

Botanicals that Alleviate Pain and Modulate Inflammation

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CHRONIC PAIN: PRIMARY HEALTH ISSUE

Chronic pain affects around 100 million Americans – a greater number than those affected by diabetes, heart disease, or cancer combined.² The annual cost of pain is greater than that of heart disease, cancer or diabetes; about 635 billion dollars in 2010.^{2,3}

Anyone who has ever been affected by pain knows how debilitating and exhausting it can be, especially over time. Acute pain from injury, illness, or headaches usually passes quickly but can develop into chronic pain. The most common chronic pain conditions include migraines, severe headaches, back pain, neck pain, facial pain, cancer pain, joint pain, and neurogenic pain.¹ Back pain is the leading cause of disability for Americans under 45 years old.² Persistent, chronic pain impacts a person's quality of life, functional capacity, and ability to work. Further, it contributes to mental and emotional distress.

Non-resolving inflammation and continual firing of pain signals in the nervous system play major roles in chronic pain. Inflammatory processes and neurotransmitters are implicated in the complex pain response. Typically, the sensation of pain is transmitted by afferent neurons from the periphery of the body to the spinal cord and from there to the brain. This elicits multiple responses, including production of natural endorphins. Feedback loops continually modulate and modify this process.

Recent studies report that spinal glial-mediated neuro-inflammation is a key factor in the development of chronic pain. This involves production of chemokines via NFκB (nuclear factor kappa-beta), which plays a major role in the inflammatory response.^{4,5,6} Since it is well-known that certain pro-inflammatory cytokines such as IL-1, IL-6, and TNF (tumor necrosis factor) are involved in the process of pathological pain,⁷ therapeutic approaches focus on analgesic and anti-inflammatory actions.

TRADITIONAL BOTANICAL THERAPIES FOR PAIN RELIEF

Pain-relieving botanicals have been used for millennia in

traditional medical systems. Scientists in the field of pain research are studying botanical extracts as they search for compounds that work through pathways other than the opioid receptors without causing side effects or dependency. Through this research we are gaining a deeper understanding of the complex biological mechanisms that modulate pain.

Scientists are also discovering the advantage of using whole herbs, which contain a complex array of biochemical compounds in a natural polypharmacy. In this way, medicine is slowly expanding from a single-target based model to explore multi-targeted approaches. Botanical medicines, especially when combined in harmonious formulations, naturally provide a synergistic and multi-targeted effect that supports the body's return to health.

For thousands of years, medical herbalists in most cultures have utilized the power of whole herbs to promote health and support the body's ability to heal from illness. Trained herbal practitioners combine multiple herbs to work together in a formula because experience shows that the body responds best to what we would today call a multi-targeted approach. Skillfully crafted botanical formulations have a history of safe, efficacious use for millennia as documented in Ayurvedic and Chinese medicines. These botanical formulations, still in use today, act powerfully to support and modulate complex physiological systems, most often with very few and minor side effects. They can also enhance benefits from medications.^{8,9}

BOTANICALS TRADITIONALLY USED FOR PAIN RELIEF

The botanicals reviewed in this paper have a long history of safe and efficacious use to help calm inflammation and relieve pain through various pathways. Corydalis and Notoginseng are two of the most highly-regarded botanicals used in Chinese medicine to relieve pain and promote healing. They are used to address both chronic and acute pain, including traumatic injuries. They are blended in formulas with herbs appropriate for the condition and person being treated.

The combination of White Peony and Licorice Root is widely-

known for its ability to relieve muscle spasms and pain and is included in formulations to support pain relief and enhance tissue healing. In the traditional understanding of Chinese medicine, Boswellia, Myrrh, Notoginseng, White Peony root, and Wild Turmeric are often used together in various combinations to move stagnation from the tissues, nourish the blood, relieve pain, and promote the healing response.

A clinical trial with 201 patients suffering from degenerative osteoarthritis of the knees were given a combination of Curcumin and Boswellia extracts. The combination of the two compounds was found to be more effective than either agent alone or than placebo.¹⁰

Many studies report that the herbs reviewed in this paper exert specific analgesic and anti-inflammatory properties along pathways that modulate pain and inflammation without development of tolerance. These herbs work on pathways other than the opioid receptors – for example, through modulating dopamine and cannabinoid receptors or through mediating neuroglial inflammation, particularly in the spine.^{5,6,9} Combined in a formula, these botanicals can benefit those with mild, acute, and chronic pain, and can be used along with standard pain approaches, especially when combined with appropriate exercise, diet, and lifestyle.

