

# Rationale For Contifin™ -

# Glucosamine Complex™ -

# Arthegic™

The body is comprised of organs, the organs are made up of tissues, and the tissues are made up of cells. Holding all of this structure together and filling the voids is connective tissue. Connective tissue produces a biochemical framework that holds water, and it gives organisms resiliency, fluidity, elasticity and resistance to compression. It is also a medium within which infective agents are fought and intercellular communication occurs.

## CONNECTIVE TISSUE SUPPLEMENTS

W Y S O N G

### PURPOSE:

To supply natural nutrients to support the health of joints, cartilage, tendons, intervertebral discs, blood vessels, and all connective tissues.

### INGREDIENTS:

**Contifin™:** Proteoglycans, Glycosaminoglycans, Collagen [as cartilage digest (bovine), hydrolyzed cartilage (avian), hydrolyzed collagen (types I-IX), gelatin peptone].

**Glucosamine Complex™:** d-Glucosamines (n-acetyl, hydrochloride and sulfates).

**Arthegic™:** Natural Phytonutrient Extracts and Concentrates of *Boswellia serrata*, Sea Cucumber, Turmeric, Ginger, Devil's Claw, Yucca and Red Pepper; Cetyl Myristoleate.

- Contain no additives -

### DIRECTIONS:

**Contifin™ Suggested Dosage:** Begin with 2 capsules 3 times daily. After 30 days decrease dose to 1 capsule 3 times daily if desired effect is maintained. Rotate with Glucosamine Complex™ every 2-3 days.

**Glucosamine Complex™ Suggested Dosage:** 1 capsule twice daily. Rotate with Contifin™ every 2-3 days.

**Arthegic™ Suggested Dosage:** 2 capsules 3 times daily.



Optimal health is not possible without connective tissue health, and virtually all disease has connective tissue dysfunction in common. The loss of elasticity in arteries, the wrinkling of skin, delayed healing, susceptibility to injury, and the loss of water hydration in flaccid tissues – all common to aging – are a result of connective tissue degeneration.

The interlacing connective framework woven throughout the body is manufactured by specialized cells. Fibroblast cells create fibrous elastic and web-like connective tissue, chondroblast cells form cartilage and joint lubricating fluids, and osteoblast cells manufacture the matrix of bone.

These cells are able to manufacture and secrete filamentous-type molecules, such as collagen and proteoglycans, which interlace together and bind with water. They are able to manufacture these structural elements from substrates such as sugars, amino acids and more complex proteins and carbohydrates derived directly from the diet.

Until recently the nutritional basis for connective tissue health has been little understood and by-and-large ignored. This amorphous material that weaves throughout the body and holds it together is not nearly as exciting as a thinking brain, a beating heart or hormone-secreting glands. But since everything in life is interconnected and connective tissue is the interconnector, it is logical that without paying attention to connective tissue we cannot adequately understand or address the health of the organs within the body, or the health of the being as a whole.

Connective tissue is important in skin, fingernails, bones, tendons, ligaments, eyes, cartilage, teeth, joint synovial fluids, heart valves, mucous membranes lining the respiratory and digestive tract, intervertebral discs,

the lining of blood vessels, and the framework of organs everywhere. Collagen, a protein secreted by connective tissue cells, is the most abundant protein in the body. Proteoglycans – another biochemical secreted by connective tissue cells – are the next most abundant biochemical in the body. Their abundance should not make us take them for granted, but rather alert us to their extreme importance.

Not only does connective tissue hold things together and create form and resiliency, it is also important on a functional basis. Proteoglycans are incorporated into cell membranes and help regulate the flow of nutrients into cells from the blood. Connective tissue mucus blocks the path of disease-causing organisms that attempt to enter through the respiratory or digestive tract. Connective tissue biochemicals serve a broad range of bioregulatory functions, permitting tissues to intercommunicate: alerting the body to the invasion of pathogens, the need for repair, the control of growth, the integrity of tissues (helping to make sure liver cells produce more liver cells and not brain or bone cells), and calling for the need for nutrients or the removal of waste.

There is constant turnover of connective tissue, with damaged or aged material being removed and then replenished by the blast (building) cells. When injury occurs, this turnover can be remarkably accelerated to over three times greater than normal, thus increasing demand on nutritional raw materials.

When balance does not exist between breakdown and synthesis, net degeneration can occur. Age, decreased ability to digest connective tissue raw materials in food, disease,

stress, trauma and physical stresses from occupation or athletics can tip the balance in favor of breakdown.

Catabolic (tissue breakdown) enzymes (such as glycosidase, collagenase and catabolin) can turn elastic arteries brittle, causing joint lubricant to disappear, cartilage to thin, skin to sag, eyes to lose accommodation, disease resistance to lower, gums to recede, teeth to loosen and organs to fail. To prevent this, connective tissue must be constantly supplied with the raw materials to stimulate anabolism (tissue build up) and counteract catabolism.

To best understand how nutrition can affect the health of connective tissue, it is important to understand how basic nutritional elements form these tissues. If you were to cut into any tissue you would find that after the incision was made – other than at the cut – all tissue holds together. If you attempt to pull the tissue apart it resists tearing due to an elastic network of fibrous-like elements. This “mesh”, if you will, is made up of connective tissue cells which have secreted, long chain-like chemicals – predominantly collagen and proteoglycans. (Discussion resumes on Contifin page 4.)

**For The More  
Technical Reader:**

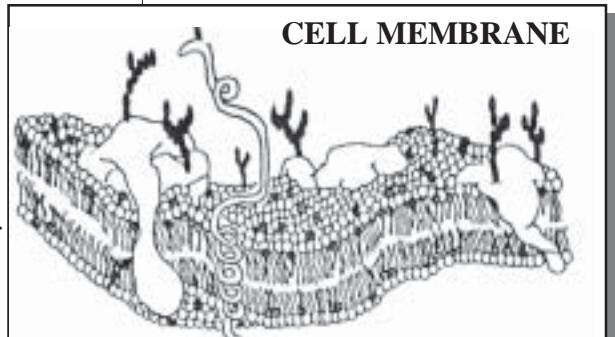
*Collagen is a protein made up of long, non-elastic chains of amino acids (predominantly proline, glycine, and lysine) interlaced with a more complex negatively charged biochemical, proteoglycan, which has the ability to hold to its surface water molecules. The protein that makes up collagen is in the form of a triple helix – three amino acid chains woven around each other. The resulting strength is such that it would take almost 25 pounds of*

*pressure to break a 1 millimeter collagen fiber. The combination of collagen, proteoglycans and water is what creates the moistness, strength, lubrication, tear strength and resiliency of living tissue.*

