

**ARE MODERN DAY PAIN KILLERS OUR ONLY ALTERNATIVE
TO PAIN MANAGEMENT:: AYURVEDA [INDIA] IS THE
ANSWER**

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ABSTRACT

It would be not at all wrong to say “There would be no doctor who has not prescribed an NSAID for pain ever in modern day practice”. Usually called NSAIDs which stand for “non steroidal anti inflammatory drug” are the commonest class of drug used to treat pain and which also has a long list of side effects and interactions. So while treating elderly patients a physician must know the other medications the elderly patient is taking to prevent any side effects that it can cause. On the contrary the natural herbs which have effective pain management have less or no side effects if they are prescribed by an Ayurvedic practitioner. Pain is something for which herbal medicines are commonly used. It is much easy to make a multi herb combination which not only take care of pain but yes can work on other factors which are required to improve joint pain.

This review aims to investigate how the NSAIDs work [pharmacokinetics & pharmacodynamics], as well as their side effects and interactions with other medications. Together with are gathered generally accessible herbal painkillers that can be used in place of or in addition to conventional painkillers or with pain management techniques.

HOW THE NSAIDs WORK ::

There are two types of cyclo-oxygenase enzymes [1][2][3][4].

COX 1 :- makes prostaglandins and thromboxane A₂ that protect the gastric mucosa, platelet aggregation and renal homeostasis etc.

COX 2 :- makes prostaglandins that play major role in fever, pain and inflammation.

Selective NSAIDs block only COX 2 enzyme but nonetheless have high cardiac and nephrotoxic side effects. On the contrary nonselective NSAIDs block both COX 1 and 2 and have various side effects combined with high gastric adverse effects because they damage the mucosal lining. NSAIDs are typically broken down in liver and eliminated via urine.

NSAIDs are prescribed to patients in cases of acute pain, that is anything causing acute musculoskeletal injury and also in pain due to arthritis as they possess anti inflammatory properties[5] [6]

KNOWN ADVERSE EFFECTS ::

1] NSAIDs AND YOUR HEART :- A study was conducted where patients with congestive heart failure were evaluated. It was observed, people who were taking any sort of NSAIDs were at high risk for getting admitted to hospital for first time due to congestive heart failure [7]. All kind of NSAIDs (selective and non-selective) are associated with increased risk of cardiovascular adverse effects. Each medications risk and benefit profile should be evaluated before prescribing it to any patient [8].

2] NSAIDs AND YOUR GASTROINTESTINAL TRACT :- The reason why NSAIDs cause GI side effects is because they prevent the production of prostaglandins, which weakens the GI mucosal barrier and makes a person more prone to GI bleeding. Now to prevent the GI ulcers and bleeding one can use the COX 2 inhibitors but using them increases high chance of cardio and nephrology side effects [9].

3] NSAIDs AND YOUR KIDNEYS :- Prostaglandin and thromboxane production is inhibited by NSAIDs, which leads to renal constriction of renal vessels and that decreases renal perfusion. Side effects of NSAIDs related to kidneys are less common than GI and cardiovascular but older population is more likely to experience NSAID-induced nephrotoxicity in the form of

renal papillary necrosis, acute interstitial nephritis, reduced GFR, hyperkalemia, edema, nephrotic syndrome, sodium retention and CKD [1].

4] NSAIDs AND YOUR BLOOD PRESSURE :- There are 2 mechanism by which NSAIDs are thought to increase blood pressure.

A] By inhibiting the prostaglandin synthesis , which leads to interfere blood supply to kidney and thus manipulate the blood pressure in the body.

B] NSAIDs have shown to increase serum aldosterone, which results in sodium retention and thus increases blood pressure [10].

The typical increase in blood pressure caused by NSAIDs is 5 mmHg. A study shows that NSAIDs were prescribed along with hypertensive medication or CHF medication in around 60% of older population [11].

5] NSAIDs AND YOUR BRAIN :- Studies have shown that use of long term NSAIDs increases the risk of stroke [12]. A study in 2011 showed how use of NSAIDs on long term basis increased the risk of cardiac event and stroke by almost 64% at two years time [13]. NSAIDs can cause hypertension, a key risk factor for stroke, by interfering with salt excretion and vasoconstriction. Moreover, these drugs have the ability to promote platelet aggregation and boost thrombus formation [14].

