Inflamagesic

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Compounding Without Compromise Since 1962

Studies have demonstrated that most Americans are in a hyper-inflamed and exacerbated state of pain because of our high consumption of sugar and animal products in the form of dairy, meat, fish, and eggs. Added to this is the exposure to environmental chemicals and genetically modified organisms, as well as ubiquitously low hormone production. We are the largest patrons of anti-inflammatory drugs, both prescription and over-the-counter. We lead the world in autoimmune diseases. The obvious primary combatant of this existence, as well as prevention, is a change in diet that becomes organic and plant based. However, in the mean time while these transitions are taking place, a product called Inflamagesic has been designed to effectively reduce pain and inflammation throughout the entire body while promoting collagen formation and healing.

Synthetic steroids, such as prednisone, and non-steroidal anti-inflammatory drugs (NSAIDS), such as ibuprofen and naproxen, work to cut off all inflammation. However, some inflammation is required for healing tendons, skin, and joints properly. NSAIDS and steroids even prevent the repair of tissues from daily wear and tear causing cartilage, tendons, ligaments, and muscles to thin out and therefore rendering them more susceptible to injury. This is especially detrimental to the elderly and to women, who with age, lose their ability to produce collagen. Dramatic examples of this effect are the bleed-outs and perforated ulcers due to extreme thinning of the stomach lining. Kidney and liver damage are other common but potentially devastating side-effects of NSAIDS, as are bronchospasm, blood dyscrasias, fluid retention, congestive heart failure, stroke, constipation, drowsiness, dizziness, and delayed ovulation.

Although some inflammation is necessary to catalyze the healing and repair process, too much inhibits these vital functions. Inflamagesic allows enough inflammation for healing while cutting down on the excessive and deleterious amounts of inflammation, maximizing the body's ability to recover from injury and maintain everyday health. It supports the structure and function of connective tissues and joints. It reduces the generation of eicosanoids and cytokines, such as prostaglandins, leukotrienes, and nitric oxide, by targeting the enzyme pathways of COX and LOX enzymes. (You've heard of the COX/LOX pathways in inflammation?) Inflamagesic can accomplish this without causing any of the issues associated with NSAIDs or steroids. Think of Inflamagesic as your healthy alternative to conventional anti-inflammatory drugs.

Inflamagesic is a blend of traditional herbs, including tumeric, boswellia, devils's claw, ginger, and yucca, as well as bromelian and quercetin. These botanicals and health supportive nutrients reduce allergic and asthmatic reactions, inhibit formation of inflammatory compounds, provide antioxidant protection against the damaging effects of free radicals, and reduce growth and metastases of tumors. Many of these herbs have been used for centuries in Ayurvedic medicine, and have proven beneficial in treating rheumatoid and osteoarthritis, headaches, and cardiovascular disease. The ingredients in Inflamagesic have been successfully used for brain and central nervous system inflammation that is involved in cases of depression, autism, TBI, and degenerative neurological diseases like Parkinson's, Alzheimers, and Multiple Sclerosis.

Getting Down to the Nitty-Gritty:

Tumeric, an herb used for centuries in Ayurvedic medicine, has been the subject of many research studies. Curcumin, one of turmeric's most active constituents, has been found to reduce inflammation and pain via several biochemical pathways that are similar to how NSAIDs work, but more gently and in balance. First, it drives down arachidonic acid release from phospholipids by reducing the activity of an enzyme called phospholipase A2. Second, it inhibits cycloxygenase-2 (COX-

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2) expression. Third, it lessens the macrophage production of nitric oxide. And fourth, it lowers TNFa's activation of nuclear factor kappa-beta (NF-kB). NF-kB elevates in response to stressors such as injury, stress, infection, chemical exposure, and consumption of animal products, as do all the other markers mentioned here. Tumeric's curcumin was even compared to phenylbutazone for its anti-inflammatory effect with favorable results. Tumeric also reduces pain by depleting substance P, the messenger molecule that carries the sensation of pain to our brains. A fabulous benefit is that there is virtually no toxicity at normal doses.

Boswellic acids are pentacyclic triterpenes thought to be the active ingredients of boswellia serrata gum resin, also known as Frankincense. Frankincense resin, a traditional herb of the Ayurvedic pharmacopoeia, has been used for centuries as an astringent, anti-arthritic, antiseptic, stimulant, and expectorant. It has an inhibitory and apoptotic affect against leukemia cells. Studies support the use of boswellia serrata in all inflammatory bowel diseases, asthma, arthritis, and autoimmune diseases.