*Collagen fibrils provide the tensile strength to hold the gel-like material produced when proteoglycans attract water. The production of collagen is primarily dependent upon the right amino acids being available in the diet to build the protein chain, along with vitamin and mineral enhancers. Of particular importance to collagen is vitamin C, a deficiency of which can cause scurvy.*

*In 1536 the explorer Cartier described the disease in his men. Notice how the description is what we would expect from the loss of strength in connective tissue: “Some did lose all their strength, and could not stand on their feet... Others also had all their skins spotted of blood of a purple colour: then did it ascend up to their ankles, knees, thighs, shoulders, arms, and necks. Their mouths became stinking, their gums so rotten, that all the flesh did fall off, even to the roots of the teeth, which did also almost all fall out.”*

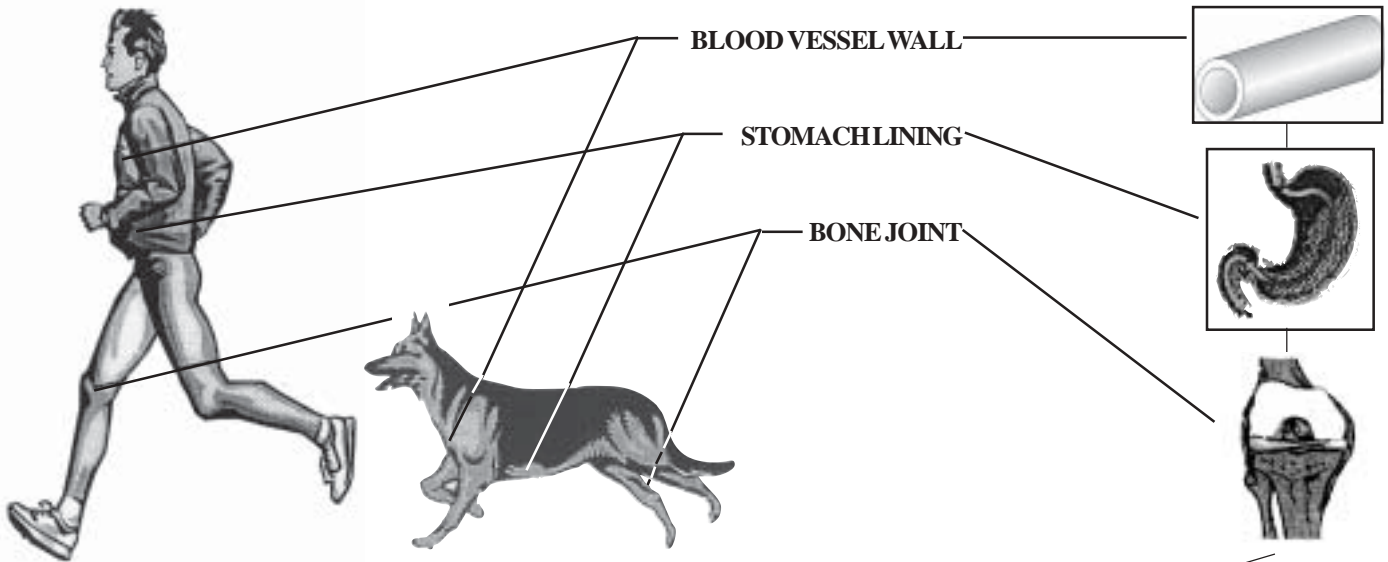
*There are many levels of nutritional deficiency, not always so dramatic as scurvy. Connective tissue*



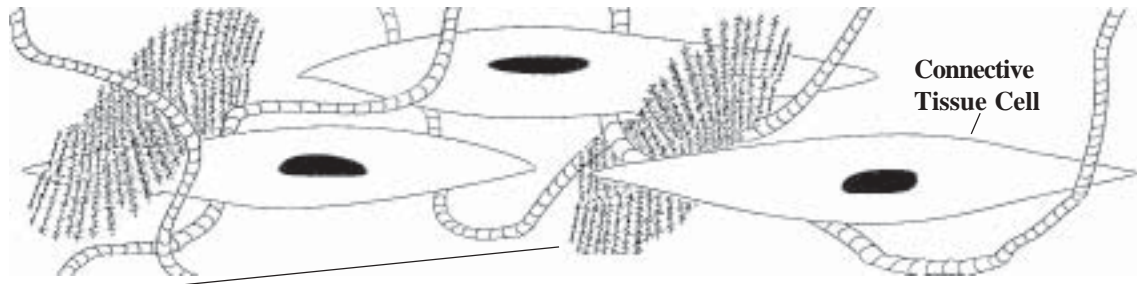
Section of a cell membrane showing various proteins, carbohydrates, and proteoglycans penetrating the surface. (Wysong RL. Lipid Nutrition: Understanding Fats And Oils In Health And Disease, p26. 1990.)

Figure 1.

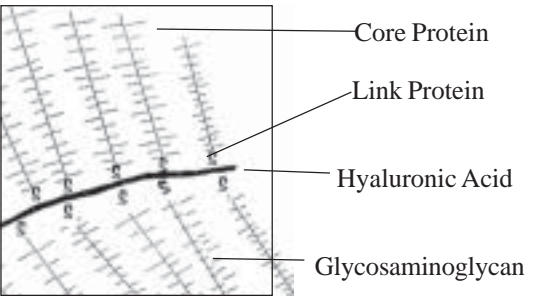
# CONNECTIVE TISSUE IS FOUND THROUGHOUT THE BODY



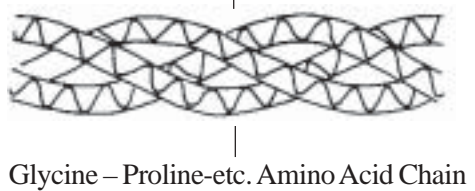
## CONNECTIVE TISSUE MATRIX



**Proteoglycans**  
(resiliency, water binding)



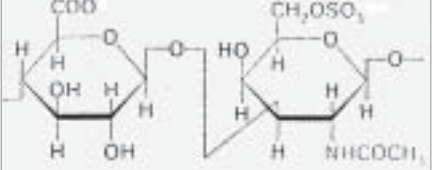
**Collagen**  
(tensile strength)



### Glycosaminoglycans

(Composition: Glucosamine, Galactosamine, Glucuronic Acid, Iduronic Acid, Galactose)

Example of repeating units of Chondroitin, a Glycosaminoglycan.