6] NSAIDs WITH YOUR DAILY DRUGS :- After a certain age many people have to use certain drugs for their daily use like anti hypertensives, anti diabetics or thyroid medication to name a few. Following are drugs with cause a reaction when used along with NSAIDs.

a] Gastrointestinal bleeding chances increase if the patient is on steroids, anti platelets, anti coagulants or selective serotonin re- uptake inhibitors along with NSAIDs.

b] Chances of increase in blood pressure occurs if the patient is taking ACE inhibitor, Angiotensin Receptor Blocker's, beta blockers, calcium antagonists and diuretics along with NSAIDs.

AYURVEDA [INDIA] ALTERNATE AND EFFECTIVE ANSWER TO PAIN

A patient in pain will look around for every possible solution for his pain and any possible way they can avoid as much adverse effects [15]. In the current time when ayurveda is finding its shelf space and is growing in popularity [16], we certainly need to educate people more about its use and safety to prevent side effects with modern medicine. Debilitating chronic pain places a significant social and financial burden on the healthcare system [4]. The purpose of the following review is to compile safety and efficacy information on some of the most popular herbal painkillers.

a] Ginger [*Zingiber officinale*] :- Herbalists across China and India have been using it as medicine for the past 2500 years its active ingredient particularly is 6-gingerol [17]. By preventing the metabolism of arachidonic acid, it gets its anti-inflammatory properties [18][19]. According to data, there is a delayed therapeutic response, thus it cannot be used to treat acute pain situations but good for long term pain management [20][21][22] [23]. Used for headaches, arthritic pain, muscle pain and has huge antioxidant properties.

b] Turmeric [*Curcuma longa*] :- The active compound is called curcumin. As it can control NF-kappa B, AP-1 and JAK-STAT signalling pathways as well as inflammatory cytokines like interleukin-1 beta, IL-6, IL-12, tumour necrosis factor alpha, and interferon gamma, this gives curcumin its anti-inflammatory, analgesic, antiseptic and antioxidant properties [24][25].

c] Capsaicin [natural chilli extract] :- From centuries topical application of capsaicin extract have been used to reduce pain[26]. Capsaicin causes selective and reversible loss of nociceptive nerve terminals after prolonged or intense exposure. The pain sensitivity is reduced for a long time to most stimulations, thus pain fibres cannot convey pain signals even after pain receptors are formed [27][28]. According to a trial, topical use of diclofenac combined with capsaicin provided better pain relief when diclofenac and capsaicin are used together then used alone [29].

d] Ashwagandha [*Withania somnifera*] :- Out of all herbal medicines it is one of the widely used Ayurvedic medicine for the purpose of joint pain. Its active component is withanolide glycosides which is extracted from its leaves. Treatment with *W. somnifera* resulted in a substantial decrease in the severity of pain and disability which was proved by a study with individuals suffering with OA. Moreover, it functions as an analgesic to calm the nerve system and reduce pain [30]. Due to its anti-inflammatory effects, *W. somnifera* has been shown to be useful in treating a number of rheumatologic disorders [31]. The plant's roots are said to have rejuvenating, immunomodulatory, anti-stress, anti-inflammatory, and antitumor effects [32].

e] Yograj Guggul :- a poly-herbal formulation extensively used by Ayurvedic practitioners to treat inflammatory conditions [33]. It gains its anti-inflammatory effect by inhibiting both COX 1, COX 2 along with 5-Lipoxygenase (LOX) enzymes. But as it inhibits very less of COX 1 it has bare minimal GI side effects.

f] Rasna [*Vanda roxburghii*] :- Heptacosane and octacosanol are the active components of rasna and they exhibit strong anti-inflammatory action [34]. The herb also eases osteoporosis-related joint discomfort [35].

g] Shudh shalaki [*Boswellia serrata*] :- The main component, boswellic acid, has a potent inhibitory impact on 5-lipoxygenase (5-LOX) and thus show anti-inflammatory and anti-arthritic properties [36][37]. Studies also show that even at high doses it is a safe drug of choice [38][39]

h] Tamarind [*Tamarindus indica*] :- Tamarind is a powerful anti-arthritic, anti-inflammatory, and anti-stress agent. It has high capacity to reduce inflammatory mediators that are involved in the cartilage degradation and bone degradation. It also helps to reduce physical and haematological changes involved with arthritis [40].

