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Title: COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING
INFLAMMATORY DISEASES INCLUDING DIABETES MELLITUS
10 TYPE I AND TYPE II AND THYROID DISEASES

FIELD AND BACKGROUND OF THE INVENTION

15 The present invention, in some embodiments thereof, relates to compositions and methods for treating or preventing inflammatory diseases.

Inflammation involves the activation of the immune system in response to harmful stimuli, such as, e.g., a pathogen, infection, irritant, or damage to cells. As a stereotyped response, inflammation is a mechanism of innate immunity, as compared to adaptive
20 immunity, which is specific for each pathogen. Inflammation can be classified as either acute or chronic. Generally speaking, acute inflammation is mediated by granulocytes, while chronic inflammation is mediated by mononuclear cells such as monocytes and lymphocytes.

Acute inflammation is an initial protective response of the body to remove an
25 injurious stimulus by maintaining tissue integrity and contributing to tissue repair. It is a part of the body's natural defense system against injury and disease, and in the absence of acute inflammation, wounds and infections would never heal and progressive destruction of the tissue would compromise the survival of the organism.

The process of acute inflammation is initiated by cells already present in all tissues,
30 mainly resident macrophages, dendritic cells, histiocytes, Kupffer cells, mastocytes, vascular endothelial cells, and vascular smooth muscle cells. At the onset of a harmful stimulus, these cells undergo activation and release inflammatory mediating and sensitizing molecules, such as, e.g., pro-inflammatory cytokines, pro-inflammatory prostaglandins, leukotrienes, histamine, serotonin, neutral proteases, bradykinin and nitric
35 oxide. These inflammatory molecules modulate a complex series of biological events involving cellular and acellular components of the local vascular system, the immune system, and the injured tissue site to propagate and mature the inflammatory response.

These events are responsible for eliciting an acute inflammatory response, typically characterized by 1) vasodilatation which increases blood flow into the tissue thereby causing erythema (redness and warmth), which may extend beyond this site (the flare response); 2) blood vessel permeability which increases plasma leakage into the tissue
5 thereby causing edema (swelling); 3) alter the excitability of certain sensory neurons causing hypersensitivity and pain; 4) stimulate the release of inflammation inducing molecules such as, e.g., neuropeptides like substance P (SP) and calcitonin gene-related peptide (CGRP), prostaglandins, and amino acids like glutamate, from the peripheral nerve endings; and 5) increase migration of leukocytes, mainly granulocytes, from the blood
10 vessels into the tissue. An acute inflammatory response requires constant stimulation to be sustained and must be actively terminated when no longer needed. Hence, acute inflammation ceases once the injurious stimulus has been removed.

However, severe or prolonged noxious stimulation results in a chronic inflammatory response that leads to a progressive shift in the type of cells present at the
15 site of tissue injury. Chronic inflammation may be characterized as the simultaneous destruction and healing of tissue from the inflammatory process, with the net result of provoking injury rather than mediating repair. As such, chronic inflammation is a disease. As an inflammatory response can occur anywhere in the body, chronic inflammation has been implicated in the pathophysiology of a wide range of seemingly unrelated disorders
20 which underlay a large and varied group of human diseases. For example, chronic inflammation is involved in diseases as diverse as cardiovascular diseases, cancers, allergies, obesity, diabetes, digestive system diseases, degenerative diseases, auto-immune disorders, and Alzheimer's disease or other related dementia e.g., vascular dementia, mixed dementia, fronto-temporal dementia, Lewy-body dementia, cholesterol disorders, hair loss,
25 depression, hormonal disorders.

Attempts to treat chronic inflammation have met with limited success. This is due, in part, to the fact that the etiology of chronic inflammation is a complex response based in part on the various inflammation inducing molecules and the multitude of inflammation mediating and sensitizing molecules that appear to elicit inflammation via redundant
30 mechanism. In addition, besides blocking pro-inflammatory molecules, many anti-inflammatory drugs, also inhibit regulatory loops that release endogenous anti-inflammatory molecules. For example, NSAIDs reduce inflammation by blocking the enzymatic activity of cyclooxygenase, a key enzyme that catalyzes the conversion of

arachidonic acid to prostaglandins and leukotrienes. Thus, NSAIDs reduce inflammation by preventing the synthesis of all prostaglandins. However, NSAIDs not only prevents the synthesis of proinflammatory prostaglandins, these compounds also prevent the synthesis of anti-inflammatory prostaglandins. Hence, NSAIDs have limited success as they block
5 endogenous anti-inflammatory response, which in some instances may prolong chronic inflammation. Therefore, compounds, compositions, uses, and methods preferentially inhibiting pro-inflammatory responses would be highly desirable for the treatment of inflammation.

Type I diabetes mellitus (T1DM) is a multi-factorial autoimmune disease
10 characterized by an immune-mediated destruction of pancreatic β cells. Studies have shown that environmental factors contribute to the constant rise of T1DM all overtheworld. Viral infections represent one of the environmental risk, epidemiological data show that T1DM incidence increases after epidemics due to enteroviruses, and that enteroviral RNA can be detected in the blood of >50%ofT1DM patients at the time of
15 disease onset (See Galleri et al, 2012).

Studies have shown that the chronic HCV infection is associated with an increased risk of developing insulin resistance (IR) and type 2 diabetes (T2D). Clinical and experimental data suggest that HCV contributes to its pathogenesis (Negro et. al, 2009). Patients with chronic HCV infection have an increased prevalence of type 2 diabetes, and
20 this prevalence is independent of cirrhosis (see Knobler et.al 2000)

It is clear that there is a long felt and unmet need to provide effective compositions for inflammatory diseases including diabetes I, II and gestational diabetes.

The thyroid, is a gland of the endocrinic system. It is located at the front of the neck consisting of two lobes, connected by a thin band called the thyroid isthmus. The thyroid
25 secretes three hormones: triiodothyronine (T_3), thyroxine (T_4) and calcitonin. T_3 and T_4 influence the metabolic rate, protein synthesis, and in children, growth and development. Calcitonin plays a role in calcium homeostasis. A part from thyroid types of cancer, there are several specific diseases of the thyroid, that may result in either Hyperthyroidism or Hypothyroidism according to there effect on the throid. Hyperthyroidism related diseases,
30 Hashimoto's disease, Grave's disease, Goieter disease, Thyroid Nodules disease. Hypothyroidism mainly related to Hashimoto's disease.

SUMMARY OF THE INVENTION

According to an aspect of the invention there is provided a method of preventing or treating an inflammatory disease in a subject in need thereof, the method comprising administering to the subject an effective amount of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein the component is capable of ameliorating inflammation and wherein the plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

According to an aspect of the invention there is provided a pharmaceutical composition comprising an effective amount of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein the component is capable of ameliorating inflammation and wherein the plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng* for use in preventing or treating an inflammatory disease.

According to an aspect of the invention there is provided a composition of matter comprising at least 2 of a plant species or genus thereof-derived components selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein the component is capable of ameliorating inflammation and wherein the plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

According to an aspect of the invention there is provided a food supplement comprising a combination of at least 2 of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein the component is capable of ameliorating inflammation and wherein the plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*,

Thymus vulgaris, Origanum syriacum, Thymbra spicata, Satujera thymbra, Sesamum indicum Rhus coriaria, Gynostemma pentaphyllum, Boswellia sacra and Panax ginseng.

According to an aspect of the invention there is provided a food supplement, composition or extracts further including "Beduin Tea" comprising

- 5 Rose Leaves Micromeria fruticose, Salvia, cymbopgon (Cital,) Aloysia ,verbena officinalis, origanum majorana, menthe

According to an aspect of the invention there is provided a food supplement, composition or extracts further including "Beduin Tea" comprising

Thyme,sage,cardamom,cinnamon,,black tea,habuk, Marmaya.

- 10 Further details of components of Thyme Vulgaris are included in APPENDIX1.

- 15 According to some embodiments, the component comprises at least 2 components.
 According to some embodiments, the component comprises at least 3 components.
 According to some embodiments, the component comprises at least 4 components.
 According to some embodiments, the component comprises at least 5 components.
 According to some embodiments, the component comprises 5-10 components.

- 20 According to some embodiments, the component comprises thymoquinone or an analog thereof.

 According to some embodiments, the component comprises thymol or an analog thereof.

- 25 According to some embodiments, the component comprises carvacrol or an analog thereof.

In some embodiments of the present invention the component comprises tryptophan, analogs of tryptophan or extract of plants containing tryptophan such as sesame or oregano.

- 30 According to some embodiments, the inflammatory disease comprises an autoimmune disease.

 According to some embodiments, the inflammatory disease comprises an acute inflammatory disease.

According to some embodiments, the inflammatory disease comprises an autoimmune disease.

According to some embodiments, the inflammatory disease comprises diabetes.

According to some embodiments, the diabetes comprises type I diabetes.

5 According to some embodiments, the diabetes comprises type II diabetes.

According to some embodiments, the diabetes comprises gestational diabetes.

Unless otherwise defined, all technical and/or scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. Although methods and materials similar or equivalent to those
10 described herein can be used in the practice or testing of embodiments of the invention, exemplary methods and/or materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be necessarily limiting.

15 BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S)

Some embodiments of the invention are herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of embodiments of the invention. In this regard, the description
20 taken with the drawings makes apparent to those skilled in the art how embodiments of the invention may be practiced.

In the drawings:

FIGs. 1A-C shows embodiments in plant extraction methods as taken from berkem(dot)com. Figure 1A - scheme describing the general principle of plant extraction;
25 Figure 1B - scheme describing the main separation process according to some embodiments; Figure 1C - scheme describing parameters that may influence the process. Figure 2 - depicting SDS-page of the SARS-CoV-2 S1 subunit protein digestion assay with the tested extracts following an incubation time of 6h at 37°C. Figure 3 - depicting SDS-page of the SARS-CoV-2 S2 subunit protein digestion assay with
30 the tested extracts following an incubation time of 6h at 37°C. Figure 4 - depicting SDS-page of the SARS-CoV-2 Nucleocapsid digestion assay with the tested extracts following an incubation time of 6h at 37°C.

Figure 5 - depicting a graphic representation of the densitometry test of the SARS-CoV-2 S1 subunit protein digestion assay with the tested extracts following an incubation time of 6h at 37°C.

Figure 6 - depicting a graphic representation of the densitometry test of the SARS-CoV-2 S2 subunit protein digestion assay with the tested extracts following an incubation time of 6h at 37°C.

Figure 7 - depicting a graphic representation of the densitometry test of the SARS-CoV-2 Nucleocapsid digestion assay with the tested extracts following an incubation time of 6h at 37°C.

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DESCRIPTION OF SPECIFIC EMBODIMENTS OF THE INVENTION

The present invention, in some embodiments thereof, relates to compositions and methods for treating or preventing inflammatory diseases.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not necessarily limited in its application to the details set forth in the following description or exemplified by the Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways.

Inflammatory diseases and autoimmune diseases exert a devastating personal and economic burden. Inflammatory diseases occur when an inflammatory response is initiated that is inappropriate and/or does not resolve in the normal manner but rather persists and results in a chronic inflammatory state, which is cureless.

Thus, according to an aspect of the invention, there is provided a method of preventing or treating an inflammatory disease in a subject in need thereof, the method comprising administering to the subject an effective amount of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein said component is capable of ameliorating inflammation and wherein said plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

According to an additional or an alternative aspect there is provided a pharmaceutical composition comprising an effective amount of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein said component is capable of ameliorating inflammation and wherein said plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng* for use in preventing or treating an inflammatory disease.

According to an additional or an alternative aspect there is provided a composition of matter comprising at least 2 of a plant species or genus thereof-derived components selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein said component is capable of ameliorating inflammation and wherein said plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

According to an additional or an alternative aspect there is provided a food supplement comprising a combination of at least 2 of a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein said component is capable of ameliorating inflammation and wherein said plant species is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

According to an aspect of the present invention there is provided compositions or food supplements comprising Bromelain or pineapple extracts comprising Bromelain.

As early as 1899 H.F. Harris have reported "A case of diabetes mellitus quickly following Mumps". A significant number of viruses have been associated with type 1 diabetes, including enteroviruses such as Coxsackievirus B (CVB), but also rotavirus, mumps virus, and cytomegalovirus. Rubella virus has been suggested to cause type 1

diabetes (see Filippi and. Von Herrath, 2008) The combined incidence of diabetes and latent diabetes in this group of patients was nine out of forty-four (20%). These findings suggest a causative relationship between congenital rubella infection and diabetes mellitus. Further more, epidemiological studies have suggested a linkage between type 2 diabetes
5 and chronic hepatitis C virus (HCV) infection (Yoshizumi Shinatai et.al, 2005).

It is acknowledged herein that the Glycoproteins that are on the surfaces of many viruses, including coronavirus, help them to bind to host cells.

There are Sugars/glycans on the surface of the Coronavirus Spike Protein ("Sugary
10 Camouflage on Coronavirus offers vaccine clues"
Sugars on Coronavirus Spike Protein Offer Vaccine Clues | Quanta Magazine)

Tryptophan is important in glycan-protein interaction
15 ("The Sugar Code").

The study of glycan-protein interactions provides insight into the mechanism of cell=signaling and allows to create better-diagnosing tools for many diseases including cancer. "Indeed there are no known types of cancer that do not involve erratic patterns of protein glycosylation
20 The sweet spot: defining virus-sialic acid interactions | Nature Reviews Microbiology

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It is further herein acknowledged that SGLT2 inhibitor drugs are diabetes medications.

In order for glucose to reach cells in the human body, there are proteins on the cell
30 membranes that are carriers of glucose and sodium. These carrier proteins are called Sodium-Glucose Transport protein. There are about five types of SGLT, with the kidneys with a protein from this family called SGLT2. This protein is responsible for

nearly 90% reuptake of kidney glucose[2]. Knowing this mechanism was the groundwork for the formation of the drugs that inhibit SGLT2.

SGLT2 inhibitors inhibit the protein responsible for absorbing glucose from urine into the blood and cause:

- 5 • Secretion of glucose in the urine
- Lowering blood glucose levels

Tryptophan is important in glycan-protein interaction - as explained above.

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Thus, according to an aspect of the invention, there is provided a method of
20 reducing the infectivity of a diabetes mediated virus by modifying the viral entry
mechanism proteins in a subject in need thereof, the method comprising administering to
the subject an effective amount of a plant species or genus thereof-derived component
selected from the group consisting of a plant part, extract thereof, fraction thereof, active
ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof,
25 wherein said component is capable of attenuating viral entry and wherein said plant species
is selected from the group consisting of *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*,
Origanum syriacum, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*, *Rhus*
coriaria, *Gynostemma pentaphyllum*, *Boswellia sacra* and *Panax ginseng*.

It is further herein acknowledged that, in some embodiments of the present invention,
30 Tryptophan, or tryptophan analogues or extracts of plants containing tryptophan are
used in the method of treatment or compositions of the present invention.