### Predominant Locations

- Hyaluronan ..... All tissues, synovial fluid, vitreous humor, cartilage
- Chondroitin sulfates ..... Cartilage, arterial walls, skin, bones, most tissues
- Keratan sulfates ..... Cartilage, arterial walls
- Dermatan sulfates      Skin, skeletal tissues (cartilage, bone, intervertebral discs, tendons), cornea, blood vessel walls
- Heparan sulfates ..... Arteries, lungs, cell membranes (not in skeletal tissues), Heparin Mast cells, lungs, liver, intestines

Figure 2.

or vitamin C deficiency can cause subtle weakening of tissues which may go undetected for years or be manifested in degenerative tissue diseases in the gums, kidney, joint, eye, or the digestive or respiratory systems. It may create symptoms easily passed off as aging, infection, tiredness, lingering colds, allergies, weakness, and sore back and neck.

In the blood vessel wall, weakness in connective tissue can result in tearing and inflammation. This can result in the development of atherosclerotic plaque, particularly in coronary vessels which experience constant mechanical stress from the beating of the heart. Decades later, a heart attack or stroke is not “just one of those things,” but rather due to a lifetime of low grade nutrient deficiency and connective tissue degeneration.

Proteoglycans are far more complex than collagen. They consist of amino sugars and organic acids arranged into long chains of repeating disaccharides called glycosaminoglycans (formerly named mucopolysaccharides). An important amino sugar is glucosamine sulfate. The long chain glycosaminoglycans are then attached like a bottle brush to a core protein. The resulting combination is called a proteoglycan. If that isn't complicated enough, these bottle brush-like proteoglycans are then connected by connecting proteins to another long compound called hyaluronic acid. This conglomerate is then known as an aggregating proteoglycan.

There are many kinds of proteoglycan configurations, from very large complex aggregates to simple forms with a small protein chain having one glycosaminoglycan chain attached to it.

Collagen and proteoglycans are ubiquitous throughout the body. But for them to be produced in the body the right building blocks must be present. Though they can be synthesized from basic food chemicals such as sugars and amino acids, this ability is limited and varies from individual to individual, as well as being suppressed in states of stress, advanced age or disease conditions.

It has now been found that by consuming preformed collagen and proteoglycans, the more complex, ready-made subunits (such as glucosamine sulfate, and fragments of proteoglycans such as chondroitin sulfate and keratan), can be directly incorporated into proteoglycans and greatly augment and stimulate their

and chondroitin sulfate are effective in herbivores (such as race horses), but are of more limited effectiveness if given orally.

(End of Technical Section)

**Broad Potential**

Understanding that connective tissue compounds are present in all tissues – including synovial lubricating fluid in joints, the vitreous humor in the eye, cartilage, the walls of arteries, skin, bone, intervertebral discs, tendons, the cornea of the eye, the lungs, the liver, the lining of the intestines, the respiratory tract, and even in immune cells – gives a hint about the broad potential of making readily available the important nutritional building blocks to permit continued health

**Glycosaminoglycans**

Results of One-Year Study in 140 patients.

Parameter	Placebo	Glycosaminoglycans
Lequesne Index –	Unchanged	Reduced
Echographic measure –	13% reduction	37% increase of cartilage thickness.

Murray, M. , Vital Communications, Inc. Figure 3.

manufacture. For example, since glucosamine sulfate is a rate limiting step in glycosaminoglycan synthesis, if it is deficient, connective tissue will not properly form.

It is interesting to note that not all animals have the ability to digest connective tissue in food. Research has shown that only those creatures adapted to eating flesh have the necessary digestive enzyme capability to incorporate these compounds into the body to be used as building blocks for connective tissue. Humans, dogs and cats have this ability, whereas herbivores such as deer and cattle do not. It is for this reason that injectable forms of connective tissue biochemicals such as cartilage, glucosamine sulfate

or repair of these tissues if damage or disease strikes. Glucosamines have been the subject of over 300 scientific investigations and over 20 double-blind studies.

**Wound Healing**

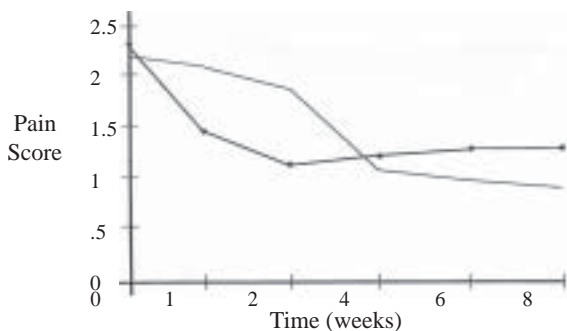
Clinical studies have proven, for example, that rubbing cartilage powder on open wounds or surgical incisions will greatly accelerate healing and increase the tensile strength of the healed tissue union. Glycosaminoglycans are proven effective in the treatment of corneal and other eye injuries.

**Heart Disease**

Proteoglycans have been demonstrated to decrease acute cardiac incidents. In one study over a

## Glycosaminoglycans vs. Ibuprofen

— Glycosaminoglycans —•— Ibuprofen



Murray, M. N. D., Vital Communications, Inc.  
Figure 4.

six-year period, 4 out of 60 people receiving chondroitin sulfate (a glycosaminoglycan) died, whereas 13 out of 60 of those not receiving the supplement died. Six out of 60 receiving the supplement experienced heart attacks, while 42 out of 60 not receiving the supplement did.

### Cancer

Several clinical studies have demonstrated the ability of cartilage supplements to arrest, and even reverse, some cancers.

### Joint Problems

The use of connective tissue supplements has not only been proven to reduce the pain and immobility of joint disease such as osteoarthritis and rheumatoid arthritis, it also reverses the condition and stimulates the regrowth of cartilage within degenerating joints. This has led researchers conducting the trials to conclude that these compounds are the treatment of choice, and far superior to conventional pharmaceutical agents such as nonsteroidal anti-inflammatory drugs, (NSAIDS such as ibuprofen and indomethacin). These may quickly relieve pain, but they do nothing to repair damaged joints. They also carry a variety of adverse side effects. Patients using steroids and NSAIDs experience an acceleration of

degeneration over time and are also subject to a host of side effects. Connective tissue supplements, on the other hand, give promise of healing and restoration over time and are without toxicity even in doses many times higher than effective ranges.

### Today's Diet Insufficient

Why is today's diet not sufficient in supplying the raw material for connective tissue? The answer lies in the fact that modern diets have veered dramatically from the natural archetypal makeup. Humans, as well as the pets within their care, now consume primarily processed foods that have been fabricated, fractionated and devitalized by a variety of processing methods. In contrast, the natural diet is raw and consists only of those foods that can be consumed and digested whole, directly from nature. This would include meats, organs, nuts, fruits and vegetables. But today's diet is comprised primarily of industrially-farmed grains and carbohydrates that have been milled and fractionated, with various food additives, and meat products that have been degraded through processing. Eating an apple, for example, is not the same as drinking a reconstituted, pasteurized and "fortified" glass of apple juice.

