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(57) Abstract: The invention provides methods for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health in an animal. The methods comprise administering green tea extract to the animals, preferably in amounts of from about 0.005 to about 100 mg/kg/day.



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METHODS AND COMPOSITIONS FOR PREVENTING OR TREATING OSTEOARTHRITIS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Serial No. 61/403943 filed September 23, 2010, the disclosure of which is incorporated herein by this reference.

BACKGROUND OF THE INVENTION

Field of the Invention

[0002] The invention relates generally to methods for preventing or treating osteoarthritis and particularly to methods for using green tea extract for preventing or treating osteoarthritis.

Description of Related Art

[0003] Osteoarthritis (OA), also commonly referred to as degenerative joint disease, is characterized by the imbalance between the synthesis and degradation of articular cartilage. The breakdown of joint cartilage often results in joint pain and loss of mobility. OA commonly affects the hands, feet, spine, and the large weight bearing joints, such as the hips and knees. Symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion. A variety of causes, such as hereditary, developmental, metabolic, and mechanical, may initiate processes leading to loss of cartilage.

[0004] *Camellia sinensis* is the species of plant whose leaves and leaf buds are used to produce tea. White tea, green tea, oolong, pu-erh tea and black tea are all harvested from this species, but are processed differently to attain different levels of oxidation. Green tea extract is the derivative from leaves of *Camellia sinensis* that have undergone minimal oxidation during processing. Green tea contains salubrious polyphenols, particularly catechins, the most abundant of which is epigallocatechin gallate (EGCG). Green tea also contains carotenoids, tocopherols, ascorbic acid (vitamin C), minerals such as chromium, manganese, selenium or zinc, and certain phytochemical compounds.

[0005] Osteoarthritis is a painful condition and is adverse to the health and wellness of an animal and result in a lower quality of life for an animal. There is, therefore, a need for methods and compositions useful for promoting the health and wellness and improving the quality of life for animals by preventing or treating osteoarthritis.

SUMMARY OF THE INVENTION

[0006] It is, therefore, an object of the present invention to provide methods and compositions useful for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health.

[0007] It is another object of the invention to provide methods for promoting the health or wellness of animals.

[0008] It is another object of the invention to provide methods for extending the prime years of an animal's life.

[0009] One or more of these or other objects are achieved by administering green tea extract to animals in therapeutically effective amounts for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health. In general embodiments, green tea extract is administered to the animals in amounts of from about 0.005 to about 100 milligrams per kilogram of body weight per day (g/kg/day) for as long as there is a need for such treatment.

[0010] Other and further objects, features, and advantages of the invention will be readily apparent to those skilled in the art.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0011] The term "animal" means any animal that has a need for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health in an animal, including human, avian, bovine, canine, equine, feline, hircine, lupine, murine, ovine, or porcine animals.

[0012] The term "companion animal" means domesticated animals such as cats, dogs, rabbits, guinea pigs, ferrets, hamsters, mice, gerbils, horses, cows, goats, sheep, donkeys, pigs, and the like.

[0013] The term "therapeutically-effective amount" means an amount of a compound of the present invention that (i) treats or prevents the particular disease, condition, or disorder, (ii) attenuates, ameliorates, or eliminates one or more symptoms of the particular disease, condition, or disorder, or (iii) prevents or delays the onset of one or more symptoms of the particular disease, condition, or disorder described herein.

[0014] The terms "treating", "treat", and "treatment" embrace both preventative, *i.e.*, prophylactic, and palliative treatment.

[0015] The terms “pharmaceutically acceptable” and “nutraceutically acceptable” indicates that the substance or composition must be compatible chemically and/or toxicologically, with the other ingredients comprising a formulation, and/or the mammal being treated therewith.

[0016] The term “health and/or wellness of an animal” means the complete physical, mental, and social well being of the animal, not merely the absence of disease or infirmity.

[0017] The term “extending the prime” means extending the number of years an animal lives a healthy life and not just extending the number of years an animal lives, *e.g.*, an animal would be healthy in the prime of its life for a relatively longer time.

[0018] The term “degenerative joint disorder” refers to any etiological or pathological symptom affecting a joint. Such symptoms and etiology include swelling, pain and/or stiffness of a joint such that complete or partial loss of function and/or damage to the joint and/or a reduction of the joint mobility. The term also includes chronic inflammation, primarily of the synovial tissue, pannus formation, destruction of articular cartilage and release of various enzymes, for example, collagenase and lysosomal enzymes, in an affected joint, osteoarthritis, rheumatic disorders with cartilage breakdown, rheumatoid arthritis, chondrolysis after joint trauma, for example, after meniscus or patella injuries or torn ligaments, or chondrolysis associated with prolonged immobilization of joints. By way of example, degenerative joint disorder includes osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, tendonitis, ankylosing spondylitis, bursitis, spinal disc injuries, and temporomandibular joint disorder.

[0019] The term “in conjunction” means that green tea extract or other compounds or other compositions of the invention are administered to an animal (1) together in a food composition or (2) separately at the same or different frequency using the same or different administration routes at about the same time or periodically. “Periodically” means that green tea extract or other compounds or other compositions are administered on a schedule acceptable for specific compounds or compositions. “About the same time” generally means that green tea extract or other compounds or compositions are administered at the same time or within about 72 hours of each other.

[0020] The term “dietary supplement” means a product that is intended to be ingested in addition to a normal animal diet. Dietary supplements may be in any form, *e.g.*, solid, liquid, gel, tablet, capsule, powder, and the like. Preferably they are provided in convenient dosage forms, *e.g.*, in sachets. Dietary supplements can be provided in bulk consumer packages such as bulk powders, liquids, gels, or oils. Similarly such supplements can be provided in bulk

quantities to be included in other food items such as snacks, treats, supplement bars, beverages, and the like.

[0021] The term “aging” means being of an advanced age such that an animal has reached or exceeded 50% of the average life expectancy for the animal’s species and/or breed within such species. For example, if the average life expectancy for a given breed of dog is 12 years, then an “aging animal” within that breed is 6 years old or older.

