

# Naturopathic Pain Management

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**C**ontrolling pain in patients is perhaps one of the physician's greatest challenges. Pain, quite often, is not the disease but is almost always a symptom of imbalance in one or more areas of the body. Because pain tends to be the greatest motivator for a person to seek medical care, this symptom often takes precedence over any others.

Pain, as discussed in this article, refers to that which is derived from the physical realm (to separate it from mental, emotional, and psychologic types of pain). More specifically, pain derived from soft tissues often has the best chance of being treated most efficaciously, depending on whether its cause can be discerned. After all, one of the main tenets of naturopathic medicine is "find the cause."

However, this approach is easily overlooked by some physicians who help patients deal with symptoms of pain, regardless of duration. Pain management from a naturopathic perspective includes several aspects of treatment in addition to using medicines that elicit a physiologic change in the patient's perspective of pain.

It is true that conventional pain medicines (many of which are derived from plant substances) offer strong and fast-acting modes of treatment and are quite useful in instances when pain is unbearable for patients (e.g., traumatic injuries, cancer).

## Naturopathic Approach to Treating Pain

In the naturopathic tradition, pain and disease are considered to be the result of such factors as inadequate diet, improper care of the body (sedentary lifestyle), and other lifestyle overindulgences and excesses. This is based on the concept that an organism is more likely to be healthier than one that is deprived in some fashion. A healthier organism also will be able to resist disease and pain better even if both come from external causes. In addition, the early naturopathic doctors prescribed fresh air, sunshine, proper diet, exercise, "scientific relaxation," (i.e., an early form of Western meditation designed to relax the mind), constructive thinking, and a positive mental attitude, with prayer and meditation to create a sound mind in a sound body.

These extremely simplistic recommendations provide the basic

framework for health; but striving for health when one has poor lifestyle habits is self-defeating at best. Thus, people need additional treatment using botanical medicines, nutraceuticals, or pharmaceuticals until a better state of health can be achieved.

The technique of pain control with natural medicines involves identifying, treating, and, if possible, removing the source of the discomfort. In addition, when treatment is focused this way, ideally, a patient can avoid the addictive perils of pharmaceutical pain medicines as well as their sometimes strong and toxic side-effects. Most importantly, from the perspective of removing the cause, physicians perhaps do their greatest service by altering the course of a person's health away from a protracted period of pain and concomitant disability.

The first intervention involves setting a course for healing the tissues that are the source of the pain. Removing dietary perils that prevent the body from being in its optimum state of health include limiting refined carbohydrates and optimizing protein, micronutrient, and fatty-acid intakes. Excess carbohydrate intake exerts a negative effect on insulin metabolism, provoking weight gain and the inflammatory cascade. Insufficient protein intake, at levels less than 30 percent of the Recommended Daily Allowance (0.8 g of protein per kg of body weight per day), may limit repair and regeneration.

An excess of foods that contain omega-6 fatty acids is a known promoter of inflammation, cancer, autoimmune conditions, and circulatory compromise.<sup>1</sup> Protein synthesis is compromised by a number of conditions, and protein-energy malnutrition is associated with impaired muscle function, immune dysfunction, decreased bone mass, impaired cognitive function, delayed wound healing (even wounds caused by surgical interventions), and increased morbidity.<sup>2</sup>

Medical conditions, including gastrointestinal (GI) disease, malabsorption syndromes, and chronic and acute infections, can lead to micronutrient deficiencies as well as increased protein and energy requirements. Patients with chronic pain often use prescription medicines heavily, which can, in turn, compound nutrient malabsorption, GI conditions, and loss of appetite.

## Proteolytic Enzymes

Proteolytic enzymes have analgesic effects in addition to their well-recognized anti-inflammatory and antiedemic properties. Enzyme-derived analgesia is based on inhibition of the inflam-

matory cascade as well as exerting a direct influence on nociceptors.<sup>3</sup> Bromelain (pineapple; *Ananas comosus*) is used orally to treat acute swelling and inflammation following trauma.

Bromelain is a grouping of proteolytic enzymes obtained from the stem and fruit of pineapple (*Ananas comosus*).<sup>4</sup> Bromelain is thought to exert its anti-inflammatory effect by altering leukocyte migration and activation. Other mechanisms of action include proteolysis at point of inflammation, fibrinolysis via the plasminogen-plasmin system, depletion of kininogen, inhibition of inflammatory prostaglandins, and induction of prostaglandin E1 (an anti-inflammatory prostaglandin).