Boswellic acids have been found to inhibit the 5-lipoxygenase (5-LOX) enzyme, thereby lowering the synthesis of leukotrienes from arachidonic acid. Boswellia dramatically reduces immune globulin synthesis and the leukotrienes before they can cause bronchospasm, helping to prevent asthma attacks. These boswellic acids also drive down leukocyte elastase involved in emphysema and the mucus production in cystic fibrosis, chronic bronchitis, and respiratory distress syndrome.

Research has also suggested that boswellia's beneficial effects are a result of its ability to prevent the expression of VCAM-1 and ICAM-1 induced by TNFa , making it useful in allaying atherosclerosis, rheumatoid arthritis, and other inflammatory conditions.

NSAIDS thin tissues through glycosaminoglycan degradation, opening up the susceptible tissues to injury. Boswellia, on the other hand, does not disturb glycosaminoglycan synthesis and promotes tissue and collagen growth.

Bromelain is the name given to a group of proteolytic (protein-digesting) enzymes, derived from the stem and fruit of pineapple. Bromelain reduces swelling, bruising, healing time, blood clotting, and tumor growth. It also rebuilds muscles and collagen, supports normal mucosal tissue function, and enhances the absorption of quercetin. Bromelain administration has been found to interfere with the inflammatory arachidonic acid cascade as well as lead to significant reductions in concentrations of 2-series prostaglandins, while simultaneously promoting the anti-inflammatory prostaglandin 3 series. It continues to modulate the immune system by reducing kininogen, which in turn inhibits bradykinin release. Research has also found that it lowers substance P, contributing to it analgesic properties. By way of degrading fibrin and fibrinogen, bromelain helps prevent the excess formation of blood clots.

Ginger has a long history of use in both Ayurvedic and Asian systems for health and well-being. It naturally contains a matrix of active constituents including gingerols, beta-carotene, capsaicin, curcumin, and salicylate. Ginger inhibits inflammatory prostaglandins, reduces pain and swelling, and has documented anti-ulcer and analgesic effects. Ginger has been found to reduce biosynthesis of leukotrienes, nitric oxide, and 2-series prostaglandins. The unique actions of ginger are a reflection of it being an inhibitor of both COX and LOX enzymes. Ginger has long been used for nausea, vomiting, and vascular inflammation.

Devil's claw is an herb that is native to Southern Africa. Related to sesame, the root was traditionally used as a digestive aid and to treat arthritis and fever. It is recognized in the European Pharmacopoeia as an analgesic, a sedative, a diuretic, and an anti-rheumatic. Both the whole herb and one of its major constituents, the iridoid harpagoside, have been shown to reduce cytokine production, including the inhibition of NF-kB activation and its subsequent inducible expression of COX-2 and nitric oxide. Harpagosides are the main anti-inflammatory constituents, acting as a COX-2 enzyme inhibitor, reducing prostaglandin E2 synthesis, and inhibiting cysteinyl leukotrienes. Devil's Claw was compared favorably to Vioxx in studies for back pain.

Quercetin, a flavonoid phytonutrient, is naturally occurring in onions, apples, broccoli, chocolate, wine, and citrus fruits. It travels in nature with vitamin C and other bioflavonoids such as rutin and hesperidin. Not only does quercetin have strong antioxidant activity, but results from studies suggest it also prevents mast cell and basophil degranulation, reduces leukotriene synthesis, and inhibits the activity of the NF-kB pathway; the latter mechanism may in turn decrease nitric oxide synthase expression. All of these mechanisms give it powerful abilities to stabilize the immune system and drive down allergic reactions. Quercetin promotes sinus and respiratory health and is excellent for use in patients with asthma. It is beneficial not only for reducing inflammation but also in rebuilding tissue. Quercetin inhibits the pathways of inflammatory prostaglandins without disturbing the prostaglandins that promote healing.

Yucca is a plant native to the Southwestern United States and Mexico. Related to agave, yucca contains yuccaols, phenols, sterols, gloriosaols, and resveratrols that act as steroids, COX 1&2 pro-inflammatory enzymes, and powerful antioxidants. Recently, researchers have identified the presence of not only resveratrol, but also resveratrol-like stilbenes in yucca. Resveratrol is the phytonutrient present in red wine that has been attributed with many of its health promoting benefits. Among its other numerous actions suggested by studies, resveratrol has been found to inhibit NF-kB activation and nitric oxide.

