Abstract: Compositions comprising a mixture of one or more omega 3 extracts of one or more marine oils and use of the composition to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer or depression.
FIELD OF THE INVENTION

[0001] The present invention relates to anti-inflammatory compositions and uses thereof and in particular to compositions comprising a mixture of one or more marine oils with one or more omega 3 extracts of one or more marine oils and use of the compositions to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.

BACKGROUND

[0002] Conditions associated with abnormal or undesirable inflammation such as soft tissue injuries and rheumatoid arthritis can be difficult to manage (Scott et al, 1998). Marine oils high in EPA (eicosapentaenoic acid; 20:5 (n-3); eicosa-5,8,11,14,17-pentaenoic acid) and DHA (docosahexaenoic acid; 22:6 (n-3); docosa-4,7,10,13,16,19-hexaenoic acid) are reported to be useful as anti-inflammatory products including for the treatment of rheumatoid arthritis and related conditions (Cleland et al, 2003; Cleland and James, 2006) with steroid-sparing effects (Galarraga et al, 2008). Tissue extracts from the green shell mussel (GSM) Perna canaliculus are also reported to be useful as anti-inflammatory products. Individual subjects may respond differently to anti-inflammatory agents (Noble et al, 2000). The availability of improved or alternative anti-inflammatory agents is desirable for subjects suffering conditions associated with abnormal or undesirable inflammation. It would therefore be desirable to provide an improved or alternative anti-inflammatory composition.

SUMMARY OF THE INVENTION

[0003] Accordingly, in one aspect the present invention relates to a composition comprising, consisting essentially of, or consisting of a mixture of

(a) an omega 3 fatty acid extract of one or more marine oils, and

(b) one or more marine oils.

[0004] In another aspect the present invention relates to a method of treating or preventing inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression, the method comprising separate, simultaneous, or sequential administration to a subject in need thereof of an effective amount of
(a) an omega 3 fatty acid extract of one or more marine oils, and
(b) one or more oils more marine oils.

[0005] In another aspect the present invention relates to use of
(a) an omega 3 fatty acid extract of one or more marine oils, and
(b) one or more marine oils,
to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression. In one embodiment where the use is in the manufacture of a medicament, the medicament may be formulated for separate, simultaneous, or sequential administration of the extract and the one or more oils.

[0006] In another aspect the present invention relates to a product containing
(a) an omega 3 fatty acid extract of one or more marine oils, and
(b) one or more marine oils,
as a combined preparation for separate, simultaneous, or sequential use to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.

[0007] The following embodiments may relate to any of the above aspects.

[0008] In one embodiment the mixture is a blend or admixture. In one embodiment the one or more omega 3 fatty acid extracts is a mixture, blend or admixture of two or more omega 3 fatty acid extracts, or three or more omega 3 fatty acid extracts, or four or more omega 3 fatty acid extracts. In one embodiment the omega 3 fatty acid extract comprises at least about 60, 65, 70, 75, 80, 85, 90, or 95% by weight omega 3 fatty acids or esters thereof. In one embodiment the extract is prepared by supercritical fluid extraction of one or more marine oils, preferably supercritical CO₂ extraction of one or more marine oils.

[0009] In one embodiment the omega 3 fatty acid extract (also referred to as the omega 3 extract) comprises one or more fatty acids or one or more esters thereof or combinations thereof selected from α-linolenic acid (ALA) (18:3 (n-3); octadeca-9,12,15-trienoic acid), esters of ALA, stearidonic acid (SA) (18:4 (n-3); octadeca-6,9,12,15-tetraenoic acid), esters of SA, eicosatetraenoic acid (ETA) (20:4 (n-3); eicosa-8,11,14,17-tetraenoic acid), esters of ETA, eicosapentaenoic acid (EPA) (20:5 (n-3); eicosa-5,8,11,14,17-pentaeinoic acid), esters of EPA, docosapentaenoic acid (DPA) (22:5 (n-3); docosa-7,10,13,16,19-pentaeinoic acid), esters of DPA, and docosahexaenoic acid
(DHA) (22:6 (n-3); docosa-4,7,10,13,16,19-hexaenoic acid), esters of DHA, of a combination of any
two or more thereof. The fatty acids may be free fatty acids or esterified, preferably esterified.

Useful esterified fatty acids include methyl, ethyl, and propyl esters, and lipids (including
glycerophospholipids, glycerophospholipids, and phospholipids) or a combination of any two or more
thereof.

[0010] The omega 3 fatty acid extract is an extract of one or more marine oils. Preferred
methods of extraction include solvent extraction, supercritical solvent extraction including
supercritical CO$_2$ extraction, distillation, and chromatographic separation. Preferred methods of
solvent extraction include ethanol extraction. In one embodiment the extract is prepared by solvent
extraction, such as ethanol extraction, followed by distillation or supercritical extraction. In one
preferred embodiment the extract is preparedly conversion of the marine oil, preferably a hoki oil,
to ethyl esters followed by extraction of omega 3 fatty acids using supercritical CO$_2$. In alternative
embodiments, an additional extract from a plant oil, a marine oil, eggs, milk fat, or micro-algae, or a
combination of any two or more thereof may also be added to the composition.

[0011] In one embodiment the marine oil selected from one or more marine mammal oils
(such as one or more oils from seals of the families Odobenidae, Otariidae or Phocidae), one or
more shellfish oils, one or more cephalopod oils (such as one or more whole cephalopod oils or one
or more cephalopod offal oils or a combination thereof), and one or more fish oils, or a
combination of any two or more thereof. In various embodiments the oil is a seal oil, or a squid oil,
or a fish oil.

[0012] In one embodiment the cephalopod oil is an octopus oil (from cephalopods of the
order Octopoda) or a squid oil (from cephalopods of the order Teuthida such as JLoligopki, Loligo
bkekert, Nototodarus gotildi, and Nototodarus sloanii).

[0013] In one embodiment the fish oil is selected from alfonsino (a fish of the family Berycidae
such as Betyx decadactylus), anchovy, barracouta (Thysites atun), barracuda (a fish of the genus
Sphyraena), baikal, bloater, cacha, cardinalfish (such as black cardinalfish), carp, cod (such as red cod
and black cod), common mora (Mora moro, Ribaldo), dogfish (such as spiny dogfish Squalus acanthias),
dory (such as John dory Zeus faber or smooth oreo dory Pseudocytta maculatus), eel, elephant fish,
eulachon, frost fish, gemfish, hake, herring, hilsa, hold (Macrironus novae-elandiae), jack fish (such as
leather) acket Oligopilus saums), katla, kahawai (a fish of the family Arripidae such as Arripis sylabion or
A. trutta.), kipper, ling (including burbot Lota lota, blue ling Molva dypterygia, cobia Rachycentron
canadum, common ling Molva molva, pink cusk-eel Genypterus blacodes and red hake Urophysa chuss),
mackerel (such as blue mackerel Scomber australasias and Jack mackerel Trachurus symmetrica),

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morwong (such as tarakihi Nemadactylus macropterus), taut (a fish of the family Mugilidae, such as grey mullet Mugil cephalus) orange roughy, pangas, pilchard, rig, salmon, sardine, sea perch, shark (such as school shark Gakorhimis gakns and pale ghost shark *Hydrologus bemisi*), sprat, stargazer (a fish of the family Uranoscopidae), swordfish, trevally, trout, tuna (including species of the genera *Timmus* and other fish in the family Scombridae commonly known as 'tuna', such as slender tuna *A-lothannusfallai*), wharehou (such as common wharehou *S. octa bra*ma, white warehou *Seriolella caenika* and silver warehou *Seriolellapunctata*), whitebait, and whiting (such as southern blue whiting Microtesistius australis) oils, or a combination of any two or more thereof. In various embodiments the fish oil comprises an oil selected from one or more fish oils, one or more head oils, one or more offal oils, and one or more liver oils, or a combination of any two or more thereof.