Eating pastas, breads, rolls and pastries that consist of refined flours are almost devoid of any basic building blocks of connective tissue like proteoglycans (which is now considered healthy by modern logic). But consumption of such substances in our natural state would have been impossible. A person or animal would starve to death long before they would ever be able to gather enough grains in the wild for sustenance. Even if

grains were to be found and eaten in their raw, uncooked, unprocessed state, they would be toxic.

Likewise, modern meat products have been separated from much of their connective tissue due to the removal of skin, fat, cartilage, tendons and ligaments, prior to cooking and preserving. This is not the same as eating whole flesh. When people eat meat, they are careful to trim away as much of the connective tissue elements (such as skin, grizzle and cartilage) as possible. The result is that we do not get the quantity of these connective tissue building blocks that would naturally be a part of our diet.

### Animals

Pets, on the other hand, are fed so-called "100% complete and balanced" packaged foods, made up primarily of grains. Consumers are told by authorities not to feed their pets table scraps and bones (rich in connective tissue).

The result is a whole host of connective tissue degenerative diseases now found in our companion animals: in the skin, eyes, digestive system, respiratory tract, immune system, organs, bones, joints, and intervertebral discs.

### Proof of Effectiveness

The mere fact that supplementation with connective tissue products (such as cartilage, chondroitin sulfate, collagen, and glucosamine sulfate) provides dramatic benefits is proof that our diets have veered from their natural makeup. If a supplement is capable of preventing or reversing a disease condition, that is evident proof of its essentiality, at least for the individuals it assists.

## The Wysong Spectrum

Contifin and Glucosamine Complex are designed to supply a spectrum of connective tissue elements to provide the appropriate building blocks for the maintenance of connective tissue health and the recovery from damage. Although isolated connective tissue elements (such as glucosamine sulfate, chondroitin sulfate, and cartilage powder) have proven to be effective supplements, they are more narrowed in their application. By combining the full spectrum of connective tissue elements in their more natural whole food form, Contifin and Glucosamine Complex recognize the complexity of tissue and the variation between individuals in requirements. The spectrum of connective tissue elements in these supplements can thus be utilized by the body based upon need.

Each kind of tissue has its own characteristically predominant type of collagen and proteoglycan. The following are known types of collagen: Type I is prevalent in tendons, Type II in intervertebral discs, Type IV in the lens of the eye, Type IX in the aorta, etc... Notice all the different kinds of proteoglycans and glycosaminoglycans. If only certain fragments, such as glucosamine or chondroitin are consumed, one could only hope for partial effectiveness, and the full potential of connective tissue nutrition would not be realized.

Contifin, Glucosamine Complex, and Arthegic should be used in combination with all other Wysong Diets for pets and lifestyle recommendations designed to restore natural, archetypal patterns. This includes: conversion of the diet to fresh, whole, raw, organic foods to the degree possible, given pure water, fresh air, daily sunshine and exercise, and elimination of chronic stress and exposure to home or occupational pollutants.

## ADDENDUM- ARTHRITIS

### (OSTEOARTHRITIS, RHEUMATOID ARTHRITIS)

The conventional approach to the pain of joint degeneration is to mask the symptoms. Little is done to address the causes, prevention, or reversal of the disease process.

Arthritic conditions are not simple problems easily resolved with a pill or a shot. They develop over long periods of time. To attempt a real resolution may require a variety of lifestyle changes, as well as significant amount of time. It cannot be expected that a degenerative condition, sometimes developing over decades, will be cured in days.

Arthritic conditions can be caused by overuse of a particular joint, allergic reactions within the joint tissue, aging degeneration and genetic predisposition. All of these causes can be either eliminated or moderated.

If allergy is the problem, finding the allergen is the key. Eliminating foods from the night shade family, including white potatoes, tomatoes, egg plant and peppers (not black) can reverse the problem for some people. Other food allergies may have to be discovered and the offending allergen eliminated through elimination-provocation diets. (See *Wysong Health Letter*, Vol. 6, No. 12.)

For others, allergic reactions to the body's own joint protein, such as in rheumatoid arthritis, may be reversed by oral toleration through consuming joint biochemicals such as those found in Contifin and Glucosamine Complex. Tolerization results from consuming the very nutritional elements the body is attacking in the joints. The digestive tract

and immune system begin to recognize joint tissues as friend rather than foe. In addition to supplementation with Contifin and Glucosamine Complex the preparation of home prepared soup stocks using bones and cartilage provides an additional dietary supply of the important collagens and proteoglycans which can produce tolerization.

In one case, a father who was exasperated by modern medicine's inability to help his child suffering from rheumatoid arthritis took matters into his own hands. By grinding up raw chicken cartilage (cooked didn't work), and feeding it to his child, the child experienced complete recovery. (Rheumatoid arthritis is an autoimmune [toleration] disease in which the body attacks its own joint cartilage. By feeding cartilage to the body, the digestive track begins to tolerate cartilage and the attack on the joints ends.)

If overuse of a joint is the problem, the obvious solution is to modify the activity or eliminate it altogether. This does not mean a person should become totally inactive because of the pain of arthritis. Non-painful exercise, such as isometrics and swimming, stimulates metabolism and circulation to help the healing process to proceed.

Anti-inflammatory drugs such as aspirin, cortisone and NSAIDs (e.g. ibuprofen, indomethacin, naproxyn) may give immediate pain relief, but they put people on a dead-end spiral headed straight for joint replacement surgery. The body sends pain signals as a warning not to overuse the part. Drugs, on the other hand, mute this warning and permit continued use of the part – causing even more joint inflammation, which furthers the degeneration of the joint. Taking drugs is like turning off the fire alarm as the fire continues to smolder in the closet.

In some individuals, particularly as they age and the body loses its digestive capability, (especially its ability to secrete stomach acid responsible for proper digestion of minerals and proteins), insufficient nutrients are absorbed. Modifying the diet to an increasing consistence of fresh, whole, raw nutrients will help increase nutrient bioavailability and digestibility. In addition, enzyme supplements such as Wysong Probiosyn™ and Panzyme™ will assist in digestion, and in some instances supplementation of hydrochloric acid may be necessary. (The use of hydrochloric acid should be explored and treatment initiated by a nutritionally oriented health care professional.)