Botanical Ingredients for Alleviating Pain



White Willow Bark (*Salix alba*)

The ancient Greek and Roman physicians, including Hippocrates, Galen, and Dioscorides, valued White Willow bark to reduce fever and inflammation. Native Americans valued the bark to calm joint pain.¹¹⁻¹⁷ In the 1760s it was used medicinally for feverish conditions.¹⁶⁻¹⁸

In the early 1800s a French pharmacist isolated salicin from Willow bark and an Italian chemist synthesized salicylic acid from salicin. Several chemists synthesized acetylsalicylic acid (a derivative of salicylic acid) including Charles Gerhardt and later, three researchers from Bayer laboratories, including Felix Hoffman. This compound, noted for its antifebrile and analgesic activity, was first marketed in 1899 as aspirin.^{16,18,19}

Modern studies with White Willow bark confirm its effectiveness and safety as an analgesic, giving relief in arthritic joint pain, low back pain, and headaches.¹¹⁻¹⁵ The analgesic and anti-inflammatory actions of White Willow bark are attributed to its high concentration of flavonoids and polyphenols. These are found to inhibit cytokine production.²⁰ A number of studies show that White Willow bark extract modulates inflammatory mediators including TNF, NFκB, and interleukin factors.^{20,21}

Research finds that White Willow bark offers a multi-faceted spectrum of activity due to the many compounds found within the bark. Because of this, White Willow bark extract is found to exert very few to no adverse effects.^{21,22} Natural products standardized to contain higher amounts of salicin still contain the naturally-occurring polyphenols, salicylates, flavonoids, and other compounds that play therapeutic roles in modulating inflammation.^{20,21}

Salicin, a potent anti-inflammatory agent, inhibits over-expression of COX-2 and NF-κB factors, which are implicated in inflammation and abnormal gene expression.^{23,24} Several randomized controlled trials found that standardized White Willow bark providing 240 mg salicin effectively reduced pain from osteoarthritis and low back pain in patients compared to placebo.^{11,25}

Corydalis Rhizome (*Corydalis yanhusuo*)



Corydalis is the premier herb in traditional Chinese medicine to relieve pain of all kinds, most often in combination with appropriate and synergistic herbs.

Corydalis is known for its hemostatic qualities and is considered a primary herb for pain from traumatic injury. It is often used by itself and is traditionally valued to promote blood circulation, which helps bring fresh blood to areas of injury. This, in turn, helps relieve pain and promote tissue healing. While used to treat pain in any part of the body, it is especially

used for chest pain, abdominal pain, and dysmenorrhea.

The whole herb, Corydalis, is considered highly beneficial and efficacious. Modern studies report that Corydalis demonstrates potent analgesic and anti-inflammatory activity.²⁶⁻³⁰ The analgesic effect of Corydalis is found to involve participation of the cannabinoid receptors.²⁶ Studies show that Corydalis may offer a useful therapeutic approach for trigeminal neuropathic pain⁹ and for dysmenorrhea.³⁰

Research reports that its bioactive constituents work through several known pathways.³¹ Several bioactive alkaloids isolated from Corydalis are of great interest to researchers. These include tetrahydropalmatine (THP), dl-Tetrahydropalmatine (dl-THP), and dehydrocorybulbine (DHCB). Of these, THP and DHCB demonstrate the most potent analgesic and sedative effects on the CNS.^{32,34,35} In one study, 75mg THP showed nerve pain reduction in 78% of patients tested.²⁹ THP and DHCB are structurally similar and are found in Corydalis in almost equal amounts. They exert a very mild agonist effect on the μ-opioid receptor.³²

However, the affinity of DHCB for dopamine receptors is greater than 100 times its affinity for the μ-opioid receptor.³² THP and DHCB bind to dopamine receptors where they act as potent antagonists.³² Their analgesic effect is mediated by dopamine receptors, which suggests that dopamine plays a role in pain modulation. Many studies show dopamine plays a role in modulating pain circuits in the brain. Studies with mice engineered to be deficient in dopamine were found to be more sensitive to pain – suggesting that dopamine is also involved with pain threshold.⁹

The alkaloid DHCB exerts analgesic effects independent of the opioid receptors and is non-sedative. It is found effective in both inflammatory and neuropathic pain models with repeated use and without inducing tolerance. The Herbalome project is currently working on a DHCB-based drug for pain.³²

Wild Turmeric Rhizome (*Curcuma aromatica*)