[0014] In one embodiment the oil is a winterised oil or a non-winterised oil or a combination thereof. Preferred marine oils include hoki (*Macrurots* novae*elandiae*) oil and winterised hoki oil. In one embodiment the oil is winterised oil that has been chilled to at least about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15°C and any solids removed by, for example, filtration or decanting. In one embodiment the oil is a food grade oil. In another embodiment the oil has been deodorised, preferably steam deodorised. In yet another embodiment the oil is a cold-pressed oil or a neutralised oil or a cold-pressed neutralised oil.

[0015] In one embodiment the omega 3 extract comprises at least about 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95% by weight omega 3 fatty acids or esters thereof, and useful ranges may be selected between any of these foregoing values (for example, about 25 to 50, 30 to 50, 35 to 50, 40 to 50, 25 to 60, 30 to 60, 35 to 60, 40 to 60, 45 to 60, 50 to 60, 25 to 70, 30 to 70, 35 to 70, 40 to 70, 45 to 70, 50 to 70, 55 to 70, 60 to 70, 25 to 80, 30 to 80, 35 to 80, 40 to 80, 45 to 80, 50 to 80, 55 to 80, 60 to 80, 65 to 80, 70 to 80, 25 to 90, 30 to 90, 35 to 90, 40 to 90, 45 to 90, 50 to 90, 55 to 90, 60 to 90, 65 to 90, 70 to 90, 75 to 90, 80 to 90, 25 to 95, 30 to 95, 35 to 95, 40 to 95, 45 to 95, 50 to 95, 55 to 95, 60 to 95, 65 to 95, 70 to 95, 75 to 95 and 80 to 95%). In one preferred embodiment the omega 3 extract comprises at least about 25% by weight omega 3 fatty acids or esters thereof.

[0016] In one embodiment the composition comprises or the medicament comprises at least about 0.1, 0.2, 0.5, 1, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 99, 99.5, 99.8 or 99.9% by weight of one or more omega 3 extracts and useful ranges may be selected between any of these foregoing values (for example, about 0.1 to 50, 0.2 to 50, 0.5 to 50, 1 to 50, 5 to 50, 10 to 50, 15 to 50, 20 to 50, 25 to 50, 30 to 50, 35 to 50, 40 to 50, 45 to 50, 0.1 to 60, 0.2 to 60, 0.5 to 60, 1 to 60, 5 to 60, 10 to 60, 15 to 60, 20 to 60, 25 to 60, 30 to 60, 35 to 60, 40 to 60, 45 to 60, 0.1 to 70, 0.2 to 70, 0.5 to 70, 1 to 70, 5 to 70, 10 to 70, 15 to 70, 20 to 70, 25 to 70, 30 to 70,
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35 to 70, 40 to 70, 45 to 70, 0.1 to 80, 0.2 to 80, 0.5 to 80, 1 to 80, 5 to 80, 10 to 80, 15 to 80, 20 to 80, 25 to 80, 30 to 80, 35 to 80, 40 to 80, 45 to 80, 0.1 to 90, 0.2 to 90, 0.5 to 90, 1 to 90, 5 to 90, 10 to 90, 15 to 90, 20 to 90, 25 to 90, 30 to 90, 35 to 90, 40 to 90, 45 to 90, 0.1 to 99, 0.2 to 99, 0.5 to 99, 1 to 99, 5 to 99, 10 to 99, 15 to 99, 20 to 99, 25 to 99, 30 to 99, 35 to 99, 40 to 99 and 45 to 99%). Preferably the composition or medicament comprises at least about 30 to 90% by weight of the one or more omega 3 extracts.

[0017] In one embodiment the composition comprises or the medicament comprises at least about 0.1, 0.2, 0.5, 1, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 99, 99.5, 99.8 or 99.9% by weight of one or more marine oils, and useful ranges may be selected between any of these foregoing values (for example, about 0.1 to 50, 0.2 to 50, 0.5 to 50, 1 to 50, 5 to 50, 10 to 50, 15 to 50, 20 to 50, 25 to 50, 30 to 50, 35 to 50, 40 to 50, 45 to 50, 0.1 to 60, 0.2 to 60, 0.5 to 60, 1 to 60, 5 to 60, 10 to 60, 15 to 60, 20 to 60, 25 to 60, 30 to 60, 35 to 60, 40 to 60, 45 to 60, 0.1 to 70, 0.2 to 70, 0.5 to 70, 1 to 70, 5 to 70, 10 to 70, 15 to 70, 20 to 70, 25 to 70, 30 to 70, 35 to 70, 40 to 70, 45 to 70, 0.1 to 80, 0.2 to 80, 0.5 to 80, 1 to 80, 5 to 80, 10 to 80, 15 to 80, 20 to 80, 25 to 80, 30 to 80, 35 to 80, 40 to 80, 45 to 80, 0.1 to 90, 0.2 to 90, 0.5 to 90, 1 to 90, 5 to 90, 10 to 90, 15 to 90, 20 to 90, 25 to 90, 30 to 90, 35 to 90, 40 to 90, 45 to 90, 0.1 to 99, 0.2 to 99, 0.5 to 99, 1 to 99, 5 to 99, 10 to 99, 15 to 99, 20 to 99, 25 to 99, 30 to 99, 35 to 99, 40 to 99 and 45 to 99%).

[0018] In one embodiment the ratio of the omega 3 extract to the oil in the composition is about 1:100 to about 100:1, about 1:10 to about 10:1, about 1:5 to about 5:1, about 1:2 to about 2:1, preferably about 2:3 or about 3:2.

[0019] In one embodiment the composition comprises at least about 0.001, 0.01, 0.05, 0.1, 0.15, 0.2, 0.3, 0.4, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19 grams of the omega 3 extract and useful ranges may be selected between any of these foregoing values (for example, from about 0.01 to about 1 grams, about 0.01 to about 10 grams, about 0.01 to about 19 grams, from about 0.1 to about 1 grams, about 0.1 to about 10 grams, about 0.1 to about 19 grams, from about 1 to about 5 grams, about 1 to about 10 grams, about 1 to about 19 grams, about 5 to about 10 grams, and about 5 to about 19 grams).