A Few Examples of Scientific Research

In a double-blind study published by Deodhar, et al, (1980), administration of 1200mg of curcumin for 2 weeks was found to improve morning joint comfort and walking time in individuals with joint concerns. One serving of Inflamagesic contains 750mg of turmeric standardized to contain 713mg of curcuminoids.

A double-blind, crossover trial performed by Kimmatkar, et al, (2003) found improvements in joint comfort as well as an increase in knee flexion and walking distance in participants who received 999mg per day of boswellia for 8 weeks. Once serving of Inflamagesic contains 500mg of boswellia.

In an open, non-placebo controlled trial of healthy adults with recently developed, mild joint concerns, Walker, et al, (2002) found that those receiving either 200mg or 400mg per day of bromelain for 30 days reported improvements in joint comfort. One serving of Inflamagesic contains 75mg of bromelain.

The results of a double-blind, placebo controlled, crossover study by Wigler, et al, (2003) found that individuals receiving 1000mg per day of ginger extract for 60 days had improvements in joint comfort on movement measured by a visual analog scale. One serving of Inflamagesic contains 100mg of ginger.

References:

Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum. 2001 Nov; 44(11):2531-8

Ammon HP, Safayhi H, Mack T. Sabieraj J. Mechanism of anti-inflammatory actions of curcumin and boswellic acids. J Ethnopharmacol. 1993 Mar; 38(2-3):113-9

Andersen ML, Santos EH, Seabra Mde L, daSilva AA, Tufik S. Evaluation of acute and chronic treatments with Harpagophytum procumbens on Freund's adjuvant-induced arthritis in rats. J Ethnopharmacol. 2004 Apr; 91(2-3):325-30

Banerjee M, Tripathi LM, Srivastava VM, Puri A, Schakal R. Modulation of inflammatory mediators by ibuprofen and curcumin treatment during chronic inflammation in rat. Immunopharmacol Immunotoxicol. 2003 May; 25(2):213-24

Basch E. Boon H, Davies-Heerema T. Foppo I, Hashmi S. Hasskarl J, Sollars D, Ulbricht C. Boswellia: an evidence-based systematic review by the Natural Standard Research Collaboration. J Herb Pharmacother. 2004; 4(3):63-83

Bingham R. Bellew BA, Bellew JG. Yucca plant saponin in the management of arthritis. J App Nutr. 1975: 27:45-50

Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of turmeric (Curcuma longa). J Altern Complement Med. 2003 Feb; 9(1):161-8

Comalada M, Camuesco D, Sierra S, Ballester I, Haus J, Galvez J, Zarzuelo A. In vivo quercitrin anti-inflammatory effect involves release of quercetin, which inhibits inflammation through down-regulation of the NF-kappaB pathway. Our J Immunol 2005 Feb; 35(2):584-92

Deodhar SD, Sethi R, Srimal RC. Preliminary study on anti rheumatic activity of curcumin (diferuloyl methane). Indian J Med Res. 1980 Apr; 71:632-4

Formica JV, Regelson W. Review of the biology of Quercetin and related bioflavonoids. Food Chem Toxicol. 1995 Dec; 33(12): 1061-80

Gagnier JJ, Chrubasik S, Manheimer E. Harpgophytum procumbent for osteoarthritis and low back pain: a systematic review. BMC Complement Altern Med. 2004 Sep; 15;4:13

Gaspani L, Limiroli E. Ferrario P, Bianchi M. In vivo and in vitro effects of bromelain on PGE(2) and SP concentrations in the inflammatory exudate in rats. Pharmacology. 2002 May; 65(2): 83-6

Grzanna R, Lindmark L, Frondoza CG. Ginger - an herbal medicinal product with broad anti-inflammatory actions. J med Food. 2005 Summer; 8(2):125-32

Guardia T, Rotelli AE, Juarez AO, Pelzer LE. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin, and hesperidin on adjuvant arthritis in rat. Farmaco. 2001 Sep; 56(9):683-7

Huang TH, Tran VH, Duke RK, Tan S, Chrubasik S, Roufogalis BD, Duke CC. Harpagoside suppresses lipopolysaccharide-induced iNOS and COX-2 expression through inhibition of NF-kappaB activation. J Ethnopharmacol. 2005 Sep30; [Epub ahead of print]