[0022] The term “food” or “food product” or “food composition” means a product or composition that is intended for ingestion by an animal, including a human, and provides nutrition to the animal.

[0023] The term “regular basis” means at least monthly dosing with green tea extract and more preferably weekly dosing. More frequent dosing or consumption, such as twice or three times weekly, is preferred in certain embodiments. Still more preferred are regimens that comprise at least once daily consumption, *e.g.*, when green tea extract is a component of a food composition that is consumed at least once daily.

[0024] The term “single package” means that the components of a kit are physically associated in or with one or more containers and considered a unit for manufacture, distribution, sale, or use. Containers include, but are not limited to, bags, boxes, cartons, bottles, packages such as shrink wrap packages, stapled or otherwise affixed components, or combinations thereof. A single package may be containers of individual green tea extract and food compositions physically associated such that they are considered a unit for manufacture, distribution, sale, or use.

[0025] The term “virtual package” means that the components of a kit are associated by directions on one or more physical or virtual kit components instructing the user how to obtain the other components, *e.g.*, in a bag or other container containing one component and directions instructing the user to go to a website, contact a recorded message or a fax-back service, view a visual message, or contact a caregiver or instructor to obtain instructions on how to use the kit or safety or technical information about one or more components of a kit.

[0026] The dosages expressed herein are in milligrams per kilogram of body weight per day (mg/kg/day) unless expressed otherwise.

[0027] All percentages expressed herein are by weight of the composition on a dry matter basis unless specifically stated otherwise. The skilled artisan will appreciate that the term “dry matter basis” means that an ingredient’s concentration or percentage in a composition is measured or determined after any free moisture in the composition has been removed.

[0028] As used herein, ranges are used herein in shorthand, so as to avoid having to list and describe each and every value within the range. Any appropriate value within the range can be selected, where appropriate, as the upper value, lower value, or the terminus of the range.

[0029] As used herein, the singular form of a word includes the plural, and vice versa, unless the context clearly dictates otherwise. Thus, the references “a”, “an”, and “the” are generally inclusive of the plurals of the respective terms. For example, reference to “a supplement”, “a method”, or “a food” includes a plurality of such “supplements”, “methods”, or “foods.” Similarly, the words “comprise”, “comprises”, and “comprising” are to be interpreted inclusively rather than exclusively. Likewise the terms “include”, “including” and “or” should all be construed to be inclusive, unless such a construction is clearly prohibited from the context. Similarly, the term “examples,” particularly when followed by a listing of terms, is merely exemplary and illustrative and should not be deemed to be exclusive or comprehensive.

[0030] The methods and compositions and other advances disclosed here are not limited to particular methodology, protocols, and reagents described herein because, as the skilled artisan will appreciate, they may vary. Further, the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to, and does not, limit the scope of that which is disclosed or claimed.

[0031] Unless defined otherwise, all technical and scientific terms, terms of art, and acronyms used herein have the meanings commonly understood by one of ordinary skill in the art in the field(s) of the invention, or in the field(s) where the term is used. Although any compositions, methods, articles of manufacture, or other means or materials similar or equivalent to those described herein can be used in the practice of the present invention, the preferred compositions, methods, articles of manufacture, or other means or materials are described herein.

[0032] All patents, patent applications, publications, technical and/or scholarly articles, and other references cited or referred to herein are in their entirety incorporated herein by reference to the extent allowed by law. The discussion of those references is intended merely to summarize the assertions made therein. No admission is made that any such patents, patent applications, publications or references, or any portion thereof, are relevant, material, or prior art. The right to challenge the accuracy and pertinence of any assertion of such patents, patent applications, publications, and other references as relevant, material, or prior art is specifically reserved.

The Invention

[0033] In one aspect, the invention provides methods for preventing or treating osteoarthritis in an animal. The methods comprise administering to the animal a therapeutically effective amount of green tea extract.

[0034] In another aspect, the invention provides methods for preventing or treating the degradation of articular cartilage in an animal. The methods comprise administering to the animal a therapeutically effective amount of green tea extract.

[0035] In another aspect, the invention provides methods for promoting and maintaining joint health in an animal. The methods comprise administering to the animal a therapeutically effective amount of green tea extract.

[0036] In a further aspect, the invention provides methods for promoting the health or wellness of an animal. The methods comprise administering to an animal a health or wellness promoting amount of green tea extract.

[0037] In another aspect, the present invention provides methods for extending the prime years of an animal's life. The methods comprise administering green tea extract to the animals in an amount effective for extending the prime for the animal.

[0038] The inventions are based upon the discovery that green tea extracts are able to positively modulate osteoarthritis markers. Specifically, green tea extracts are able to decrease the gene expression of Matrix Metalloproteinase 13 (MMP-13, also known as collagenase II) and Insulin-like Growth Factor 2 (IGF-2) while increasing the gene expression of SRY-box containing gene 9 (SOX-9) and the Geneva gene (2252B). Some genes associated with osteoarthritis have been previously identified in WO2005075685. The methods of the present invention may also be useful in the treatment of inflammatory related conditions, cancer metastasis and other degenerative joint disorders.

[0039] Any therapeutically effective amount of *Camellia sinensis* derivative may be used in the present invention. In various embodiments the derivative is white tea, green tea, oolong, pu-erh tea, black tea or combinations thereof. In a preferred embodiment the derivative is green tea, preferably green tea extract.

[0040] In the methods of the invention, green tea extract is administered to an animal in amounts of from about 0.005 to about 5 mg/kg/day, preferably from about 0.01 to about 50 mg/kg/day, most preferably from about 0.05 to about 10 mg/kg/day.

[0041] Green tea extract can be administered to the animal in any suitable form using any suitable administration route. For example, green tea extract can be administered in a green

tea extract composition, in a food composition, in a dietary supplement, in a pharmaceutical composition, in a nutraceutical composition, or as a medicament. Similarly, green tea extract can be administered using a variety of administration routes, including oral, intranasal, intravenous, intramuscular, intragastric, transpyloric, subcutaneous, rectal, and the like. Preferably, green tea extract is administered to an animal orally. Most preferably, green tea extract is administered orally to an animal as a dietary supplement or as an ingredient in a food composition.