[0020] In one embodiment the composition comprises at least about 0.001, 0.01, 0.05, 0.1, 0.15, 0.2, 0.3, 0.4, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19 grams of the oil and useful ranges may be selected between any of these foregoing values (for example, from about 0.01 to about 1 grams, about 0.01 to about 10 grams, about 0.01 to about 19 grams, from about 0.1 to about 1 grams, about 0.1 to about 10 grams, about 0.1 to about 19 grams, from about 1 to about
[0021] In one embodiment the composition comprises, the medicament comprises, or the method comprises administration of about 5% to about 50% by weight omega 3 extract and about 50% to 90% by weight of one or more marine oils. In one embodiment the marine oil is hoki oil.

[0022] In one embodiment the composition further comprises, consists essentially of or consists of about 0.1, 0.5, 1, 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50% by weight another anti-inflammatory agent and useful ranges may be selected between any of these foregoing values (for example, from about 0.1 to about 50%, from about 0.2 to about 50%, from about 0.5 to about 50%, from about 1 to about 50%, from about 5 to about 50%, from about 10 to about 50%, from about 15 to about 50%, from about 20 to about 50%, from about 25 to about 50%, from about 30 to about 50%, from about 35 to about 50%, from about 40 to about 50%, and from about 45 to about 50%).

[0023] In one embodiment the composition further comprises a pharmaceutically acceptable carrier. In one embodiment the composition further comprises, the medicament further comprises, or the method further comprises administration of one or more agents selected from one or more antihistamines, one or more anti-inflammatories, one or more anti-rheumatics, one or more corticosteroids, one or more muscle relaxants, one or more greenshell mussel extracts, glucosamine or a salt thereof, vitamin E, and vitamin C, or a combination of any two or more thereof.

[0024] In one embodiment the composition further comprises, the medicament further comprises, or the method further comprises administration of a greenshell mussel (GSM) extract (including whole-tissue extracts, gonad extracts, protein extracts, lipid extracts, or a combination of any two or more thereof, in liquid, dried, or powdered form), glucosamine (including salts thereof), or a combination of any two or more thereof.

[0025] In one embodiment the composition further comprises, the medicament further comprises, or the method further comprises administration of one or more anti-inflammatory food components selected from vitamin E; vitamin C; greenshell mussel (GSM) extracts; Lyprinol™ GSM extract; bromelain; a bioflavonoid mixture extracted from Pinus maritime (pine bark) such as Pycnogenol™; garlic; extracts of Ginkgo biloba leaves; Ephedra (ma-huang); a combination of three Chinese herbal extracts (Ling-Zhi (Ganoderma lucidum), Ku-Shen (Radix Sophora flavescentis) and Gan-Cao (Radix Glycyrrhiza uralensis)) known as ASHMI for "anti-asthma herbal medicine intervention"; Oxy 17™ available from Progressive Health Nutraceuticals, Inc. (USA); extracts from
the mushrooms Cordyceps sinensis, Ganoderma lucidum (Reishi), and Tremella fuciformis (Silver-Ear); perilla leaf extract; rosmarinic acid; flavonoids (such as luteolin, fisetin and apigenin); simple sugars (such as L-fucose and N-acetylenuraminic acid); methylsulfonylmethane; soy protein or genistein or both; quercetin; spkulina; forskolin; and mixtures of any two or more thereof.

[0026] In one embodiment the composition further comprises a plant oil selected from coconut oil, corn oil, cottonseed oil, canola oil, rapeseed oil, olive oil, palm oil, peanut oil, ground nut oil, safflower oil, sesame oil, soybean oil, sunflower oil, nut oil, hazelnut oil, almond oil, cashew oil, macadamia oil, pecan oil, pistachio oil, walnut oil, oils from melon and gourd seeds, bottle gourd oil, buffalo gourd oil, pumpkin seed oil, watermelon seed oil, acai oil, blackcurrant seed oil, borage seed oil, evening primrose oil, carob seed oil, amaranth oil, apricot oil, argan oil, artichoke oil, avocado oil, babassu oil, ben oil, boroneo tallow nut oil, cohune oil, coriander seed oil, flax oil, flax seed oil, coriander seeds oil, grape seed oil, hemp oil, kapok seed oil, kiwi fruit oil, lallemantia oil, meadowfoam seed oil, linseed oil, mustard oil, okra seed oil, perilla seed oil, pequi oil, pine nut oil, poppyseed oil, prune kernel oil, quinoa oil, ramtil oil, rice bran oil, tea oil, and wheat germ oil, or a combination of any two or more thereof. Preferred plant oils are those high in omega 3 fatty acids.

[0027] In one embodiment the composition is in the form of a tablet, a caplet, a pill, a hard or soft capsule or a lozenge. In one embodiment the composition is in the form of a cachet, a dispensable powder, granules, a suspension, an elixir, a liquid, or any other form that can be added to food or drink, including for example water or fruit juice. In one embodiment the composition further comprises one or more constituents (such as antioxidants) which prevent or reduce degradation of the composition during storage or after administration.

[0028] In one embodiment the composition is or is formulated as a food, drink, food additive, drink additive, dietary supplement, nutritional product, medical food, nutraceutical, medicament or pharmaceutical. Preferably, the composition is formulated as a powder, liquid, food bar, spread, sauce, ointment, tablet or capsule.

[0029] In one embodiment the composition is formulated for oral, nasal or parenteral (including topical, subcutaneous, intramuscular and intravenous) administration. In one embodiment the composition is formulated for ingestion, inhalation or topical application. Where the composition is formulated for inhalation, preferably it is formulated as an inhalable powder, solution or aerosol. Where the composition is formulated for topical application, preferably it is formulated as an ointment, cream or lotion.
In one embodiment the composition is formulated for separate, simultaneous or sequential administration of the extract and the oil. In one embodiment separate compositions are formulated for separate, simultaneous or sequential administration of the extract and the oil. In one embodiment the composition described above and an agent selected from therapeutic agents including but not limited to antihistamines, antiinflammatories, anti-rheumatics, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase-2 selective inhibitors, and muscle relaxants, including a combination of any two or more thereof, are administered separately, simultaneously or sequentially. In one embodiment the agent is selected from a greenshell mussel extract (including whole-tissue extracts, gonad extracts, protein extracts, and Hpid extracts, or a combination of any two or more thereof), glucosamine (including salts thereof), anti-inflammatory food component (as described above), or a combination of any two or more thereof.

In one embodiment the inflammation is joint inflammation, muscle inflammation, tendon inflammation, ligament inflammation, joint damage, joint sprain or strain, muscle sprain, muscle strain, cartilage damage, osteoarthritis, or rheumatoid arthritis. In one embodiment the condition is an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression. In one preferred embodiment the inflammation is joint inflammation. In another preferred embodiment the inflammation is muscle inflammation, tendon inflammation, ligament inflammation, joint damage, joint sprain or strain, muscle sprain or strain, or cartilage damage. In another preferred embodiment the conditions is osteoarthritis or rheumatoid arthritis. In another preferred embodiment the condition is an atopic condition. In another preferred embodiment the condition is an allergy. In yet another preferred embodiment the condition is arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression. In various embodiments, the treatment is with steroid sparing effect.