According to an aspect of the invention there is provided a food supplement,
composition or extracts further including "Beduin Tea" comprising
 Rose Leaves Micromeria fruticose, Salvia, cymbopgon (Cital,) Aloysia ,verbena
 officinalis, origanum majorana, menthe

- 5 According to an aspect of the invention there is provided a food supplement,
composition or extracts further including "Beduin Tea" comprising
 Thyme,sage,cardamom,cinnamon,,black tea,habuk, Marmaya.

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- 15 The term "plant" as used herein encompasses whole plants, a grafted plant,
 ancestors and progeny of the plants and plant parts, including seeds, flowers, bark, shoots,
 stems, roots (including tubers), fruit, rootstock, scion, and plant cells, tissues and organs.

According to a specific embodiment, the plant part is a seed.

According to a specific embodiment, the plant part is a fruit.

- 20 According to a specific embodiment, the plant part is a leaf.

According to a specific embodiment, the plant part is a stem.

According to a specific embodiment, the plant part is a flower.

The plant part can be a solid part or a non-solid part such as oil or aqueous portions
 of the plant.

- 25 The plant may be in any form including suspension cultures, embryos, meristematic
 regions, callus tissue, leaves, gametophytes, sporophytes, pollen, and microspores.

The term plant refers to a wild plant or a cultivated variety thereof.

- As used herein the term "plant species" refers to a sub-group of one or more plants
 within the genus. These plants will share similar characteristics with each other. There may
 30 be a single plant within a species, or there may be many hundreds of plants. The term
 intends to include subspecies, such as grown or can be found in different geographical
 location, e.g., Lebanese Sumac and Syrian Sumac or Korean Ginseng and American
 Ginseng.

As used herein "plant genus" refers to a taxonomic rank below family and above species.

It will be appreciated that the relevant species and genera and listed below and each option or combination thereof represents a different embodiment of the invention.

5 The term "extraction" refers to a separation process which relies on the separation of one or more analytes from the components of a sample other than the one or more analytes. Extractions are processes that typically use two immiscible phases to separate one or more solutes from one phase into the other. The distribution of a solute between two phases is an equilibrium condition described by partition theory. For example, boiling tea
10 leaves in water extracts the tannins, theobromine, and caffeine out of the leaves and into the water. More typical extractions performed typically but not only in a laboratory are settings of organic compounds out of an aqueous phase and into an organic phase. Common extractants are arranged from ethyl acetate to water (ethyl acetate<acetone<ethanol<methanol<acetone: water (7:3)<ethanol:water
15 (8:2)<methanol:water (8:2)<water) in increasing order of polarity according to the Hildebrand solubility parameter. Procedures for plant extraction are provided in Figures 1A-C.

The term "extract" as used herein refers to the result of such process of separation that can take the form of a solution formulation or other chemical form depending on the
20 extraction process. In particular, the term extract can relate to a substance made by extracting a part of a sample (e.g. a raw material), such as by using a solvent such as ethanol or water. In various instances an extract relates to a solvent that is enriched in one or more solute. In particular, a "plant extract" in the sense of the present disclosure typically comprises a concentrated preparation of a plant material obtained by isolating or
25 purifying desired active constituents with one or more extraction processes.

The choice of the solvent depends on the desired component to be obtained. For example, to extract polar components in an extraction process suggested solvents include, but are not limited to, water, ethanol methanol or butanol while for non polar compounds diethyl ether, hexane or chloroform depending on the use of the extract. For midpolar one
30 may choose Ethyl acetate but other solvents can be used as well.

The general procedure of solid/liquid extraction can be scaled in five different ways:

Maceration: the contact stage is maintained at room temperature.

Decoction or reflux: the contact stage is maintained at the boiling point of the solvent.

Digestion: the contact stage is maintained at a temperature in between those of the previous two cases.

5 Infusion: the boiling solvent is poured over the solid, then left to cool for a set time.

Leaching or percolation: the solvent passes through the biomass.

It is also possible to combine these methods with each other or with other processes such as distillation, steam distillation, rectification, etc.

10 According to another embodiment, the use of various solvents, either successively or in combination is contemplated and the ordinary skilled of organic chemistry will know which to choose according to the active ingredient as described below.

Extraction may be further assisted by other means such as ultrafiltration, reverse osmosis, high pressure (supercritical CO₂), microwaves, ultrasound, etc.

15 In some embodiments, the plant part is contacted with a polar solvent (e.g. ethanol) or nonpolar solvent (e.g., hexane or pentane) for several minutes, e.g., 15 minutes or more, about 30 minutes or more, about 1 hour or more, about 2 hours or more, or about 5 hours or more.

Temperature can also be controlled during the contacting.

20 According to specific embodiments, the plant part is contacted with the solvent (e.g. ethanol) while being constantly mixed e.g. on a shaker.

It will be appreciated that the extraction process can also be solvent-free.

For example, solvent-free microwave extraction (SFME) has been proposed as a green method for the extraction of essential oil from aromatic herbs that are extensively
25 used in the food industry. This technique is a combination of microwave heating and dry distillation performed at atmospheric pressure without any added solvent or water. The isolation and concentration of volatile compounds is performed in a single stage. In some embodiments, SFME and/or hydro-distillation (HD)), are used for the extraction of essential oil from the plants of the invention.

30 In some embodiments, the process of the present invention comprises isolating a liquid extract (i.e. filtered extract) from the mixture (i.e. crude extract) comprising the liquid extract and solids. Suitable means for isolating the liquid extract (i.e. filtered extract) include those known in the art of organic synthesis and include, but are not limited

to, gravity filtration, suction and/or vacuum filtration, centrifuging, setting and decanting, and the like. In some embodiments, the isolating comprises filtering a liquid extract through a porous membrane, syringe, sponge, zeolite, paper, or the like having a pore size of about 1-5 μm , about 0.5-5 μm , about 0.1-5 μm , about 1-2 μm , about 0.5-2 μm , about 5 0.1-2 μm , about 0.5-1 μm , about 0.1-1 μm , about 0.25-0.45 μm , or about 0.1-0.5 μm (e.g. about 2 μm , about 1 μm , about 0.45 μm , or about 0.25 μm).

According to specific embodiments, the present invention contemplates drying (i.e. removal of the polar/non-polar solvent) and/or freezing the filtered extract following generation thereof.

10 The method for drying the filtered extract (i.e. removing the polar solvent) is not particularly limited, and can include solvent evaporation at a reduced pressure (e.g., sub-atmospheric pressure) and/or an elevated temperature (e.g., above about 25 °C). In some embodiments, it can be difficult to completely remove a solvent from a liquid extract by standard solvent removal procedures such as evaporation. In some embodiments, processes 15 such as co-evaporation, lyophilization, and the like can be used to completely remove the polar solvent from a liquid fraction to form a dry powder, dry pellet, dry granulate, paste, and the like. According to a specific embodiment the polar solvent is evaporated with a vacuum evaporator.

The selection of the extraction process much depends on the component to be 20 isolated.

It will be appreciated that following generation of the extract, specific embodiments of the present invention further contemplate additional purification steps so as to further isolate/purify active agents from the extract, for example, by fractionating the filtered extract.

25 As used herein "a fraction" refers to a portion of the extract that contains only certain chemical ingredients of the extract but not all.

Fractionating can be performed by processes such as, but not limited to: column chromatography, preparative high performance liquid chromatography ("HPLC"), reduced pressure distillation, and combinations thereof.

30 According to a specific embodiment, fractionating is performed by HPLC.

In some embodiments, fractionating comprises re-suspending the filtered extract in a polar solvent (such as methanol, as discussed above), applying the polar extract to a

separation column, and isolating the extract having the anti-respiratory disease (e.g. anti-fibrotic, anti-inflammatory) activity by column chromatography (preparative HPLC).

An eluting solvent is applied to the separation column with the polar extract to elute fractions from the polar extract. Suitable eluting solvents for use include, but are not limited to, methanol, ethanol, propanol, acetone, acetic acid, carbon dioxide, methylethyl ketone, acetonitrile, butyronitrile, carbon dioxide, ethyl acetate, tetrahydrofuran, di-isopropylether, ammonia, triethylamine, N,N-dimethylformamide, N,N-dimethylacetamide, and the like, and combinations thereof.

According to an alternative or an additional embodiment, liquid chromatography comprises high performance liquid chromatography (HPLC).

According to an alternative or an additional embodiment, liquid chromatography is performed on a reverse stationary phase.

The fractions may be characterized by analytical methods such as, but not limited to, spectroscopic methods such as, but not limited to, ultraviolet-visible spectroscopy ("UV-Vis"), infrared spectroscopy ("IR"), and the like; mass-spectrometry ("MS") methods such as, but not limited to, time-of-flight MS; quadrupole MS; electrospray MS, Fourier-transform MS, Matrix-Assisted Laser Desorption/Ionization ("MALDI"), and the like; chromatographic methods such as, but not limited to, gas-chromatography ("GC"), liquid chromatograph ("LC"), high-performance liquid chromatography ("HPLC"), and the like; and combinations thereof (e.g., GC/MS, LC/MS, HPLC/UV-Vis, and the like), and other analytical methods known to persons of ordinary skill in the art.

The component (active ingredients, extract and/or fractions) obtained may be tested for ameliorating inflammation. Exemplary methods for testing the effect are further described herein below.

For example, there are a few so-called markers that help diagnose inflammation in the body. These include, but are not limited to: Serum protein electrophoresis (SPE), C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR), plasma viscosity and more.

Alternatively or additionally, inflammation can be determined at the whole body level (e.g., by the determination of fecer, sweating, swelling, fever, redness).

However, to be more accurate, the inflammation should be determined using a test specific for the disease. For instance, MRI in multiple sclerosis (MS), or molecular markers which are specific for MS, or in rheumatoid arthritis joint pain, swelling, stiffness, or loss of joint function.

The active ingredients, extract and/or fraction described herein may be immediately used or stored until further used.

According to specific embodiments, the active ingredients, extract and/or fractions is kept frozen, e.g. in a freezer, until further use (e.g. at about -20 °C to -90 °C, at about -70
5 °C to -90 °C, e.g. at -80 °C), for any required length of time.

According to other specific embodiments, the active ingredients, extract and/or fractions is immediately used (e.g. within a few minutes e.g., up to 30 minutes).

The active ingredients, extract and/or fractions may be used separately. Alternatively, different active ingredients, extract and/or fractions (e.g. from different
10 plants or from separate extraction procedures) may be pooled together. Likewise, different active ingredients, extract and/or fractions (from the same extract, from different extracts, from different plants and/or from separate extraction procedures) may be pooled together.

Using the present teachings, the present inventor was able to identify not only plants and extracts that can be used to effectively treat or prevent inflammation, but also
15 active ingredients thereof.

“Active ingredient” refers to a defined chemical composition which is responsible for the anti (preventive or therapeutic) effect against inflammation.

The active ingredient can be purified from a plant or chemically synthesized (artificial, man-made).

20 Also contemplated herein are analogs and derivatives of the active ingredients as long as the anti- inflammation effect is maintained, which are also referred to as mimetics.

Following are some non-limiting examples for extraction of active ingredients from selected plants of the present invention.

Extraction from leaves of *T. capitatus* - The Aerial parts of *T. capitatus* (leaves)
25 samples are collected. Leaves separated from branches are dehydrated at room temperature for 7 days and slightly blended into fine powders for extractions.

Essential oil (EO) extraction - hydro-distillation is used to extract EO from the plant, e.g., dried aerial parts of *T. capitatus*. In brief, the extraction is conducted for several hours for example, 3 h, by mixing 100 g of plants in 500 mL of distilled water. The
30 extract is dried and concentrated using sodium sulphate and rotatory evaporator under reduced pressure. The EO yield is established by quantity of the obtained oil in mL for 100 g of dried plant. Finally, the pure EO is stored at -4 °C until further analyzed.

Essential oil analysis - The chemical composition of EO is examined by GC and GC-MS. GC analysis is conducted using gas chromatograph. The proportion of the constituents is determined by the integration of peak areas. In addition, mass spectrometry (MS) can be used to analyze the EO typically under the same conditions as described above for gas chromatography. The identification of the different compounds is defined by comparison of their retention indexes (determined relatively to the retention times of a series of n-alkanes) with those of standards of the Wiley library search routines¹², based on fit and purity of mass spectra. Such conditions are used for determining the active ingredients as described below.

Extraction from *Satujera Thymbra*:

Air dried aerial parts from *S. thymbra* were collected in Lebanon at random during April 2009. For 3 h the plant material was submitted to steam distillation using a clevenger-type apparatus to produce the essential oil with a yield of 0.84% (w/w). Oil is dried using anhydrous magnesium sulfate and stored at 4°C. *S. thymbra* oil was analyzed by GC/MS.

Extraction from *Rhus coriaria* (Sumac)

In order to isolate, determine and identify the compounds from the *Rhus coriaria* fruits, different extracts are taken from the fruit or leaves of the Sumac plant. Some are isolated from aqueous extracts, others from alcoholic extracts and some from lipid extracts. Hydrolysable tannins compose the highest percentage in the Sumac fruits, followed by flavonoids. This emphasizes the antioxidant potential of the fruit. Following hydrolysable tannins, comprising almost 20% of the fruit's mass, are other unidentified compounds. Subsequently there are anthocyanins, isoflavonoids, terpenoids and diterpenes. Analysis of the chemical properties of sumac fruit is conducted on ripe fruits and have found a 2.6% protein content, 7.4% fat content, 14.6% fiber content, 1.8% ash. Also, a calorimetric calculation showed that 100g of sumac fruit contains 147.8 kcal.

Extraction of thymoquinone from *Nigella sativa*

Various methods can be used including microwave-assisted extraction system having temperature controlling function as well as other extraction methods, Soxhlet and conventional solid/liquid extraction.