[0042] In a preferred embodiment, green tea extract is administered to an animal as an ingredient in a food composition suitable for consumption by an animal, including humans and companion animals such as dogs and cats. Such compositions include complete foods intended to supply the necessary dietary requirements for an animal or food supplements such as animal treats.

[0043] In various embodiments, food compositions such as pet food compositions or pet treat compositions comprise from about 5% to about 50% crude protein. The crude protein material may comprise vegetable proteins such as soybean meal, soy protein concentrate, corn gluten meal, wheat gluten, cottonseed, and peanut meal, or animal proteins such as casein, albumin, and meat protein. Examples of meat protein useful herein include beef, pork, lamb, equine, poultry, fish, and mixtures thereof.

[0044] The food compositions may further comprise from about 5% to about 40% fat. Examples of suitable fats include animal fats and vegetable fats. Preferably the fat source is an animal fat source such as tallow or grease. Vegetable oils such as corn oil, sunflower oil, safflower oil, rape seed oil, soy bean oil, olive oil and other oils rich in monounsaturated and polyunsaturated fatty acids, may also be used.

[0045] The food compositions may further comprise from about 10% to about 60% carbohydrate. Examples of suitable carbohydrates include grains or cereals such as rice, corn, millet, sorghum, alfalfa, barley, soybeans, canola, oats, wheat, rye, triticale and mixtures thereof. The compositions may also optionally comprise other materials such as dried whey and other dairy by-products.

[0046] The moisture content for such food compositions varies depending on the nature of the food composition. The food compositions may be dry compositions (*e.g.*, kibble), semi-moist compositions, wet compositions, or any mixture thereof. In a preferred embodiment, the composition is a complete and nutritionally balanced pet food. In this embodiment, the pet food may be a “wet food”, “dry food”, or food of “intermediate moisture” content. “Wet

food” describes pet food that is typically sold in cans or foil bags and has a moisture content typically in the range of about 70% to about 90%. “Dry food” describes pet food that is of a similar composition to wet food but contains a limited moisture content typically in the range of about 5% to about 15% or 20% (typically in the form of small biscuit-like kibbles). In one preferred embodiment, the compositions have moisture content from about 5% to about 20%. Dry food products include a variety of foods of various moisture contents, such that they are relatively shelf-stable and resistant to microbial or fungal deterioration or contamination. Also preferred are dry food compositions that are extruded food products such as pet foods or snack foods for either humans or companion animals.

[0047] The food compositions may also comprise one or more fiber sources. The term “fiber” includes all sources of “bulk” in the food whether digestible or indigestible, soluble or insoluble, fermentable or nonfermentable. Preferred fibers are from plant sources such as marine plants but microbial sources of fiber may also be used. A variety of soluble or insoluble fibers may be utilized, as will be known to those of ordinary skill in the art. The fiber source can be beet pulp (from sugar beet), gum arabic, gum talha, psyllium, rice bran, carob bean gum, citrus pulp, pectin, fructooligosaccharide, short chain oligofructose, mannanoligofructose, soy fiber, arabinogalactan, galactooligosaccharide, arabinoxylan, or mixtures thereof.

[0048] Alternatively, the fiber source can be a fermentable fiber. Fermentable fiber has previously been described to provide a benefit to the immune system of a companion animal. Fermentable fiber or other compositions known to skilled artisans that provide a prebiotic to enhance the growth of probiotics within the intestine may also be incorporated into the composition to aid in the enhancement of the benefit provided by the present invention to the immune system of an animal.

[0049] In some embodiments, the ash content of the food composition ranges from less than 1% to about 15%, preferably from about 5% to about 10%.

[0050] In a preferred embodiment, the composition is a food composition comprising green tea extract and from about 15% to about 50% protein, from about 5% to about 40% fat, from about 5% to about 10% ash content, and having a moisture content of about 5% to about 20%. In other embodiments, the food composition further comprises prebiotics or probiotics as described herein.

[0051] When administered in a food composition, green tea extract comprises from about 0.1 to about 40% of the food composition, preferably from about 3 to about 30%, more

preferably from about 5 to about 20%. In various embodiments, food compositions comprise about 1%, 2%, 4%, 6%, 8%, 10%, 12%, 14%, 16%, 18%, 20%, 22%, 24%, 26%, 28%, 30%, 32%, 34%, 36%, 38%, or 40%.

[0052] In another embodiment, green tea extract is administered to an animal in a dietary supplement. The dietary supplement can have any suitable form such as a gravy, drinking water, beverage, yogurt, powder, granule, paste, suspension, chew, morsel, treat, snack, pellet, pill, capsule, tablet, sachet, or any other suitable delivery form. The dietary supplement can comprise green tea extract and optional compounds such as vitamins, preservatives, probiotics, prebiotics, and antioxidants. This permits the supplement to be administered to the animal in small amounts, or in the alternative, can be diluted before administration to an animal. The dietary supplement may require admixing with a food composition or with water or other diluent prior to administration to the animal. When administered in a dietary supplement, green tea extract comprises from about 0.1 to about 90% of the supplement, preferably from about 3 to about 70%, more preferably from about 5 to about 60%.

[0053] In another embodiment, green tea extract is administered to an animal in a pharmaceutical or nutraceutical composition. The pharmaceutical composition comprises green tea extract and one or more pharmaceutically or nutraceutically acceptable carriers, diluents, or excipients. Generally, pharmaceutical compositions are prepared by admixing a compound or composition with excipients, buffers, binders, plasticizers, colorants, diluents, compressing agents, lubricants, flavorants, moistening agents, and the like, including other ingredients known to skilled artisans to be useful for producing pharmaceuticals and formulating compositions that are suitable for administration to an animal as pharmaceuticals. When administered in a pharmaceutical or nutraceutical composition, green tea extract comprises from about 0.1 to about 90% of the composition, preferably from about 3 to about 70%, more preferably from about 5 to about 60%.