In this specification where reference has been made to patent specifications, other external documents, or other sources of information, this is generally for the purpose of providing a context for discussing the features of the invention. Unless specifically stated otherwise, reference to such external documents is not to be construed as an admission that such documents, or such sources of information, in any jurisdiction, are prior art, or form part of the common general knowledge in the art.

It is intended that reference to a range of numbers disclosed herein (for example, 1 to 10) also incorporates reference to all rational numbers within that range (for example, 1, 1.1, 2, 3, 3.9, 4, 5, 6, 6.5, 7, 8, 9 and 10) and also any range of rational numbers within that range (for example, 2 to 8, 1.5 to 5.5 and 3.1 to 4.7) and, therefore, all sub-ranges of all ranges expressly
disclosed herein are hereby expressly disclosed. These are only examples of what is specifically intended and all possible combinations of numerical values between the lowest value and the highest value enumerated are to be considered to be expressly stated in this application in a similar manner.

**BRIEF DESCRIPTION OF THE DRAWINGS**

5 [0034] Figure 1 is a graph showing the inhibition of neutrophil superoxide production by aspirin (in EtOH), hoki oil, hoki omega 3 extract, and 33% w/w hoki omega 3 extract plus 67% w/w hoki oil (actual). Also shown is the expected result for 33% w/w hoki omega 3 extract plus 67% w/w hoki oil based on results for individual components. Test materials were assessed at concentrations of 100 µg/ml, 200 µg/ml, 400 µg/ml, and 800 µg/ml against a control assay with no test sample added. Statistical significance was assessed relative to control with an independent Student t-test. Aspirin (all concentrations), hoki oil plus hoki SFE (all concentrations): P<0.01: Hoki oil (200 and 200 ug/ml), hoki SFE (200 ug/ml): P<0.05.

**DETAILED DESCRIPTION OF THE INVENTION**

[0035] The present invention is based on the discovery that compositions comprising a mixture of (a) one or more omega 3 fatty acid extracts of one or more marine oils, and (b) one or more marine oils have useful, preferably synergistic, activity to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.. In particular, the present invention is based on the discovery that combinations of (1) an omega 3 fatty acid extract that comprises about 70% by weight omega 3 fatty acids; and (2) winterised hoki oil, have useful, preferably synergistic, anti-inflammatory activity. A preferred composition is 33% w/w hoki omega 3 extract plus 67% w/w hoki oil.

1. **Definitions**

[0036] The term "comprising" as used in this specification means "consisting at least in part of. When interpreting statements in this specification which include that term, the features, prefaced by that term in each statement or claim, all need to be present but other features can also be present. The related terms "comprises" and "comprised" are to be interpreted similarly.

[0037] An "effective amount" is the amount required to confer therapeutic effect. The interrelationship of dosages for animals and humans (based on milligrams per meter squared of body surface) is described by Freireich, et al. (1966). Body surface area can be approximately
determined from height and weight of the subject. See, e.g., Scientific Tables, Geigy Pharmaceuticals, Aïdley, New York, 1970, 537. Effective doses also vary, as recognized by those skilled in the art, dependent on route of administration, carrier usage, and the like.

[0038] The term "pharmaceutically acceptable carrier" is intended to refer to a carrier including but not limited to an excipient, diluent or auxiliary that can be administered to a subject as a component of a composition of the invention that does not reduce the activity of the composition and is not toxic when administered in doses sufficient to deliver an effective amount of one or more active agents. The formulations can be administered orally, nasally or parenterally (including topically, intramuscularly, inttaperitoneally, subcutaneously and intravenously).

[0039] The term "steroid sparing" is intended to mean that the dose of steroidal medication administered to a subject is able to be reduced to a level below that administered before the subject began taking a composition of the present invention or began using a method of the present invention. Preferably the daily or weekly or monthly dose of steroids is able to be reduced by at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 99%.

[0040] A "subject" in accordance with the invention is an animal, preferably a mammal, more preferably a mammalian companion animal or human. Preferred companion animals include cats, dogs and horses.

[0041] The term "synergy" as used in this specification means the effects of compositions useful herein are superior, as measured by, for example, the extent of the effect in vitro or in vivo or both, compared to use of individual agents alone. For example, the effect of the combination of an omega 3 extract and an oil is synergistic if the effect is superior to the effect achievable with the extract alone or the oil alone. Further, the effect of the combination is synergistic if a beneficial effect is obtained in a group of patients that does not respond (or responds poorly) to an extract alone or an oil alone. In addition, the effect of the combination is synergistic if one of the components is used at its conventional dose and the other component is used at a reduced dose and the effect, as measured by, for example, the extent of the effect in vitro or in vivo or both, is equivalent to or better than that achievable with conventional amounts of either one of the components of the combination treatment alone. Related terms such as "synergistic" are to be interpreted similarly.

[0042] The term "treat" and its derivatives should be interpreted in their broadest possible context. The term should not be taken to imply that a subject is treated until total recovery.
Accordingly, "treat" broadly includes amelioration and/or prevention of the onset of the symptoms or severity of a particular condition.

2. Marine oils

[0043] Marine oils are known sources of omega 3 fatty acids. The omega 3 fatty acids are ω-linolenic acid (ALA) (18:3 (n-3); octadeca-9,12,15-trienoic acid), stearidonic acid (SA) (18:4 (n-3); octadeca-6,9,12,15-tetraenoic acid), eicosatetraenoic acid (ETA) (20:4 (n-3); eicoso-8,11,14,17-tetraenoic acid), eicosapentaenoic acid (EPA) (20:5 (n-3); eicoso-5,8,11,14,17-pentaenoic acid), docosapentaenoic acid (DPA) (22:5 (n-3); docosa-7,10,13,16,19-pentaenoic acid), and docosahexaenoic acid (DHA) (22:6 (n-3); docosa-4,7,10,13,16,19-hexaenoic acid). These fatty acids are present in different amounts and proportions in different oils. Fatty acids useful herein include free fatty acids or esterified fatty acids or mixtures thereof. Useful esterified fatty acids include methyl, ethyl, and propyl esters, and lipids (including glycerolipids, glycerophospholipids, and phospholipids).

[0044] In one embodiment the marine oil selected from one or more marine mammal oils (such as one or more seal oils from the families Odobenidae, Otariidae and Phocidae), one or more shellfish oils, one or more cephalopod oils (such as one or more whole cephalopod oils or one or more cephalopod offal oils or a combination thereof), and one or more fish oils, or a combination of any two or more thereof. In various embodiments the oil is a seal oil, or a squid oil, or a fish oil. In one embodiment the cephalopod oil is an octopus oil (order Octopoda) or a squid oil (order Teuthida).