Side-effects of taking bromelain may include GI upset with diarrhea. Immunoglobulin E (IgE)-mediated allergic reactions are possible but this has not yet been widely documented.<sup>5</sup>

#### Research on Efficacy

A 3-month study was conducted on the anti-inflammatory and analgesic effects of bromelain in osteoarthritis (OA) and rheumatoid arthritis.<sup>6</sup> The researchers tested bromelain's effects on mild, acute knee pain at a dose of either 200 mg or 400 mg per day. Total pain symptom scores were reduced by 41 percent and 59 percent, respectively, in each treatment group. Additional scores for stiffness and physical function were significantly decreased in the high-dose (400 mg per day) group compared to the low-dose (200 mg per day) group. In addition, the researchers noticed that, compared to baseline, overall psychologic well-being was significantly improved in both groups following treatment, indicating a significant dose-response relationship.

In another study, efficacy and tolerability of an oral enzyme preparation (Phlogenzym,<sup>®</sup> MUCOS Pharma GmbH & Co., Geretsried, Germany) containing 90 mg of bromelain was compared to the nonsteroidal anti-inflammatory drug (NSAID) diclofenac for treating OA.<sup>7</sup> This trial lasted 3 weeks and involved patients, ages 40–75 years, with active OA of the knee joint. Both groups experienced comparable reductions in joint tenderness, pain, and swelling, and slight improvements in range of motion (ROM) at 7 weeks' follow-up, with greater reduction of joint tenderness reduction in the Phlogenzym-treatment group. The investigators concluded that the enzyme preparation was equally efficacious and as well-tolerated as diclofenac for treating active OA.

Enzymes, particularly bromelain, have been shown to be helpful for treating postsurgical pain and edema. An interesting study divided postsurgical fracture patients into two treatment groups; the first was treated with a standard antiedemic medication and the other group was given an oral proteolytic enzyme preparation.<sup>8</sup>

Subjects who were treated with the enzyme preparation took it three times per day, in the first 3 days following surgery, then twice per day in the follow-up period. These patients experienced a continuous and significantly more rapid reduction in postoperative swelling compared to the control group (on the standard medication).

Furthermore, the enzyme-treated group had an average reduction of limb fluid volume by 8 percent while the control group experienced an increase of 100-percent fluid volume. The investi-



California poppy (*Eschscholtzia californica*).

gators also noted an analgesic effect; the total amount of analgesics taken by the enzyme-treatment group was significantly lower (especially in the early postoperative period) compared to analgesic intake in the control group.

Bromelain is useful for treating athletic injuries (namely, bruising and edema) and for speeding healing time. Healing of musculoskeletal injuries such as muscle strains and sprains, ligamentous tears, and contusions is helped by bromelain's ability to decrease fibrin, thereby promoting circulation and assisting resorption of post-traumatic inflammatory factors.

An in-office clinical study found that orthopedic patients treated with bromelain experienced reductions in swelling, pain at rest and during movement, and tenderness on all subsequent follow-up visits compared to baseline.<sup>9</sup> In addition, patient tolerance was noted to be very good.

These studies highlight the positive effects of enzymes for treating pain, inflammation, and edema. In addition, enzymes increase speed of healing and pain relief, and decrease inflammation. These are all distinct advantages of enzymes for treating painful conditions; in addition, these effects promote the healing process.

## Botanical Medicines

Several herbal medicines are useful for treating pain; the herbs addressed in the following section were selected because of their analgesic and anti-inflammatory effects. (There are several other herbs that are useful for treating painful conditions, so this coverage is not complete). These herbs exert beneficial effects on pain via their analgesic, anti-inflammatory, anxiolytic, and sedative properties. Using a combination of herbs that are best suited for certain conditions produces the best result. It is important to consider how pain affects each individual when offering a course of treatment for each patient.

### *Jamaican Dogwood*

Jamaican dogwood (*Piscidia erythrina*; piscidia) is a shrub found in tropical America and the West Indies. The medicine is derived from the bark. Jamaican dogwood has several pain-relieving effects. These include sedative, anti-inflammatory, and antispasmodic (smooth muscle) effects.<sup>10</sup> Historically, this herb has been used to treat neuralgia, migraine headaches, toothaches, insomnia, and smooth-muscle spasms (GI spasms). The herb has also been used for treating insomnia resulting from neuralgia or nervous tension.