[0054] Green tea extract can be administered to the animal on an as-needed, on an as-desired basis, or on a regular basis. A goal of administration on a regular basis is to provide the animal with a regular and consistent dose of green tea extract or the direct or indirect metabolites that result from such ingestion. Such regular and consistent dosing will tend to create constant blood levels of green tea extract and its direct or indirect metabolites. Thus, administration on a regular basis can be once monthly, once weekly, once daily, or more than once daily. Similarly, administration can be every other day, week, or month, every third day,

week, or month, every fourth day, week, or month, and the like. Administration can be multiple times per day. When utilized as a supplement to ordinary dietetic requirements, green tea extract may be administered directly to the animal, *e.g.*, orally or otherwise. Green tea extract can alternatively be contacted with, or admixed with, daily feed or food, including a fluid, such as drinking water, or an intravenous connection for an animal that is receiving such treatment. Administration can also be carried out as part of a dietary regimen for an animal. For example, a dietary regimen may comprise causing the regular ingestion by the animal of green tea extract in an amount effective to accomplish the methods of the present invention.

[0055] According to the methods of the invention, green tea extract administration, including administration as part of a dietary regimen, can span a period ranging from parturition through the adult life of the animal. In various embodiments, the animal is a human or companion animal such as a dog or cat. In certain embodiments, the animal is a young or growing animal. In more preferred embodiments, the animal is an aging animal. In other embodiments administration begins, for example, on a regular or extended regular basis, when the animal has reached more than about 30%, 40%, or 50% of its projected or anticipated lifespan. In some embodiments, the animal has attained 40, 45, or 50% of its anticipated lifespan. In yet other embodiments, the animal is older having reached 60, 66, 70, 75, or 80% of its likely lifespan. A determination of lifespan may be based on actuarial tables, calculations, estimates, or the like, and may consider past, present, and future influences or factors that are known to positively or negatively affect lifespan. Consideration of species, gender, size, genetic factors, environmental factors and stressors, present and past health status, past and present nutritional status, stressors, and the like may also influence or be taken into consideration when determining lifespan.

[0056] Green tea extract is administered to an animal for a time required to accomplish one or more objectives of the invention, *e.g.*, preventing or treating osteoarthritis in an animal; preventing or treating the degradation of articular cartilage; promoting and maintaining joint health; improving the quality of life; and promoting the health and wellness in an animal. Preferably, green tea extract is administered to an animal on a regular basis.

[0057] In another aspect, the invention provides compositions comprising green tea extract in a therapeutically effective amount for one or more of preventing or treating osteoarthritis in an animal; preventing or treating the degradation of articular cartilage in an animal; promoting and maintaining joint health in an animal; improving the quality of life in an

animal; and promoting the health and wellness in an animal. The compositions contain green tea extract in amounts sufficient to administer green tea extract to an animal in amounts of from about 0.005 to about 100 mg/kg/day, preferably from about 0.01 to about 50 mg/kg/day, most preferably from about 0.05 to about 10 mg/kg/day when the compositions are administered as anticipated or recommended for a particular composition. Typically, green tea extract comprises from about 1 to about 90% of a composition, preferably from about 3 to about 70%, more preferably from about 5 to about 60%. In various embodiments, food compositions comprise about 1%, 2%, 4%, 6%, 8%, 10%, 12%, 14%, 16%, 18%, 20%, 22%, 24%, 26%, 28%, 30%, 32%, 34%, 36%, 38%, 40%, 45%, 50%, 55%, 60%, 70%, or 80%.

[0058] Green tea extract compositions such as food, dietary, pharmaceutical, and other compositions may further comprise one or more substances such as vitamins, minerals, probiotics, prebiotics, salts, and functional additives such as palatants, colorants, emulsifiers, and antimicrobial or other preservatives. Minerals that may be useful in such compositions include, for example, calcium, phosphorous, potassium, sodium, iron, chloride, boron, copper, zinc, magnesium, manganese, iodine, selenium, and the like. Examples of additional vitamins useful herein include such fat soluble vitamins as A, D, E, and K. Inulin, amino acids, enzymes, coenzymes, and the like may be useful to include in various embodiments.

[0059] In various embodiments, the green tea extract compositions contain at least one of (1) one or more probiotics; (2) one or more inactivated probiotics; (3) one or more components of inactivated probiotics that promote health benefits similar to or the same as the probiotics, *e.g.*, proteins, lipids, glycoproteins, and the like; (4) one or more prebiotics; and (5) combinations thereof. The probiotics or their components can be integrated into the green tea extract compositions (*e.g.*, uniformly or non-uniformly distributed in the compositions) or applied to the green tea extract compositions (*e.g.*, topically applied with or without a carrier). Such methods are known to skilled artisans, *e.g.*, US5968569 and related patents.

[0060] Typical probiotics include, but are not limited to, probiotic strains selected from *Lactobacilli*, *Bifidobacteria*, or *Enterococci*, *e.g.*, *Lactobacillus reutei*, *Lactobacillus acidophilus*, *Lactobacillus animalis*, *Lactobacillus ruminis*, *Lactobacillus johnsonii*, *Lactobacillus casei*, *Lactobacillus paracasei*, *Lactobacillus rhamnosus*, *Lactobacillus fermentum*, and *Bifidobacterium sp.*, *Enterococcus faecium* and *Enterococcus sp.* In some embodiments, the probiotic strain is selected from the group consisting of *Lactobacillus reuteri* (NCC2581; CNCM I-2448), *Lactobacillus reuteri* (NCC2592; CNCM I-2450),

Lactobacillus rhamnosus (NCC2583; CNCM I-2449), *Lactobacillus reuteri* (NCC2603; CNCM I-2451), *Lactobacillus reuteri* (NCC2613; CNCM I-2452), *Lactobacillus acidophilus* (NCC2628; CNCM I-2453), *Bifidobacterium adolescentis* (e.g. NCC2627), *Bifidobacterium sp.* NCC2657 or *Enterococcus faecium* SF68 (NCIMB 10415). The green tea extract compositions contain probiotics in amounts sufficient to supply from about 10^4 to about 10^{12} cfu/animal/day, preferably from 10^5 to about 10^{11} cfu/animal/day, most preferably from 10^7 to 10^{10} cfu/animal/day. When the probiotics are killed or inactivated, the amount of killed or inactivated probiotics or their components should produce a similar beneficial effect as the live microorganisms. Many such probiotics and their benefits are known to skilled artisans, e.g., EP1213970B1, EP1143806B1, US7189390, EP1482811B1, EP1296565B1, and US6929793. In a preferred embodiment, the probiotic is *Enterococcus faecium* SF68 (NCIMB 10415). In one embodiment, the probiotics are encapsulated in a carrier using methods and materials known to skilled artisans.

