

Topical and Oral Herbal Pain Remedies

Editorial

The World Health Organization has proclaimed the years 2000-2010 the Decade of Joint Health, because joint health is such a widespread public health concern. Arthritis is a general term used to describe a large grouping of health conditions, all of which manifest symptoms of pain and stiffness. Commonly diagnosed forms of arthritis include osteoarthritis, rheumatoid arthritis (autoimmune involvement), gout, psoriatic arthritis, ankylosing spondylitis, fibromyalgia and infectious arthritis (such as Lyme's Disease). The most prevalent debilitating forms are rheumatoid arthritis (RA), affecting 3 million people in the U.S., and the far more common osteoarthritis (OA). Some estimate that as many as 40 million Americans suffer with osteoarthritis. The most commonly recognized causes of arthritis are genetic predisposition, advancing age, obesity, trauma and "wear and tear." However, the 'wear and tear' theory is probably an oversimplification, because many elderly people never develop arthritis, after years of wear and tear [1]. The degeneration of joints in all types of arthritis involves ongoing biochemical processes that negatively alter metabolism essential to maintaining healthy joints. Although conventional medical diagnostics attempt to assign patients a differential diagnosis of one specific kind of arthritis, in reality, many patients exhibit a continuum of symptoms. For example, even in those individuals who are officially diagnosed with osteoarthritis, many pro-inflammatory cytokines are released. This may not be due to the immune dysregulation associated with rheumatoid arthritis, but instead can be caused by a myriad of other factors, such as toxicity and high levels of oxidative stress, which lead to accelerated tissue destruction [2].

Pain Management

In natural medicine, the goal is to address the causative factors of illness through an examination of diet, lifestyle, allergies, toxic load, gut integrity, presence of microorganisms and psychological factors. Uncovering these factors, and making the behavioral changes that will positively affect the disease process, ultimately will lead to increased wellness. However, these steps take time, and the issue of pain management needs to be addressed immediately, while the body readjusts to a less inflammatory state. While pharmaceutical drugs offer effective pain relief, their use long term is not desirable due a large number adverse secondary effects. NSAIDs, in particular, actually make the overall disease process of arthritis worse, by increasing the destruction of the tight junctures in the gastrointestinal mucosa, commonly known as 'leaky gut' and by

depleting the very nutrients necessary for joint repair, including iron [3], folic acid [4] and zinc [5]. COX 2 inhibitors, introduced with a media blitz touting them as a much safer drug therapy, are now known to also have serious side effects [6]. In this article, we will review several oral and topical botanical approaches to the pain and inflammation associated with arthritis, and other in-

flammatory conditions.

Topicals For Pain

For eons of time, humankind has searched for effective pain relief through the use of natural medicines applied topically over a painful or injured area. When some part of the body is injured, the innate, natural response is to rub the afflicted area. This act of rubbing itself seems to be therapeutic; however, the use of herbs when applied topically can enhance the healing response. Many botanicals offer excellent relief of pain and inflammation when massaged over muscles, tendons, ligaments and joints that are aching, tender, or traumatized.

Boswellia (Boswellia serrata)

Boswellia is a well researched herb that is a useful anti-inflammatory and can be used both internally and topically. For a full referenced discussion of Boswellia, please visit the section below in "Botanicals Taken Orally" below.

Teasel (Radix dipsacus) Xu Duan

Teasel is often referred to as Dipsacus. It is a dramatic tall flowering plant which has been used as a 'comb' both to groom animal and human hair and to pull wool on a weaving loom. It is commonly used in formulas for osteoarthritis in Traditional Chinese Medicine. Dipsacus tonifies the liver and kidneys, two of the organs most affected in arthritis. Dipsacus helps strengthen the bones and tendons and prevents damage from wear and tear. It also promotes the circulation of blood and helps "moisten" the joints. While research on Dipsacus as a solo herb is sparse in the medical literature, Dipsacus has shown clinical effectiveness in treating arthritis as part of TCM formulas such as Wangbi Chongji [7] and Shuguan Wenjing [8].

Angelica (Angelica pubescence, Angelica dahuricae)

The genus Angelica has many species which are traditionally used to assist in the moving of Qi and blood, eliminating blockages into the afflicted body part. Both topical and oral applications have demonstrated anti nociceptive action, thereby mitigating soreness and tenderness [9,10].