Nigella Sativa

24-ETHYL-LOPHENOL	Seed Oil		
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<u>24-METHYL-LOPHENOL</u>	Seed Oil		
<u>24-METHYLENE-CYCLOARTANOL</u>	Seed Oil		
<u>5-DEHYDRO-AVENASTEROL</u>	Seed Oil		
<u>7-DEHYDRO-AVENASTEROL</u>	Seed Oil		
<u>ALANINE</u>	Seed	8,000	10,255
<u>ALPHA-SPINASTEROL</u>	Seed Oil		
	Seed		
<u>ARABIC-ACID</u>	Seed		
<u>ARACHIDIC-ACID</u>	Seed Oil		1,900
<u>ARACHIDONIC-ACID</u>	Seed Oil		24,900
<u>ARGININE</u>	Seed	41,500	53,050
<u>ASCORBIC-ACID</u>	Leaf		2,577
<u>ASH</u>	Seed	38,000	53,000
<u>ASPARAGINE</u>	Seed		0
<u>ASPARTIC-ACID</u>	Seed	10,670	13,650
<u>ASTRAGALIN</u>	Seed		200
<u>BETA-AMYRIN</u>	Seed Oil		
<u>BETA-SITOSTEROL</u>	Seed Oil		
	Seed		3,218
<u>BUTYROSPERMOL</u>	Seed Oil		
<u>CALCIUM</u>	Seed		10,600
<u>CAMPESTANOL</u>	Seed Oil		
<u>CAMPESTEROL</u>	Seed Oil		
	Seed		
<u>CARBOHYDRATES</u>	Seed		339,600
<u>CARVONE</u>	Seed Essent. Oil		
	Seed	2,250	9,600
<u>CHOLESTEROL</u>	Seed Oil		
	Seed		
<u>CITROSTADIENOL</u>	Seed Oil		
<u>CYCLOARTENOL</u>	Seed Oil		
<u>CYCLOEUCALENOL</u>	Seed Oil		
<u>CYMENE</u>	Seed		
<u>CYSTINE</u>	Seed		
<u>D-LIMONENE</u>	Seed		
<u>DAMASCENINE</u>	Plant		
<u>DEHYDROASCORBIC-ACID</u>	Leaf		295
<u>DITHYMOQUINONE</u>	Seed Oil		
<u>EICOSADIENOIC-ACID</u>	Seed Oil		25,000

	Seed	8,979	10,525
<u>EO</u>	Seed Oil		4,500
	Seed	4,000	16,000
<u>FAT</u>	Seed	354,900	416,000
<u>FIBER</u>	Seed		55,000
<u>FIXED-OIL</u>	Seed		380,000
<u>GLUCOSE</u>	Seed		
<u>GLUTAMIC-ACID</u>	Seed	28,085	35,900
<u>GLYCINE</u>	Seed	8,840	20,700
<u>GRAMISTEROL</u>	Seed Oil		
<u>hederagenin</u>	Seed		10,000
<u>INDOLE-3-ACETIC-ACID</u>	Tissue Culture		14
<u>IRON</u>	Seed		140
<u>ISOLEUCINE</u>	Seed	8,570	10,960
<u>KAEMPFEROL-3-O-BETA-GLUCOPYRANOSYL-(1.2)-O-BETA-GALACTOPYRANOSYL-(1.2)-BETA-GLUCOPYRANOSIDE</u>	Seed		100
<u>LEUCINE</u>	Seed	23,130	29,595
<u>LINOLEIC-ACID</u>	Seed Oil	487,600	576,300
	Seed	128,124	233,459
<u>LINOLENIC-ACID</u>	Seed Oil	5,700	7,000
	Seed	2,484	2,912
<u>LIPASE</u>	Seed		
<u>LOPHENOL</u>	Seed Oil		
<u>LYSINE</u>	Seed	16,200	20,700
<u>MELANTHIGENIN</u>	Seed		
<u>MELANTHIN</u>	Plant		15,000
	Seed		15,000
<u>METHIONINE</u>	Seed	13,100	16,750
<u>MYRISTIC-ACID</u>	Seed Oil	1,900	18,000
	Seed	567	1,082
<u>NIGELLICINE</u>	Seed		
<u>NIGELLIDINE</u>	Seed		
<u>NIGELLIMINE</u>	Seed		0.13
<u>NIGELLIMINE-N-OXIDE</u>	Seed		0.2
<u>NIGELLIN</u>	Seed		
<u>NIGELLINE</u>	Seed Essent. Oil		
	Seed Essent. Oil		
<u>NIGELLONE</u>	Plant		
	Seed		

<u>OBTUSIFOLIOL</u>	Seed Oil		
<u>OLEIC-ACID</u>	Seed Oil	244,600	262,400
	Seed	89,911	184,912
<u>PALMITIC-ACID</u>	Seed Oil	120,000	171,200
	Seed	22,464	50,523
<u>PALMITOLEIC-ACID</u>	Seed Oil		2,000
<u>PHENYLALANINE</u>	Seed	16,850	21,560
<u>PHYTOSTEROLS</u>	Seed		5,100
<u>POTASSIUM</u>	Seed		5,820
<u>PROLINE</u>	Seed	11,350	14,520
<u>PROTEIN</u>	Seed	210,000	271,900
<u>QUERCETIN-3'-GLUCOSIDE</u>	Seed		440
<u>QUERCETIN-3-O-(6-FERULOYL-BETA-GLUCOPYRANOSYL)-(1,2)-BETA-GALACTOPYRANOSYL-(1,2)-BETA-GLUCOPYRANOSIDE</u>	Seed		240
<u>QUERCETIN-3-O-BETA-GLUCOPYRANOSYL-(1,2)-O-BETA-GALACTOPYRANOSYL-(1,2)-BETA-GLUCOPYRANOSIDE</u>	Seed		1,380
<u>RESIN</u>	Seed		
<u>RUTIN</u>	Seed		200
<u>SERINE</u>	Seed	4,210	5,385
<u>SODIUM</u>	Seed		980
<u>STEARIC-ACID</u>	Seed Oil	18,100	60,400
	Seed	8,722	10,192
<u>STIGMAST-7-EN-3-BETA-OL</u>	Seed Oil		
<u>STIGMASTANOL</u>	Seed Oil		
<u>STIGMASTEROL</u>	Seed Oil		
	Seed		
<u>TANNIN</u>	Seed		
<u>TARAXEROL</u>	Seed Oil		
<u>TELFAIRIC-ACID</u>	Seed Oil		
<u>THREONINE</u>	Seed	2,615	3,345
<u>THYMOHYDROQUINONE</u>	Seed		
<u>THYMOL</u>	Seed Oil		
<u>THYMOQUINONE</u>	Seed Essent. Oil		
	Seed Oil		
	Seed		
<u>TIRUCALLOL</u>	Seed Oil		
<u>TRYPTOPHAN</u>	Seed		
<u>TYROSINE</u>	Seed	12,925	16,530
<u>VALINE</u>	Seed	6,500	8,325

According to a specific embodiment, active ingredients (e.g., which can be obtained by supercritical carbon dioxide extraction method) include but are not limited to:

Compound	RI _{exp}	RI _{lit}	SFE 1	SFE 2	HD SFE	Identification
<i>n</i> -Nonane ^a	905	900	0.12	—	—	RI, MS
Tricyclene	926	926	tr	—	—	RI, MS
Camphene	953	953	—	—	1.64	RI, MS
β -Pinene	958	959	—	—	0.40	RI, MS
2,4,(10)-Thujadiene	967	960	4.74	0.19	—	RI, MS
Sabinene	978	977	1.05	—	—	RI, MS
β -Myrcene	990	991	0.31	—	—	RI, MS
1,8-Cineole	1013	1010	—	—	0.98	RI, MS
α -Terpinene	1025	1026	2.34	—	—	RI, MS
Limonene	1034	1034	0.18	0.38	1.03	RI, MS
γ -Terpinene	1054	1056	27.46	13.20	12.87	RI, MS
<i>cis</i> -Sabinene hydrate	1063	1068	—	0.38	Tr	RI, MS
<i>allo</i> -Ocimenol ^a	1079	1071	—	0.11	—	RI, MS
Linalool	1087	1080	0.25	0.19	—	RI, MS
Terpinolene	1091	1088	—	—	Tr	RI, MS
<i>trans</i> -Sabinene hydrate	1099	1097	0.37	—	—	RI, MS
Terpinen-1-ol ^a	1124	1120	—	—	0.11	RI, MS
1,5,8-p-Menthatriene ^a	1130	1135	0.43	0.38	—	RI, MS
Borneol	1152	1152	—	—	1.02	RI, MS
Pinocarvone	1167	1165	2.96	3.00	—	RI, MS
<i>trans</i> -Dihydrocarvone	1208	1202	—	0.19	—	RI, MS
Dihydrocarvone ^a	1215	1214	0.37	2.06	—	RI, MS
Ocimenone (E) ^a	1249	1239	1.54	1.50	—	RI, MS

Compound	RI _{exp}	RI _{lit}	SFE 1	SFE 2	HD SFE	Identification
Thymoquinone	1250	1250	35.05	33.12	38.41	RI, MS,NMR
Thymol	1283	1288	7.43	5.30	16.95	RI, MS,NMR
Carvacrol	1299	1299	1.98	1.73	0.81	RI, MS
2-Undecanone	1312	1315	—	—	13.72	RI, MS
<i>n</i> -Octyl isobutyrate ^a	1323	1326	—	—	0.12	RI, MS
α -Longipinene	1330	1334	0.26	—	—	RI, MS
Citronellyl acetate ^a	1339	1336	—	—	0.50	RI, MS
Thymohydroquinone methyl ether ^a	1353	1351	—	—	Tr	RI, MS
Cyclosativene	1367	1366	—	—	1.43	RI, MS
α -Longicyclene	1381	1380	0.43	5.25	—	RI, MS
α -Copaene	1385	1383	1.54	2.00	0.41	RI, MS
α -Longifolene	1391	1387	—	—	0.51	RI, MS
(<i>Z</i>)-Caryophyllene ^a	1395	1395	0.23	—	—	RI, MS
β -Caryophyllene	1420	1417	2.89	5.07	4.80	RI, MS
Thymohydroquinone dimethylether ^a	1429	1425	0.43	—	—	RI, MS
Aromadendrene ^a	1437	1438	—	—	1.04	RI, MS
Thymohydroquinone	1515	1509	1.17	1.12	2.31	RI,MS,NMR
Davanone ^a	1587	1586	0.31	—	—	RI, MS
8-Heptadecene ^a	1683	1680	1.23	1.13	0.86	RI, MS
Dihydrofarnesyl acetate	1841	1840	2.28	4.69	—	RI, MS
Pimaradiene ^a	1934	1935	1.23	2.25	—	RI, MS
Palmitic acid	1947	1946	0.18	—	—	RI, MS
Pimara-8(14),15-diene	1968	1966	0.92	—	—	RI, MS
Octadecanoic acid	2145	2157	0.26	12.31	—	RI, MS

Compound	RI _{exp}	RI _{lit}	SFE 1	SFE 2	HD SFE	Identification
Total identified			99.94	95.55	99.92	
Grouped compounds:						
Quinones			44.08	39.54	57.67	
Monoterpene hydrocarbons			36.51	14.15	15.94	
Oxygenated monoterpenes			7.47	9.16	17.14	
Sesquiterpene hydrocarbons			5.35	12.32	8.19	
Oxygenated sesquiterpenes			2.59	4.69	—	
Diterpenes			2.15	2.25	—	
Alkane			0.12	—	—	
Alkenes			1.23	1.13	0.86	
Fatty acids			0.44	12.31	—	
Fatty acid esters			—	—	0.12	

Additional plants that are contemplated herein are of the genus *Nigella*.

Nigella is a genus of 18 species of annual plants in the family Ranunculaceae, native to Southern Europe, North Africa, South Asia, Southwest Asia and Middle East.

- 5 Common names applied to members of this genus are nigella, devil-in-a-bush or love-in-a-mist.

Nigella arvensis

Nigella carpatha

Nigella damascena

- 10 *Nigella degenii*

Nigella deserti

Nigella doerfleri

Nigella elata

Nigella fumariifolia

Nigella hispanica

Nigella latisepta

Nigella nigellastrum

5 *Nigella orientalis*

Nigella oxypetala

Nigella papillosa

Nigella sativa

Nigella segetalis

10 *Nigella stricta*

Nigella unguicularis

According to a specific embodiment the active ingredient is thymoquinone.

Additional plants containing thymoquinone include, but are not limited to:

Monarda fistulos (of the genus *Monarda*);

15 *Satureja montana* (of the genus *Satureja*);

Additional families containing thymoquinone include, but are not limited to:

Asteraceae - examples include, but are not limited to the subfamilies:

- Barnadesioideae Bremer & Jansen
- Carduoideae Sweet
- 20 • Cichorioideae Chevallier
- Corymbioideae Panero & Funk
- Famatinanthoideae S.E. Freire, Ariza & Panero
- Gochnatioideae Panero & Funk
- Gymnarrhenioideae Panero & Funk
- 25 • Hecastocleidoideae Panero & Funk
- Mutisioideae Lindley
- Pertyoideae Panero & Funk
- Stifftioideae Panero
- Wunderlichioideae Panero & Funk

30 Cupressaceae

-
- Cunninghamioideae
 - Taiwanoideae
 - Athrotaxidoideae

- Sequoioideae
 - Taxodioideae
 - Callitroideae
 - Cupressoideae
 - 5 • *Incertae sedis*
 - Lamiacea
 - Ranunculacea
 - Hydrastidoideae
 - Glaucidoideae
 - 10 • Coptoideae
 - Thalictrioideae
 - Ranunculoideae
- List of plants that contain Carvacrol include, but are not limited to:
- Monarda didyma*
- 15 *Nigella sativa*
- Origanum compactum*
- Origanum dictamnus*
- Origanum microphyllum*
- Origanum onites*
- 20 *Origanum scabrum*
- Origanum syriacum*
- Origanum vulgare*
- Plectranthus amboinicus*
- Thymus glandulosus*
- 25 *Lavandula multifida*
- Origanum minutiflorum*
- Satureja thymbra*

Active ingredients found in Thymus Capitatus

No	RI	Compound	%
1	935	α -Thujene	0.54
2	940	α -Pinene	0.38
3	991	Myrcene	0.87

No	RI	Compound	%
4	1019	α -terpinene	1.11
5	1025	p-Cymene	6.25
6	1063	γ -Terpinene	6.75
7	1089	α -terpinolene	0.26
8	1101	Linalool	1.51
9	1179	Terpinen-4-ol	1.40
10	1185	4-Carvomenthenol	0.94
11	1260	Geraniol	0.25
12	1309	Carvacrol	65.38
13	1310	Thymol	1.35
14	1358	Eugenol	0.21
15	1408	Carvacryl Acetate	0.45
16	1427	β -Caryophyllene	4.94
17	1461	α -Humulene	0.10
18	1487	allo-aromadendrene	0.18
19	1685	α -Bisabolol	0.35
20	1774	α -Bisabolol oxide A	0.11
21	1815	Hexadecanal	0.14
22	1870	1-Hexadecanol	0.46
23	1879	1-Hexadecanol	0.13
24	1894	Rimuene	0.28
25	1957	Hexadecanoic acid	0.68
		Total identified	95.02
		Unknown	4.98

Additional plants contemplated herein are of the genus *Thymus*.

The genus *Thymus* (/ˈtɑːməʊ/ TY-məs; thymes) contains about 350 species of aromatic perennial herbaceous plants and subshrubs to 40 cm tall in the family Lamiaceae, native to temperate regions in Europe, North Africa and Asia.

Stems tend to be narrow or even wiry; leaves are evergreen in most species, arranged in opposite pairs, oval, entire, and small, 4–20 mm long, and usually aromatic.

Thyme flowers are in dense terminal heads with an uneven calyx, with the upper lip three-lobed, and are yellow, white, or purple.

Several members of the genus are cultivated as culinary herbs or ornamentals, when they are also called thyme after its best-known species, *Thymus vulgaris* or common
5 thyme.