Kimmatkar N, thawani V, Hingorani L, Khiyani R. Efficacy and tolerability of Boswellia serrata extract in treatment of osteoarthritis of knee - a randomized double blind placebo controlled trial. Phytomedicine. 2003 Jan; 10(1):3-7

Kumakura S, Yamashita M, Tsurufuji S. Effect of bromelain on kaolin-induced inflammation in rats. Eur J Pharmacol. 1998 Jun; 150(3):295-301

Marzocco S, Piacente S, Pizza C, Oleszek W, Stochmal A, Pinto A, Sorrentino R, Autore G. Inhibition of inducible nitric oxide synthase expression by yuccaol C from Yucca schidigera roezl. Life Sci. 2004 Aug 6; 75(12):1491-501

Piacente S, Montoro P, Oleszek W, Pizza C. Yucca schidigera bark: phenolic constituents and antioxidant activity. J Nat Prod. 2004 May; 67(5):882-5

Reddy GK, Chandrakasan, G, Dhar SC. Studies on the metabolism of glycosaminoglycans under the influence of new herbal anti-inflammatory agents. Biochem Pharmacol. 1989 Oct 15; 38(20):3527-34

Roy S, Khanna S, Shah H, Rink C, Phillips C, Preuss H, Subbaraju GV, Trimurtulu G, Krishnaraju AV, Bagchi M, Bagchi D, Sen CK. Human genome screen to identify the genetic basis of the anti-inflammatory effects of Boswellia in microvascular endothelial cells. DNA Cell Biol. 2005 Apr; 24(4):244-55

Sato M, Miyazaki T, Kambe F, Maeda K, Seo H. Quercetin, a bioflavonoid, inhibits the induction of interleukin 8 and monocyte chemoattractant protein-1 expression by tumor necrosis factor-alpha in cultured human synovial cells. J Rheumatol. 1997 Sep; 24(9):1680-4

Setty AR, Sigal LH. Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy, and side effects. Semin Arthritis Rheum. 2005 Jun; 34(6):773-84

Shen CL, Hong KJ, Kim SW. Comparative effects of ginger root (Zingiber official Rosc.) on the production of inflammatory mediators in normal and osteoarthritic sow chondrocytes. J Med Food. 2005 Summer; 8(2):149-53

Surh YJ, Chun KS, Cha HH, Han SS, Keum YS, Park KK, Lee SS. Molecular mechanisms underlying chemopreventive activities of anti-inflammatory phytochemical: down-regulation of COX-2 and iNOS through suppression of NF-kappaB activation. Mutat Res. 2001 Sep 1; 480-481:243-68

Thomson M, Al-Qattan KK, Al-Sawan SM, Alnaqeeb MA, Khan I, Ali M. The use of ginger (Zingiber official Rosc.) as a potential anti-inflammatory and antithrombotic agent. Prostaglandins Leukot Essent Fatty Acids. 2002 Dec; 67(6):475-8

Tsai SH, Lin-Shiau SY, Lin JK. Suppression of nitric oxide synthase and the down-regulation of the activation of NF-kappB in macrophages by resveratrol. Br J Pharmacol. 1990 Feb; 126(3):673-80

Vellini M, Desideri D, Milanese A, Omini C, Daffonchio L, Hernandez A, Brunelli G. Possible involvement of eicosanoids in the pharmacological action of bromelain. Arzneimittelforschung. 1986; 36(1):110-2

Walker AF, Bundy R, Hicks SM, Middleton RW. Bromelain reduces mild acute knee pain and improves well-being in a dose-dependent fashion in an open study of otherwise healthy adults. Phytomedicine. 2002 Dec; 9(8):681-6

Wallace JM. Nutritional and botanical modulation of the inflammatory cascade - eicosanoids, cyclooxygenases, and lipoxygenases - as an adjunct in cancer therapy. Integr Cancer Ther. 2002 Mar; 1(1):7-37

Werbach M. (1993). *Nutritional Influences on Illness; A Sourcebook of Clinical Research, 2nd Ed.* Tarzana, CA: Third Line Press

Werbach M., and Murray M. (1994). *Botanical Influences on Illness; A Sourebook of Clinical Research.* Tarzana, CA: Third Line Press

Wigler I, Grotto I, Caspi D, Yaron M. The effects of Zintona EC (a ginger extract) on symptomatic gonarthritis. Osteoarthritis Cartilage. 2003 Nov; 11(11):783-9