Plants in the genus *Curcuma* (part of the Ginger family) are highly valued for their powerful therapeutic benefits. These botanicals are traditionally known as foods, medicines, dyes, and cosmetics. Wild Turmeric, also known as Yellow Zedoary, grows wild in India. This form of Turmeric is widely used, second only to *Curcuma longa* – common Turmeric. Wild Turmeric rhizome, noted in Chinese medicine to promote blood circulation and relieve pain, is particularly utilized for pain in the abdominal and hypochondriac regions. It is also known for its calming influence.³⁶

Wild Turmeric contains a higher volatile oil content than common Turmeric, including camphor.³⁶ Studies find that Wild Turmeric exerts anti-inflammatory, antiplatelet, antioxidant, and free radical scavenging activity. It is found to promote wound healing. As an anti-inflammatory, it mediates several pathways including the COX pathways.³⁶⁻³⁹

Curcuminoids, the active constituents in Turmeric, are yellowish-orange, lipid-soluble, natural phenolic compounds. Highly researched, they demonstrate many protective health benefits and offer powerful anti-inflammatory, antioxidant, antineoplastic, antiviral, and immunomodulatory activity.⁴⁰

Curcumin calms inflammatory pathways including NFkB, TNF, and multiple IL (interleukin) factors.^{41,42} NFkB is a key factor that modulates inflammatory signaling response. It is often associated with the expression of multiple disorders including arthritis and cellular disturbances.⁴³ Curcumin inhibits COX-2 and 5-LOX expression^{44,45} and also demonstrates neuroprotective qualities.^{46,47}

Indian Frankincense (*Boswellia serrata*)



Frankincense resin is highly revered as a sacred and potent medicine in many cultures.⁴⁸⁻⁴⁹ Ayurvedic and Chinese medicine practitioners especially value the resin for its ability to promote blood circulation and enhance health. It is traditionally used in Ayurvedic medicine to alleviate both rheumatoid arthritis and osteoarthritis. Studies with *Boswellia* extract confirm these benefits.^{49,50} A Japanese study found *Boswellia* extract to alleviate knee pain in healthy adults.⁵¹

Frankincense contains gum-like resinous constituents known as boswellic acids that exhibit powerful anti-inflammatory, analgesic, and health-promoting activity. *Boswellia* extract is found to benefit those with inflammatory bowel conditions.⁵²

Boswellic acid extracts are found to down-regulate multiple inflammatory pathways including 5-LOX, COX-2, and NFkB. LOX acts as a biological fuel for cellular dysfunction by stimulating EGF (epidermal growth factor), VEGF (vascular endothelial growth factor), and other growth factors.⁵³⁻⁵⁵ These extracts are also found to induce apoptosis, modulate cell-signaling, and to exert immunomodulatory influence.^{54,56-60}

Hops (*Humulus lupulus*)



Hops is a vigorous climbing plant whose flowers were first used for their ability to preserve and add flavor to beer in the middle ages in Europe.⁶¹ Paracelsus and other physicians in the 15th and 16th centuries noted hops benefits as a digestive aid and diuretic. The noted botanist and physician Avicenna (980-1037 AD) described the calmative and digestive influence of hops.

Native Americans utilized hops as a sedative, antirheumatic, and analgesic among other uses.⁶¹

Iso-alpha acids from hops flowers demonstrate anti-inflammatory activity in vitro and in animal studies of rheumatoid arthritis.⁶² In vitro studies found that a hops flower extract high in alpha acids was selective for inhibition of COX-2 inflammatory pathways.⁶³

Myrrh Gum (*Commiphora myrrha*)



Myrrh resin is a highly renowned medicinal throughout the ancient and modern world. Myrrh is traditionally used to treat multiple conditions including wounds and infections. It was one of the three gifts offered to the infant Jesus by the Magi and was revered by both ancient Egyptian and Arab physicians. Traditional herbalists value Myrrh for its ability to treat sore throats, canker sores, and gingivitis.^{64,65}

Both Chinese and Ayurvedic medicine value its ability to calm inflammation and move blood stagnation. Myrrh resin is widely revered in Chinese medicine to treat injuries due to trauma, arthritis, and blood stagnation.⁶⁵ The origins of Frankincense and Myrrh are thought to be on the Arabian Peninsula. Both are used to treat traumatic injuries as they are traditionally known to move stagnant blood, help relieve swelling, and promote circulation of fresh blood to an afflicted area. They are also known to help calm inflammation and alleviate pain. Frankincense and Myrrh are often used together because of their similar and complementary actions and it is noted that combining them together enhances their powerful actions.⁶⁶