[0061] As stated, the green tea extract compositions may contain one or more prebiotics, e.g., fructo-oligosaccharides, gluco-oligosaccharides, galacto-oligosaccharides, isomalto-oligosaccharides, xylo-oligosaccharides, soybean oligosaccharides, lactosucrose, lactulose, and isomaltulose. In one embodiment, the prebiotic is chicory root, chicory root extract, inulin, or combinations thereof. Generally, prebiotics are administered in amounts sufficient to positively stimulate the healthy microflora in the gut and cause these “good” bacteria to reproduce. Typical amounts are from about one to about 10 grams per serving or from about 5% to about 40% of the recommended daily dietary fiber for an animal. The probiotics and prebiotics can be made part of the composition by any suitable means. Generally, the agents are mixed with the composition or applied to the surface of the composition, e.g., by sprinkling or spraying. When the agents are part of a kit, the agents can be admixed with other materials or in their own package. Typically, the food composition contains from about 0.1 to about 10% prebiotic, preferably from about 0.3 to about 7%, most preferably from about 0.5 to 5%, on a dry matter basis. The prebiotics can be integrated into the compositions using methods known to skilled artisans, e.g., US5952033.

[0062] A skilled artisan can determine the appropriate amount of green tea extract, food ingredients, vitamins, minerals, probiotics, prebiotics, antioxidants, or other ingredients to be use to make a particular composition to be administered to a particular animal. Such artisan can consider the animal’s species, age, size, weight, health, and the like in determining how best to formulate a particular composition comprising green tea extract and other ingredients.

Other factors that may be considered include the type of composition (*e.g.*, pet food composition versus dietary supplement), the desired dosage of each component, the average consumption of specific types of compositions by different animals (*e.g.*, based on species, body weight, activity/energy demands, and the like), and the manufacturing requirements for the composition.

[0063] In a further aspect, the invention provides kits suitable for administering green tea extract to animals. The kits comprise in separate containers in a single package or in separate containers in a virtual package, as appropriate for the kit component, green tea extract and one or more of (1) one or more ingredients suitable for consumption by an animal; (2) instructions for how to combine green tea extract and other kit components to produce a composition useful for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, promoting and maintaining joint health; (3) instructions for how to use green tea extract for preventing or treating osteoarthritis; (4) instructions for how to use green tea extract for preventing or treating the degradation of articular cartilage; (5) instructions for how to use green tea extract for promoting and maintaining joint health; (6) one or more probiotics; (7) one or more inactivated probiotics; (8) one or more components of inactivated probiotics that promote health benefits similar to or the same as the probiotics, *e.g.*, proteins, lipids, glycoproteins, and the like; (9) one or more prebiotics; (10) a device for preparing or combining the kit components to produce a composition suitable for administration to an animal; and (11) a device for administering the combined or prepared kit components to an animal. In one embodiment, the kit comprises green tea extract and one or more ingredients suitable for consumption by an animal. In another embodiment, the kit comprises instructions for how to combine green tea extract and the ingredients to produce a composition useful for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health.

[0064] When the kit comprises a virtual package, the kit is limited to instructions in a virtual environment in combination with one or more physical kit components. The kit contains green tea extract and other components in amounts sufficient for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health. Typically, green tea extract and the other suitable kit components are admixed just prior to consumption by an animal. The kits may contain the kit components in any of various combinations and/or mixtures. In one embodiment, the kit contains a packet containing green tea extract and a container of food for consumption by an

animal. The kit may contain additional items such as a device for mixing green tea extract and ingredients or a device for containing the admixture, *e.g.*, a food bowl. In another embodiment, green tea extract is mixed with additional nutritional supplements such as vitamins and minerals that promote good health in an animal. The components are each provided in separate containers in a single package or in mixtures of various components in different packages. In preferred embodiments, the kits comprise green tea extract and one or more other ingredients suitable for consumption by an animal. Preferably such kits comprise instructions describing how to combine green tea extract with the other ingredients to form a food composition for consumption by the animal, generally by mixing green tea extract with the other ingredients or by applying green tea extract to the other ingredients, *e.g.*, by sprinkling green tea extract on a food composition.

[0065] In a further aspect, the invention provides a means for communicating information about or instructions for one or more of (1) using green tea extract for preventing or treating osteoarthritis; (2) using green tea extract for preventing and treating degradation of articular cartilage; (3); using green tea extract for promoting and maintaining joint health; (4) contact information for consumers to use if they have a question regarding the methods and compositions of the invention; and (5) nutritional information about green tea extract. The communication means is useful for instructing on the benefits of using the invention and communicating the approved methods for administering green tea extract and food compositions containing green tea extract to an animal. The means comprises one or more of a physical or electronic document, digital storage media, optical storage media, audio presentation, audiovisual display, or visual display containing the information or instructions. Preferably, the means is selected from the group consisting of a displayed website, a visual display kiosk, a brochure, a product label, a package insert, an advertisement, a handout, a public announcement, an audiotape, a videotape, a DVD, a CD-ROM, a computer readable chip, a computer readable card, a computer readable disk, a USB device, a FireWire device, a computer memory, and any combination thereof.

[0066] In another aspect, the invention provides methods for manufacturing a food composition comprising green tea extract and one or more other ingredients suitable for consumption by an animal, *e.g.*, one or more of protein, fat, carbohydrate, fiber, vitamins, minerals, probiotics, prebiotics, and the like. The methods comprise admixing one or more ingredients suitable for consumption by an animal with green tea extract. Alternatively, the methods comprise applying green tea extract alone or in conjunction or combination with

other ingredients onto the food composition, *e.g.*, as a coating or topping. Green tea extract can be added at any time during the manufacture and/or processing of the food composition. The composition can be made according to any method suitable in the art.

