COMPOSITION AND METHOD OF TREATING ARTHRITIS

This application is a continuation-in-part of U.S. patent application Ser. No. 09/350,380 filed Jul. 8, 1999, now U.S. Pat. No. 6,346,519, which is a continuation-in-part of U.S. patent application Ser. No. 09/149,241, filed Sep. 8, 1998, now abandoned.

FIELD OF THE INVENTION

The present invention concerns compositions and methods of treating and preventing arthritis, repairing of articular joint surfaces and relief of symptoms associated with arthritis.

BACKGROUND OF THE INVENTION

Arthritis, a musculoskeletal disorder, is the leading cause of disability in the United States. The Centers for Disease Control and Prevention (CDC) stated that arthritis and other rheumatic conditions accounted for about 744,000 hospitalizations and 4 million days of care in 1997. Forty million Americans, representing 15% of the population, have some form of arthritis, and that figure is expected to increase to 59.4 million (18.2%) by the year 2020, an increase of 57% in the number of persons affected. Arthritis patients make more than 315 million physician visits and are hospitalized more than 8 million times a year. Arthritis costs the nation $65 billion annually in medical costs and lost productivity. Osteoarthritis (OA), or degenerative joint disease, is the most common type of arthritis, affecting 20.7 million people, (12.1%) of U.S. adults in 1990, now estimated at 37 million, and trailed chronic heart disease as the leading cause of Social Security payments due to long-term absence from work. Lawrence R C, et al. Arthritis & Rheumatism 1998; 41 :778–799.

Approximately 1–2% of the population suffers from rheumatoid arthritis (RA), which is characterized as an imbalance in the immune system that causes an overproduction of pro-inflammatory cytokines, e.g., tumor necrosis factor alpha (TNFα), interleukin 1 (IL-1), and a lack of anti-inflammatory cytokines, e.g. IL-10, IL-11. RA is characterized by synovial inflammation, which progresses to cartilage destruction, bone erosion and subsequent joint deformity. The primary symptoms of RA are joint inflammation, swelling, difficulty moving, and pain. During the inflammatory process, polymorphonuclear cells, macrophages, and lymphocytes are released. Activated T-lymphocytes produce cytotoxins and pro-inflammatory cytokines, while macrophages stimulate the release of prostaglandins and cytotoxins. Vasoactive substances (histamine, kinins, and prostaglandins) are released at the site of inflammation and cause edema, warmth, erythema, and pain associated with inflamed joints.

Osteoarthritis usually presents as pain, which worsens with exercise or simply an X-ray that clearly shows thinning cartilage. Common joints affected are the knees, hips and spine, finger, base of thumb and base of the big toe. Osteoarthritis is characterized by degenerative changes in the articular cartilage and subsequent new bone formation at the articular margins. The primary defect in hyaline cartilage, at the articular surface of the joint, is an alteration in the ratio of total glycosaminoglyeans to that of the collagen fiber content in the matrix. Yasuda K. Hokkaido Igaku Zasshi July 1997;72(4):369–76. Paleontologists have found osteoarthritis to exist in almost every vertebrate. By age 60, almost all Americans have osteoarthritis in their

necks or spines. Joint cartilage consists of only 5 percent cells, and that joint cartilage lesions do heal. Tindall W N. Business & Health December 1997;47–48. Bones directly underneath the cartilage in joints is called subchondral bone. This bone nourishes the cartilage with oxygen, water, and nutrients conveyed through microscopic channels. This supply route carries "chondroprotective agents" from the bloodstream to the cartilage.

Cartilage is the supporting structure of the body, but has no blood vessels, nerves or lymphatics, and consists of thick bundles of fibrous protein (collagen) which are woven to form the articular surface. Proteoglycans fill the extracellular spaces not occupied by collagen, and are a combination of protein and sugar. Each proteoglycan subunit contains a protein core attached to hundreds of long chains of specially modified sugars called glycosaminoglycans (GAGs). Glucosamine is the single most important component and precursor for GAGs. Glucosamine is almost completely absorbed by the GI tract into the bloodstream. Cartilage rebuilding is only as good as its GAG synthesis. Chondrocytes in the cartilage obtain glucosamine from the subchondral blood vessels and manufacture N-acetylglucosamine (NAG) and glucuronic acid, which make hyaluronan, which is half glucosamine, and provides the lubricating ability of joints.

There is no definitive answer regarding the cause of osteoarthritis. A natural erosion of cartilage occurs with age, but excessive loads placed on joints, obesity, heredity, trauma, decreased circulation, poor bone alignment, and repetitive stress motion play a role. Osteoarthritis may also be the result of free radical damage, thought to be a major cause of many diseases, including the aging process, cancer, heart disease and degenerative diseases.

Free radicals affect the immune system causing rheumatoid arthritis and osteoarthritis. Free radicals are atoms or atomic groups that are byproducts of normal metabolism, tobacco smoke, pollutants, car exhaust, bacteria, radiation, and chemicals which oxidize or damage otherwise healthy cells. They damage DNA, corrode cell membranes, and may play a role in the development of cancer, heart and lung disease, cataracts, and cause or accelerate the aging process. Bucci wrote that there is conclusive evidence that free radicals do most of their damage in rheumatoid arthritis, but also to the cartilage in osteoarthritis. Bucci L. Healing Arthritis the Natural Way Arlington, Tex.: Summit Publishing Group, 1995, pp. 34–5. In his best seller, Theodosakis stated that "Osteoarthritis may be the result of free radical damage. And to make matters worse, joint inflammation itself may trigger an even faster rate of new free radical formation. Prevention of free radical damage is a critical feature in treating and preventing osteoarthritis." Theodosakis J, Adderly B, Fox B. The Arthritis Cure New York, St. Martins Press, 1997, p 147–9. Unless the damage caused by free radical formation is addressed, any benefits obtained by using only chondroprotective agents could be nullified; similar to trying to fill a sieve with water, the relief is transient but pathology progresses.

There is no known drug that claims to reverse osteoarthritis. Most therapeutic agents are directed at reducing the inflammation and relieving pain. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first line of treatment for osteoarthritis, but long-term use can lead to gastric ulcers, kidney damage, hearing loss and even inhibit cartilage formation.

SUMMARY OF THE INVENTION

This invention relates to the compositions and method of treating and preventing arthritis, repairing of articular joint