Although Jamaican dogwood is a powerful sedative, relatively little research has been performed on this herb. *Piscidia* also acts as an antitussive and antipyretic.

Because of its potent neuromuscular sedative effects, piscidia is considered to be a toxic herb. This herb's reputation as a toxin stems from its use as a fish poison. Crushed leaves were used to stupefy fish, enabling them to be caught easily. The constituent responsible for this, rotenone, interferes with oxygen consumption in cold-blooded animals, acting as a toxin to them.

### *Corydalis and California Poppy*

*Corydalis* (*Corydalis cava*) and California poppy (*Eschscholtzia californica*) are herbs with historical use in pain management. The medicinal parts of corydalis are the tuber and root. Typically, corydalis was used for treating nerve damage, tremors, and muscle spasms because of the herb's effects as a mild sedative and tranquilizer. *Corydalis* was also used to treat hypertension and intestinal spasms.

Similarly, California poppy has been used historically to treat insomnia, sedation, aches and pains, nervous conditions, childhood enuresis, and bladder disorders. The dried stems and leaves are used. The active constituents are thought to be isoquinoline alkaloids<sup>11</sup>; among these active constituents is tetrahydropalmatine, which can cause liver toxicity if not monitored carefully. California poppy is sometimes confused with the opium poppy (*Papaver somniferum*). These plants are distantly related (they are in the same family in different genera); *Eschscholtzia* does not produce opium.

Several studies on these plants have been performed in combination because of their similar effects. Alkaloids derived from the corydalis rhizome (protoberberine alkaloids) have been shown to bind positively to gamma aminobutyric acid (GABA) receptors *in vitro*,<sup>12</sup> with the derivatives of corydalis exerting stronger effects than nonderivatives. GABA receptors in the human brain, when activated, typically facilitate downregulatory functions. That is, when stimulated, activation of GABA receptors leads to downregulation of certain neural activities. This activity is correlated with a calming/sedative effect.

A grouping of peptide structures in the brain—endorphins and enkephalins—have pain-modulating effects. These molecules are thought to bear much of the responsibility for altering pain responses in humans under a number of physical stressors. Typically, these peptides bind to opioid receptors in the nociceptive areas of the brain, thereby altering pain perception.

In one study, extracts of corydalis and California poppy have inhibited a particular degradation process (dimerization) of cer-

tain pain-modulating peptides in the brain. This effect is thought to prolong the activity of these pain-relieving molecules.<sup>13</sup> *Corydalis*, in this investigation, appeared to have positive modulatory effects on human endogenous pain-relieving molecules to a greater degree than California poppy did.

This study revealed the additive effects of both herbs on promoting and preserving elevated catecholamine levels. This effect is thought to explain the two herbs' sedative, hypnotic, and antidepressive activities.

These studies have demonstrated the unique effects of these herbs and their influence on neurotransmitter metabolism. While much research into the exact mechanisms of these herbs needs to be conducted, existing studies provide some information on the pain-modulating effects of these plant medicines.

### *Ginger*

Ginger (*Zingiber officinale*) is one of the more widely used herbal medicines. It acts as an antipyretic, antiemetic, antitussive, cardiac inotropic, antibiotic, antifungal, sedative, and analgesic.<sup>14</sup> These effects are varied and are dependent on the particular herb preparation used. The active constituents of ginger (gingerols and gingerdione) are derived from the rhizome and root of the plant.

Ginger is used for pain management because the herb is an analgesic and antioxidant, and inhibitor of inflammatory prostaglandins, thromboxanes, and leukotriene synthesis.<sup>15</sup> Ginger also produces antiplatelet aggregation effects,<sup>16</sup> thereby speeding healing of contusions and bruises. The analgesic effect of ginger may be related to one of its constituents known as shogaol. This substance has inhibitory effects on the release of substance P, a neurotransmitter that is used by the sensory neurons involved in the perception of intense pain.<sup>17</sup>

Ginger has been shown to have a mild effect on OA-related pain. Patients with moderate-to-severe OA pain were given a ginger supplement twice per day in a placebo-controlled, double-blinded study for 6 weeks.<sup>18</sup> At the end of the study, the researchers concluded that the ginger extract's effects on OA pain were statistically significant for reducing symptoms of knee pain, producing a moderate effect. Subjects who were treated with ginger reported less pain on standing and following walking. Adverse effects in the treatment group included mild GI upset. Ginger is a botanical medicine that can modulate pain via several effects. It has been shown to be an effective medicine for treating mild pain; side-effects are limited and are of short duration.