[0067] In another aspect, the invention provides a package comprising green tea extract and a label affixed to the package containing a word or words, picture, design, acronym, slogan, phrase, or other device, or combination thereof that indicates that the contents of the package contains green tea extract with beneficial properties relating to osteoarthritis. Typically, such device comprises the words “prevents and treats osteoarthritis”, “prevents and treats the degradation of articular cartilage”, “promotes and maintains joint health”, or an equivalent expression printed on the package. Any package or packaging material suitable for containing the composition is useful in the invention, *e.g.*, bag, box, bottle, can, pouch, and the like manufactured from paper, plastic, foil, metal, and the like. In a preferred embodiment, the package contains a food composition adapted for a particular animal such as a human, canine, or feline, as appropriate for the label, preferably a companion animal food composition for dogs or cats. In a preferred embodiment, the package is a can or pouch comprising a food composition of the invention.

[0068] In another aspect, the invention provides for use of green tea extract to prepare a medicament for one or more of preventing or treating osteoarthritis; preventing or treating the degradation of articular cartilage; promoting and maintaining joint health; improving the quality of life; and promoting the health and wellness in an animal. Generally, medicaments are prepared by admixing a compound or composition, *i.e.*, green tea extract or a green tea extract composition, with excipients, buffers, binders, plasticizers, colorants, diluents, compressing agents, lubricants, flavorants, moistening agents, and other ingredients known to skilled artisans to be useful for producing medicaments and formulating medicaments that are suitable for administration to an animal.

[0069] In another aspect, the invention provides a package useful for containing green tea extract of the invention. The package comprises at least one material suitable for containing the green tea extract and a label affixed to the material containing a word or words, picture, design, acronym, slogan, phrase, or other device, or combination thereof, that indicates that the package contains the green tea extract. Typically, such device comprises the words “prevents or treats osteoarthritis” or “prevents or treats degradation of articular cartilage” or “maintains joint health” or an equivalent expression printed on the material. Any package configuration and packaging material suitable for containing the green tea extract are useful

in the invention, *e.g.*, a bag, box, bottle, can, pouch, and the like manufactured from paper, plastic, foil, metal, and the like. In preferred embodiments, the package further comprises a green tea extract of the invention. In various embodiments, the package further comprises at least one window that permit the package contents to be viewed without opening the package. In some embodiments, the window is a transparent portion of the packaging material. In others, the window is a missing portion of the packaging material.

EXAMPLES

[0070] The invention can be further illustrated by the following example, although it will be understood that this example is included merely for purposes of illustration and is not intended to limit the scope of the invention unless otherwise specifically indicated.

[0071] Green tea extracts were prepared according to the following method. 100g of dried *Camellia sinensis* leaves were mixed with 500ml hexane for 30 minutes to remove the fatty acids. The solution was filtered to separate the solids from the liquid. The liquid was discarded. This process was repeated two more times with the remaining solids.

[0072] The remaining solids were mixed with 500ml methanol/water (50/50; v/v) for 30 minutes. The solution was filtered to separate the solids from the liquid. This process was repeated two more times with the remaining solids. The solids were discarded and the methanol/water solutions were pooled. The methanol was evaporated under vacuum and the remaining solution was freeze dried to give 30g of green tea extract. Extracts from both a first harvest (April-May) and a second harvest (June to July) were prepared.

Example 1

[0073] Canine cartilage was digested in a 37°C shaking water bath using the following enzymes: trypsin (0.25%) for 25 minutes, hyaluronidase (150U/ml) for 1 hour, and collagenase (0.78%) overnight. Digested cartilage was filtered to obtain chondrocytes. Dulbecco's Modified Eagle Medium (DMEM) + 2.4% alginate (low melting) + cells were dropped from a 10cc syringe into calcium chloride (102 mM) to form "beads." Chondrocyte beads were cultured in DMEM/F12 + P/S (100 U/mL penicillin and 100 µg/mL streptomycin) + 10% Fetal Bovine Serum (FBS). Media was changed every other day. At the end of the treatment, the chondrocyte beads were dissolved in sodium citrate (55mM) and EDTA (30mM). Suspensions were centrifuged at 1800 rpm for 10 minutes. Cells were washed with phosphate buffer and centrifuged again at 1800 rpm for 5 minutes. One mL RNAqueous™ lysis binding solution (Ambion, Austin, TX) was added to the isolated canine

chondrocyte pellet, mixed thoroughly and stored at -80°C until RNA isolation could be performed.

[0074] Samples were vortexed and homogenized using a Qiashredder column (Qiagen, Valencia, CA) according to manufacturer's directions. The homogenized lysate was collected and 1 equal volume of 64% ethanol was added to it. This mixture was then applied to an RNAqueous™ filter cartridge, 700 uL at a time, and centrifuged for 1 minute at 10,000 rpm. The cartridge was washed using 700uL wash solution #1 and 500 uL wash solution #2/3 with centrifugation at 10,000 rpm for 1 minute for each wash. The filter cartridge was dried by centrifugation (10,000 rpm) for 1 minute. RNA was eluted 3 times by centrifugation (as above) using 30 uL aliquots of 95-100°C elution solution. The resulting RNA was DNase-treated and quantitated in a Beckman DU 640B spectrophotometer (Beckman Coulter, Inc., Brea, CA) at 260 nm. Additionally, quantity and quality were assessed using a bioanalyzer (Agilent, Santa Clara, CA) according to manufacturer's directions.

[0075] Chondrocytes were treated with first harvest or second harvest green tea (*Camellia sinensis*) extracts at 10 ug/ml or 100 ug/ml. 50% methanol was used as a vehicle (0.05, 0.005% final methanol concentration). The same quantity of 50% methanol used in the treatment was used as a control. Cells were treated for one week in DMEM/HAMS + P/S + 10% FBS. Media was changed every other day.