Myrrh contains volatile oils, resin, gum, and a bitter principle. It is well-known for its anti-inflammatory, antibacterial, antioxidant, and antimycobacterial activity.^{64,65,67} Myrrh's effective antimicrobial activity is largely attributed to its unique sesquiterpenoids.^{64,65,67}

Panax Notoginseng Root (*Panax notoginseng*)



Traditional Chinese medicine often refers to Notoginseng as *the miracle root for the preservation of life*. It is used both internally and externally as a powerful hemostatic to reduce or stop bleeding especially after traumatic injuries. Notoginseng is the primary herb for all traumatic injuries including falls, fractures, and contusions. It is also noted to help alleviate pain.

Notoginseng promotes healthy blood flow to and from areas of injury, which supports healthy healing of damaged tissues. It has been used in this manner successfully for thousands of years either by itself or in combination with other botanical medicines, including Corydalis and Peony. Chinese medicine practitioners value it to vitalize blood circulation and as a

protector of the heart and vascular system.

Notoginseng is rich in saponins and immune-enhancing polysaccharides.⁶⁸ It is found to have the ability to address hypoxia and anoxia.⁶⁹ As a potent anti-inflammatory, Notoginseng modulates various inflammatory pathways and exerts a pain-relieving effect in animal studies.⁷⁰⁻⁷³ It is noted to significantly improve the status of those with rheumatoid arthritis with both anti-inflammatory and analgesic activity.⁷²

Notoginseng is also found to be neuroprotective and research suggests it may benefit recovery from spinal cord injuries.⁷⁴ One study that combined Notoginseng with conventional treatment for multiple fractured ribs and pulmonary contusions helped improve clinical outcome.⁷⁵

White Peony (*Paeonia lactiflora*)

Peony is perhaps best known for its beautiful flowers, which symbolize longevity in Asian art. Peony root has been a treasured medicinal for over 3000 years in China and around 500 years in Europe. Valued for numerous health benefits, it is known for its ability to enhance relaxation. In Chinese medicine, White Peony root is one of the main herbs used to nourish the blood and is combined with appropriate herbs to address pain or muscle spasm. It is particularly used for flank, chest, or abdominal pain patterns. It is also used to alleviate abdominal spasms and cramping pain or spasm in the hands or feet.



Peony root contains glycosides, flavonoids, proanthocyanidins, tannins, terpenoids, and complex polysaccharides. The glycoside paeoniflorin, the monoterpenoids, and other constituents of White Peony are known to be spasmolytic. Clinical trials find White Peony effective for many types of muscle cramps and to calm pain and spasm.⁷⁶⁻⁷⁹

The compound paeoniflorin is found to calm pain and joint swelling and to lessen the decline of bone and cartilage in experimental arthritis. It suppresses multiple inflammatory processes including prostaglandin and leukotriene production, reactive oxygen species, proinflammatory cytokines, and chemokines. It inhibits formation of new blood vessels and production of matrix metalloproteinases. Paeoniflorin is found beneficial to relieve both signs and symptoms of rheumatoid arthritis.⁸⁰⁻⁸³

Bromelain (from Pineapple Stem)

Bromelain, a proteolytic enzyme, is a component of pineapple commonly used as a digestive aid. It demonstrates anti-edematous, anti-inflammatory, and fibrinolytic activities. It exerts immunomodulatory influence and is noted to modulate cytokine expression.⁸⁴⁻⁸⁶



Bromelain is well-absorbed orally and therapeutic effects are often enhanced with higher doses.⁸⁷ Clinical studies demonstrate promising results as an analgesic and anti-inflammatory for the treatment of osteoarthritis.⁸⁶ Research suggests that it works as an analgesic through influencing pain mediators.⁸⁸

Licorice Root (*Glycyrrhiza uralensis*)

Licorice root is traditionally used in Chinese medicine as a synergist to moderate and harmonize the characteristics of other botanicals in a formula. Since it is soothing to the mucus membranes, Licorice is valued as a demulcent in Western herbal medicine. Research notes its anti-inflammatory, immunomodulatory influence.⁸⁹⁻⁹¹



Licorice extract is shown to increase immune function including production of interferon and NK (natural killer) cells.⁹² Multiple flavonoids have been isolated from Licorice, many of which show broad-spectrum antibacterial effects.⁹³⁻⁹⁷

For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email info@naturaedu.com.

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