## Physical Medicine/Modalities

Physical medicines, the application of therapies to the body externally, are numerous and are excellent for identifying, treating, and resolving pain and its sources. While beyond the scope of this article, therapies such as traditional hydrotherapy, electronic therapies such as ultrasound and electric stimulation in all of its forms, myofascial trigger-point injections, acupuncture, and manual (osseous manipulation) medicine all provide excellent pain relief in and of themselves. Each of these modalities has a long history of use as well an excellent record of safety and effi-

cacy for pain treatment. Used in various combinations, the above therapies are powerful tools for moving patients from states of helpless pain to health and pain-free vitality.

### Prolotherapy and Regenerative Injection Therapy

Another form of physical medicine, prolotherapy, is an excellent technique for treating musculoskeletal pain. Prolotherapy generally uses intra-articular injection that causes growth of normal cells or tissue—ligamentous and tendinous tissues at the fibro-osseous junction—leading to stronger, more taut tendons, thereby disrupting pain patterns.

Regenerative injection therapy (RIT) is a modernized form of prolotherapy that utilizes injections into the fibro-osseous junction of the tendon or ligament that is causing the pain. Prolotherapy originated in the 1930s and is based on the theory that ligament and tendon laxity result in the generation of pain at the fibro-osseous junction; this was postulated by one of the technique's pioneers, George Hackett, M.D., who was a consulting surgeon at Mercy Hospital, in Canton, Ohio.

Dr. Hackett is credited with bringing the technique to mainstream medicine via his large clinical trial during which he observed 656 patients ranging in age from 15 to 88 years old with various forms of ligamentous joint pain. Dr. Hackett followed this patient population for 12 years and it is estimated that he administered 18,000 prolotherapy injections over this time period. He observed that 82 percent of his patients considered themselves cured during the follow-up period.

In addition, Dr. Hackett mapped common pain-referral patterns from tendon and ligamentous instability that are still applicable today.

As noted above, the RIT technique involved injection of a proliferative substance into the fibro-osseous junction in the tendon or ligament that caused pain. A large body of supportive research has examined different types of proliferative substances. The most often-researched and utilized substance today is dextrose solution. Dextrose produces several proliferative effects, including elevation of extracellular glucose levels to as little as 0.5 percent. This has been shown to raise levels of insulin-like growth factor 1, insulin-like growth factor 2, and transforming growth factor-beta in a variety of human cell types.<sup>19,20</sup>

The cellular response to extracellular glucose is quite rapid; levels of DNA rise within minutes to hours following exposure.<sup>21</sup> It is thought that as many as 15 different genes are induced, with exposure to elevated concentrations of glucose, to produce various cellular proteins associated with growth and repair.<sup>22</sup> There is a great deal of research that explains the mechanism of action of dextrose on connective tissue; a search through the literature will offer more information on prolotherapy.

#### Research on Efficacy

In addition to investigations of RIT's effectiveness for inducing connective tissue regeneration, other studies have explored the effectiveness of RIT for relieving musculoskeletal joint-related pain. Several studies explored the ability of RIT to lessen joint-specific pain.

### Botanicals for Treating Pain

Latin binomials	Common names	Doses
<i>Piscidia erythrina</i>	Jamaican dogwood; piscidia	Dried root bark: 2–4 g or via decoction per day Liquid extract: 1:1 in 30% alcohol, 1–2 mL per day Tincture: 5–15 mL per day
<i>Corydalis cava</i>	Corydalis	Infusion: 2–4 g of dried herb brewed, one time per day Tincture: 1–2 mL per day
<i>Eschscholtzia californica</i>	California poppy	Infusion: 1–2 tsp. of herb in 1 cup water per day Tincture: 1–4 mL per day
<i>Ananas comosus</i>	Pineapple (contains bromelain)	300 mg, three times per day
<i>Zingiber officinale</i>	Ginger	200–300 mg, three times per day

One study investigated RIT's effect on anterior cruciate ligament (ACL) laxity from treatment through 3 years' postinjection.<sup>23</sup> Subjects were enrolled if they had suffered from 6 or more months of knee pain in addition to documented ACL laxity (defined by a KT1000 anterior displacement difference [ADD] of 2 mm or more). RIT was performed, using 6–9 cc of 10-percent or 25-percent dextrose, every 2 months over a 10-month period.