CONCLUSION

Given that NSAIDS are the most often given painkillers, it is important to comprehend their pharmacodynamics, pharmacokinetics, and adverse drug reactions in order to provide comprehensive care for pain in every patient. Elderly people should receive extra attention because they are more likely to experience these reactions and always have a lot of prescriptions on hand.

Stroke risk assessment should be carefully done and gastrointestinal, renal, and cardiovascular effects be monitored. These dangers and benefits should be carefully weighed in each patient to achieve the best possible results, especially in the case of the elderly.

This analysis offers a summary and an overview of the information that is currently accessible about the main herbs of interest which can be used as substitutes in managing pain. With the usage of herbal medicine becoming more and more popular every year, rigorous scientific and methodical investigations should be carried to bring more of such preparations in the market.

Reference

1. Harirforoosh S, Asghar W, Jamali F (2013). Advers effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. *J Pharm Pharm Sci*, 16: 821-847 [PubMed] [Google Scholar]
2. Vane JR, Botting RM (1998). Mechanism of action of nonsteroidal anti-inflammatory drugs. *Am J Med*, 104: 2S-8S [PubMed] [Google Scholar]
3. Cashman JN (1996). The mechanisms of action of NSAIDs in analgesia. *Drugs*, 52 Suppl 5: 13-23 [PubMed] [Google Scholar]
4. Rainsford KD (2007). Anti-inflammatory drugs in the 21st century. *Subcell Biochem*, 42: 3-27 [PubMed] [Google Scholar]
5. Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D, et al. (2013). Guidance on the management of pain in older people. *Age Ageing*, 42 Suppl 1: i1–57. [PubMed] [Google Scholar]
6. Malec M, Shega JW (2015). Pain management in the elderly. *Med Clin North Am*, 99: 337-350 [PubMed] [Google Scholar].
7. Page J, Henry D (2000). Consumption of NSAIDs and the development of congestive heart failure in elderly patients: an underrecognized public health problem. *Arch Intern Med*, 160: 777-784 [PubMed] [Google Scholar].
8. Rahme E, Bardou M, Dasgupta K, Toubouti Y, Ghosn J, Barkun AN (2007). Hospitalization for gastrointestinal bleeding associated with non-steroidal anti-inflammatory drugs among elderly patients using low-dose aspirin: a retrospective cohort study. *Rheumatology (Oxford)*, 46: 265-272 [PubMed] [Google Scholar].
9. Rostom A, Dube C, Wells G, Tugwell P, Welch V, Jolicoeur E, et al. (2002). Prevention of NSAID-induced gastroduodenal ulcers. *Cochrane Database Syst Rev*: CD002296. [PubMed] [Google Scholar].
10. Kumar B, Swee ML (2015). Nonsteroidal Anti-inflammatory Drug Use in a Patient With Hypertension: A Teachable Moment. *JAMA Intern Med*, 175: 892-893 [PubMed] [Google Scholar]
11. Vandraas KF, Spigset O, Mahic M, Slordal L (2010). Non-steroidal anti-inflammatory drugs: use and co-treatment with potentially interacting medications in the elderly. *Eur J Clin Pharmacol*, 66: 823-829 [PubMed] [Google Scholar].