Modern dietary choices, with an emphasis on refined, processed foods, can cause the body to become too acidic metabolically. This can result in a variety of problems including increased susceptibility to disease. Pathogens thrive better in an acid environment, tartar is more readily deposited on the teeth, joints degenerate and inflammation is stimulated. By converting the diet to its more natural, raw, whole form emphasizing high quality protein, fruits and vegetables, and drinking a glass of water with one half of a lemon squeezed into it each morning (or enhanced with Wysong Wellspring™), combined with Wysong Probiosyn to supply enzymes and probiotic cultures, this metabolic acidosis can be reversed and the proper environment set within tissues for healing to proceed.

Wysong EFA™ and Marine Lipids™ will help to provide important fatty acids which can naturally modify the inflammatory response in the joint, decreasing pain and stimulating healing. (See my book, *Lipid Nutrition - Understanding Fats and Oils in Health and Disease*.)

Probiotics – dietary friendly microbial cultures – such as found in Wysong Probiosyn, have also been proven to be effective in arthritic conditions. By populating the digestive tract with beneficial organisms, the digestive process is enhanced, micronutrients are synthesized and absorbed, pathogens are inhibited, and the immune response is modified.

Antioxidants – particularly beta carotene, vitamin A, and vitamins C and E are also important in decreasing the damage that can result to the joint from inflammatory processes. Wysong Food ACE™, Food C™, Spectrox™ and Mega C™ are excellent concentrated food sources of these important nutrients.

Vitamin B<sub>3</sub> (niacin) has also been reported to be effective in arthritic conditions. Fairly high doses are required and this may bring certain side effects. It would be wise to undertake this approach with a nutritionally-oriented health care professional.

There is also significant scientific evidence demonstrating that a variety of plant-based nutrients may ease the pain of arthritis, decrease the inflammatory reaction and help speed the healing process. These include ginger, capsaicin, turmeric, hawthorne, blueberries, boswellia, devil's claw, and yucca. A special Nutrient Support Formula incorporating many of these proven plant substances, Arthegic™, is available from Wysong.

### **Additional Beneficial Supplements**

To increase the effectiveness of Contifin and help prevent the development of food sensitivities or intolerances, rotate every 2-3 days with Glucosamine Complex. If digestive intolerance occurs with either product, use

the other. Additionally, if pain and inflammation are present, use Arthegic in combination with Contifin and Glucosamine Complex.

The following complementary supplements will provide synergistic nutritional benefits when using Nutrient Support Formulas. For humans, all NSF products should be taken in combination with all Wysong Foundation Formulas. In animals, Contifin, Glucosamine Complex, and Arthegic should be combined in the Optimal Health Program for animals.

---

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*

# SCIENTIFIC REFERENCES

## CONNECTIVE TISSUE NUTRITION AND ARTHRITIS, RHEUMATOID ARTHRITIS AND AUTOIMMUNITY

- Altman R. New Directions in therapy of osteoarthritis 17(2)1-2. 1987. (CS-3)
- Altman R, et al. Design and conduct of clinical trials in patients with osteoarthritis: Recommendations from a task force of the Osteoarthritis Research Society. *Osteoarthritis Cart.* 4, in press. 1996. *American Journal of Surgery.* 119:560-564. (CS-2)
- Barinaga M. Treating arthritis with tolerance. *Science.* 261:1669-1670. 1993.
- Bassler C, et al. Effects of glucosamine on differentiated human chondrocytes cultivated in clusters. *Rev Esp Reumatol.* 20 (suppl 1), Mo95 (abs). 1993.
- Birkenfeld P. Cross-Reactivity between the EBNA-1 p107 peptide, collagen and keratin: Implications for the pathogenesis of rheumatoid arthritis. *Clinical Immunology and Immunopathology.* 54:14-25. 1990.
- Bland JH. Osteoarthritis: A review of the cell biology involved and evidence for reversibility. *Sem Arthr Rheum.* 14:106-33. 1984. (GS-2)
- Blankenhorn G. Clinical efficacy of spondylvit (Vitamin E) in activated arthroses. *Z Orthop Ihre Grenzgeb.* 124:340-343. 1986. (CS-3)
- Bohmer D. Treatment of chondropathia patellae in young athletes with glucosamine sulfate. *Current Topics in Sports Medicine.* 1982. (GS-9)
- Brandt K. Pathogenesis of osteoarthritis. In:00:1417-1432 (CS-3)
- Breedveld GC. An arthritogenic lymphokine in the Rat. *J. Experimental Med.* November:1531-1545. 1987.
- Bucci L. Mucopolysaccharides (Chondroitin Sulfates) As dietary supplements: Sources, production and comparative bioavailability. *Chiropractic Products.* October:54-56. 1988. (CS-4)
- Bucci L. Reversal of osteoarthritis by nutritional intervention. *ACA Journal of Chiropractic.* November:69-72. 1990. (CS-3)
- Bucci L. Glucosamine - A new potent nutraceutical for connective tissues. *AAO Journal.* Summer:17. 1993. (GS-1)
- Burkhardt H. Oxygen radicals as effectors of cartilage destruction. *Arth Rheum.* 29(3)379-387. 1986. (CS-3)
- Burkhardt D. Laboratory evaluation of antiarthritic drugs as potential chondroprotective agents. *Sm Arth Rheum.* 17(2)35-53. 1987. (CS-3)
- Carney S. The structure and function of cartilage proteoglycans. *Physiol. Rev.* 68:858-910. 1988. (GS-3)
- Christensen K. Comparison of nutritional supplement effects in functional assessments of lower back patients measured by an objective computer-assisted tester. *Second Symposium on Nutrition and Chiropractic.* Palmer College. 19-22. 1989.
- Crolle G. Glucosamine sulphate for the management of arthrosis: A controlled clinical investigation. *Curr Med Res Opin.* 7:104-114. 1980. (GS-2)
- D'Ambrosio E. Glucosamine sulphate: A controlled clinical investigation in arthrosis. *Pharmatherapeutica.* 2(8)504-8. 1981. (GS-2) (GS-5) (GS-7) (GS-16)
- Dougados M, et al. The group of the respect of ethics and excellence in science. Recommendations for the registration of drugs used in the treatment of osteoarthritis. *Ann Rheum Dis.* 55:552-557. 1996.
- Drovanti A. Therapeutic activity of oral glucosamine sulphate in osteoarthritis: A placebo controlled double-blind investigation. *Clin Ther.* 3:260-272. 1980.
- Durie B. An assessment of the anti-mitotic activity of catrinx-S in the human stem cell Assay. *Journal of Biological Response Modifiers.* 4:590-95. 1985.
- Fialkova M. The effect of chondroitin sulfate preparations on wound healing and the strength of the surgical scar. *Biulleten Eksperimentalnoi Biologii I Medistiny.* 108(9)350-351. 1989. (CS-1)
- Giacovelli G, et al. Clinical efficacy of glucosamine sulfate in osteoarthritis of the spine. *Rev Esp Reumatol.* 20 (Suppl 1), Mo96 (abs). 1993.
- Greenwald R. Effect of oxygen-derived free radicals on connective tissue macromolecules. *Biological and Clinical Aspects of Superoxide and Superoxide Dismutase.* 160-171. 1980. (CS-3)
- Hamerman D. The biology of osteoarthritis. *New England Journal of Medicine.* 320(20)1322-1329. 1989. (CS-3)
- Harab R. Increase of chondroitin 4-sulfate concentration in the endochondral ossification cartilage of normal dogs. *Biochimica Et Biophysica Acta.* 992(2)237-240. 1989. (CS-1)
- Hassell JR. Proteoglycan core protein families. *Ann Rev Biochem.* 55:539. 1986.
- Hook M. Cell-surface glycosaminoglycans. *Ann Rev Biochem.* 53:847-869. 1984.
- Hunold H. Ergebnisse einer Kurzzeittherapie mit Dona 200-S. *Z. Allg. Med.* 57:1686. 1981. (GS-7)
- Ishikawa K. Clinical evaluation of the intra-articular injection of glycosaminoglycanpolysulphate for osteoarthritis of the knee joint: A Multicentric Double Blind Controlled Study. *Z Orthop.* 120:708-716. 1982. (CS-3)
- Jones, W. The benefits of MP supplements. *Horseman's Journal.* March, 1991. (CS-7)
- Krystal G. Stimulation of DNA synthesis by ascorbate in cultures of articular chondrocytes. *Arth Rheum.* 25(3)318-325. 1982. (CS-3)
- Kuder AU. Chicken Collagen Added to Orange Juice to Control Arthritis. *Arthritis Research News Alert Letter.* Received March 3, 1994.
- Lequesne M, et al. Guidelines for testing slow-acting drugs in osteoarthritis. *J Rheumatol.* 21:65-73. 1994.
- Londei M. Persistence of collagen Type-II specific T-cell clones in the synovial membrane of a patient with rheumatoid arthritis. *Proc Natl Acad Sci.* January:636-640. 1989.
- Lukaczer D. Natural treatment for sports injuries. *NFM's Nutritional Science News.* June:16-18. 1996. (GS-9)
- Machtley I. Tocopherol in osteoarthritis: A controlled pilot study. *J Am Ger Soc.* 26(7)328-330. 1978. (CS-3)
- Maier A. Connective-tissue macromolecules in golgi chicken tendon organs and at their interface with muscle fibers and adjoining tendinous structures. *American Journal of Anatomy.* 188(3)239-48. 1990. (CS-1)
- Mankin H. Biochemical and metabolic aspects of osteoarthritis. *Orthop Clin N Am.* 2(1)19-31. 1971. (CS-3)
- Modulation of native chondroitin sulphate structure in tissue development and in disease. *Journal of Cell Science.* November:411-417. 1990. (CS-1)