About 350 species, including:

- Thymus adamovicii*
- Thymus altaicus*
- Thymus amurensis*
- 10 *Thymus boissieri*
- Thymus bracteosus*
- Thymus broussonetii*
- Thymus caespititius*
- Thymus camphoratus*
- 15 *Thymus capitatus*
- Thymus capitellatus*
- Thymus camphoratus*
- Thymus carnosus*
- Thymus cephalotus*
- 20 *Thymus cherlerioides*
- Thymus ciliatus*
- Thymus cilicicus*
- Thymus cimicinus*
- Thymus citriodorus* (*Thymus* × *citriodorus*) syn. *T. fragrantissimus*, *T. serpyllum*
- 25 *citratus*, *T. serpyllum citriodorum*.^[7] – citrus thyme
- Thymus comosus*
- Thymus comptus*
- Thymus curtus*
- Thymus decussatus*
- 30 *Thymus disjunctus*
- Thymus doerfleri*
- Thymus glabrescens*
- Thymus herba-barona*

- Thymus hirsutus*
Thymus hyemalis
Thymus inaequalis
Thymus integer
- 5 *Thymus lanuginosus*, syn. *T. serpyllum* – woolly thyme
 Thymus leucospermus
 Thymus leucotrichus
 Thymus longicaulis
 Thymus longiflorus
- 10 *Thymus mandschuricus*
 Thymus marschallianus
 Thymus mastichina
 Thymus membranaceus
 Thymus mongolicus
- 15 *Thymus moroderi*
 Thymus nervulosus
 Thymus nummularis
 Thymus odoratissimus
 Thymus pallasianus
- 20 *Thymus pallidus*
 Thymus pannonicus
 Thymus praecox – creeping thyme
 Thymus proximus
 Thymus pseudolanuginosus, syn. *T. serpyllum* – woolly thyme
- 25 *Thymus pulegioides* – lemon thyme ^[8]
 Thymus quinquecostatus
 Thymus richardii
 Thymus satureioides
 Thymus serpyllum
- 30 *Thymus sibthorpii*
 Thymus striatus
 Thymus thracicus – lavender thyme
 Thymus villosus

Thymus vulgaris – common thyme

Thymus zygis

List of plants that contain thymol include, but are not limited to:

Euphrasia rostkoviana

5 *Lagoecia cuminoides*

Monarda didyma

Monarda fistulosa

Mosla chinensis, Xiang Ru

Origanum compactum

10 *Origanum dictamnus*

Origanum onites

Origanum vulgare

Satureja thymbra

Thymus glandulosus

15 *Thymus hyemalis*

Thymus vulgaris

Thymus zygis

Trachyspermum ammi

Active ingredients in *Thymus vulgaris*:

Chemical	Plant part	Low ppm	High ppm
<u>1-OCTEN-3-OL</u>	Shoot		150
	Shoot		65
	Shoot		80
<u>2,5-DIETHYL-TETRAHYDROFURAN</u>	Shoot		0
	Shoot		6
	Shoot		6
<u>3-OCTANOL</u>	Shoot		110
	Shoot		12
	Shoot		30
<u>ALPHA-GUAIENE</u>	Shoot		0.1
	Shoot		6
	Shoot		0
<u>ALPHA-HUMULENE</u>	Shoot		45
	Shoot		20
	Shoot		55

<u>ALPHA-PHELLANDRENE</u>	Shoot	0
	Shoot	40
	Shoot	12
<u>ALPHA-PINENE</u>	Shoot	0
	Shoot	265
	Shoot	325
<u>ALPHA-TERPINENE</u>	Shoot	840
	Shoot	990
	Shoot	990
<u>ALPHA-TERPINEOL</u>	Shoot	55
	Shoot	55
	Shoot	25
<u>ALPHA-THUJENE</u>	Shoot	320
	Shoot	0
	Shoot	0
<u>BETA-CARYOPHYLLENE</u>	Shoot	175
	Shoot	185
	Shoot	200
<u>BETA-GUAIENE</u>	Shoot	0.1
	Shoot	0
	Shoot	3
<u>BETA-PHELLANDRENE</u>	Shoot	80
	Shoot	60
<u>BETA-PHELLLANDRENE</u>	Shoot	70
<u>BETA-PINENE</u>	Shoot	30
	Shoot	30
	Shoot	560
<u>BORNEOL</u>	Shoot	55
	Shoot	30
	Shoot	15
<u>CAMPHENE</u>	Shoot	30
	Shoot	25
	Shoot	40
<u>CAMPHOR</u>	Shoot	0
	Shoot	0.1
	Shoot	0
<u>CARVACROL</u>	Shoot	1,285
	Shoot	24,850
	Shoot	23,765
<u>CARVONE</u>	Shoot	15

	Shoot		20
	Shoot		0.1
	Shoot		75
<u>CARYOPHYLLENE-OXIDE</u>	Shoot		55
	Shoot		45
	Shoot		0
<u>CIS-CARVEOL</u>	Shoot		0
	Shoot		3
	Shoot		20
<u>CIS-SABINENE-HYDRATE</u>	Shoot		0
	Shoot		55
	Shoot		12
<u>CITRONELLOL</u>	Shoot		0.1
	Shoot		0
<u>CITRONELLOL-BUTYRATE</u>	Shoot		0
<u>CITRONELLYL-BUTYRATE</u>	Shoot		0
	Shoot		15
	Shoot		0
<u>DIHYDROCARVONE</u>	Shoot		0
	Shoot		12
<u>EHTYL-CINNAMATE</u>	Shoot		0
	Shoot		31,000
<u>EO</u>	Shoot		31,000
	Shoot		31,000
<u>ETHYL-CINNAMATE</u>	Shoot		0
	Shoot		30
	Shoot		2,700
<u>GAMMA-TERPINENE</u>	Shoot		1,015
	Shoot		240
	Shoot		0
<u>GERANIOL</u>	Shoot		0
	Shoot		65
	Shoot		0
<u>GERANYL-ACETATE</u>	Shoot		0
	Shoot		15
	Shoot		0
<u>GERANYL-BUTYRATE</u>	Shoot		20
	Shoot		0
	Shoot		0
<u>GERANYL-HEXANOATE</u>	Shoot		0
	Shoot		0

	Shoot		6
	Shoot		0
<u>GERANYL-PROPIONATE</u>	Shoot		0
	Shoot		70
	Shoot		0
<u>GERMACRENE-D</u>	Shoot		0
	Shoot		50
	Shoot		110
<u>LIMONENE</u>	Shoot		55
	Shoot		90
	Shoot		35
<u>LINALOL</u>	Shoot		55
	Shoot		25
	Shoot		6
<u>METHYL-2-METHYL-BUTYRATE</u>	Shoot		12
	Shoot		9
	Shoot		750
<u>MYRCENE</u>	Shoot		565
	Shoot		0.1
	Shoot		4,445
<u>P-CYMENE</u>	Shoot		1,880
	Shoot		3,135
	Shoot		6
<u>TERPINEN-1-OL</u>	Shoot		15
	Shoot		0
	Shoot		435
<u>TERPINEN-4-OL</u>	Shoot		315
	Shoot		335
	Shoot		0
<u>TERPINOLENE</u>	Shoot		0.1
	Shoot		45
	Shoot		18,560
<u>THYMOL</u>	Shoot		385
	Shoot		280
<u>TRANS-BERGAMOTENE</u>	Shoot		9
	Shoot		9
<u>TRANS-BERGAMOTTENE</u>	Shoot		9
	Shoot		25
<u>TRANS-SABINENE-HYDRATE</u>	Shoot		120
	Shoot		0

TRICYCLEN	Shoot		0
	Shoot		0
	Shoot		3

Active ingredients on the EO of *Thymus vulgaris* according to some embodiments of the invention, include, but are not limited to:

No.	RT (min)	Area % of total	Constituents*
1	5.39	1.06	alpha-Thujene
2	5.63	1.07	alpha-Pinene
3	6.89	0.37	beta-Pinene
4	6.97	1.53	beta-Myrcene
5	7.53	0.33	alpha-Phellandrene
6	7.77	3.76	Carene<δ-2->
7	8.04	0.29	D-Limonene
8	8.26	0.21	beta-Phellandrene
9	8.46	8.41	para-Cymene
10	8.96	30.90	gamma-Terpinene
11	9.48	0.47	Terpineol
12	12.55	0.46	Terpinen-4-ol
13	16.17	47.59	Thymol
14	17.32	2.68	Caryophyllene
15	19.03	0.78	Cyclohexene, 1-methyl-4-(5-methylmethylene-4-hexenyl)
Total		99.91%	

5 Active ingredients of *Satureja Thymbra*:

Air dried aerial parts from *S. thymbra* were collected in Lebanon at random during April 2009. For 3 h the plant material was submitted to steam distillation using a cleverger-type apparatus to produce the essential oil with a yield of 0.84% (w/w). Oil was dried using anhydrous magnesium sulfate and stored at 4°C. *S. thymbra* oil are analyzed by

GC/MS. Nineteen compounds representing 98.8% of the oil sample are identified. The major components of *Satureja thymbra* L. oil are γ -terpinene (34.06%), carvacrol (23.07%) and thymol (18.82%). Also abundant are p -cymene (7.58%), caryophyllene (3.96%), α -terpinene (3.53%) and myrcene (1.70%).

5 Also contemplated herein are plants of the genus *Satureja*.

Satureja is a genus of aromatic plants of the family Lamiaceae, related to rosemary and thyme. It is native to North Africa, southern and southeastern Europe, the Middle East, and Central Asia. A few New World species were formerly included in *Satureja*, but they have all been moved to other genera. Several species are cultivated as
10 culinary herbs called savory, and they have become established in the wild in a few places.

Examples include, but are not limited to:

- Satureja adamovicii* Šilic - Balkans
- Satureja aintabensis* P.H.Davis - Turkey
- Satureja amani* P.H.Davis - Turkey
- 15 *Satureja atropatana* Bunge - Iran
- Satureja avromanica* Maroofi - Iran
- Satureja bachtiarica* Bunge - Iran
- Satureja boissieri* Hausskn. ex Boiss. - Turkey, Iran
- Satureja bzybica* Woronow - Caucasus
- 20 *Satureja* $\times$ *caroli-pau* G.López - Spain (*S. innotata* $\times$ *S. montana*)
- Satureja cilicica* P.H.Davis - Turkey
- Satureja coerulea* Janka - Bulgaria, Romania, Turkey
- Satureja cuneifolia* Ten - Spain, Italy, Greece, Albania, Yugoslavia, Iraq
- Satureja* $\times$ *delpozoi* Sánchez-Gómez, J.F.Jiménez & R.Morales - Spain (*S. cuneifolia* $\times$ *S.*
- 25 *intricata* var. *gracilis*)
- Satureja edmondii* Briq. - Iran
- Satureja* $\times$ *expectata* G.López - Spain (*S. intricata* var. *gracilis* $\times$ *S. montana*)
- Satureja fukarekii* Šilic - Yugoslavia
- Satureja hellenica* Halácsy - Greece
- 30 *Satureja hortensis* L.
- Satureja horvatii* Šilic - Greece, Yugoslavia
- Satureja icarica* P.H.Davis - Greek Islands
- Satureja innotata* (Pau) Font Quer - Spain

- Satureja intermedia* C.A.Mey. - Iran, Caucasus
- Satureja intricata* Lange - Spain
- Satureja isophylla* Rech.f. - Iran
- Satureja kallarica* Jamzad - Iran
- 5 *Satureja kermanshahensis* Jamzad - Iran
- Satureja khuzistanica* Jamzad - Iran
- Satureja kitaibelii* Wierzb. ex Heuff. - Bulgaria, Romania, Yugoslavia
- Satureja laxiflora* K.Koch - Iran, Iraq, Turkey, Caucasus
- Satureja linearifolia* (Brullo & Furnari) Greuter - Cyrenaica region of Libya
- 10 *Satureja macrantha* C.A.Mey. - Iran, Iraq, Turkey, Caucasus
- Satureja metastasiantha* Rech.f. - Iraq
- Satureja montana* L. – winter savory - southern Europe, Turkey, Syria
- Satureja mutica* Fisch. & C.A.Mey. - Caucasus, Iran, Turkmenistan
- Satureja nabateorum* Danin & Hedge - Jordan
- 15 *Satureja* × *orjenzii* Šilic - Yugoslavia (*S. horvatii* × *S. montana*)
- Satureja pallaryi* J.Thiébaud - Syria
- Satureja parnassica* Heldr. & Sart. ex Boiss. - Greece, Turkey
- Satureja pilosa* Velen. - Italy, Greece, Bulgaria
- Satureja rumelica* Velen. - Bulgaria
- 20 *Satureja sahendica* Bornm. - Iran
- Satureja salzmännii* (Kuntze) P.W.Ball - Morocco, Spain
- Satureja spicigera* (K.Koch) Boiss. - Turkey, Iran, Caucasus
- Satureja spinosa* L. - Turkey, Greek Islands including Crete
- Satureja subspicata* Bartl. ex Vis. - Austria, Yugoslavia, Albania, Bulgaria, Italy
- 25 *Satureja taurica* Velen. - Crimea
- Satureja thymbra* L. - Libya, southeastern Europe from Sardinia to Turkey; Cyprus, Lebanon, Palestine
- Satureja thymbriifolia* Hedge & Feinbrun - Israel, Saudi Arabia
- Satureja visianii* Šilic. - Yugoslavia
- 30 *Satureja wiedemanniana* (Ave-Lall.) Velen. – Turkey

Active ingredients of Thymbra spicata:

Compounds	%	RI ¹	RT ²
α -pinene	0.56	1028	3.64
α -phellandrene	0.64	1033	3.71
camphene	0.06	1073	4.36
β -pinene	0.10	1113	5.16
δ -3-carene	0.05	1155	6.10
β -myrcene	1.04	1170	6.51
α -terpinene	1.48	1184	6.90
dl-limonene	0.17	1202	7.43
β -phellandrene	0.12	1212	7.69
γ -terpinene	10.73	1252	8.86
p-cymene	12.18	1276	9.69
α -terpinolene	0.05	1286	10.04
oct-1-en-3-ol	0.11	1454	16.17
trans sabinene hydrate	0.05	1465	16.59
cis sabinene hydrate	0.03	1547	19.73
linalool	0.03	1551	19.91
trans caryophyllene	1.28	1589	21.39
4-terpineol	0.53	1598	21.79
isoborneol	0.21	1694	25.36
d-carvone	0.02	1728	26.55
anethole	0.04	1826	30.05
caryophyllene oxide	0.65	1968	34.87
spathulenol	0.15	2125	39.56
thymol	2.77	2218	41.80
carvacrol	66.86	2239	42.61
naphthalene ³	0.08	2281	44.26

¹ RT – retention time; ² RI – retention index; ³ naphthalene, 1,2,3,4,4a, 5,6,7-octahydro-4a-methyl

Also contemplated herein are plants of the genus *Thymbra*.

Thymbra, common name Mediterranean thyme, is a genus of plants in the family Lamiaceae. As currently categorized, the genus has seven species and one subspecies. It is native to the Mediterranean region of southern Europe, North Africa, and the Middle East.