Editorial

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Rue (*Ruta graveolens*)

Ruta contains many anti-inflammatory flavonoids [11], which can inhibit inflammation and reduce oxidative damage related to arthritis and other inflammatory conditions [12]. Rue is particularly useful for ligaments and tight muscles following injuries. (i.e pulled hamstrings) It can be used topically or in homeopathic doses. Rue should not be used internally due to toxicity issues.

Aconite (*Aconitum napellus*)

The great healer Paracelsus has been quoted as saying... “Everything is poison...nothing is poison...only the dose permits something not to be poisonous. “Toxic substances may be harmless in small doses, while ordinarily harmless substances can be deadly if over-consumed: Even water !

Aconite, also referred to as Monkshood, is an herb feared by many due to its powerful effects and high degree of toxicity. However, in the proper small dose, it is unrivaled in its analgesic effects. Aconite first stimulates and later sedates nerves that are involved with pain, touch and temperature. The initial tingling gives way to a long continued anesthetic action. The famous Eclectic MD, Dr. Ellingwood, found that aconite could be extremely useful in the relief of acute pain. He suggested,... “perhaps the most immediate influence obtainable in acute pain is to put 5 drops each of Menthol and Aconite into the palm of the hand and hold it over the seat of pain for 2-3 minutes. The effect is instantaneous and marvelous.” One of the alkaloids found in Aconite, mesaconitine, shows efficacy in pain relief greater than can be achieved by the use of morphine [13]. However, the mechanism of action differs, since mesaconitine does not bind to opioid receptors, but via 5-HT receptors (5-hydroxytryptamine receptors) [14]. The 1968 Medicines Act recommends the use of aconite in topical preparations that does not exceed 1.3 parts of aconite to 100 parts of the topical applicant. This has been found to be below the amount that may cause a toxic reaction.

Bryonia (*Bryonia alba*)

The Eclectic medical doctors prominent in the late 1800's and early 1900's, recommended minute doses of bryonia as a remedy for arthritis. Indications for bryonia include:

- 1) Red or warm joints
- 2) Joint pain that is worse with exertion and better with rest
ing or after applying support such as a brace or ace bandage
- 3) Joint pain that is worse in cold wet weather, but improved
by heat

Bryonia contains several bitter glycosides including bryonin, bryoamaride, bryoniosides A-G, bryodulcoside, cucurbitacins, dihydrocucurbitacins, bryoioid, cabenoside and chrysophanic acid [15].

Cayenne (*Capsicum spp.*)

The oleoresin, capsaicin, is a resin found in many species of “hot peppers”. Shamans and folk healers traditionally used capsaicin as a skin rub for pain. More recent scientific studies have proven that this action depletes “Substance P”, a chemical released in response to injury and inflammation, which is believed

to be overabundant in the peripheral nerves of patients with arthritis, fibromyalgia and other painful syndromes.

Capsaicin binds to nociceptors in the skin, which stimulate afferent thinly-myelinated A and un-myelinated C nerve pain fibers. One of the main receptors is the Vanilloid Receptor 1 (VR1). VR1s are found in the peripheral neurons in the skin, specifically the A and C nerve fibers. Some VR1s are found in the brain, notably glutaminergic VRs exist in the hypothalamus where they are believed to be associated with the mediation of hypothermic actions [16,17]. VR1 is a non selective, cation channel which mediates stimuli from both chemical and physical triggers, including heat, low pH, capsaicin and chemical bi-products released due to inflammation. When the VR1 receptor is not activated it remains closed. Upon activation (ie. capsaicin binding), the VR1 channel opens. When capsaicin binds and the VR1 channel opens, a flood of calcium ions results in a depolarization of the nerve and an action potential. When the neurons containing these receptors are stimulated, they release the neurotransmitter, substance P. Substance P communicates a message perceived as an itch, burning sensation, or pain. If capsicum therapy is repeated often, the body cannot replenish substance P quickly enough to trigger the perception of pain. The depleted level of substance P results in analgesia for many types of pain: nociceptive pain (transmitted by normal physiologic pathways),

neuropathic pain (due to diabetic neuropathy), shingles, post-amputation pain syndrome and trigeminal neuralgia [16,17]. In addition to the depletion of substance P, some researchers have discovered that on-going treatment with capsaicin results in an irreversible destruction of primary afferent terminals related to the peripheral nerves, leading to analgesia. If the capsicum treatment is discontinued, the nerves can regenerate, leading to a return of sensation and pain [18,19].