At follow-up, pain at rest, pain on walking, and pain on stair use were reduced by 45 percent, 43 percent, and 35 percent respectively. Subjective measurements showed a 63-percent reduction in swelling, knee ROM improved by 10.5°, and the anterior displacement difference was reduced by 71 percent. RIT also produced clinically and statistically significant reductions in ACL pain.

RIT was also effective for treating pain related to knee OA. Patients with grade 2 or more joint narrowing and/or grade 2 or more osteophytic changes in any knee compartments were treated with RIT, using a 10-percent dextrose solution.<sup>24</sup> After treatment with one injection every 2 months over the course of 1 year, RIT-treated patients had a 44-percent decrease in pain, a 63-percent decrease in swelling, and an 85-percent decrease in knee buckling. Flexion ROM was increased by 14°. In addition, radiographic variables (lateral patellofemoral cartilage thickness and distal femur width in mm) remained stable at 1 year and ACL laxity was also reduced.

This study showed that RIT relieved OA complications such as pain and swelling. Perhaps even more importantly, this therapy stabilized joint degradation while reducing pain-related symptoms. This is a key factor in using preventive medicine techniques in pain medicine; the cause of pain is addressed and modulated.

RIT is used to treat numerous ligament- and tendon-related pain syndromes. Clinical studies have demonstrated efficacy for treating OA-related pain in the finger joints,<sup>25</sup> cervicothoracic pain and cervicogenic headaches,<sup>26</sup> and low-back pain.<sup>27</sup> RIT has generated much interest in recent years in the realm of interventional pain management. The use of steroidal and nonsteroidal medications have limited appeal for treating degenerative connective-tissue conditions while RIT offers a preventive and curative form of therapy. (The treatment is also relatively inexpensive when one considers the savings in reduced office visits, pain-medicine prescriptions cost, and life and work-related disability).

## Mesotherapy

Mesotherapy involves the injection of small amounts of combinations of natural and pharmaceutical medicines in the superficial tissues of the skin. Defined mainly by its unique style of injection, mesotherapy protocols are wide-ranging. Intracutaneous injections of medicines allow them to remain in the injected area longer. These injected solutions continue to penetrate deeper tissues in a time-release manner.

Mesotherapy is indicated primarily for treating pain that originates from injured musculoskeletal tissues, including both overlying muscles and connective tissues within injured joints.

The technique was founded in France in the late 1950s; it continues to be widely used in that country for a variety of purposes today. Considered to be a part of mainstream medicine in France, mesotherapy is used by approximately 16,000 practitioners there, primarily for sports medicine and pain management.<sup>28</sup> Mesotherapy has gained popularity in numerous other countries around the world today with many established national organizations. However, although primarily used for pain reduction, mesotherapy is just gaining recognition in the United States as a form of cosmetic medicine.

Originated by Michel Pistor, M.D., who practiced in France, mesotherapy is based on treating the tissues that originated from the mesoderm. The name of the therapy was based on Dr. Pistor's reasoning that: "[t]he action on the tissues originating from the mesoderm is so extensive that these treatments should be called mesotherapy." He advocated using the smallest dose of medicine, as infrequently as possible, in the correct location in order to achieve a clinical effect.

An analysis of the mesotherapy technique via radioisotope-serial scanning has shown that the more superficial the injection, the longer the solution remained in the treatment area.<sup>29</sup> Another study utilizing measurement of the injected medicine via venous blood draws showed that at 1 and 3 hours postinjection, lesser amounts of the injected medicine were found in the venous circulation according to the respective depth of injection.<sup>30</sup>

Overall, the mechanism of action of mesotherapy in pain medicine is derived from the novel form of injection whereby the dermis acts as a time-release dosing system, allowing relatively minute amounts of medicine to be absorbed both locally and systemically over a prolonged period of time.

A typical procedure involves using injection depths ranging from 2 to 4 mm directly over pain-affected structures or in corre-

sponding acupuncture points. The amount of medicine injected at each point is only 0.02–0.05 cc of solution. Classical mesotherapy solutions contain a base solution comprised of a local anesthetic and a vasodilatory pharmaceutical drug. Other medicines are added depending on individual indications.