## SCIENTIFIC REFERENCES

- Moriizumi T. Pain-induced changes in the guinea pig knee joint with special reference to cartilage healing. *Virchow's Arch.* B-51:461-474. 1986. (GS-3)
- Mourao P. Distribution of chondroitin 4-sulfate and chondroitin 6-sulfate in human articular and growth cartilage. *Arthritis and Rheumatism.* 31(8)1028-33. 1988. (CS-1)
- Mund-Hoym W. Konservative Behandlung von Wirbelsaulenarthrosen Mit Glukosaminosulfat und Phenylbutazon. *Therapiewoche.* 30:5922-5928. 1980. (GS-7)
- Mund-Hoym W. Die Behandlung von Huft-und Kniegelenk-arthrosen. *Z Allg Med.* 56:2153-2159. 1980. (GS-7)
- Murray M. Natural relief for osteoarthritis. *Health Counselor.* 3:36-38. 1994. (GS-11)
- Newnham RE. Essentiality of boron for healthy bones and joints. *Environ Health Perspect* 102(Suppl 7): 83-85. 1994.
- Noack W, et al. Glucosamine sulfate in osteoarthritis of the knee. *Osteoarthritis Cart.* 2, 51-59. 1994.
- Palmieri L. Metabolic fate of exogenous chondroitin sulfate in the experimental animal *Arzneimittel-Forschung.* 40(3)319-23. 1990. (CS-1)
- Palmoski M. Effect of salicylate on proteoglycan metabolism in normal canine articular cartilage *in vitro.* *Arth Rheum.* 22(7)746-754. 1979. (CS-3)
- Palmoski M. Effects of some nonsteroidal anti-inflammatory drugs on proteoglycan metabolism and organization in canine articular cartilage. *Arth Rheum.* 23(9)1010-1020. 1980. (CS-3)
- Perry GH. Spontaneous recovery of the hip joint space in degenerative hip disease. *Ann Rheum Dis.* 31:440-8. 1972. (GS-2)
- Prudden JF. Summary of bovine tracheal cartilage research programs. New York. Foundation for Cartilage and Immunology Research. 3-5. 1993.
- Pujalte J. Double-blind clinical evaluation of oral glucosamine sulphate in the basic treatment of osteoarthrosis. *Curr Med Res Opin.* 7(2)110-114. 1980. (CS-3)
- Radin E. Hypothesis: Joints can heal. *Sem Arth Rheum.* 13(3)293-302. 1984. (CS-3)
- Recer P. Protein aids arthritis. *Reader's Digest.* February:76. 1994.
- Reese KM. Chicken collagen helps rheumatoid arthritis. *C&E News.* November 15:80.
- Reimann I. Observations of reversibility of glycosaminoglycan depletion in articular cartilage. *Clin Orthop.* 168:258-264. 1982. (CS-3)
- Rejholec, V. Long term studies of antiosteoarthritic drugs: An assessment. *Sem Arth Rheum.* 17(2)35-53. 1987. (CS-3)
- Rosen J. Immunoregulatory effects of catrrix. *Journal of Biological Response Modifiers.* 7:498-512. 1988.
- Roudier J. Susceptibility to rheumatoid arthritis maps to T-cell epitope shared by the IILA-Dw4 DR beta-1 chain and the Epstein-Barr virus glycoprotein gp 110. *Proc Natl Acad Sci.* July:5104-5108. 1989.
- Rovati LC, et al. A large randomized placebo controlled double-blind study of glucosamine sulfate vs. piroxicam in knee osteoarthritis. *Osteoarthritis and cartilage.* 2 (suppl 1), 56. 1994.
- Schwartz E. The modulation of osteoarthritic development by vitamins C and E. *Int J Vit Nutr Res. Suppl* 26:141-146. 1984. (CS-3)
- Science. Collagen soothes arthritis. *Modern Medicine.* November 1993.
- Seminars in arthritis and rheumatism,* 1974. 3;4.
- Setnikar I. Antiarthritic effects of glucosamine sulfate studied in animal models. *Rotta Research Laboratorium.* 542. (GS-4)
- Setnikar I, et al. Absorption, distribution and excretion of radioactivity after a single intravenous or oral administration of [<sup>14</sup>C]-glucosamine to the rat. *Pharmatherapeutica.* 3: 538-550. 1984.
- Setnikar I. Pharmacokinetics of glucosamine in the dog and in man. *Arzneim-Forsch.* 36:729. 1986. (GS-6)
- Setnikar I. Antiarthritic effects of glucosamine sulfate studied in Animal models. *Arzneim-Forsch.* 41:542-545. 1991. (GS-2)
- Setnikar I, et al. Pharmacokinetics of glucosamine in man. *Arzneim-Forsch.* 43:1109-1113. 1993.
- Sewell KL. Pathogenesis of rheumatoid arthritis. *Lancet.* January 30:283-286. 1993.
- Slattery K. Understanding glucosamine. *Health Supplement Retailer.* June:22. 1996. (GS-10)
- Stuart JM. Collagen-induced arthritis in rats. *Arthritis and Rheumatism.* April;4. 1979.