Ginger (*Zingiber officinale*)

Ginger is a medicinal plant that has been widely used in Chinese, Ayurvedic and Tibb- Unani herbal medicines all over the world since antiquity. It has applications for a wide array of unrelated ailments that include arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, constipation, indigestion, nausea, vomiting, hypertension, dementia, fever, infectious diseases and helminthiasis [20]. Ginger's name is derived

from an ancient Sanskrit name, ‘singabera’(grows like a horn), which closely describes the appearance of the ginger rhizome. Ginger contains zingerberol, gingerols, shogaols, bisabolene, borneol, zingabaine and capsaicin [21]. Ginger suppresses prostaglandin synthesis through the inhibition of cyclooxygenase-1 and cyclooxygenase-2, and suppresses leukotriene biosynthesis by inhibiting 5-lipoxygenase, as well as modulating the cytokine, NF-Kappa Beta. Dual inhibition of cyclooxygenase and 5-lipoxygenase distinguishes ginger from nonsteroidal anti-inflammatory drugs (NSAID'S), and partially accounts for its positive therapeutic profile, while having fewer side effects than nonsteroidal anti-inflammatory drugs [22,23]. Ginger has been shown to decrease pain in arthritis. Studies have demonstrated strong anti-inflammatory and anodyne properties that can use useful in Osteoarthritis, Rheumatoid arthritis and gouty arthritis [24-26]. Ginger has been shown to be excellent as a topical application for pain, [27] and can be ingested as well [28].

Cinnamon (*Cinnamomum spp.*)

Cinnamon is the source of a penetrating, medicinal oil derived from the bark {cortex} twigs or leaves of a tropical tree. In Chinese medicine, cinnamon is one of the most widely used warming herbs for promoting circulation in joints and limbs [29]. Cinnamon also aids in blood sugar regulation, which helps the body control overall inflammation. Topical application of cinnamon helps to improve circulation and ease discomfort. When applied topically, Cinnamon may redden the skin and produce a warming sensation.

When rubbed into painful, stiff joints, ligaments and muscles, traditional Chinese medicine believes that it “invigorates the blood and relieves stagnation, thus relieving pain. Cinnamon oil applied topically acts to release bradykinins. Continuous application results in depletion of bradykinins and reduction of muscle and joint aching and tenderness [30]. Cinnamon may also modulate inflammation by influencing NfKB receptors [31].

Wintergreen (*Gaultheria procumbens*)

Wintergreen is a low-growing evergreen shrub found in the damp woods of the Eastern United States. Methyl salicylate is one of the chief components that naturally occurs in wintergreen oil which is expressed from the plant. It has a distinctive pleasant aroma, and is often used as an extract for flavoring purposes. Methyl salicylate has chemical properties similar to salicylic acid - an aspirin like compound with the ability to allay

Pain [32]. Methyl salicylate is a common ingredient found in many over the counter salves and ointments. Many companies choose to use synthetic, petrochemically based methylsalicylate, instead of natural Wintergreen Oil.

Peppermint (*Mentha piperita*)

Menthol is one of the principle essential oils derived from peppermint, and it has been historically used in Traditional Chinese Medicine (TCM). Menthol acts as a powerful analgesic when applied topically for various types of pain [33-34]. When menthol is applied to the skin, it initially produces a cooling sensation to inflamed areas, followed by a profound warmth.