5 Examples include, but are not limited to:

Thymbra calostachya (Rech.f.) Rech.f. - Crete

Thymbra capitata (L.) Cav. - widespread from Morocco + Portugal to Turkey + Palestine

Thymbra sintenisii Bornm. & Azn. - Iraq, Turkey

Thymbra spicata L. - Greece, Turkey, Syria, Lebanon, Palestine, Israel, Iraq, Iran

10 *Thymbra thymbrifolia* (Hedge & Feinbrun) Bräuchler, comb. nov. - Israel, Palestine, Judean Desert, Khirbet el Mird

Thymbra nabateorum (Danin & Hedge) Bräuchler, comb. nov. - W of Jordan and the adjacent N of Saudi Arabia

Thymbra linearifolia (Brullo & Furnari) Bräuchler, comb. nov. - Libya

15 **Chemical Composition of *Rhus coriaria* (Sumac)**

Characterization and identification of chemical compounds of Sumac using HPLC-MS method identified 191 compounds in *Rhus coriaria* and classified them as generally being:

- 20 • 78 hydrolysable tannins (e.g., gallotannins, e.g., penta, hexa, hepta, octa, nona and decagalloyl-glucoside)
- 59 flavonoids (e.g., Quercetin, Myrecetin 3-rhamnoside and Quercetin 3-glucoside)
- 9 anthocyanins (e.g., Delphinidin-3-glucoside, Cyanidin 3-(2"-galloyl)galactoside, Cyanidin-3-glucoside, 7-methyl-cyanidin-3-(2"-galloyl)galactoside, 7-methyl-cyanidin-3-galactoside)
- 25 • 2 isoflavonoids
- 2 terpenoids
- 1 diterpene
- 38 other unidentified compounds.

30 According to specific embodiments, the phenolic compounds in Sumac are the compounds that constitute its phytochemical activity along with anthocyanins. The most abundant phenolic compound in sumac fruits was found to be Gallic acid.

Hydrolysable tannins compose the highest percentage in the Sumac fruits, followed by flavonoids. This emphasizes the antioxidant potential of the fruit, a plant part

contemplated herein as a specific embodiment. Following hydrolysable tannins, comprising almost 20% of the fruit's mass, are other unidentified compounds. Subsequently there are anthocyanins, isoflavonoids, terpenoids and diterpenes. The chemical properties of sumac fruit is conducted on ripe fruits and have found a 2.6%
 5 protein content, 7.4% fat content, 14.6% fiber content, 1.8% ash. Also, a calorimetric calculation showed that 100g of sumac fruit contains 147.8 kcal.

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 10 compounds. Subsequently there are anthocyanins, isoflavonoids, terpenoids and diterpenes. The chemical properties of sumac fruit is conducted on ripe fruits and have found a 2.6% protein content, 7.4% fat content, 14.6% fiber content, 1.8% ash. Also, a calorimetric calculation showed that 100g of sumac fruit contains 147.8 kcal.

Other active ingredients or any combinations thereof include, but are not limited to,
 15 methyl gallate, gathisflavone, sumaflavone, hinfikflavone, photocatechuic acid, pentagalloylglucose, hinokiflavone, β -caryophyllene, Delphinidin-3-glucoside, Cyanidin 3-(2"-galloyl)galactoside, Cyanidin-3-glucoside, 7-methyl-cyanidin-3-(2"-galloyl)galactoside, 7-methyl-cyanidin-3-galactoside, quercetin-3-glucoside, kampferol, myricetin, butein, D-limonene.

20 According to a specific embodiment, the active ingredient or combination thereof includes a volatile compound, e.g., terpene hydrocarbons, monoterpene and sesquiterpene hydrocarbons, specifically β -caryophyllene and α -pinene, Coriarianaphthyl ether, Coriarioic acid and Coriariacthracenyl ester.

According to a specific embodiment, the active ingredient or combination thereof
 25 includes a fatty acid, e.g., oleic acid, linoleic acid, palmitic acid, β -caryophyllene, cembrene stearic acid, Myristic acid, α -linolenic acid.

According to a specific embodiment, the active ingredient or combination thereof includes a mineral, e.g., potassium, calcium, magnesium, phosphorus, aluminum, iron, sodium, boron, zinc, cadmium, selenium.

30 According to a specific embodiment, the active ingredient or combination thereof includes a vitamin, e.g., thiamin B₁, riboflavin B₂, pyridoxine B₆, cyanocobalamin B₁₂, nicotinamide, biotin and ascorbic acid.

According to a specific embodiment, a methanol or ethanol extract is performed, e.g., ethanol concentration is 80%; extraction time is 1 h; extraction temperature is 40 °C; particle size 1.0mm; and solvent to sumac ratios 15:1 ml/g. Other extraction procedures include, but are not limited to, those described in Sakhr and Khatib Heliyon. 2020 Jan;

5 6(1): e03207, which is hereby incorporated by reference in its entirety.

According to another embodiment, the plant part is leaf.

Also contemplated herein are plants of the genus *Rhus*.

Examples include, but are not limited to:

Asia and southern Europe

10 *Rhus chinensis* Mill. – Chinese sumac

Rhus coriaria – Tanner's sumac

Rhus delavayi Franchet

Australia, Pacific

Rhus taitensis Guill. (Northeast Australia, Malesia, Micronesia, French Polynesia)

15 *Rhus sandwicensis* A.Gray – *neneleau* (Hawaii)

North America

Rhus aromatica – fragrant sumac

Rhus copallinum – winged or shining sumac

Rhus glabra – smooth sumac

20 *Rhus integrifolia* – lemonade sumac

Rhus kearneyi – Kearney sumac

Rhus lanceolata – prairie sumac

†*Rhus malloryi* Wolfe & Wehr – Ypresian, Washington

Rhus michauxii – Michaux's sumac

25 *Rhus microphylla* – desert sumac, littleleaf sumac

Rhus ovata – sugar sumac

†*Rhus republicensis* Flynn, DeVore, & Pigg-Ypresian, Washington

†*Rhus rooseae* Manchester – Middle Eocene, Oregon

Rhus trilobata Nutt. – skunkbush sumac

30 *Rhus typhina* – staghorn sumac

Rhus virens Lindh. ex A.Gray – evergreen sumac

Chemical Composition of Panax ginseng (Ginseng)

Characterization and identification of chemical compounds of Ginseng using a variety of methods identified a large variety of compounds in *Panax ginseng* and classified them as generally being:

- Saponin Glycosides (e.g., ginsenosides)
- 5 • Phytosterols (e.g. stigmasterol, beta-sterol)
- Sesquiterpenes (e.g. beta-alamene and beta-selinine)
- Flavenoids (e.g. Kaempferol)
- Polyacetylenes (e.g. panaxynol, ginsenoyne A)
- Alkaloids (e.g. fumarine, girinimbin)
- 10 • Polysaccharides
- Phenolic compounds (e.g. elemicin, dauricin, maltol).

According to specific embodiments, the saponin compounds in Ginseng and the polysaccharide compounds are the compounds that constitute its phytochemical activity. The most abundant saponin compound in ginseng root was found to be ginsenoside. Polysaccharides from ginseng have been identified as NGP, WGP, 1-KGP, 4-KGP, WGPE and EGP, with WGP and WGPE being the most abundant, depending on the species of ginseng plant material used for extraction.

Most ginseng saponins belong to a family of steroids with a four trans-ring rigid steroid skeleton. They are also referred to as ginsenosides, triterpenoid saponins or dammarane derivatives. More than 200 saponins have been isolated from ginseng plants. In addition to ginseng root, saponins have been identified in ginseng leaves and stems, flower buds, fruits, berries, and seeds. Because steaming or heating changes the saponin profile of ginseng products, ginseng saponins have also been identified in the processed root, leaf, flower-bud and berry.

25 Ginseng saponins are divided into several groups. Two major groups are the protopanaxadiol (PPD)-type saponins with sugar moieties attached to the C-3 and/or C-20 and the protopanaxatriol (PPT) group with sugar moieties at C-6 and/or at C-20. Other groups include the ocotillol-type with a five-membered epoxy ring at C-20, the oleanane-type with a nonsteroidal structure, and the dammarane type with a modified C-20 side chain. As techniques are developed for chemical purification and structural identification, novel ginseng saponins continue to be discovered.

The table below shows ginsenoside compounds recovered from ginseng extracts prepared by different extraction procedures:

GINSENOSES

Material	Solvent system ^a (volume ratio)	Detection ^b	Obtained compound	Isolation efficiency ^c	
<i>P. notoginseng</i> , root	Hex- <i>n</i> -BuOH-H ₂ O (3 : 4 : 7)	TLC	Ginsenosides Rb1, Re, Rg1 And notoginsenoside	157, 13, 56, and 17 mg of Rb1, Re, Rg1 and R1 from 283 mg MeOH extract of five tablets	
<i>P. ginseng</i> , root	CH ₂ Cl ₂ -MeOH-NH ₄ OAc-iPrOH (6 : 2 : 4 : 3)	ELSD	Ginsenosides Rf, Rd, Re, and Rb1	10.7, 11.0, 13.4 and 13.9 mg of Rf, Rd, Re and Rb1 from 480 mg enriched fraction by macroporous res	
<i>P. notoginseng</i> , root	CHCl ₃ -MeOH-2-BuOH-H ₂ O (5 : 6 : 1 : 4) EtOAc- <i>n</i> -BuOH-H ₂ O (1 : 1 : 2)	ELSD	Ginsenosides Rg1, Rd, Re, Rb1 and notoginsenoside R1	Not provided	
Red <i>P. ginseng</i> , steamed root	CH ₂ Cl ₂ -MeOH-H ₂ O-iPrOH (6 : 6 : 4 : 1)	ELSD	Ginsenosides Rg3, Rk1, Rg5 and F4	32.2, 26.6, 28.6 and 8.1 mg of Rg3, Rk1, Rg5 and F4 from 350 mg enriched fraction by RP-C ₁₈ column	
<i>P. ginseng</i> , root	EtOAc-iPrOH-0.1% formic acid H ₂ O (3 : 5)	UV	Ginsenoside Ro	61 mg Ro from 100 mg enriched sample by normal-phase MPLC	

^aAbbreviations: Hex; *n*-hexane; BuOH: butanol; CH₂Cl₂: methylene chloride; MeOH: methanol; NH₄OAc: ammonium acetate; iPrOH: isopropanol; CHCl₃: chloroform; EtOAc: ethyl acetate.

^bAbbreviations: TLC: thin layer chromatography; ELSD: evaporative light scattering detection; UV: ultraviolet.

^cAbbreviations: RP: reversed-phase; MPLC: medium-pressure liquid chromatography.

10 The table below shows the chemical formulae of 123 dammarane-type saponins isolated from various parts of *Panax* plants. They are placed in the order of the structure type.

Dammarane – type saponin ginsenosides

Name	Formula	Plant Material	
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Name	Formula	Plant Material
Floralginsenoside M	C ₅₃ H ₉₀ O ₂₂	Flower buds of <i>P. ginseng</i>
Floralginsenoside N	C ₅₃ H ₉₀ O ₂₂	Flower buds of <i>P. ginseng</i>
Floralquinquenoside E	C ₅₃ H ₉₀ O ₂₂	Flower buds of <i>P. quinquefolius</i>
Ginsenoside Rh5	C ₃₇ H ₆₄ O ₉	Roots and rhizomes of <i>P. vietnamensis</i>
Notoginsenoside FP1	C ₄₇ H ₈₀ O ₁₈	Fruit pedicels of <i>P. notoginseng</i>
Notoginsenoside M	C ₄₈ H ₈₂ O ₁₉	Roots of <i>P. notoginseng</i>
Notoginsenoside N	C ₄₈ H ₈₂ O ₁₉	Roots of <i>P. notoginseng</i>
Notoginsenoside Rw1	C ₄₆ H ₇₈ O ₁₇	Rhizomes of <i>P. notoginseng</i>
Notoginsenoside T3	C ₃₈ H ₆₆ O ₉	Acid hydrolysate roots of <i>P. notoginseng</i>
Notoginsenoside U	C ₄₂ H ₇₂ O ₁₄	Roots of <i>P. notoginseng</i>
Quinquenoside L17	C ₄₇ H ₈₀ O ₁₈	Leaves and stems of <i>P. quinquefolius</i>
Yesanchinoside D	C ₄₄ H ₇₄ O ₁₅	Underground part of <i>P. japonicus</i>
Yesanchinoside E	C ₅₄ H ₉₂ O ₂₃	Underground part of <i>P. japonicus</i>
Yesanchinoside F	C ₅₆ H ₉₄ O ₂₄	Underground part of <i>P. japonicus</i>
20(S)-acetylated Rg2	C ₄₄ H ₇₄ O ₁₄	Roots of <i>P. quinquefolius</i>
20(R)-acetylated Rg2	C ₄₄ H ₇₄ O ₁₄	Roots of <i>P. quinquefolius</i>
Malonylginsenoside Ra3	C ₆₂ H ₁₀₂ O ₃₀	Fresh roots of <i>P. ginseng</i>
Malonylnotoginsenoside R4	C ₆₂ H ₁₀₂ O ₃₀	Roots of <i>P. ginseng</i>
Notoginsenoside FP2	C ₅₈ H ₉₈ O ₂₆	Fruit pedicels of <i>P. notoginseng</i>
Notoginsenoside FT1	C ₄₇ H ₈₀ O ₁₇	Acid hydrolysate roots of <i>P. notoginseng</i>
Notoginsenoside L	C ₅₃ H ₉₀ O ₂₂	Roots of <i>P. notoginseng</i>
Notoginsenoside O	C ₅₂ H ₈₈ O ₂₁	Flower buds of <i>P. notoginseng</i>
Notoginsenoside P	C ₅₂ H ₈₈ O ₂₁	Flower buds of <i>P. notoginseng</i>
Notoginsenoside Q	C ₆₃ H ₁₀₆ O ₃₀	Flower buds of <i>P. notoginseng</i>
Notoginsenoside S	C ₆₃ H ₁₀₆ O ₃₀	Flower buds of <i>P. notoginseng</i>
Notoginsenoside T	C ₆₄ H ₁₀₈ O ₃₁	Flower buds of <i>P. notoginseng</i>
Quinquenoside L10	C ₄₇ H ₈₀ O ₁₇	Leaves and stems of <i>P. quinquefolius</i>
Quinquenoside L14	C ₄₇ H ₈₀ O ₁₇	Leaves and stems of <i>P. quinquefolius</i>
Yesanchinoside J	C ₆₁ H ₁₀₂ O ₂₈	Underground part of <i>P. japonicus</i>