- Swaak A. Free Radicals and arthritic diseases. *Rijswijk:Eurage.* 1986. (CS-3)
- Tapadinhas MJ. Oral glucosamine sulphate in the management of arthrosis: Report on a multi-centre open investigation in Portugal. *Pharmatherapeutica.* 3(3)157-68. 1982. (GS-2) (GS-7)
- Tarkowski A. Secretion of antibodies to Types I and II collagen by synovial tissue cells in patients with rheumatoid arthritis. *Arthritis and Rheumatism.* September 1989.
- Thomas L. Reversible collapse of rabbit ears after intravenous papain, and prevention of recovery by cortisone. *J Exp Med.* 104:245-251. 1956. (GS-3)
- Times News Service. New rheumatoid arthritis therapy shows promise. *NDN.* September 24, 1993.
- Trentham DE. Autoimmunity to Type II collagen and experimental model of arthritis. *The Journal of Experimental Medicine.* 146:857-868. 1977.
- Trentham DE. Autoimmunity to collagen in adjuvant arthritis of rats. *The Journal of Clinical Investigation.* November:1109-1117. 1980.
- Trentham DE. Effects of oral administration of Type II collagen on rheumatoid arthritis. *Science.* 261:1727-1730. 1993.
- Varma R. Glycosaminoglycans and proteoglycans in physiological and pathological processes of body systems. Basel:Karger. 1982.
- Vaz A. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulfate in the management of osteoarthritis of the knee in outpatients. *Curr Med Res Opin.* 8:145-49. 1982. (GS-2)
- Vidal y Plana R. Glukosamin: Seine Bedeutung fur den Knorpelstoffwechsel der Gelenke 1. *Forschr Med.* 98:555-594. 1980. (GS-13)
- Vidal y Plana R. Glukosamin: Seine Bedeutung fur den Knorpelstoffwechsel der Gelenke 2. *Forschr Med.* 98:801-806. 1980. (GS-13)
- Walker M. Glucosamine providing osteoarthritic relief. *Health Foods Business.* P.23. July 1994. (GS-8)
- Wegrowski Y. Stimulation of sulfated glycosaminoglycan synthesis by the tripeptide-copper complex Glycyl-L-Histidyl-L-Lysine-Cu<sup>2+</sup>. *Life Sciences.* 51:1049-1056. 1992. (GS-12)

# SCIENTIFIC REFERENCES

Wong SF. The role of superoxide and hydroxyl radicals in the degradation of hyaluronic acid induced by metal ions and by ascorbic acid. *J Inorg Biochem.* 14:127-134. 1981. (CS-3)

Wooley PH. Passive transfer of arthritis to mice by injection of human anti-Type II collagen antibody. *Mayo Clin Proc.* 59:737-743. 1984.

Zhang ZJ. Suppression of adjuvant arthritis in lewis rats by oral administration of Type II collagen. *Journal of Immunology.* 145:2489-2493. 1990.

## CONNECTIVE TISSUE NUTRITION AND CANCER

Kirchhof DC. The successful use of bovine tracheal cartilage in the treatment of cancer. Krieger & Associates Publishers. 1995.

Langer R. Shark cartilage contains inhibitors of tumor angiogenesis. *Science.* 221:1185-87. 1983.

Prudden JF. The treatment of human cancer with agents prepared from bovine cartilage. *Journal of Biological Response Modifiers.* 4:583. 1985.

Puccio C. The treatment of metastatic renal cell carcinoma with catrux. Proceedings from the annual meeting of the American Society of Clinical Oncology. 13:A769. 1994.

## CONNECTIVE TISSUE NUTRITION AND THE CARDIOVASCULAR SYSTEM

*Atherosclerosis.* 25:199-204

Bucci L. Mucopolysaccharides (Chondroitin Sulfates) As dietary supplements: Sources, production and comparative bioavailability. *Chiropractic Products.* P.54-56. October 1988. (CS-4)

Morrison LM.. Prolongation of the plasma thrombus formation time of dogs administered chonroitin sulfates A and C. *Experimental Medical Surgery.* 28:188-193. 1970 (CS-6)

*Proc Soc Exp Biol Med.* 118:770. (CS-5)

## CONNECTIVE TISSUE NUTRITION AND DIABETES

Deckert T. Possible genetic defects in regulation of glycosaminoglycans in patients with diabetic nephropathy. *Diabetes.* 40:764. 1991. (GS-14)

## CONNECTIVE TISSUE NUTRITION AND ENTERITIS

Jones W. The Benefits of MP supplements. *Horseman's Journal.* March 1991. (CS-7)

## CONNECTIVE TISSUE NUTRITION AND THE EYE

Keates R. Extending corneal storage with 2.5% chondroitin sulfate (K-Sol). *Ophthalmic Surgery.* 19(11)817-20. 1988. (CS-1)

Kurkinen M. Fibronectin in the development of chick eye. *Dev Biol.* 69:589-600. 1979.