[0076] All samples were run singularly against each primer/probe set to determine what standard curve should be used. Standard curves were generated using serial dilutions of liver RNA or RNA from experimental samples. Alternately, if the samples did not fall within either of the curve ranges, the sample with the lowest C_T (cycle threshold) would be re-reverse transcribed and a 1:10 serial dilution would be used as the standard curve for that primer/probe set. Values were normalized to cyclophilin A levels as determined by quantitative PCR. Inductions were calculated from each of the lowest sample's normalized value. Each set was run with n=4 except the following: CYTL-1 (first harvest 10 ug/ml, n=2; first harvest 100 ug/ml, n=3 and second harvest 10 ug/ml, n=3)

Table 1

Quantitative PCR expression values.

Gene	10 ug/ml			100 ug/ml		
	Control	1st Harvest	2nd Harvest	Control	1st Harvest	2nd Harvest

	10 ug/ml			100 ug/ml		
Gene	Control	1st Harvest	2nd Harvest	Control	1st Harvest	2nd Harvest
IL-6	8.3	39.6	34.8	9.9	115.6	92.6
2252B	2.7	3.3	2.7	2.1	11.4	13.1
MMP-9	205.9	84.3	54.5	264.9	68.8	77.4
IGF-2	8.8	3.5	5.3	5.9	3.5	3.9
TNF-alpha	24.2	186.4	147.4	52.7	1413.7	1607.6
GRIA-4	7.4	4.4	4.2	6.2	4.1	5.6
IL-1	9.2	16.1	13.8	6.4	7.5	7.9
IL-8	4.4	41.1	33.9	5.6	255.5	264.3
MMP-2	3.5	4.4	3.4	3.1	2.2	2.6
MMP-13	12.1	8.7	5.4	14.0	9.4	9.5
PC-2A	109.6	9.6	23.5	79.3	2.6	3.4
CYTL-1	31.2	6.9	9.5	19.7	18.8	14.5
SOX-9	1.8	3.8	3.1	1.8	21.9	12.4

Values represent relative average induction values. Abbreviations: Interleukin (IL); Matrix Metalloproteinase (MMP); Insulin-like Growth Factor (IGF); Tumor Necrosis Factor (TNF); Procollagen (PC); Cytokine-like (CYTL); Glutamate Receptor, Ionotropic, AMPA (GRIA); SRY (sex determining region Y)-box (SOX).

[0077] In the specification, there have been disclosed typical preferred embodiments of the invention. Although specific terms are employed, they are used in a generic and descriptive sense only and not for purposes of limitation. The scope of the invention is set forth in the claims. Obviously many modifications and variations of the invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise than as specifically described.

CLAIMS

What is Claimed is:

1. A method for preventing or treating osteoarthritis in an animal comprising administering to the animal a therapeutically effective amount of green tea extract.
2. The method of claim 1 wherein green tea extract is administered in amounts of from about 0.005 to about 100 mg/kg/day.
3. The method of claim 1 wherein green tea extract is administered to the animal on a regular basis.
4. The method of claim 1 wherein the animal is suffering from osteoarthritis.
5. The method of claim 1 wherein green tea extract is administered as a dietary supplement or a food composition.
6. The method of claim 5 wherein the composition is a food composition and green tea extract comprises from about 0.1 to about 40% of the food composition.
7. The method of claim 5 wherein the composition or dietary supplement further comprises one or more probiotics; inactivated probiotics; components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; and one or more prebiotics.
8. The method of claim 1 wherein the animal is a human or a companion animal.
9. The method of claim 8 wherein the companion animal is a canine.
10. The method of claim 8 wherein the companion animal is a feline.
11. The method of claim 1 wherein the animal is an aging animal.
12. A method for preventing or treating the degradation of articular cartilage in an animal comprising administering to the animal a therapeutically effective amount of green tea extract.
13. The method of claim 12 wherein green tea extract is administered in amounts of from about 0.005 to about 100 mg/kg/day.
14. The method of claim 12 wherein green tea extract is administered to the animal on a regular basis.
15. The method of claim 12 wherein the animal is suffering from the degradation of articular cartilage.
16. The method of claim 12 wherein green tea extract is administered as a dietary supplement or a food composition.

17. The method of claim 16 wherein the composition is a food composition and green tea extract comprises from about 0.1 to about 40% of the food composition.
18. The method of claim 16 wherein the composition or dietary supplement further comprises one or more probiotics; inactivated probiotics; components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; and one or more prebiotics.
19. The method of claim 12 wherein the animal is a human or a companion animal.
20. The method of claim 19 wherein the companion animal is a canine.
21. The method of claim 19 wherein the companion animal is a feline.
22. The method of claim 12 wherein the animal is an aging animal.
23. A method for promoting and maintaining joint health in an animal comprising administering to the animal a therapeutically effective amount of green tea extract.
24. The method of claim 23 wherein green tea extract is administered in amounts of from about 0.005 to about 100 mg/kg/day.
25. The method of claim 23 wherein green tea extract is administered to the animal on a regular basis.
26. The method of claim 23 wherein green tea extract is administered as a dietary supplement or a food composition.
27. The method of claim 26 wherein the composition is a food composition and green tea extract comprises from about 0.1 to about 40% of the food composition.
28. The method of claim 26 wherein the composition or dietary supplement further comprises one or more probiotics; inactivated probiotics; components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; and one or more prebiotics.
29. The method of claim 23 wherein the animal is a human or a companion animal.
30. The method of claim 29 wherein the companion animal is a canine.
31. The method of claim 29 wherein the companion animal is a feline.
32. The method of claim 23 wherein the animal is an aging animal.
33. A method for improving the quality of life in an animal comprising administering to the animal a therapeutically effective amount of green tea extract.
34. The method of claim 33 wherein green tea extract is administered in amounts of from about 0.005 to about 100 mg/kg/day.