[0045] In one embodiment the fish oil is selected from alfonsino (a fish of the family Berycidae such as Beryx decadactylus), anchovy, barracouta (Thyrsites atun), barracuda (a fish of the genus Sphirraend), baikal, bloater, cacha, cardinalfish (such as black cardinalfish), carp, cod (such as red cod and black cod), common mora (Mora mow, Ribaldo), dogfish (such as spiny dogfish Squahts acanthias), dory (such as John dory Zeusfaber or smooth oreo dory Pseidocytthus maculatus), eel, elephant fish, eulachon, frost fish, gemfish, hake, herring, hilsa, hoki (Macruronus novae-elandiae), hilsa, jack fish (such as leatherjacket Oligoplites saunis), katla, kahawai (a fish of the family Arripidae such as A.r pis xylabion oiA.mpis trutta.), kipper, ling (including burbot Lota lota, blue ling Molva dypterygia, cobia Raýçentron canadum, common ling Molva molva, pink cusk-eel Genyptertis blacodes and red hake Orophyôs òwass), mackerel (such as blue mackerel Scomber australasicus and Jack mackerel Tráwuras symmetricus), morwong (such as tarakrhi Nemadactylus macroptetns), mullet (a fish of the family Mugilidae, such as grey mullet Mugil cephalus) orange roughy, pangsas, pilchard, rig, black cod, salmon, sardine, sea perch, shark (such as school shark Gahorhinus galeus and pale ghost shark Hydrolagm...
bemisi), sprat, stargazer (a fish of the family Uranoscopidae), swordfish, trevally, trout, tuna
(including species of the genera *Timno*us and other fish in the family Scombridae commonly known
as 'tuna', such as slender tuna *Allothunmis falla*), wharehou (such as common wharehou *Serioklla
bra?jia*, white wharehou *Serioklla caerulea* and silver wharehou *Serioklla punctata*), whitebait, and whiting
(such as southern blue whiting *Micromesistius australis*) and swordfish oils, or a combination of any
two or more thereof. In various embodiments the fish oil comprises an oil selected from one or
more whole fish oils, one or more head oils, one or more offal oils, and one or more liver oils, or a
combination of any two or more thereof. The fatty acid profiles of some whole fish oils are
provided in Table 1. The omega-3 fatty acid profiles of some whole fish oils are provided in Table
2.

[0046] In one embodiment the oil is a winterised oil. Preferred marine oils include hoki
(*Macruronus nopaegelandiae*) oil and winterised hold oil. In one embodiment the oil is winterised oil
that has been chilled to at least about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15°C and any solids
removed by, for example, filtration or decanting. In one embodiment the oil is a food grade oil. In
another embodiment the oil has been deodorised, preferably steam deodorised. In yet another
embodiment the oil is a cold-pressed oil.

[0047] In one embodiment the oil is winterised oil. Winterised oils are produced by cooling the
oil to between 4 and 15°C and removing any solids. In one embodiment the oil is chilled to at least
about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15°C and any solids removed. Winterising can be a batch
or continuous process. The winterising process can be conducted by cooling oil in a heat exchanger,
and decanting or filtering solids from the oil. The oil temperature may be raised just before
filtration to reduce viscosity and aid filtration. With or without winterising, an oil may be processed
to deodorise (such as by steam deoderisation) it or to remove unwanted components. For example,
oils may be a neutralised by treatment with an absorbent or treated by any conventional oil refining
process. Preferred oils are food grade oils such as cold-pressed oils or neutralised oils.

[0048] In one embodiment the oil is a hold oil. Preferred hoki oils include but are not Limited
to whole fish oils and oils prepared from part of the hoki including the head, offal, liver and any
combination of any two or more thereof. The vitamin E content of the oil of Table 1 is 9 mg/100g
and the vitamin A content is 38 mg/100g.
Table 1 – Fatty acid profile of some whole fish oils

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Hoki</th>
<th>Hoki¹</th>
<th>Jack Mackeral²</th>
<th>Arrow Squid²</th>
<th>Tarakihi²</th>
<th>Cod Liver³</th>
<th>Tuna⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:0 myristic acid</td>
<td>4.0</td>
<td>3.9</td>
<td></td>
<td></td>
<td></td>
<td>3.4</td>
<td>2.5</td>
</tr>
<tr>
<td>14:1</td>
<td>0.2</td>
<td>0.2</td>
<td></td>
<td>0.2</td>
<td></td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>15:0</td>
<td>0.6</td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>16:0 palmitic acid</td>
<td>16.0</td>
<td>16.8</td>
<td>20.6</td>
<td>22.9</td>
<td>18.7</td>
<td>12.3</td>
<td>17.8</td>
</tr>
<tr>
<td>16:1 palmitoleic acid</td>
<td>5.4</td>
<td>5.0</td>
<td>5.4</td>
<td>0.7</td>
<td>3.7</td>
<td>9.6</td>
<td>3.6</td>
</tr>
<tr>
<td>16:3n4</td>
<td>0.3</td>
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<td></td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>17:0</td>
<td>0.3</td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>17:1</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>18:0 stearic acid</td>
<td>2.6</td>
<td>2.6</td>
<td>5.4</td>
<td>4.4</td>
<td>7.7</td>
<td>2.5</td>
<td>5.1</td>
</tr>
<tr>
<td>18:1 n7</td>
<td>3.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.0</td>
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<tr>
<td>18:1 n9 oleic acid</td>
<td>22.9</td>
<td>22.8</td>
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<td>11.2</td>
<td>29.3</td>
<td>13.2</td>
</tr>
<tr>
<td>18:1n9</td>
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<td></td>
<td></td>
<td>3.7</td>
<td>1.2</td>
</tr>
<tr>
<td>18:2 n6 linoleic acid</td>
<td>3.3</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
<td>2.8</td>
<td>0.9</td>
</tr>
<tr>
<td>18:3 n3 alpha linolenic acid (ALA)</td>
<td>0.9</td>
<td>0.6</td>
<td>2.8</td>
<td>0.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:3 n6 gamma linolenic acid (GLA)</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:3 n4</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>18:4n3 stearidonic acid (OTA)</td>
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<td>0.8</td>
<td></td>
<td>0.2</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>20:0 arachidic acid</td>
<td>0.2</td>
<td>0.2</td>
<td></td>
<td></td>
<td></td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>20:1 gadoleic acid</td>
<td>7.1</td>
<td>8.7</td>
<td></td>
<td></td>
<td></td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>20:1 n9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>20:2 n6</td>
<td>1.2</td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>20:3 n3</td>
<td>0.4</td>
<td>0.2</td>
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<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Fatty Acid</td>
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<td>20:4 n6</td>
<td>20:4 n3 arachidonic acid (EPA)</td>
<td>20:5 n3 (EPA)</td>
<td>22:1 n9</td>
<td>22:2 dicosadienoic acid</td>
<td>22:4 n6</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------</td>
<td>--------</td>
<td>-------------------------------</td>
<td>---------------</td>
<td>---------</td>
<td>------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>20:3n6</td>
<td>2.6</td>
<td>0.7</td>
<td>1.4</td>
<td>1.7</td>
<td>4.2</td>
<td>0.0</td>
<td>2.1</td>
</tr>
<tr>
<td>20:4 n6</td>
<td></td>
<td>2.5</td>
<td>1.4</td>
<td>1.7</td>
<td>4.2</td>
<td>0.0</td>
<td>2.1</td>
</tr>
<tr>
<td>20:4 n3 arachidonic acid</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20:5 n3 (EPA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>22:1 n9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22:2 dicosadienoic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22:4 n6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22:5 n3 (DPA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>22:5 n6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22:6 n3 (DHA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24:0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24:1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Fatty Acids</td>
<td>95.1</td>
<td>93.6</td>
<td>80.4</td>
<td>90.4</td>
<td>85.5</td>
<td>94.4</td>
<td>94.9</td>
</tr>
<tr>
<td>Total Omega-3</td>
<td>20.1</td>
<td>22.5</td>
<td>31.6</td>
<td>58.3</td>
<td>40.0</td>
<td>23.5</td>
<td>38.2</td>
</tr>
<tr>
<td>Total Omega-6</td>
<td>8.2</td>
<td>6.4</td>
<td>1.4</td>
<td>1.7</td>
<td>4.2</td>
<td>3.7</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Blank cells ate either less than 0.1 or not detected