Miller WV. Using polysulfated glycosaminoglycan to treat persistent corneal erosions in dogs. *Veterinary Medicine.* P.916-922. October 1996.

Selonen EM. Plasmin in tear fluid of patients with corneal ulcers: Basis for new therapy. *Acta Ophthalmol.* 65:3-12. 1987.

Tervo T. Distribution of fibronectin in human and rabbit corneas. *Exp Eye Res.* 42:399-406. 1986.

## CONNECTIVE TISSUE NUTRITION AND WOUND HEALING

Boyce S. Reduced wound contraction after grafting of full-thickness burns with a collagen and chondroitin-6-sulfate (GAG) dermal skin substitute and coverage with biobrane. *Journal of Burn Care and Rehabilitation.* 9(4)364-70. 1988. (CS-1)

Fialkova M. The effect of chondroitin sulfate preparations on wound healing and the strength of the surgical scar. *Biulleten Eksperimentalnoi Biologii I Medistiny.* 108(9)350-351. 1989. (CS-1)

Prudden JF. Acceleration of wound healing with cartilage-1. *Surgery, Gynecology and Obstetrics.* 105:283. 1957.

## ANTI-INFLAMMATORY REFERENCES

Ammon HP, et al. Inhibition of leukotriene B4 formation in peritoneal neutrophils by an ethanolic extract of the gum resin exudate of *Boswellia serrata*. *Planta Med.* 57(3):203-207. 1991.

Arora R, et al. Anti-inflammatory studies on *Curcuma longa* (turmeric). *Ind J Med Res.* 59:1289-95. 1971.

Baghdikian B, et al. An analytical study, anti-inflammatory and analgesic effects of *Harpagophytum procumbens* and *Harpagophytum zeyheri*. *Planta Med.* 63(2)171-176. 1997.

Bhargava KP, et al. Anti-inflammatory activity of saponins and other natural products. *Indian J Med Res.* 58(6)724-30. 1970.

Bingham R, et al. Yucca plant saponin in the management of arthritis. *J Appl Nutr.* 27:45-50. 1975.

Carleson J, et al. Effects of capsaicin in tempromandibular joint arthritis in rats. *Arch Oral Biol* 42(12)869-76. 1997.

Chandra D, et al. Anti-inflammatory and anti-arthritic activity of volatile oil of *Curcuma longa*. *India J Med Res* 60:138-42. 1972.

Deal CL, et al. Treatment of arthritis with topical capsaicin: A double-blind trial. *Clin Ther* 13(3)383-95. 1991.

Deodhar SD, et al. Preliminary studies on antirheumatic activity of curcumin (diferloyl methane). *Indian J Med Res* 71:632-4. 1980.

Diehl HW, et al. Cetyl myristoleate isolated from Swiss albino mice: An apparent protective agent against adjuvant arthritis in rats. *J Pharm Sci* 83(3)296-9. 1986.

Donaldson LF, et al. Neuropeptide gene expression and capsaicin-sensitive primary afferents: Maintenance and spread of adjuvant arthritis in the rat. *J Physiol (Lond)* 486(Pt. 2)473-82. 1995.

Eichler O, et al. Antiphlogistic, analgesic and spasmolytic effect of harpagoside, a glycoside from the root of *Harpagophytum procumbens* DC. *Arzneimittelforschung* 20(1)107-9. 1970.

Kiuchi F, et al. Inhibitors of prostaglandin biosynthesis from ginger. *Chem Pharm Bull* 30:754-7. 1982.

Kulkarni RR, et al. Treatment of osteoarthritis with herbomineral formulation: A double-blind, placebo-controlled, cross-over study. *J Ethnopharmacol* 33(1-2)91-5. 1991.

Lanthers MC, et al. Anti-inflammatory and analgesic effects of an aqueous extract of *Harpagophytum procumbens*. *Planta Med* 58(2)117-23. 1992.

Lynn B. Capsaicin: actions on nociceptive C-fibres and therapeutic potential. *Pain* 41:61-9. 1990.

Matucci-Cerinic M, et al. Effects of capsaicin on the metabolism of rheumatoid arthritis synoviocytes *in vitro*. *Ann Rheum Dis* 49(8)598-602. 1990.

## SCIENTIFIC REFERENCES

Morales TI, et al. The effect of lipopolysaccharides on the biosynthesis and release of proteoglycans from calf articular cartilage cultures. *J Biol Chem* 259:6720-9. 1984.

Moussard C, et al. A drug used in traditional medicine. *Harpagophytum procumbens*: No evidence of NSAID-like effect on whole blood eicosanoid production in humans. *Prostaglandins Leukot Essent Fatty Acids* 46(4):283-6. 1992.

Mukhopadhyay A, et al. Anti-inflammatory and irritant activities of curcumin analogues in rats. *Agents Actions* 12:508-15. 1982.

Satsokar RR, et al. Evaluation of anti-inflammatory property of curcumin (diferuloyl methane) in patients with postoperative inflammation. *Int J Clin Pharmacol Ther Toxicol* 24:651-4. 1986.

Singh GB, et al. Pharmacology of an extract of salai guggal extract, *Boswellia serrata*, a new non-steroidal anti-inflammatory agent. *Agents Actions* 18(3-4):407-12. 1986.

Srimal R, et al. Pharmacology of diferuloyl methane (curcumin), a non-steroidal anti-inflammatory agent. *J Pharm Pharmacol* 25:447-52. 1973.

Srivastava KC, et al. Ginger (*Zingiber officinale*) and rheumatic disorders. *Med Hypothesis* 29:25-28. 1989.

Srivastava R, et al. Modification of certain inflammation-induced biochemical changes by curcumin. *Indian J Med Res* 81:215-23. 1985.

Srivastava R. Inhibition of neutrophil response by curcumin. *Agents Actions* 28:298-303. 1989.

Trotter JA, et al. Stiparin: A glycoprotein from sea cucumber dermis that aggregates collagen fibrils. *Matrix Biol* 15(2):99-110. 1996.

Vieira RP, et al. Structure of a fucose-branched chondroitin sulfate from sea cucumber. Evidence for the presence of O-sulfo-beta-D-glucuronosyl residues. *J Biol Chem* 266(21):13530-6. 1991.

Vieira RP, et al. Extensive heterogeneity of proteoglycans bearing fucose-branched chondroitin sulfate extracted from the connective tissue of sea cucumber. *Biochemistry* 32(9):2254-62. 1993.

Whitehouse LW, et al. Devil's claw (*Harpagophytum procumbens*): No evidence for anti-inflammatory activity in treatment of arthritic disease. *Can Med Assoc J* 129(3):249-51. 1983.