Name	Formula	Plant Material	
Floralginsenoside A	C ₄₂ H ₇₂ O ₁₆	Flower buds of <i>P. ginseng</i>	
Floralginsenoside C	C ₄₁ H ₇₀ O ₁₅	Flower buds of <i>P. ginseng</i>	
Floralginsenoside H	C ₅₀ H ₈₄ O ₂₁	Flower buds of <i>P. ginseng</i>	
Floralginsenoside J	C ₄₈ H ₈₂ O ₂₀	Flower buds of <i>P. ginseng</i>	
Floralginsenoside Ka	C ₃₆ H ₆₂ O ₁₁	Flower buds of <i>P. ginseng</i>	
Floralginsenoside Tc	C ₅₃ H ₉₀ O ₂₄	Flower buds of <i>P. ginseng</i>	
Floralquinquenoside B	C ₄₂ H ₇₂ O ₁₅	Flower buds of <i>P. quinquefolius</i>	
Floralquinquenoside D	C ₄₂ H ₇₂ O ₁₅	Flower buds of <i>P. quinquefolius</i>	
Floranotoginsenoside B	C ₅₃ H ₉₀ O ₂₄	Flowers of <i>P. notoginseng</i>	
Floranotoginsenoside C	C ₅₃ H ₉₀ O ₂₄	Flowers of <i>P. notoginseng</i>	
Ginsenoside I	C ₄₈ H ₈₂ O ₂₀	Flower buds of <i>P. ginseng</i>	
Ginsenoside II	C ₄₈ H ₈₂ O ₂₀	Flower buds of <i>P. ginseng</i>	
Ginsenoside SLI	C ₃₆ H ₆₂ O ₁₁	Steamed leaves of <i>P. ginseng</i>	
Floralginsenoside B	C ₄₂ H ₇₂ O ₁₆	Flower buds of <i>P. ginseng</i>	
Floralginsenoside D	C ₄₁ H ₇₀ O ₁₅	Flower buds of <i>P. ginseng</i>	
Floralginsenoside E	C ₄₂ H ₇₂ O ₁₅	Flower buds of <i>P. ginseng</i>	
Floralginsenoside F	C ₄₂ H ₇₂ O ₁₅	Flower buds of <i>P. ginseng</i>	
Floralginsenoside G	C ₅₀ H ₈₄ O ₂₁	Flower buds of <i>P. ginseng</i>	
Floralginsenoside I	C ₄₈ H ₈₂ O ₂₀	Flower buds of <i>P. ginseng</i>	
Floralginsenoside K	C ₄₈ H ₈₂ O ₂₁	Flower buds of <i>P. ginseng</i>	
Floralginsenoside O	C ₅₃ H ₉₀ O ₂₄	Flower buds of <i>P. ginseng</i>	
Floralginsenoside P	C ₅₃ H ₉₀ O ₂₃	Flower buds of <i>P. ginseng</i>	
Floralquinquenoside A	C ₃₆ H ₆₂ O ₁₁	Flower buds of <i>P. quinquefolius</i>	
Floralquinquenoside C	C ₄₂ H ₇₂ O ₁₅	Flower buds of <i>P. quinquefolius</i>	
Ginsenoside Rh6	C ₃₆ H ₆₂ O ₁₁	Leaves of <i>P. ginseng</i>	
Floralginsenoside La	C ₄₈ H ₈₂ O ₁₉	Flower buds of <i>P. ginseng</i>	
Floralginsenoside Lb	C ₄₈ H ₈₂ O ₁₉	Flower buds of <i>P. ginseng</i>	
Floranotoginsenoside D	C ₅₃ H ₉₀ O ₂₃	Flowers of <i>P. notoginseng</i>	
Ginsenoside Rg7	C ₃₆ H ₆₀ O ₉	Leaves of <i>P. ginseng</i>	

Name	Formula	Plant Material
Notopanaxoside A	C ₃₆ H ₆₂ O ₁₀	Roots of <i>P. notoginseng</i>
Notoginsenoside FT3	C ₄₇ H ₈₀ O ₁₈	Acid hydrolysate roots of <i>P. notoginseng</i>
Floranotoginsenoside A	C ₅₃ H ₉₀ O ₂₃	Flowers of <i>P. notoginseng</i>
Ginsenoside ST2	C ₃₆ H ₆₂ O ₁₀	Steamed leaves of <i>P. ginseng</i>
Notoginsenoside Rw2	C ₄₁ H ₇₀ O ₁₄	Rhizomes of <i>P. notoginseng</i>
Notoginsenoside ST5	C ₄₇ H ₈₀ O ₁₈	Steamed roots of <i>P. notoginseng</i>
Yesanchinoside H	C ₅₃ H ₉₀ O ₂₃	Underground part of <i>P. japonicus</i>
Ginsenoside Ki	C ₃₆ H ₆₂ O ₁₀	Leaves of <i>P. ginseng</i>
Ginsenoside Km	C ₃₆ H ₆₂ O ₁₀	Leaves of <i>P. ginseng</i>
Quinquenoside L2	C ₄₈ H ₈₂ O ₁₉	Leaves and stems of <i>P. quinquefolius</i>
Dammar-25(26)-ene-3,6,12,20,22,24-hexanol	C ₃₀ H ₅₂ O ₆	Leaves of <i>P. ginseng</i>
Floralginsenoside Kb	C ₄₅ H ₇₆ O ₁₉	Flower buds of <i>P. ginseng</i>
Floralginsenoside Kc	C ₄₅ H ₇₆ O ₂₀	Flower buds of <i>P. ginseng</i>
Floralginsenoside Ta	C ₃₆ H ₆₀ O ₁₀	Flower buds of <i>P. ginseng</i>
Vina-ginsenoside R25	C ₄₂ H ₇₀ O ₁₅	Roots and rhizomes of <i>P. vietnamensis</i>
Floralginsenoside Tb	C ₃₅ H ₆₂ O ₁₁	Flower buds of <i>P. ginseng</i>
Quinquenoside L9	C ₄₂ H ₇₄ O ₁₅	Leaves and stems of <i>P. quinquefolius</i>
Quinquenoside L16	C ₅₄ H ₉₄ O ₂₅	Leaves and stems of <i>P. quinquefolius</i>
25-OCH ₃ -PPD	C ₃₁ H ₅₆ O ₄	Leaves of <i>P. notoginseng</i>
25-OH-PPD	C ₃₀ H ₅₄ O ₄	Fruits of <i>P. ginseng</i>
25-OH-PPT	C ₃₀ H ₅₄ O ₅	Fruits of <i>P. ginseng</i>
Notoginsenoside FT2	C ₄₇ H ₈₂ O ₁₈	Acid hydrolysate roots of <i>P. notoginseng</i>
Notoginsenoside T4	C ₃₆ H ₆₂ O ₁₁	Acid hydrolysate roots of <i>P. notoginseng</i>
Quinquenoside L1	C ₄₈ H ₈₀ O ₁₈	Leaves and stems of <i>P. quinquefolius</i>
Quinquefoloside La	C ₅₄ H ₉₂ O ₂₃	Leaves of <i>P. quinquefolius</i>
Quinquefoloside Lc	C ₅₄ H ₉₂ O ₂₃	Leaves of <i>P. quinquefolius</i>
Dammar-(E)-20(22)-ene-3,12,25-triol	C ₃₀ H ₅₂ O ₃	Acid hydrolysate roots of <i>P. ginseng</i>

Name	Formula	Plant Material
Notoginsenoside ST1	C ₃₆ H ₆₂ O ₁₀	Steamed roots of <i>P. notoginseng</i>
Ginsenoside Rg6	C ₄₂ H ₇₀ O ₁₂	Stem-leaves of <i>P. ginseng</i>
Ginsenoside Rs4	C ₄₂ H ₇₀ O ₁₂	Steamed roots of <i>P. notoginseng</i>
Ginsenoside Rs6	C ₄₂ H ₇₀ O ₁₂	Steamed roots of <i>P. notoginseng</i>
Isoginsenoside Rh3	C ₃₆ H ₆₀ O ₇	Fruits of <i>P. ginseng</i>
Ginsenoside Rh5	C ₃₆ H ₆₀ O ₉	Leaves of <i>P. ginseng</i>
Ginsenoside SL2	C ₄₂ H ₇₀ O ₁₄	Steamed leaves of <i>P. ginseng</i>
Ginsenoside ST1	C ₃₆ H ₆₀ O ₁₀	Steamed leaves of <i>P. ginseng</i>
Notoginsenoside ST2	C ₄₃ H ₇₄ O ₁₅	Steamed roots of <i>P. notoginseng</i>
Notoginsenoside ST3	C ₄₃ H ₇₄ O ₁₅	Steamed roots of <i>P. notoginseng</i>
Ginsenoside Rg8	C ₄₂ H ₇₀ O ₁₂	Roots of <i>P. quinquefolius</i>
Notoginsenoside T1	C ₃₆ H ₆₀ O ₁₀	Acid hydrolysate roots of <i>P. notoginseng</i>
Notoginsenoside T2	C ₃₆ H ₆₂ O ₁₀	Acid hydrolysate roots of <i>P. notoginseng</i>
Ginsenoside Rg1-12,23-epoxy	C ₄₂ H ₇₀ O ₁₄	Leaves of <i>P. ginseng</i>
Ginsenoside Rh9	C ₃₆ H ₆₀ O ₉	Leaves of <i>P. ginseng</i>
Quinquefoloside-Lb	C ₅₃ H ₈₈ O ₂₂	Leaves of <i>P. quinquefolius</i>
Ginsenoside Rk1	C ₄₂ H ₇₀ O ₁₂	Processed roots of <i>P. ginseng</i>
Ginsenoside Rk2	C ₃₆ H ₆₀ O ₇	Processed roots of <i>P. ginseng</i>
Ginsenoside Rk3	C ₃₆ H ₆₀ O ₈	Processed roots of <i>P. ginseng</i>
Ginsenoside Rs5	C ₃₈ H ₆₂ O ₉	Steamed roots of <i>P. notoginseng</i>
Ginsenoside Rs7	C ₃₈ H ₆₂ O ₉	Steamed roots of <i>P. notoginseng</i>
Notoginsenoside T5	C ₄₁ H ₆₈ O ₁₂	Acid hydrolysate roots of <i>P. notoginseng</i>
Ginsenoside Rz1	C ₄₂ H ₇₀ O ₁₂	Steamed roots of <i>P. notoginseng</i>
Ginsenoside SL3	C ₄₂ H ₇₀ O ₁₄	Steamed leaves of <i>P. ginseng</i>
Ginsenoside Rh8	C ₃₆ H ₆₀ O ₉	Leaves of <i>P. ginseng</i>
Ginsenoside Rh7	C ₃₆ H ₆₀ O ₉	Leaves of <i>P. ginseng</i>
Yesanchinoside G	C ₅₃ H ₈₈ O ₂₃	Underground part of <i>P. japonicus</i>
Yesanchinoside I	C ₅₉ H ₁₀₀ O ₂₆	Underground part of <i>P. japonicus</i>

Name	Formula	Plant Material
Hexanordammaran	C ₂₄ H ₄₀ O ₄	Leaves of <i>P. ginseng</i>
Notoginsenoside R10	C ₃₀ H ₅₀ O ₉	Steamed leaves of <i>P. ginseng</i>
Yesanchinoside A	C ₄₄ H ₇₄ O ₁₆	Underground part of <i>P. japonicus</i>
Yesanchinoside B	C ₄₈ H ₈₂ O ₂₀	Underground part of <i>P. japonicus</i>
Yesanchinoside C	C ₄₇ H ₈₀ O ₁₉	Underground part of <i>P. japonicus</i>
Panaxadione	C ₃₀ H ₄₈ O ₅	Seeds of <i>P. ginseng</i>
Polyacetyleneginsenoside Ro	C ₆₅ H ₁₀₀ O ₂₁	Roots of <i>P. ginseng</i>
Isodehydroprotopanaxatriol	C ₃₀ H ₅₀ O ₃	Acid hydrolysate roots of <i>P. ginseng</i>
20,25-epoxy-dammaran-2-en-6,12-diol	C ₃₀ H ₅₀ O ₃	Acid hydrolysate roots of <i>P. ginseng</i>
3-methyl-28-nordammaran-2-en-6,12-diol	C ₃₀ H ₅₀ O ₃	Acid hydrolysate roots of <i>P. ginseng</i>

Analysis of ginseng root (Japanese ginseng) has indicated (per 100 grams root) 0.17g (0.17%) total fat, 50mg sodium, 8.82g (8.82%) total carbohydrates comprising 2.3 g dietary fiber and 3.85g sugars and 0.71g (0.71%) protein content. Calorimetric calculation showed that 100g of ginseng root contains 37 kcal.

According to a specific embodiment, the active ingredient or combination thereof includes a ginsenoside, e.g. a protopanaxadiol (PPD)-type saponin with sugar moieties attached to the C-3 and/or C-20, a protopanaxatriol (PPT) saponin with sugar moieties at C-6 and/or at C-20, an ocotillol-type saponin with a five-membered epoxy ring at C-20, an oleanane-type saponin with a nonsteroidal structure, and a dammarane type saponin. Some specific ginsenosides include, but are not limited to notoginsenosides, yesanchinosides, panaxodione, floralginsenosides and ginsenosides Rg1, Rd, Re, Rb1, R1, Rg3, Rk1, Rf, Rg5, F4, Ro.

According to a specific embodiment, the active ingredient or combination thereof includes a volatile compound, e.g., terpene hydrocarbons, monoterpene and sesquiterpene hydrocarbons, specifically β -alamene and β -selenine.

According to a specific embodiment, the active ingredient or combination thereof includes a phytosterol, e.g., stigmasterol, beta-sterol.

According to a specific embodiment, the active ingredient or combination thereof includes a polyacetylene, e.g., panaxynol, ginsenoside A.

According to a specific embodiment, the active ingredient or combination thereof includes a flavenoid, e.g., Kaempferol.

5 According to a specific embodiment, the active ingredient or combination thereof includes an alkaloid, e.g., fumarine, ginsenoside.

According to a specific embodiment, the active ingredient or combination thereof includes a polysaccharide, e.g., WGP, KGP-1, KGP-4, WGPE, NGP, EGP.

10 According to a specific embodiment, the active ingredient or combination thereof includes a phenolic compound, e.g., clemicic, dauricin, maltol.

According to a specific embodiment, the active ingredient or combination thereof includes a mineral, e.g., potassium, calcium, magnesium, phosphorus, aluminum, iron, sodium, boron, zinc, cadmium, selenium.

15 According to a specific embodiment, the active ingredient or combination thereof includes a vitamin, e.g., vitamin D, vitamin A and vitamin C.

According to a specific embodiment, a methanol or ethanol extract is performed, e.g., ethanol concentration is 80%; extraction time is 24 h; extraction temperature is 80-90 °C; particle size 1.0mm; and solvent to ginseng ratio of 20:1 ml/g. Other extraction procedures include, but are not limited to, those described in Dong et al. 2017 Phytother Res Aug; 19(8): 684-688, which is hereby incorporated by reference in its entirety.

According to another embodiment, the plant part is leaf.

Also contemplated herein are plants of the genus *Panax*.

Examples include, but are not limited to:

Ginseng Species	Common name and geographical designation
<i>P. ginseng</i>	Korean ginseng
<i>P. quinquefolius</i>	American ginseng
<i>P. notoginseng</i>	Chinese ginseng
<i>P. japonicas</i>	Japanese ginseng
<i>P. omeiensis</i>	Omei ginseng
<i>P. pseudoginseng</i>	Himalayan ginseng
<i>P. assamicus</i>	N/A
<i>P. shangianus</i>	N/A
<i>P. sinensis</i>	N/A
<i>P. stipuleanatus</i>	Pingpien ginseng
<i>P. trifolius</i>	Dwarf ginseng
<i>P. variabilis</i>	N/A

<i>P. vietnamensis</i>	Vietnamese ginseng
<i>P. wangianus</i>	Narrow-leaved
<i>P. bipinnatifidus</i>	Feather-leaf bamboo ginseng
<i>P. sokpayensis</i>	N/A
<i>P. zingiberensis</i>	Ginger ginseng

Korean ginseng cultivars suitable for use with the present invention include, but are not limited to: Chunpoong, Yunpoong, Gopoong, Sunpoong, Gumpoong, Cheongsun, Sunhyang, Sunun, Sunone, K-1, G-1 and Kowon. Chinese ginseng cultivars suitable for use with the present invention include, but are not limited to Jilin Huangguo Reshen, Jishen 01, Fuxing 01, Fuxing 02, Kangmei 01, Xinkaihe 01, Xinkaihe 02, Zhongnong Huangfengshen and Zhongda Linxiashen.