Common examples include glucosamine sulfate, methylsulfonylmethane (MSM), B vitamins (methylcobalamin, pantothenic acid, pyridoxine, and folic acid), magnesium, and various homeopathic medicines. Vasodilators are used in order to increase microcirculation over the injured area, thereby assisting with delivery of mesotherapeutic solutions and general improvement of circulatory delivery of oxygen and micronutrients. Naturally derived vasodilatory medicines may be used as well; examples of these include sweet clover (*Melilotus officinalis*) or witch hazel (*Hamamelis virginiana*).

### Research on Efficacy

Currently, the majority of research on mesotherapy is derived from case studies; other more-rigorous studies are underway. One case series revealed beneficial effects of mesotherapy treatment in 65 patients with chronic thoracic pain. The subjects' pain had various causes, including arthritis, spinal stenosis, and various sprains and strains.<sup>31</sup> These patients' pain had not been adequately controlled with NSAIDs, narcotic analgesics, or muscle relaxants.

In another case series, 267 patients with degenerative arthritic pain were treated with mesotherapy; this was deemed as an "effective and reasonable treatment option" and no adverse side-effects/reactions were noted in the treatment group.<sup>32</sup>

Another case series determined mesotherapy to be a promising treatment option that was safe and efficacious for 132 patients with back and neck pain that was not lessened by at least 3 months of conventional treatments.<sup>33</sup>

Interestingly, mesotherapy appears to be amenable to the use of several different forms of medicines; combinations of pharmaceutical and natural medicines make this an especially effective form of pain resolution and management. Additional research is being performed on this technique, and its popularity as a pain therapy in the United States is expected to grow.

## Conclusions

Naturopathic pain management entails numerous aspects of preparing the body to heal (using nutrition), alleviating pain (proteolytic enzymes and botanical medicines); and prevention of further tissue degradation (prolotherapy and nutrition). All methods mentioned in this article are applicable to nearly all forms of musculoskeletal pain. Enzyme and botanical therapies are useful for treating visceral pain as well. The magnificence of natural medicines is their ability to modulate perception of pain, prevent continuous degradation of bodily structures, and limit the duration of pain by addressing its causative factors. □

### References

1. Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. *Biomed Pharmacother* 2002;56:365–379.

