbiol App Sci. 2014;3(4):295-308.
33. Sundararaj T, Pushpavalli G, Krishnan P. Anti-inflammatory and analgesic properties of leaves of Plumeria acutifolia. J Nat Rem. 2011;11(1):48-53.
34. Farzaei MH, Abbasabadi Z, Ardekani MR. Rahimi R, Farzaei F, Pasdaran A. Identification of medicinal plants effective on allergic rhinitis based on Iranian traditional medicine. Pharmacogn Mag. 2013;9(36):56.
35. Asghar MN, Qureshi M, Choudhary BA. Anti-inflammatory and analgesic activities of Rhus javanicusLinn. Pak J Pharm Sci. 2012;25(2):269-273.
36. Medzhitov R (2010) Inflammation 2010: new adventures of an old flame. Cell 140: 771-776.
37. Dinarello C (2010) Anti-inflammatory Agents: Present and Future. Cell 140(6): 935-950.
38. Kumar S, Bajwa BS, Singh Kuldeep (2013) Synthesis and biological evaluation of substituted 4-arylthiazol-2- amino. International journal of advances in Pharmacy, Biology and Chemistry 2(2): 41-46.
39. Toth M, Matthews DE, Tracy RP, Previs MJ (2004) Agerelated differences in skeletal muscle protein synthesis: relation to markers of immune activation. Am J Physiol Endocrinol Metab 288((5): 883-889.
40. Barbosa-Filho JM, Piuvezam MR, Moura MD, Silva MS, Lima KVB, et al. (2006) Anti-inflammatory activity of alkaloids: A twenty-century review. Revista Brasileirade Farmacognosia 16(1): 109-139.
41. Iwalewa E, McGaw L, Naidoo V, Eloff J (2007) Inflammation: the foundation of diseases and disorders. A review of phytomedicines of South African origin used to treat pain and inflammatory conditions. African Journal of Biotechnology 6(25): 2868-288.
42. Villarreal G, Zagorski J, Wahl SM (2000) Inflammation: Acute. Ethno pharmacology 72: 275.
43. Dalgleish AG, O'Byrne KJ (2002) Chronic immune activation and inflammation in the pathogenesis of AIDS and cancer. Adv Cancer Res 84: 231-276.
44. Patel S, Rathod H, Kabra M, Vaishnav M, et.al (2014) Evaluation of Anti Inflammatory Activity of Hydroalcoholic Leaves Extracts of PolyherbalCombination of Vitex Negundo and Murraya Koenigiiagainst Carrageenan Induced Paw Edema in Rats. J MolPharm Org Process Res 2: 3.
45. Shimoda H, Shan SJ, Tanaka J, Seki A, Seo JW, et al. (2010) Anti-inflammatory properties of red ginger (Zingiber officinale var. Rubra) extract and suppression of nitric oxide production by its constituents. J Med Food 13(1): 156-162.
46. Verma S, Ojha S, Raish M (2010) Anti-inflammatory activity of Aconitum heterophyllum on cotton pelletinduced granuloma in rat. Journal of Medicinal Plants Research 4(15): 1566-1569.
47. Benni JM, Jayanthi MK, Suresha RN (2011) Evaluation of the antiinflammatory activity of Aegle marmelos(Bilwa) root. Indian Journal of Pharmacology 43(4): 393-397.
48. Singh M, Kumar V, Singh I, Gauttam V, Kalia AN (2010) Anti-inflammatory activity of

aqueous extract of Mirabilis jalapa Linn. leaves. Pharmacognosy Res 2(6): 364-367.
49. Ojewole J (2005) Antinociceptive, anti-inflammatory and antidiabetic effects of Bryophyllum pinnatum(Crassulaceae) leaf aqueous extract. J Ethnopharmacol99(1): 13- 19.
50. Ravi V, Saleem TSM, Patel SS, Raamamurthy J, Gauthaman K (2009) Anti-Inflammatory Effect of Methanolic Extract of Solanum nigrum Linn Berries International Journal of Applied Research in Natural Products 2(2): 33-36.
51. Silva DR, Baroni S, Svidzinski AE, Bersani-Amado CA, Cortez DA (2008) Anti-inflammatory activity of the extract, fractions and amides from the leaves of none Piper ovatum Vahl (Piperaceae)none . J Ethnopharmacol116(3): 569-753.
52. Muhammad N, Saeed M, Khan H (2012) Antipyretic, analgesic and anti-inflammatory activity of Viola betonicifolia whole plant. BMC Complement Altern Med 12: 59.
53. Ilango K, Maharajan G, Narasimhan S (2012) Antinociceptive and anti-inflammatory activities of Azadirachta indica fruit skin extract and its isolated constituent azadiradione. Nat Prod Res 27(16): 1463- 1467.
54. Goldberg AS, Mueller EC, Edward E, Desalva SJ (1991) Achillea millefolium. Journal of Pharmaceutical Sciences 58: 938-941.
55. Ismail SK, Sambasiva Rao KRS, Bhaskar M (2016) Evaluation of anti-inflammatory activity of Boswelliaserrata on carrageenan induced paw edema in albino Wistar rats. Int J Res Med Sci 4(7): 2980-2986.
56. C. Prucksunand, B. Indrasukhsri, M. Leethochawalit, and K. Hungspreugs, “Phase II clinical trial on effect of the long turmeric (Curcuma longa Linn) on healing of peptic ulcer,” The Southeast Asian Journal of Tropical Medicine and Public Health, vol. 32, no. 1, pp. 208–215, 2001.