(1) Hold oil based on average of 5 year data
(3) Cod liver oil data from National Food Institute, Denmark, www.foodcomp.dk
Table 2 - Omega-3 fatty acid profile of some whole oils

<table>
<thead>
<tr>
<th>Species</th>
<th>20:4 (n-6) AA</th>
<th>20:5 (n-3) EPA</th>
<th>22:5 (n-3)</th>
<th>22:6 (n-3) DHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmed king salmon</td>
<td>0.6</td>
<td>6.2</td>
<td>2.5</td>
<td>10.7</td>
</tr>
<tr>
<td>Farmed yellowtail kingfish</td>
<td>1.2</td>
<td>10.6</td>
<td>2.6</td>
<td>20.5</td>
</tr>
<tr>
<td>Kina</td>
<td>7.4</td>
<td>6.3</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Snapper</td>
<td>2.6</td>
<td>6.8</td>
<td>2.5</td>
<td>24.9</td>
</tr>
<tr>
<td>Hapuku</td>
<td>3.4</td>
<td>6.3</td>
<td>3.5</td>
<td>31</td>
</tr>
<tr>
<td>Gurnard</td>
<td>3.6</td>
<td>7.6</td>
<td>3.3</td>
<td>30.8</td>
</tr>
<tr>
<td>Lemonfish</td>
<td>8.1</td>
<td>9.4</td>
<td>4.3</td>
<td>31.2</td>
</tr>
<tr>
<td>Blue Cod</td>
<td>6.2</td>
<td>8.1</td>
<td>3.9</td>
<td>41</td>
</tr>
<tr>
<td>Grey Mullet</td>
<td>2.7</td>
<td>13.2</td>
<td>7</td>
<td>12.5</td>
</tr>
<tr>
<td>Kahawai</td>
<td>1.2</td>
<td>5.8</td>
<td>2.4</td>
<td>31.5</td>
</tr>
<tr>
<td>Trevelly</td>
<td>4.6</td>
<td>8</td>
<td>3</td>
<td>36.9</td>
</tr>
<tr>
<td>Crayfish</td>
<td>10.8</td>
<td>18</td>
<td>1.8</td>
<td>14.4</td>
</tr>
<tr>
<td>Mussells</td>
<td>2.1</td>
<td>14.9</td>
<td>1.3</td>
<td>27.1</td>
</tr>
</tbody>
</table>

3. Omega 3 fatty acid extracts of marine oils

[0049] Omega 3 fatty acids in free or esterified form may be extracted from marine oils and then recombined with a whole or winterised marine oil. In some embodiments a composition useful herein may also comprise one or more additional omega 3 fatty acid extracts of a plant oil, a marine oil, eggs, milk fat, micro-algae, or an micro-algal oil, or a combination of any two or more thereof. Preferred methods of extraction include solvent extraction, supercritical solvent extraction including supercritical CO2 extraction, distillation, and chromatographic separation. Preferred methods of solvent extraction include ethanol extraction. In one embodiment the extract is prepared by solvent extraction, such as ethanol extraction, followed by distillation or supercritical extraction. In another embodiment, fatty acids present in the oil are converted to alkyl esters, preferably ethyl esters, and then subjected to distillation or supercritical extraction. Useful esterified fatty acids include methyl, ethyl, and propyl esters. Useful ester forms also include lipids (including glycerolipids, glycerophosphoHpids, and phospholipids). Methods of conversion of fatty acids in lipid form to alkyl esters are well known.

[0050] In one preferred embodiment the extract is prepared by conversion of the hoki oil to ethyl esters followed by extraction of omega 3 fatty acids using supercritical CO2.

[0051] Methods of supercritical extraction of fish oil components including ethyl esters have been reported by Staby, A.and Mollerup, J. (Separation of constituents of fish oil using supercritical
5 [0052] In one embodiment the omega 3 fatty acid extract of a hoki oil is prepared by supercritical CO₂ extraction. The fatty acid profile of a preferred fatty acid extract of hoki oil is shown in Table 3 below. In a preferred embodiment the extract is prepared by a method comprising:

(a) providing a hoki oil comprising omega 3 fatty acids,

(b) converting the omega 3 fatty acids to alkyl esters,

(c) contacting the hoki oil with supercritical CO₂ to produce a first phase containing the omega 3 alkyl esters and a second phase, and

(d) separating first phase from the second phase.

Table 3 - Fatty acid profile of a preferred hoki oil extract

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Hoki Oil Extract (wt %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20:4 n3 ETA</td>
<td>3.6</td>
</tr>
<tr>
<td>20:5 n3 EPA</td>
<td>23.8</td>
</tr>
<tr>
<td>22:5 n3 DPA</td>
<td>5.6</td>
</tr>
<tr>
<td>22:6 n3 DHA</td>
<td>46.5</td>
</tr>
<tr>
<td>Total Fatty Acids</td>
<td>79.5</td>
</tr>
<tr>
<td>Total Omega-3</td>
<td>79.5</td>
</tr>
<tr>
<td>Total Omega-6</td>
<td>0.0</td>
</tr>
</tbody>
</table>

4. Methods of treatment or prevention

[0053] The combinations of an omega 3 extract and an oil as described herein are useful to treat or prevent a variety of conditions.

[0054] In one embodiment the condition is joint inflammation, muscle inflammation, tendon inflammation, ligament inflammation, joint damage, joint sprain or strain, muscle sprain, muscle strain, cartilage damage, osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression. In one embodiment the condition is joint inflammation. In one embodiment the condition is muscle inflammation, tendon inflammation, ligament inflammation, joint damage, joint sprain or strain, muscle sprain or strain, or cartilage damage. In
another embodiment the conditions is osteoarthritis or rheumatoid arthritis. In another embodiment the condition is an atopic condition. In another embodiment the condition is an allergy. In another embodiment the condition is arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.