2. Gallagher HJ, Daly JM. Malnutrition, injury, and the host immune response: Nutrient substitution. *Curr Opin Gen Surg* 1993;92–104.
3. Klein G, Kullich W. Reducing pain by oral enzyme therapy in rheumatic diseases. *Wien Med Wochenschr* 1999;149(21–22):577–580.
4. Hale LP, Greer PK, Sempowski GD. Bromelain treatment alters leukocyte expression of cell surface molecules involved in cellular adhesion and activation. *Clin Immunol* 2002;104:183–190.
5. Nettis E, Napoli G, Ferrannini A, Tursi A. IgE-mediated allergy to bromelain. *Allergy* 2001;56:257–258.
6. 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;9:681–686.
7. Tilwe GH, Beria S, Turakhia NH, Daftary GV, Schiess W. Efficacy and tolerability of oral enzyme therapy as compared to diclofenac in active osteoarthritis of knee joint: An open randomized controlled clinical trial. *J Assoc Physicians India* 2001;49:617–621.
8. Kamenicek V, Holan P, Franek P. Systemic enzyme therapy in the treatment and prevention of post-traumatic and postoperative swelling. *Acta Chir Orthop Traumatol Cech* 2001;68:45–49.
9. Masson M. Bromelain in the treatment of blunt injuries to the musculoskeletal system: A case observation study by an orthopedic surgeon in private practice. *Fortschr Med* 1995;113:303–306.
10. Newall CA, Anderson LA, Philpson JD. *Herbal Medicine: A Guide for Healthcare Professionals*. London: The Pharmaceutical Press, 1996.
11. Kleber E, Schneider W, Schafer HL, Elstner EF. Modulation of key reactions of the catecholamine metabolism by extracts from *Eschscholtzia californica* and *Corydalis cava*. *Arzneimittelforschung* 1995;45:127–131.
12. Halbsguth C, Meissner O, Haberlein H. Positive cooperation of protoberberine type 2 alkaloids from *Corydalis cava* on the GABA(A) binding site. *Planta Med* 2003;69:305–309.
13. Reimeier C, Schneider I, Schneider W, Schafer HL, Elstner EF. Effects of ethanolic extracts from *Eschscholtzia californica* and *Corydalis cava* on dimerization and oxidation of enkephalins. *Arzneimittelforschung* 1995;45:132–136.
14. Langner E, Greifenberg S, Gruenwald J. Ginger: History and use. *Adv Ther* 1998;15:25–44.
15. Srivastava KC, Mustafa T. Ginger (*Zingiber officinale*) and rheumatic disorders. *Med Hypoth* 1989;29:25–28.
16. Srivastava KC. Effect of onion and ginger consumption on platelet thromboxane production in humans. *Leukot Essent Fatty Acids* 1989;35:183–185.
17. Onogi T. Capsaicin-like effect of (6) shogaol on substance P-containing primary afferents rats: A possible mechanism of its analgesic action. *Neuropharmacology* 1992;31:1165–1169.
18. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum* 2001;44:2531–2538.
19. DiPaolo S, Gesualdo E, Grandaliano G, Schena FP. High glucose concentration induces the overexpression of transforming growth factor-beta through the activation of a platelet-derived growth factor loop in human mesangial cells. *Am J Pathol* 1996;149:2095–2106.
20. Pugliese G, Pricci F, Locuratolo N, Romeo G, Romano G, Giannini S, Cresci B, Galli G, Rotella CM, Di Mario U. Increased activity of the insulin-like growth factor system in mesangial cells cultured in high glucose conditions: Relation to glucose-enhanced extracellular matrix production. *Diabetologia* 1996;39:775–784.
21. Ongley MJ, Klein RG, Dorman TA, Eek BC, Hubert LJ. A new approach to the treatment of chronic low back pain. *Lancet* 1987;ii:143–146.
22. Murphy M, Godson C, Cannon S, Kato S, Mackenzie HS, Martin F, Brady HR. Suppression subtractive hybridization identifies high glucose levels as a stimulus for expression of connective tissue growth factor and other genes in human mesangial cells. *J Biol Chem* 1999;274:5830–5834.
23. Reeves KD, Hassanein KM. Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity. *Altern Ther Health Med* 2003;9:58–62.
24. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med* 2000;6:68–74,77–80.
25. Reeves KD, Hassanein K. Randomized, prospective, placebo-controlled double-blind study of dextrose prolotherapy for osteoarthritic thumb and finger (DIP, PIP, and trapeziometacarpal) joints: Evidence of clinical efficacy. *J Altern Complement Med* 2000;6:311–320.
26. Linetsky FS, Miguel R, Torres F. Treatment of cervicothoracic pain and cervicogenic headaches with regenerative injection therapy. *Curr Pain Headache Rep* 2004;8:41–48.
27. Yelland M, Mar C, Pirozzo S, Schoene M, Vercoe P. Prolotherapy injections for chronic low-back pain. *Cochrane Database Syst Rev* 2004;2:CD004059.
28. 9th International Mesotherapy Conference [held by the French Society of Mesotherapy; proceedings]. Paris, France, October 20–22, 2000.
29. Kaplan A. Marks of pain produced by four different ways of injection [in French]. *Bulletin SFM* 1985;in vol. 62.
30. LeCoz J. and Dupont, J.-Y. Injection in eye of the knee by way of mesotherapy provides good concentrations intra-articularly [in French]. *Quotidien du Medecin*, September 20, 1983.
31. Smail H. Anterior thoracic pain with vertebral origins [in French]. 9th International Mesotherapy Conference [held by the French Society of Mesotherapy; proceedings]. Paris, France, October 20–22, 2000.
32. Leah da Silva J, Mesquita ME. Evaluation results of two methods of treatment with mesotherapy for chronic degenerative rheumatic pain [in French]. 9th International Mesotherapy Conference [held by the French Society of Mesotherapy; proceedings]. Paris, France, October 20–22, 2000.
33. Messedi-Kamoun, N., Ben Salah FZ, Dziri C. Mesotherapy in the treatment of 132 cases of spinal pain matters [in French]. 9th International Mesotherapy Conference [held by the French Society of Mesotherapy; proceedings]. Paris, France, October 20–22, 2000.

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