Botanicals Taken Orally

White Willow Bark (*Salix alba*)

The use of willow bark dates back thousands of years, to the time of Hippocrates (400 BC) when patients were advised to chew on the bark of the White Willow tree to reduce fever and inflammation. White, Purple and Black Willow Bark (*Salix alba*, *purpurea* and *Salix nigra*), as well as members of the Poplar and Birch families, contain flavonoids, phenolic glycosides, including salicin, as well as salicin esters such as salicortin, fragalin and tremulacin. Some of these compounds are converted in the body into active salicylates, similar to the chemicals found in Aspirin. Thus, White Willow is often referred to as Nature's Aspirin. White Willow does not cause gastrointestinal bleeding as does Aspirin. This herb was traditionally used to support musculoskeletal health, ease the discomfort of aches and pains, reduce inflammation, fever and pain. Standardized extracts of Willow bark have been the subject of numerous research studies and clinical trials, which have proven its

efficacy in pain amelioration [35-40]. The effectiveness of White Willow may be reduced if dysbiosis (imbalance in the gastrointestinal microflora) exists. This situation can be helped by taking probiotics such as acidophilus.

Bromelain

Bromelain is a proteolytic enzyme extracted from the stems and fruits of the pineapple plant. Beneficial therapeutic effects of bromelain have been shown in several human inflammatory diseases, including arthritis and inflammatory bowel disease. Bromelain helps break down fibrin, which causes swelling by accumulating in inflamed areas and blocking off blood and lymph fluid. Bromelain also inhibits platelet aggregation and adherence of antigens to cell surfaces, which supports its widely observed anti-allergic function. Anti-inflammatory effects may also be linked to bromelain's ability to alter leukocyte migration and activation. Bromelain interferes with the production of prostaglandins and other substances that contribute to the inflammatory cascade, including eicosanoids, cyclooxygenases, and lipoxygenases [41,42]. Bromelain has been the subject of several successful clinical trials illustrating its efficacy in the treatment of osteoarthritis [43,44]. Bromelain is often used successfully as a digestive aid. In this situation it should be taken with food at the end of a meal. For anti-inflammatory effects, bromelain should be taken on an empty stomach. For consistent therapeutic value, its best to use supplements containing specific amounts of bromelain. The therapeutic dose ranges from 500-2,000 mg, three times daily. Bromelain can cause sensitivity in people who are allergic to bee stings, olive tree pollen, pineapple, grass pollen, and other allergens. As a digestive aid, bromelain is usually used in combination with ox bile and hydrochloric acid.

Boswellia (*Boswellia serrata*)

This botanical is derived from the gum exuded from the Indian tree, Salai guggul (*Boswellia serrata*). The tree is scraped and the resin is allowed to exude from the tree until it dries. Boswellia is listed in Chinese Herbal Medicine under the pharmaceutical name 'Gummi Olibanum' or "Frankincense" [45]. Boswellia has been used for centuries by Ayurvedic physicians for arthritic conditions. In Traditional Chinese Medicine, Boswellia is used for static blood, invigorating and promoting the circulation of Blood and Qi, while relaxing the sinews. Modern research has documented boswellia's ability to block inflammatory compounds which lead to a heightened pain response. Several constituents have been isolated, including the anti-inflammatory compounds 11-keto β -boswellic acid and Acetyl-11-keto β -boswellic acid (AKBA), which inhibit leukotriene

biosynthesis through the impairment of 5-lipoxygenase(5-LO) [46]. Other active components in boswellia include mixed acetyl-boswellic acids and pentacyclic triterpenes. These compounds also have powerful anti-inflammatory and analgesic activity, and act by decreasing the production of pro-inflammatory molecules in articular cartilage [47]. Boswellia has been shown to prevent the interference with GAG (glycosaminoglycan)

synthesis, [48] and improves blood and lymphatic circulation to the joints. Based on a rat study, the non-phenolic ration of *Boswellia serrata* gum resin (20-300mg/kg) exhibits an analgesic effect similar to morphine (4.5mg/kg) [49]. Clinical studies on

humans have also revealed the potent anti-rheumatic activity of this phytomedicine. In one study, boswellic acids given to patients with osteoarthritis for six months caused a dramatic reduction in the levels of the inflammatory marker, C-reactive protein [50]. Boswellia shows efficacy in the treatment of both Rheumatoid and Osteoarthritis in humans [51-54]. Other studies support the use of boswellia in autoimmune conditions [55].