12. Roumie CL, Mitchel EF Jr, Kaltenbach L, Arbogast PG, Gideon P, Griffin MR (2008). Nonaspirin NSAIDs, cyclooxygenase 2 inhibitors, and the risk for stroke. *Stroke*, 39: 2037-2045 [PubMed] [Google Scholar].
13. Barthelemy O, Limbourg T, Collet JP, Beygui F, Silvain J, Bellemain-Appaix A, et al. (2013). Impact of non-steroidal anti-inflammatory drugs (NSAIDs) on cardiovascular outcomes in patients with stable atherothrombosis or multiple risk factors. *Int J Cardiol*, 163: 266-271 [PubMed] [Google Scholar].
14. Park K, Bavry AA (2014). Risk of stroke associated with nonsteroidal anti-inflammatory drugs. *Vasc Health Risk Manag*, 10: 25-32 [PMC free article] [PubMed] [Google Scholar]
15. Ernst E., Willoughby M., Weihmayr T.H. Nine Possible Reasons for Choosing Complementary Medicine. *Perfusion*. 1995;11:356–359. [Google Scholar]
16. 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. doi: 10.1001/jama.280.18.1569. [PubMed] [CrossRef] [Google Scholar]
17. Ernst E., Pittler M.H. Efficacy of Ginger for Nausea and Vomiting: A Systematic Review of Randomized Clinical Trials. *Br. J. Anaesth*. 2000;84:367–371. doi: 10.1093/oxfordjournals.bja.a013442. [PubMed] [CrossRef] [Google Scholar]
18. Koo K.L., Ammit A.J., Tran V.H., Duke C.C., Roufogalis B.D. Gingerols and Related Analogues Inhibit Arachidonic Acid-Induced Human Platelet Serotonin Release and Aggregation. *Thromb. Res*. 2001;103:387–397. doi: 10.1016/S0049-3848(01)00338-3. [PubMed] [CrossRef] [Google Scholar]
19. Grant K.L., Lutz R.B. Alternative therapies: Ginger. *Am. J. Health Syst. Pharm*. 2000;57:945–947. doi: 10.1093/ajhp/57.10.945. [PubMed] [CrossRef] [Google Scholar]
20. Black C.D., Oconnor P.J. Acute Effects of Dietary Ginger on Quadriceps Muscle Pain During Moderate-Intensity Cycling Exercise. *Int. J. Sport Nutr. Exerc. Metab*. 2008;18:653–664. doi: 10.1123/ijsnem.18.6.653. [PubMed] [CrossRef] [Google Scholar]

21. Black C.D., O'Connor P.J. Acute Effects of Dietary Ginger on Muscle Pain Induced by Eccentric Exercise. *Phytother. Res.* 2010;24:1620–1626. doi: 10.1002/ptr.3148. [PubMed] [CrossRef] [Google Scholar]
22. Black C.D., Herring M.P., Hurley D.J., O'Connor P.J. Ginger (*Zingiber Officinale*) Reduces Muscle Pain Caused by Eccentric Exercise. *J. Pain.* 2010;11:894–903. doi: 10.1016/j.jpain.2009.12.013. [PubMed] [CrossRef] [Google Scholar]
23. Terry R., Posadzki P., Watson L.K., Ernst E. The Use of Ginger (*Zingiber Officinale*) for the Treatment of Pain: A Systematic Review of Clinical Trials. *Pain Med.* 2011;12:1808–1818. doi: 10.1111/j.1526-4637.2011.01261.x. [PubMed] [CrossRef] [Google Scholar]
24. Sahbaie P., Sun Y., Liang D.Y., Shi X.Y., Clark J.D. Curcumin Treatment Attenuates Pain and Enhances Functional Recovery after Incision. *Anesth. Analg.* 2014;118:1336–1344. doi: 10.1213/ANE.000000000000189. [PubMed] [CrossRef] [Google Scholar]
25. Lee J.Y., Shin T.J., Choi J.M., Seo K.S., Kim H.J., Yoon T.G., Lee Y.S., Han H., Chung H.J., Oh Y., et al. Antinociceptive Curcuminoid, Kms4034, Effects on Inflammatory and Neuropathic Pain Likely Via Modulating Trpv1 in Mice. *Br. J. Anaesth.* 2013;111:667–672. doi: 10.1093/bja/aet176. [PubMed] [CrossRef] [Google Scholar].
26. Capsaicin Neuropathic Pain: Playing with Fire. *Prescrire Int.* 2010;19:153–155. [PubMed] [Google Scholar]
27. Babbar S., Marier J.F., Mouksassi M.S., Beliveau M., Vanhove G.F., Chanda S., Bley K. Pharmacokinetic Analysis of Capsaicin after Topical Administration of a High-Concentration Capsaicin Patch to Patients with Peripheral Neuropathic Pain. *Ther. Drug. Monit.* 2009;31:502–510. doi: 10.1097/FTD.0b013e3181a8b200. [PubMed] [CrossRef] [Google Scholar]
28. Aasvang E.K., Hansen J.B., Malmstrom J., Asmussen T., Gennevois D., Struys M.M., Kehlet H. The Effect of Wound Instillation of a Novel Purified Capsaicin Formulation on Postherniotomy Pain: A Double-Blind, Randomized, Placebo-Controlled Study. *Anesth. Analg.* 2008;107:282–291. doi: 10.1213/ane.0b013e31816b94c9. [PubMed] [CrossRef] [Google Scholar]
29. Predel H.G., Ebel-Bitoun C., Peil B., Weiser T.W., Lange R. Efficacy and Safety of Diclofenac + Capsaicin Gel in Patients with Acute Back/Neck Pain: A Multicenter Randomized Controlled Study. *Pain Ther.* 2020;9:279–296.