[0055] Compositions, medicaments and methods of treatment or prevention described and useful herein may employ compositions as described below.

5. Compositions useful according to the invention

[0056] A composition useful herein may be formulated as a food, drink, food additive, drink additive, dietary supplement, nutritional product, medical food, nutraceutical, medicament or pharmaceutical. Preferably, a composition of the invention is formulated as a powder, liquid, food bar, spread, sauce, ointment, tablet or capsule. Appropriate formulations may be prepared by an art skilled worker with regard to that skill and the teaching of this specification.

[0057] The compositions useful herein may be formulated to allow for administration to a subject by any chosen route, including but not limited to oral, nasal or parenteral (including topical, subcutaneous, intramuscular and intravenous) administration.

[0058] Thus, a pharmaceutical composition of the invention may be formulated with an appropriate pharmaceutically acceptable carrier (including excipients and diluents) selected with regard to the intended route of administration and standard pharmaceutical practice. For example, a composition of the invention can be administered orally as a powder, liquid, tablet or capsule, or topically as an ointment, cream or lotion. Suitable formulations may contain additional agents as required, including emulsifying, antioxidant, flavouring or colouring agents, and may be adapted for immediate-, delayed-, modified-, sustained-, pulsed- or controlled-release.

[0059] The compositions useful herein may be used alone or in combination with one or more other therapeutic agents. The therapeutic agent may be a food, drink, food additive, drink additive, food component, drink component, dietary supplement, nutritional product, medical food, nutraceutical, medicament or pharmaceutical.

[0060] When used in combination with another therapeutic agent the administration of a composition of the invention and other therapeutic agent may be simultaneous or sequential. Simultaneous administration includes the administration of a single dosage form that comprises all components and the administration of a composition of the invention and other therapeutic agent in separate dosage forms at substantially the same time. Sequential administration includes the
administration of a composition of the invention and other therapeutic agent according to different
schedules, preferably so that there is an overlap in the periods during which the composition of the
invention and other therapeutic agent are provided.

[0061] Suitable agents with which the compositions of the invention can be co-administered
include antihistamines, anti-inflammatories, anti-rheumatics, corticosteroids, muscle relaxants, a
greenshell mussel extract (selected from whole-tissue extracts, gonad extracts, protein extracts, and
lipid extracts, or a combination of any two or more thereof), glucosamine (including salts thereof),
including a combination of any two or more thereof, and other suitable agents known in the art.

[0062] In one embodiment a composition of the invention may further comprise or be
administered with one or more anti-inflammatory food components including but not limited to
choline, vitamin E; vitamin C; greenshell mussel (GSM) extracts; Lyprinol™ GSM extract;
bromelain; a bioflavonoid mixture extracted from Pinus maritime (pine bark) such as Pycnogenol™;
garlic; extracts of Ginkgo biloba leaves; Ephedra (ma-huang); a combination of three Chinese herbal
extracts (Ling-Zhi (Ganoderma lucidum), Ku-Shen (Radix Sophora flavescens) and Gan-Cao
(Radix Glycyrrhiza uralensis)) known as ASHMI for "anti-asthma herbal medicine intervention";
Oxy 17™ available from Progressive Health Nutraceuticals, Inc. (USA); extracts from the
mushrooms Cordyceps sinensis, Ganoderma lucidum (Reishi), and Tremella fuciformis (Silver-Ear);
perilla leaf extract; rosmarinic acid; flavonoids (such as luteolin, fisetin and apigenin); simple sugars
(such as L-fucose and N-acetylmuramic acid); methylsulfonylmethane; soy protein or genistein or
both; quercetin; spirulina; forskolin; and mixtures thereof. Useful greenshell mussel extracts include
whole-tissue extracts, gonad extracts, protein extracts, and lipid extracts, or a combination of any
two or more thereof, in liquid, dried, or powdered form, produced using known methods.
Preferably the composition is a food, drink, food additive, drink additive, dietary supplement,
nutritional product, medical food or nutraceutical.

[0063] In one embodiment a composition useful herein may further comprise a plant oil
selected from coconut oil, corn oil, cottonseed oil, canola oil, rapeseed oil, olive oil, palm oil, peanut
oil, ground nut oil, safflower oil, sesame oil, soybean oil, sunflower oil, nut oil, hazelnut oil, almond
oil, cashew oil, macadamia oil, pecan oil, pistachio oil, walnut oil, oils from melon and gourd seeds,
bottle gourd oil, buffalo gourd oil, pumpkin seed oil, watermelon seed oil, acai oil, blackcurrant seed
oil, borage seed oil, evening primrose oil, carob seed oil, amaranth oil, apricot oil, argan oil,
artichoke oil, avocado oil, babassu oil, ben oil, borneo tallow nut oil, cohune oil, coriander seed oil,
flax oil, flax seed oil, coriander seeds oil, grape seed oil, hemp oil, kapok seed oil, kiwi fruit oil,
lallemantia oil, meadowfoam seed oil, linseed oil, mustard oil, okra seed oil, perilla seed oil, pequi oil,
pine nut oil, poppyseed oil, prune kernel oil, quinoa oil, ramtil oil, rice bran oil, tea oil, and wheat
germ oil, or a combination of any two or more thereof. Preferred plant oils are those high in omega 3 fatty acids.

[0064] As will be appreciated, the dose of the composition administered, the period of administration, and the general administration regime may differ between subjects depending on such variables as the severity of symptoms of a subject, the type of disorder to be treated, the mode of administration chosen, and the age, sex and/or general health of a subject. However, by way of general example, the inventors contemplate administration of from about 1 mg to about 1000 mg per kg body weight of a composition of the invention is administered per day, preferably about 50 to about 500 mg per kg per day. In one embodiment, the inventors contemplate administration of from about 0.05 mg to about 250 mg per kg body weight of a pharmaceutical composition according to the invention. It should be appreciated that administration may include a single daily dose or administration of a number of discrete divided doses as may be appropriate.

[0065] Various aspects of the invention will now be illustrated in non-limiting ways by reference to the following examples.

EXAMPLES

[0066] Hold oil was provided by Sealord Group Limited, New Zealand. The oil was an unfractionated whole fish body oil of which at least 90% was from hoki (Macruronus novaezelandiae). It contained 750ppm of mixed natural tocoferol antioxidant. Docosahexaenoic acid PHA comprised 10-14% of total fatty acids (AOCS Official Method Ce lb-89) and eicosapentaenoic acid (EPA) comprised 5-8% of total fatty acids (AOCS Official Method Ce lb-89). The total omega-3 fatty acid content was calculated to be 17-24%. A 100g sample comprised 17-21g saturated fatty acids, 38-42g monounsaturated fatty acids, and 19-23g polyunsaturated fatty acids (all by calculation).

EXAMPLE 1 - Production of winterised Hoki oil

[0067] A sample of the oil was winterized by cooling to 10°C in a refrigerator and the liquid phase decanted from the solid phase.