Jamaican Dogwood (*Piscidia spp.*)

Jamaican Dogwood was used historically as one of the most effective pain relievers by the Eclectic physicians at the turn of the 19th century. It was commonly recommended for fibromyositis, joint pain, dysmenorrhea and pain associated with bone fractures [56]. In the Amazon and Jamaican rainforests, the curanderos (healers) and 'Bush doctors' use the plant to treat migraines, joint pain, sprains, muscular aches and neuralgia [57,58].

Corydalis (*Corydalis ambigua*) Yan Huo Su

In Traditional Chinese Medicine, Yan Hu Suo (*Corydalis ambigua*), a member of the Papaveraceae family, has been used for thousands of years for its powerful analgesic properties. Many alkaloids have been isolated, with dl-tetrahydropalmatine (THP) and Corydalis L among the most potent. The analgesic potency of the rhizome is 1 to 10% that of Opium. The main alkaloids have been demonstrated to have a significant effect

that is equivalent to approximately 40% of the analgesic effects obtained by using morphine, without the addictive properties [59-61]. THP and related constituents share a naloxone-resistant analgesic action and have no affinity for opiate receptors, which accounts for their non-addictive nature. They have been found to be dopamine receptor antagonists [62]. Corydalis has been shown to strengthen the analgesic function produced by electro-acupuncture in mice [63]. In a human trial, THP and its analogues, isolated from Corydalis, combined with Angelica, possessed analgesic activity and sedative-tranquilizing and hypnotic actions [64].

Ginger (*Zingiber officinale*)

Ginger is a widely used herbal medicine to aid with pain relief both via internal and external applications. Please visit the section on ginger above in "Topicals for Pain."

Turmeric (*Curcuma longa*)

Turmeric is a bright yellow spice used in preparing curry. It has powerful anti-inflammatory properties, which are credited to the chemical component curcumin.

Research suggests that turmeric suppresses nuclear factor kappa beta and interleukin-8, while enhancing glutathione biosynthesis [65]. Turmeric also inhibits NF-kappaB activation.

Chinese skullcap (*Scutellaria baicalensis*) Huang Qin

Chinese skullcap is often referred to as Scute, and is also known as Huang Qin in the traditional Chinese materia medica. It is one of the most widely used herbs in oriental medicine. It has a expansive range of therapeutic effects, including anti-inflammatory, anti-cancer, anti-viral, anti-bacterial and amphoteric effects on the immune response. The active ingredients found in Chinese

skullcap include natural anti-inflammatory

flavonoids and flavans. The flavonoids baicalin, baicalein and wogonin, have potent anti-oxidant properties [66].

Scute displays anti-inflammatory effects by reducing the expression of nitric oxide (NO), inducible NOS (iNOS), Cyclooxygenase2 (COX-2), Prostaglandin E2 (PGE2), Nuclear Factor-kappaB (NF-kappaB) and IkappaBalpha as well as inflammatory cytokines, such as IL-1beta, IL-2, IL-6, IL-12 and TNF-alpha. This is achieved through the downregulation of IKKalpha, IkappaBalpha, NF-kappaB activation [67]. Other studies have illustrated this herb's effect on the inhibition of the 5-LO pathway of arachidonic acid metabolism [68]. Research has illustrated Scute's effectiveness in treating gout, or urate-crystal induced arthropathy, and inflammation in animal models. Scute diminished MSU crystal-induced inflammation by reducing neutrophil recruitment and expression of pro-inflammatory factors and increasing the level of the potentially anti-inflammatory prostaglandin D2 [69]. In a double blind human study, a proprietary mixture of baicalin from Scute and catechins, two anti-inflammatory flavonoids, was tested against a traditional nonsteroidal anti-inflammatory drug, naproxen, for the management of the signs and symptoms of moderate osteoarthritis (OA) in humans. In this study, 103 subjects were randomly assigned to receive either the proprietary mixture of flavonoid molecules (baicalin and catechin, referred to as flavocoxid), [500 mg twice daily (BID)] or naproxen (500 mg BID) in a 1-month onset of action trial. In this short-term pilot study, flavocoxid was found to be as effective as naproxen in controlling the signs and symptoms of OA of the knee and that it may present a safe and effective option for those individuals on conventional nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors [70]. Scute has little known toxicity. The therapeutic dose is 2-6 grams per day.

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