doi: 10.1007/s40122-020-00161-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar].

30. Kulkarni R.R., Patki P.S., Jog V.P., Gandage S.G., Patwardhan Bhushan. Treatment of osteoarthritis with a herbomineral formulation: a double-blind, placebo-controlled, cross-over study. *J Ethnopharmacol.* May–June 1991;33(1–2):91–95. [PubMed] [Google Scholar]

31. Anbalagan K., Sadique J. Influence of an Indian medicine (Ashwagandha) on acute-phase reactants in inflammation. *Indian J ExpBiol.* 1981;19:245–249. [PubMed] [Google Scholar].

32. Mishra L.C., Singh B.B., Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (ashwagandha): a review. *Altern Med.* 2000;5:334–346. [PubMed] [Google Scholar]

33. Sharma JN. Comparison of the anti-inflammatory activity of Commiphoramukul(an indigenous drug) with those of phenylbutazone and ibuprofen in experimental arthritis induced by mycobacterial adjuvant. *Arzneimittelforschung.*1977;27:1455-1457.

34. Chawla AS, Sharma AK, Handa SS, Dhar KL. Chemical studies and anti-inflammatory activity of *Vanda roxburghii* roots. *Indian Journal of Pharmaceutical Sciences,* 1992; 54: 159-161.

35. Ahmed I, Kumar L, Kumar V. Efficacy of OST-6, a polyherbal formulation in the management of osteoporosis in postmenopausal women. *Orthopaedics Today,* 2002; 4: 241-244.

36. Safayhi H, Mack T, Sabieraj J, et al. Boswellic acids: novel, specific, nonredox inhibitors of 5-lipoxygenase. *J Pharmacol Exp Ther.* 1992;26:1143– 1146. [PubMed] [Google Scholar]

37. Sailer ER, Subramanian LR, Rall B, et al. Acetyl-11-keto- β -boswellic acid (AKBA): structure requirements or binding and 5-lipoxygenase inhibitory activity. *Br J Pharmacol.* 1996;117:615–618. doi: 10.1111/j.1476-5381.1996.tb15235.x. [PMC free article] [PubMed] [CrossRef] [Google Scholar].

38. Krishnaraju AV, Sundararaju D, Vamsikrishna U, et al. Safety and toxicological evaluation of Aflapin: a novel *Boswellia*-derived anti-inflammatory product. *Toxicol Mech Methods.* 2010;20:556–563.

doi: 10.3109/15376516.2010.497978. [PubMed] [CrossRef] [Google Scholar]

39. Sengupta K, Krishnaraju AV, Vishal AA, et al. Comparative efficacy and tolerability of 5-Loxin® and Aflapin® against osteoarthritis of the knee: a double blind, randomized, placebo controlled clinical study. *Int J Med Sci.* 2010;7:366–377. doi: 10.7150/ijms.7.366. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

40. Tamarind Seed (*Tamarindus indica*) Extract Ameliorates Adjuvant-Induced Arthritis via Regulating the Mediators of Cartilage/Bone Degeneration, Inflammation and Oxidative Stress Mahalingam S. Sundaram,1 Mahadevappa Hemshekhar,1,2 Martin S. Santhosh,1,3 Manoj Paul,1 Kabburahalli Sunitha,1 Ram M. Thushara,1 Somanathapura K. NaveenKumar,1 Shivanna Naveen,4 Sannaningaiah Devaraja,5 Kanchugarakoppal S. Rangappa,a,6 Kempaiah Kemparaju,b,1 and Kesturu S. Girishc,1,5 *Sci Rep.* 2015; 5: 11117. Published online 2015 Jun 10. doi: 10.1038/srep11117