Chemical Composition of Boswellia species (Frankincense, Olibanum)

Olibanum, also known as frankincense, is a natural oleo-gum-resin that exudes from tappings in the bark of *Boswellia* trees. There are approximately 23 species of trees in the genus *Boswellia*, which grow mainly in Arabia, on the eastern coast of Africa and in India. Characterization and identification of chemical compounds of Olibanum using a variety of methods identified a large variety of compounds in the gum resin of *Boswellia* tree species and classified them as generally being:

- Alcohol-soluble resins (e.g. diterpenes, triterpenes)
- Highly aromatic essential oils (e.g. mono- and sesquiterpenes)
- Water soluble gums

According to specific embodiments, Olibanum comprises 65-85% alcohol-soluble resins, about 5-9% highly aromatic essential oils and the remainder water soluble gums.

In India, the main commercial sources of *Boswellia serrata* are Andhra Pradesh, Gujarat, Madhya Pradesh, Jharkhand and Chhattisgarh. Regionally, it is also known by different names. The botanical origin and vernacular names of *Boswellia serrata* are given in below Table 1. *Salai*, an oleo gum-resin, is a plant exudate of genus *Boswellia* (Family: Burseraceae). It is tapped from the incision made on the trunk of the tree, which is then stored in specially made bamboo basket. The semi-solid gum-resin is allowed to remain in the basket for about a month during which its fluid content locally known as 'ras' keeps flowing out. The residue, semi-solid to solid part, is the gum-resin which hardens slowly into amorphous, tear-shaped products with an aromatic scent. Then, it is broken into small pieces by wooden mallet or chopper and during this process all impurities including bark

pieces etc. are removed manually. The gum-resin is then graded according to its flavour, colour, shape and size. Generally four grades i.e. Superfine, Grade I, Grade II and Grade III are available in the market. The fresh gum obtained from the tree is hot with pleasant flavour and slightly bitter in taste. It had been the 'frankincense' of ancient Egyptians, Greeks and Romans who used it as prized incense, fumigant as well as a multipurpose aromatic. It is generally used in making incense powder and sticks.

TABLE 1
BOTANICAL ORIGIN AND VERNACULAR NAMES OF *BOSWELLIA*
SERRATA

Botanical origin	Vernacular names
Division: Spermatophyta	English: Indian Olibanum or Indian frankincense
Sub-division: Angiospermae	Hindi: Kandar, Solai
Tribe: Rosoideae	Bengali: Kandar, Solai
Sub-tribe: Rosidae S. lat.	Gujarati: Dhup, Gupli
Order: Rosales	Kannada: Chitta, Guguladhupa
Class: Anacardiales	Malayalam: Parangi, Saambraani
Family: Burseraceae	Tamil: Parangi, Saambraani
Genus: <i>Boswellia</i>	Telugu: Phirangi, Saambraani
Species: <i>serrata</i>	Sanskrit: Ashvamutri, Kudara, Shalaki.

The oleo gum-resins contain 30-60% resin, 5-10% essential oils, which are soluble in the organic solvents, and the rest is made up of polysaccharides (~ 65% arabinose, galactose, xylose) which are soluble in water. The resins have a fragrant aroma because of the presence of essential oils and this accounts for their commercial importance.

According to specific embodiments, the common components of Olibanum belonging to the terpene and sesquiterpene families, or their terpenoid derivatives include, but are not limited to α - and β -pinene, α -limonene, myrcene, linalool, α -cubebene, γ -cadinene, β -bourbonene, and α -phellandrene dimer compounds in Olibanum are the compounds that constitute its phytochemical activity. Several oxygenated isoprenoid derivatives have also been identified, such as carbonyl derivatives (e.g., carvone, fenchone) and alcohol-containing terpene and sesquiterpene derivatives (e.g., transpinocarveol, cis-verbenol, and cembrenol), as well as ester-containing compounds (e.g., α -terpinyl acetate and bornyl acetate).

Diverse investigators have reported that limonene is the most abundant volatile in Olibanum, while others have identified octanol acetate, α -pinene and α -thujene as most abundant depending on the species of *Boswellia* plant material used for extraction.

More than 300 essential oils have been isolated from *Boswellia* ssp.

- 5 The table below shows the essential oils recovered from Olibanum extracts prepared by different extraction procedures, from diverse *Boswellia* ssp.:

Number	Compound
1	5,5-Dimethyl-1-vinylbicyclo-[2.1.1]-hexane
2	Anethol
3	Benzyl tiglate
4	<i>trans</i> - α -Bergamotene
5	Bornyl acetate
6	β -Bourbonene
7	Cadinene
8	γ -Cadinene
9	Camphene
10	Camphor
11	<i>m</i> -Camphorene
12	<i>p</i> -Camphorene
13	Carene-3
14	(<i>E</i>)- β -Caryophyllene
15	Cembrene A
16	Cembrenol
17	1,8 Cineol
18	Citronellol
19	α -Copaene
20	β -Copaene
21	<i>p</i> -Cymene
22	<i>m</i> -Cymene
23	Elemol
24	Elemicine
25	<i>epi</i> -Cubenol
26	Estragol
27	Eudesmol
28	10- <i>epi</i> - γ -Eudesmol
29	Fenchone
30	Geraniol
31	Germacrene D
32	Humulene epoxide

Number	Compound
33	Isoincensole
34	Isomenthone
35	Kessane
36	Limonene
37	Linalool
38	Linalyl acetate
39	Menthone
40	Methylchavicol
41	Methylisoeugenol
42	Methyleugenol
43	γ -Muurolene
44	Myrcene
45	Neocembrene A
46	Nerolidol
47	<i>cis</i> - β -ocimene
48	(<i>Z</i>)-Ocimene
49	(<i>E</i>)- β -Ocimene
50	Perillene
51	α -Phellandrene
52	β -Phellandrene
53	α -Pinene
54	β -Pinene
55	<i>trans</i> -Pinocarveol
56	Sabinene
57	<i>cis</i> -Sabinol
58	Terpinin-4-ol
59	Terpinen-4-ol
60	Terpinolene
61	α -Terpineol
62	α -Terpinene
63	α -Terpinene
64	γ -Terpinene
65	Terpinyl acetate
66	Terpinyl isobutyrate
67	Tetrahydrolinalool
68	α -Thujene
69	α -Thujone
70	β -Thujone
71	Tricyclene

Number	Compound
72	Undecenol
73	<i>trans</i> -Verbenol
74	β -Ylangene
75	Zingiberene
76	Abieta-8,12-diene
77	α -Amorphene
78	<i>alloaromadendrene</i>
79	Benzyl benzoate
80	Beyerene
81	Bisabolene
82	Isopentyl-2-methylbutanoate
83	<i>cis</i> -Calamenene
84	α -Cadinene
85	τ -Cadinol
86	2-Carene
87	Campholenealdehyde
88	Caryophyllene oxide
89	<i>cis</i> -Carveol
90	(+) <i>trans</i> -Carveol
91	Carvone
92	α -Cedrene
93	Cedrol
94	Cembra-1,3,7,11-tetraene
95	Cembra-3,7,11,15-tetraene
96	Cembrene
97	Cembrene C
98	Citronellyl acetate
99	α -Cubebene
100	β -Cubebene
101	<i>o</i> -Cymene
102	Chrysanthenone
103	1,4-Cyclohexadiene
104	<i>p</i> -Cymen-8-ol
105	Decanol
106	Decyl acetate
107	2,6-Dimethoxytoluene
108	3,5-Dimethoxytoluene
109	Duva-3,9,13-trien-1,5 α -diol
110	Duva-4,8,13-trien-1 α ,3 α -diol

Number	Compound
111	Duva-3,9,13-trien-1,5 α -diol-1-acetate
112	Duva-3,9,13-triene-1 α -ol-5,8-oxide-1-acetate
113	β -Elemene
114	Farnesyl acetate
115	Geranyl acetate
116	α -Gurjunene
117	Hedycariol
118	1,3,6-Trimethylenecycloheptane
119	1-Hexanol
120	Hexyl acetate
121	Hexyl hexanoate
122	α -Humulene
123	Incensole
124	Incensole acetate
125	Isodurene
126	Isocembrene
127	Isophyllocladene (kaur-15-ene)
128	Kaurene
129	Ledol
130	Maaliane
131	<i>p</i> -Mentha-1,5-dien-8-ol
132	<i>o</i> -Methyl anisole
133	α -Muurolene
134	α -Muurolol
135	Myrtenal
136	Naphthalene
137	Naphthalene 1,2,3,4,4a,7-hexahydro-1,6-dimethyl-4-(1-methylethyl)
138	Neryl acetate
139	<i>cis</i> -Nerolidol
140	(<i>S</i>)- <i>trans</i> -Nerolidol
141	(<i>E</i>)-Nerolidol
142	1-Octanol
143	<i>n</i> -Octanol
144	Octanol acetate
145	Octyl acetate
146	Octyl formate
147	<i>allo</i> -Ocimene
148	Phenanthrene-7-ethenyl-9,10,10a-dodeca-hydro-1-1-4a-

Number	Compound
	7-tetramethyl
149	α -Phellandrene epoxide
150	Phyllocladene
151	α -Pinene-epoxide
152	1- β -Pinene
153	2- β -Pinene
154	Isopinocampheol
155	Piperitone
156	Pyrimidine
157	Sabinyol acetate
158	Sandaracopimara-8(14)-15-diene
159	Sclarene
160	α -Selinene
161	β -Selinene
162	δ -Selinene
163	<i>trans</i> -Terpine
164	4-Terpineol
165	Terpinolene
166	Isoterpinolene
167	2,4(10)-Thujadiene
168	Thujopsene
169	Thunbergol
170	Isomyl-valerate
171	Verticilla-4(20),7,11-triene
172	Verbenone
173	<i>cis</i> -Verbenol
174	Verticiol
175	Viridiflorol
176	Benzene, 1methoxy-2-methyl
177	<i>endo</i> -Borneol
178	γ -Campholene aldehyde
179	α -Campholene aldehyde
180	Cara-2,4-diene
181	Carvacrol
182	Carvotanacetone
183	<i>trans</i> -Dihydrocarvone
184	Cumin alcohol
185	<i>m</i> -Cymene-8-ol
186	<i>p</i> -Cymene-9-ol

Number	Compound
187	<i>p</i> -Cymenene
188	Dodecanol
189	Eucalyptol
190	Eucarvone
191	Isopropyl benzaldehyde
192	Isopropyl benzalcohol
193	<i>cis</i> -1,2-Limonene epoxide
194	8,9-Limonene epoxide II
195	8,9-Limonene-epoxide I
196	<i>trans</i> -1,2-Limonene epoxide
197	<i>cis</i> -Linalool oxide
198	<i>trans</i> -Linalool oxide
199	<i>p</i> -Mentha-1,5-diene-7-ol
200	<i>p</i> -Mentha-1,8-diene-4-ol
201	<i>cis-p</i> -Menth-2-en-1-ol
202	<i>cis-p</i> -Mentha-1(7),8-diene-2-ol
203	<i>cis-p</i> -Mentha-2,8-diene-1-ol
204	<i>trans-p</i> -Menth-2-en-1-ol
205	<i>trans-p</i> -Mentha-1(7),8-diene-2-ol
206	<i>trans-p</i> -Mentha-2,8-diene-1-ol
207	2,4(8)- <i>p</i> -Menthadiene
208	<i>p</i> -Mentha-6,8-dien-2-one
209	<i>p</i> -Methylanisole
210	Myrtenol
211	Nerol
212	<i>trans</i> -Ocimene
213	(<i>E</i>)- β -Ocimene epoxide
214	α -Phellandrene-dimer
215	α -Phellandrene-8-ol
216	α -Pinene oxide
217	Pinocamphone
218	Pinocarvone
219	Piperitenone
220	Isopiperitenone
221	<i>trans</i> -Piperitol
222	α -Terpineol
223	Sabina ketone
224	<i>cis</i> -Sabinene hydrate
225	<i>trans</i> -Sabinene hydrate

Number	Compound
226	<i>trans</i> -Sabinol
227	2,5-Dimethylstyrene
228	<i>cis</i> -1,2-Epoxy-terpin-4-ol
229	Thuj-3-en-10-al
230	Thujanol
231	Thunbergene
232	Thymol
233	Umbellulone
234	Verticellol
235	5,5-Dimethyl-1-vinylbicyclo-[2.1.1]-hexane
236	<i>p</i> -Anisaldehyde
237	Aromadendrene
238	Benzyl tigilate
239	<i>p</i> -Camphorene
240	Isocaryophyllene
241	Cumaldehyde
242	Cyclosativene
243	γ -Eudesmol
244	Guaioxide
245	5-Guaiene-11-ol
246	Isogermacrene D
247	4-Methylene-1-(1-methylethyl)-bicyclo[3.1.0]hex-2-ene
248	2-Methyl-5-(1-methylethyl)-1,3-cyclohexadiene monoepoxide
249	<i>n</i> -Pentadecan
250	Perilla alcohol
251	Perillol
252	Thujol
253	<i>m</i> -Thymol
254	α -Ylangene
255	γ -Campholene aldehyde
256	<i>n</i> -Decanoic acid
257	β -Eudesmene
258	β -Cyclogeranylacetate
259	<i>n</i> -Hexanoic acid
260	Hexylcaprylate
261	Incensyl acetate
262	Incensole oxide
263	Incensole oxide acetate
264	Lauric acid

Number	Compound
265	<i>p</i> -Methylacetophenone
266	<i>p</i> -Methyleugenol
267	β -Myrcene
268	<i>n</i> -Nonanoic acid
269	<i>n</i> -Octanoic acid
270	3,4-Dimethoxystyrene
271	α -Cadinol
272	1,Hydroxy-1,7-dimethyl-4-isopropyl-2,7-cyclodecadiene
273	1,5,5,8-Tetramethyl-12-oxabicyclo-[9.1.0]-dodeca-3,7-diene
274	1-Methyl-4-(1-methylethenyl)-1,2-cyclohexanediol
275	<i>trans-p</i> -Mentha-2,8-dienol
276	1,2,3,4,6,8a-hexahydro-1-isopropyl-4,7-dimethylnaphthalene
277	2-Isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,8a-ctahydronaphthalene
278	3,5-Dimethoxytoluene
279	(<i>Z</i>)- α -Hydroxymanol
280	Hydroxy-manol
281	Methyl linoleate
282	1-Acetyl-4-isopropenylcyclopentene
283	2,4-Dimethylacetophenone
284	α -Amyrenone
285	β -Amyrenone
286	10-Hydroxy-4-cadinen-3-one
287	2-Hydroxy-1,4-cineole
288	Cryptone
289	Eucarvone
290	Isopropylidencyclohexane
291	1,2,4-Trihydroxy- <i>p</i> -menthane
292	Δ^4 - <i>p</i> -Menthen-2-one
293	5-Hydroxy- <i>p</i> -menth-6-en-2-one
294	Myrtenoic acid
295	Nopinone
296	3,6,6,-Trimethyl-norpinan-2-one
297	<i>o</i> -Methylacetophenone
298	Perillaaldehyde
299	Phellandra
300	Pinocamphone/isopinocamphone

Number	Compound
301	Thujone
302	24-Noroleana-3,12-diene
303	24-Noroleana-3,9(11),12-triene
304	24-Norursa-3,12-diene
305	24-Norursa-3,9(11),12-triene
306	24-Norursa-3,12-dien-11-one
307	α -Amyrine
308	<i>epi</i> - α -Amyrine
309	β -Amyrine
310	Lupeol
311	Terpinenyl acetate
312	1,5-Isopropyl-2-methylbicyclo[3.1.0]hex-3-en-2-ol
313	α -Campholenal
314	(3 <i>E</i> ,5 <i>E</i>)-2,6-Dimethyl-1,3,5,7-octatetraene
315	(<i>E</i>)-2,3-Epoxycarene
316	3,4-Dimethylstyrene
317	1-(2,4-Dimethylphenyl)ethanol
318	4-Methylbenzoic acid
319	<i>p</i> -Menth-1(7)-en-2-one
320	Caryophyllene
321	Methylcycloundecanecarboxylate
322	Nonanoic acid
323	Hexadecanoic acid
324	1,4-Cineol
325	Sabinene hydrate
326	Methyl- <i>trans</i> -2- <i>cis</i> -4-decadienoate
327	2-Hydroxy-5-methoxy-acetophenone
328	(<i>E</i>)- β -Farnesene
329	2-Dodecenoic acid methyl ester
330	Calacorene
331	<i>n</i> -Dodecanoic acid
332	α -Guaiol
333	Caryophylla-3(15),7(14)-dien-6-ol
334	Cadalene
335	Eudesma-4(15),7-dien-1 β -ol
336	<i>n</i> -Heptadecane
337	<i>n</i> -Tetradecanoic acid
338	<i>n</i> -Octadecane
339	Galaxolide

Number	Compound
340	Manool

Although many *Boswellia* species produce Olibanum, the major sources of commercial Olibanum are *B. serrata* (India), *B. sacra* (Oman), and *B. carteri* (Somalia).