35. The method of claim 33 wherein green tea extract is administered to the animal on a regular basis.
36. The method of claim 33 wherein green tea extract is administered as a dietary supplement or a food composition.
37. The method of claim 36 wherein the composition is a food composition and green tea extract comprises from about 0.1 to about 40% of the food composition.
38. The method of claim 36 wherein the composition or dietary supplement further comprises one or more probiotics; inactivated probiotics; components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; and one or more prebiotics.
39. The method of claim 33 wherein the animal is a human or a companion animal.
40. The method of claim 39 wherein the companion animal is a canine.
41. The method of claim 39 wherein the companion animal is a feline.
42. The method of claim 33 wherein the animal is an aging animal.
43. A method for promoting the health and wellness in an animal comprising administering to the animal a therapeutically effective amount of green tea extract.
44. The method of claim 43 wherein green tea extract is administered in amounts of from about 0.005 to about 100 mg/kg/day.
45. The method of claim 43 wherein green tea extract is administered to the animal on a regular basis.
46. The method of claim 43 wherein green tea extract is administered as a dietary supplement or a food composition.
47. The method of claim 46 wherein the composition is a food composition and green tea extract comprises from about 0.1 to about 40% of the food composition.
48. The method of claim 46 wherein the composition or dietary supplement further comprises one or more probiotics; inactivated probiotics; components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; and one or more prebiotics.
49. The method of claim 43 wherein the animal is a human or a companion animal.
50. The method of claim 49 wherein the companion animal is a canine.
51. The method of claim 49 wherein the companion animal is a feline.
52. The method of claim 43 wherein the animal is an aging animal.

53. A composition comprising green tea extract in a therapeutically effective amount for one or more of preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, and promoting and maintaining joint health.
54. The composition of claim 53 containing green tea extract in amounts sufficient to administer green tea extract to an animal in amounts to about from about 0.005 to about 5 mg/kg/day.
55. A pharmaceutical or nutraceutical composition comprising green tea extract and one or more pharmaceutically or nutraceutically acceptable carrier, diluents or excipients
56. A package comprising green tea extract and a label affixed to the package containing a word or words, picture, design, acronym, slogan, phrase, or other device, or combination thereof that indicates that the contents of the package contains green tea extract with beneficial properties relating to osteoarthritis.
57. The package of claim 56 wherein the beneficial properties are one or more of preventing osteoarthritis, treating osteoarthritis, preventing the degradation of articular cartilage, treating the degradation of articular cartilage, promoting joint health, and maintaining joint health.
58. A means for communicating information about, or instructions for, one or more of (1) using green tea extract for preventing or treating osteoarthritis; (2) using green tea extract for preventing or treating the degradation of articular cartilage; (3) using green tea extract for promoting and maintaining joint health; (4) contact information for consumers to use if they have a question regarding the methods and compositions of the invention; and (5) nutritional information about green tea extract, the means comprising one or more of a physical or electronic document, digital storage media, optical storage media, audio presentation, audiovisual display, or visual display containing the information or instructions.
59. The means of claim 58 selected from the group consisting of a displayed website, a visual display kiosk, a brochure, a product label, a package insert, an advertisement, a handout, a public announcement, an audiotape, a videotape, a DVD, a CD-ROM, a computer readable chip, a computer readable card, a computer readable disk, a USB device, a FireWire device, a computer memory, and any combination thereof.
60. A kit suitable for administering green tea extract to an animal comprising in separate containers in a single package or in separate containers in a virtual package, as appropriate for the kit component, green tea extract and one or more of (1) one or more

- ingredients suitable for consumption by an animal; (2) instructions for how to combine green tea extract and other kit components to produce a composition useful for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, promoting and maintaining joint health; (3) instructions for how to use green tea extract for preventing or treating osteoarthritis; (4) instructions for how to use green tea extract for preventing or treating the degradation of articular cartilage; (5) instructions for how to use green tea extract for promoting and maintaining joint health; (6) one or more probiotics; (7) one or more inactivated probiotics; (8) one or more components of inactivated probiotics that promote health benefits similar to or the same as the probiotics; (9) one or more prebiotics; (10) a device for preparing or combining the kit components to produce a composition suitable for administration to an animal; and (11) a device for administering the combined or prepared kit components to an animal.
61. The kit of claim 60 wherein the green tea extract is in a sachet.
 62. The kit of claim 61 comprising green tea extract and one or more ingredients suitable for consumption by an animal.
 63. The kit of claim 62 further comprising instructions for how to combine green tea extract and the ingredients to produce a composition useful for preventing or treating osteoarthritis, preventing or treating the degradation of articular cartilage, or promoting and maintaining joint health.
 64. The kit of claim 60 comprising green tea extract and one or more probiotics.
 65. The kit of claim 64 wherein the probiotic is *Enterococcus faecium* SF68.
 66. The kit of claim 66 further comprising one or more ingredients suitable for consumption by an animal.
 67. A package comprising at least one material suitable for containing green tea extract and a label affixed to the material containing a word or words, picture, design, acronym, slogan, phrase, or other device, or combination thereof that indicates that the package contains the green tea extract.
 68. The package of claim 67 further comprising the green tea extract.
 69. The package of claim 67 further comprising at least one window.

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A23F 3/00 (2011.01)

USPC - 426/597

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): A23F 3/00 (2011.01); USPC: 426/597

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 426/435, 590, 655

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Google Scholar, Google Patents, PubWEST (PGPB,USPT,EPAB,JPAB)

Osteoarthritis, degenerate, joint, disease, cartilage, Camellia, sinensis, green, tea, animal, food, moisture, probiotic, canine, feline, aging, prebiotic, Enterococcus. Articular, joint, diet, food, dose, sachet, hyaline

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/0317885 A1 (Baker) 25 Dec 2008 (25.12.2008) paragraphs [0005], [0012]-[0013], [0055]-[0056], [0064]-[0068], [0076]-[0077], [0086], [0097]-[0098], [0114], [0120]-[0121]	1-6, 8-17, 19-27, 29-37, 39-47, 49-55
Y		7, 18, 28, 38, 48, 56-69
Y	US 2003/0190309 A1 (Zink, et al.) 09 Oct 2003 (09.10.2003) paragraphs [0012], [0080]-[0083], [0093], [0245], [0265]	7, 18, 28, 38, 48, 56-69
A	SINGH, et al. Green tea polyphenol epigallocatechin-3-gallate: inflammation and arthritis, ; Life Sci. 2010 June 19; 86(25-26): 9077918. doi:10.1016/j.lfs.2010.04.013.	1-69

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

03 Jan 2012 (03.01.2012)

Date of mailing of the international search report

19 JAN 2012

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