EXAMPLE 2 - Production of an omega 3 Hoki oil extract using supercritical CO2

[0068] A sample of the oil was subjected to supercritical CO2 extraction after first converting fatty acids to ethyl esters. Omega 3 fatty acids were concentrated from about 20% w/w in the native oil to about 70% w/w in the omega 3 extract. The process involved:

1) mixing the oil into a hot aqueous ethanolic solution containing urea to form ethyl esters, and
In some embodiments, a filtration step may be used after (1) to remove saturated fatty acid ethyl esters.

EXAMPLE 3 - Assessment of an anti-inflammatory combination

The winterized oil, omega 3 extract, and omega 3 extract in the native oil were tested in triplicate according to the method of Tan and Berridge (2000). Aspirin in ethanol was used as a positive control. Control and test materials were formulated to the concentrations identified above in the Figure descriptions using 20% ethanol. The results are shown in Figure 1 as described above. The effects of a combination of the 33% w/w hoki omega 3 extract plus 67% w/w hoki oil (actual) were greater than the effects seen for either the extract or oil alone. Also shown is the expected result for 33% w/w hoki omega 3 extract plus 67% w/w hoki oil based on results for individual components. The expected result indicates the degree of improved effect seen with the combination of the extract and the oil.

INDUSTRIAL APPLICATION

The present invention has utility in treating or preventing inflammatory conditions. The described compositions and methods of the invention may be employed to treat or prevent one or more of the conditions discussed above.

Those persons skilled in the art will understand that the above description is provided by way of illustration only and that the invention is not limited thereto.

REFERENCES


WHAT WE CLAIM IS:

1. A composition comprising a mixture of (a) one or more omega 3 fatty acid extracts of one or more marine oils, and (b) one or more marine oils.

2. A composition of claim 1 wherein the omega 3 fatty acid extract comprises at least about 60, 65, 70, 75, 80, 85, 90, or 95% by weight omega 3 fatty acids or esters thereof.

3. A composition of claim 1 or 2 wherein the omega 3 fatty acid extract is prepared by supercritical fluid extraction of one or more marine oils.

4. A composition of claim 1 or 2 wherein the omega 3 fatty acid extract is prepared by supercritical CO$_2$ extraction of one or more marine oils.

5. A composition of any one of claims 1 to 4 wherein the omega 3 fatty acid extract comprises one or more fatty acids or one or more esters thereof or combinations thereof selected from the group comprising eicosatetraenoic acid (ETA), esters of ETA, eicosapentaenoic acid (EPA), esters of EPA, docosapentaenoic acid (DPA), esters of DPA, docosahexaenoic acid (DHA), and esters of DHA, or a combination of any two or more thereof.

6. A composition of claim 5 wherein the esters are methyl, ethyl or propyl esters, or a combination of any two or more thereof.

7. A composition of any one of claims 1 to 6 wherein the marine oil is selected from the group comprising one or more marine mammal oils, one or more shellfish oils, one or more cephalopod oils, one or more fish oils, or a combination of any two or more thereof.

8. A composition of claim 7 wherein the marine mammal oil comprises one or more seal oils.

9. A composition of claim 7 wherein the cephalopod oil comprises one or more squid oils.

10. A composition of claim 7 wherein the fish oil comprises one or more oils selected from the group comprising anchovy, baikal, bloater, cacha, carp, dogfish, dory, eel, eulachon, herring, hoki, hilsa, jack fish, katla, kipper, mackerel, orange roughy, pangas, pilchard, cod, salmon, sardine, shark, sprat, trout, tuna, wharehou, whitebait, whiting, and swordfish oil, or a combination of any two or more thereof.

11. A composition of any one of claims 1 to 6 wherein the marine oil comprises one or more hold oils.
12. A composition of any one of claims 7 to 11 wherein the fish oil or hoki oil comprises one or more oils selected from the group comprising one or more whole fish oils, one or more head oils, one or more offal oils, and one or more Ever oils, or a combination of any two or more thereof.

13. A composition of any one of claims 7 to 12 wherein the marine oil, fish oil or hoki oil comprises one or more winterised oils, one or more non-winterised oils, or a combination thereof.

14. A composition of any one of claims 1 to 13 wherein the composition further comprises one or more plant oils or one or more marine oils or a combination thereof.

15. A composition of any one of claims 1 to 14 wherein the composition further comprises one or more seal oils, one or more shellfish oils, one or more fish oils, or a combination of any two or more thereof.

16. A composition of any one of claims 1 to 15 wherein the composition comprises at least about 30 to 90% by weight of the one or more omega 3 extracts.

17. A composition of any one of claims 1 to 16 wherein the composition further comprises one or more additional agents selected from one or more antihistamines, one or more anti-inflammatory agents, one or more anti-rheumatics, one or more corticosteroids, one or more muscle relaxants, one or more greenshell mussel extracts, glucosamine or a salt thereof, vitamin E, vitamin C, or a combination of any two or more thereof.

18. A composition of any one of claims 1 to 17 wherein the composition further comprises a pharmaceutically acceptable carrier.

19. A method of treating or preventing inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression, the method comprising separate, simultaneous, or sequential administration to a subject in need thereof of an effective amount of (a) one or more omega 3 fatty acid extracts of one or more marine oils, and (b) one or more marine oils.

20. A method of claim 19 comprising administration of a composition of any one of claims 1 to 18.

21. Use of (a) one or more omega 3 fatty acid extracts of one or more marine oils, and (b) one or more marine oils, to treat or prevent inflammation or a condition selected from osteoarthritis,
rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.

22. Use of a composition of any one of claims 1 to 18 to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression.

23. A method or use of any one of claims 19 to 22 to treat or prevent inflammation or a condition selected from osteoarthritis, rheumatoid arthritis, an atopic condition, an allergy, arteriosclerosis, atherosclerosis, heart disease, high blood pressure, blood clots, hypotension, vasoconstriction, cancer, or depression, with steroid sparing effect.

24. A method or use of any one of claims 19 to 23 wherein the inflammation is joint inflammation, muscle inflammation, tendon inflammation, ligament inflammation, or inflammation associated with joint damage, joint sprain, joint strain, muscle sprain, muscle strain, cartilage damage, osteoarthritis, or rheumatoid arthritis.
FIGURE 1
INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2008/000146

A. CLASSIFICATION OF SUBJECT MATTER

Int C1
A61K 35/60 (2006 01)  A61P 29/00 (2006 01)
A61K 31/232 (2006 01)

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)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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

WPIDS and MEDLINE (Omega3 or n3_fatty or -linolenic or ala or eicosatetraenoic or eta or eicosapentaenoic or epa or docosapentaenoic or dpa or docosahexaenoic or dha) and acid9 (Marine or +fish+ or cephalopoda Or squid or hoki or seal) and oil? (Super critical+ or co 2+ 5d extract)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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* Further documents are listed in the continuation of Box C  X See patent family annex

* Special categories of cited documents
  "X" 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 September 2008

Date of mailing of the international search report
1 1 SEP 2008

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This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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