The table below shows the major components of Olibanum derived from diverse *Boswellia*

5 species, according to their percentage representation:

<i>Boswellia</i> specie	Source of resin	Predominant compound(s)	Percentage	
<i>B. serrata</i>	Commercial (Hamburg, Germany)	Myrcene	38	
<i>B. serrata</i>	NA	α -Thujene	22.7–47.4	
<i>B. serrata</i>	NA	α -Thujene	29.3	
<i>B. serrata</i>	NA	α -Thujene	61.36	
<i>B. carteri</i>	Purchased from the local market of herbs and spices in Egypt	Duva-3,9,13-triene-1a-ol-5,8-oxide-1-acetate	21.4	
<i>B. sacra</i>	Botanically certified oleogum resin	<i>E</i> - β -Ocimene	32.3	
<i>B. carteri</i> / <i>sacra</i>	NM	Octanol acetate	45.2	
<i>B. carteri</i>	Authentic sample from Ethiopia certified for its authenticity from the Agricultural Department of the Ethiopian government	Octyl acetate	39.3	
<i>B. rivae</i>	NA	Limonene	28.0	
<i>B. rivae</i>	Authentic sample from Ethiopia	α -Pinene	16.7	
<i>B. rivae</i>	NA	α -Pinene	13.3	
<i>B. rivae</i>	NA	Octanol	17.8	
<i>B. neglecta</i>	NA	α -Pinene	16.7	
<i>B. neglecta</i>	Authentic sample from Ethiopia	α -Pinene	21.3	
<i>B. papyrifera</i>	NA	Octyl acetate	63.5	
<i>B. papyrifera</i>	NA	Octyl acetate	56.0	
<i>B. pirottae</i>	NA	<i>Trans</i> -Verbenol	15.5	
<i>B. pirottae</i>	NA	Terpinen-4-ol	14.6	
<i>B. frereana</i>	Commercial (Hamburg, Germany)	α -Pinene	38.0	

One exemplary analysis of Olibanum has indicated the following components

- Acid resin (6%), soluble in alcohol and having the formula $C_{20}H_{32}O_4$
- gum (similar to gum arabic) 30–36%
- 3-acetyl-beta-boswellic acid (*Boswellia sacra*)

10

- alpha-boswellic acid (*Boswellia sacra*)
- incensole acetate, $C_{21}H_{34}O_3$
- phellandrene

Another analysis of *B. serrata* resin revealed that the resinous part of *Boswellia*
serrata contains monoterpenes (α -thujene); diterpenes (macrocyclic diterpenoids such as
 incensole, incensole oxide, iso-incensole oxide, a diterpene alcohol [serratol]); triterpenes
 (such as α - and β -amyrins); pentacyclic triterpenic acids (boswellic acids); tetracyclic
 triterpenic acids (tirucall-8,24-dien-21-oic acids). The structures of four major pentacyclic
 triterpenic acids (boswellic acids) as also some of their characteristic features of four
 pentacyclic triterpene acids (Boswellic acid) are given in the following table:

Properties	8-Boswellic acid	Acetyl-8-Boswellic acid	11-keto-8-Boswellic acid	Acetyl-11-keto-8-Boswellic acid
Molecular formula	$C_{30}H_{48}O_4$	$C_{32}H_{48}O_5$	$C_{30}H_{46}O_5$	$C_{32}H_{46}O_6$
Molecular weight	456.7	498.74	479.69	512.73
Chemical name	3 α -Hydroxy-urs-12-en-23-oic acid	3 α -Acetoxy-urs-12-en-23-oic acid	3 α -Hydroxy-urs-12-en-11-keto-23-oic acid	3 α -Acetoxy-urs-12-en-11-keto-23-oic acid
Melting point	226-228°	232-235°	195-197°	271-274°
Specific rotation	+106.8°	+138°	+78.5°	+88.9°
UV-MeOH	Maxima at 208 nm	Maxima at 208 nm	Maxima at 250 nm	Maxima at 250 nm
NMR (in $CDCl_3$, δ ppm)	5.15, CH=C; 4.68, CH-OH; 2.3-1.1, Methylenes and methines, 23 protons; 1.1-0.7 Methyls, 21 protons	5.31, CH=C; 5.2, CH-OAc; 2.3, COCH ₃ ; 1.9-1.25, Methylenes and methines, 23 protons; 1.2-0.7, Methyls, 21 protons	5.55, CH=C; 4.88, CH-OH; 2.6-1.4, Methylenes and methines, 21 protons; 1.25-0.75, Methyls, 21 protons	5.55, CH=C; 5.2, CH-OAc; 2.6-1.4, Methylenes and methines, 21 protons; 1.25-0.75, Methyls, 21 protons
FTIR (in KBr, cm ⁻¹)	3500 (OH), 1699.5 (COOH)	1732 (OAc), 1701 (COOH)	3460 (OH), 1693 (COOH)	1740 (Ac), 1701 (COOH), 647 (C=C-unsaturated carbonyl)
GC-MS	794 (M-68[44 due to -CO ₂ and 18 due to -H ₂ O]); Other fragments: 203, 189, 175, 161.	794 (M-104[44 due to -CO ₂ and 60 due to -HOAc]); 218 (base peak)	408 (M-68[44 due to -CO ₂ and 18 due to -H ₂ O]); 232 (base peak); Other fragments: 217, 175, 161, 133	408 (M-68[44 due to -CO ₂ and 18 due to -HOAc]); 232 (base peak); Other fragments: 217, 175, 161, 133

The Olibanum gum component contains polysaccharides and polymeric
 components. The proteoglycans in Olibanum comprise mainly D-galactose units in the
 main chain and glucuronic acid, uronic acids, 4-O-methyl-glucuronic acid and arabinose in
 the side chains.

According to a specific embodiment, the active ingredient or combination thereof
 includes an alcohol soluble acid resin, a water soluble gum, an alpha-boswellic acid, an
 incensole acetate and a phellandrene.

According to a specific embodiment, the active ingredient or combination thereof
 includes a volatile compound, e.g. α -Thujene, Duva-3,9,13-triene-1 α -ol-5,8-oxide-1-

acetate, *E*- β -Ocimene, Octanol acetate, Octyl acetate, Limonene, α -Pinene, Octanol, *Trans*-Verbenol and Terpinen-4-ol.

According to a specific embodiment, the active ingredient or combination thereof includes a mineral, e.g., potassium, calcium, magnesium, phosphorus, aluminum, iron,
5 sodium, boron, zinc, cadmium, selenium.

According to a specific embodiment, a water or alcohol extract is performed.

In some embodiments, the Olibanum is prepared by water extract. An exemplary water extract is described herein:

Preparation of olibanum extract by water. At first, Olibanum is carefully powdered.
10 The powder (25 g) is mixed with 200 ml of deionized water and stirred with 800 rpm overnight at room temperature. This mixture is centrifuged at 1,500 rpm for 10 min and the supernatant collected. Thereafter, the supernatant is again centrifuged at 2,500 rpm for 10 min and successively at 10,000 rpm for 20 min, and then filtered. The filtrates can be stored at -20 C and then freeze-dried -58 C and 0.5 Torr for 24 h to yield 4.02 gr of water
15 soluble extract. At the next step, the resulted powder is dissolved in 100ml methanol and stirred for 12 hr. at room temperature, then allowed to settle. The precipitate phase is collected and dried in an oven. Again the powder is dissolved in deionized water, centrifuged repeatedly and refiltered. The filtrates can be stored and then freeze-dried.

In some embodiments, the Olibanum is prepared by alcohol extract. An exemplary
20 alcohol extract is described herein:

Preparation of olibanum extract by alcohol: In this method, 100 gr of Olibanum powder with 400 ml of methanol is mixed. This mixture is then stirred at 650 rpm for 24 hours. The resulting mixture is made up of two phases, the upper phase is alcoholic and yellow, and contains substances that are soluble in alcohol. The material is then dried in an
25 oven at 50 C. The bottom phase has a sedimentary and white state, which is set to in the oven until dry. The resulting powder in the water is well dissolved and the obtained solution is centrifuged at 1,500 rpm for 10 min and the supernatant collected. Thereafter, the supernatant is again centrifuged at 2,500 rpm for 10 min and successively at 10,000 rpm for 20 min, and then filtered. The filtrates can be stored at -20 C and then freeze-dried.

30 Other extraction procedures include, but are not limited to, those described in Mertens et al, et al. 2009, Flavor and Fragrance, 24:279-300 and Hamm et al, Phytochemistry 2005, 66:1499-1514, which are hereby incorporated by reference in their entirety.

Also contemplated herein are Olibarum and other compositions from trees of the genus *Boswellia*.

Examples include, but are not limited to:

Some <i>Boswellia</i> Species
<i>B. socotrana</i>
<i>B. elongata</i>
<i>B. ameero</i>
<i>B. carteri</i>
<i>B. neglecta</i>
<i>B. sacra</i>
<i>B. thurifera</i>
<i>B. frereana</i>
<i>B. dioscorides</i>
<i>B. rivaie</i>
<i>B. papyrifera</i>
<i>B. serrata</i>

5 **Chemical Composition of *Gynostemma pentaphyllum* (Jiaogulan)**

Gynostemma pentaphyllum is a perennial herb from the Cucurbitaceae family, with 5-lobed leaves and a gourd-like, inedible fruit which grows in forests, thickets or roadside on mountain slopes in many areas of Northeast and Southeast Asia, including China, Taiwan, S Korea, Japan, Thailand, Vietnam and Laos. *G. pentaphyllum* also grows in
10 Bangladesh, Bhutan, India, Indonesia, Malaysia, Myanmar, Nepal, New Guinea and Sri Lanka. Jiaogulan is prized for its reputation as a “longevity plant”. Characterization and identification of chemical compounds of *Gynostemma pentaphyllum* using a variety of methods identified a large variety of compounds in *Gynostemma pentaphyllum* (Thun.) Makino and classified them as generally being:

- 15 • Saponin Glycosides (e.g., gypenosides)
- Phenolic compounds
- Flavenoids (e.g. Kaempferol, quercetin, rutin, ombuin, isorahmnetin)
- Polysaccharides
- Sterols (e.g. ergostane, cholestane, stigmastane)
- 20 • Trace elements (e.g. Cu, Fe, Zn, Mn, Co, Ni, Se, Mo and Sr)
- Carotenoids
- Volatiles (e.g. malonic acid, benzyl-O-beta-D-glucopyranoside, lutein, vomifoliol, palmitic acid, linoleic acid)

According to specific embodiments, the saponin compounds in Jiaogulan and the polysaccharide compounds are the compounds that constitute its phytochemical activity. The most abundant saponin compound in Jiaogulan was found to be gypenoside.

Most Jiaogulan saponins belong to a family of triterpenoid saponins. They are also referred to as gypenosides, and dammarane derivatives. More than 150 saponins have been isolated from *G. pentaphyllum* plants. Saponins have been identified in Jiaogulan leaves and stems, flower buds, fruits, berries, and seeds.

The table below shows the phytochemical properties of 5 different *Gynostemma pentaphyllum* samples from different sources:

10

SAMPLE	SOLVENT	TPC (mg GAE/g)	TSC (mg GE/g)	TFC (mg RE/g)	RUTIN CONTENT (ug/g)	QUERCETIN CONTENT (ug/g)	R+Q (umol QE/g)
GP1	50% acetone	44.3	38.02	21.44	3049.5	4906.5	21.2
	50% ethanol	37.5	41.39	26.40	7948.2	7431.8	37.6
	100% ethanol	33.6	87.28	26.87	11235.4	7279.1	42.5
GP2	50% acetone	14.9	90.17	10.6	2527.3	117.5	4.5
	50% ethanol	12.9	114.48	14.27	3588.1	136.2	6.3
	100% ethanol	6.9	132.57	13.84	2131.9	166.2	4.0
GP3	50% acetone	12.3	47.62	10.52	8614.9	358.9	15.3
	50% ethanol	10.6	59.13	9.51	9954.0	411.0	17.7
	100% ethanol	6.7	64.57	8.05	7193.0	549.4	13.6
GP4	50% acetone	43.2	77.64	63.48	1409.2	241.3	3.1
	50% ethanol	30.4	82.12	54.04	680.2	150.8	1.6
	100% ethanol	17.7	104.1	36.47	579.4	151.3	1.4
GP5	50% acetone	13.1	23.61	14.55	nd	nd	
	50% ethanol	10.2	60.7	16.53	nd	nd	
	100% ethanol	8.9	123.97	22.11	nd	nd	

GP1-5 represent *G. pentaphyllum* samples from different sources. Data are per gram of dry botanical basis and are expressed as mean (SD). Different letters represent significant differences ($P < 0.05$). nd stands for not detectable. TPC, TSC, and TFC stand for total phenolic content, total saponin content, and total flavonoid content by spectrometric methods, respectively. GAE, GE, RE, and QE stand for gallic acid equivalents, gypenoside equivalents, rutin equivalents, and quercetin equivalents. Rutin and quercetin contents were flavonoid profile obtained by HPLC. R + Q stands for total amount of rutin and quercetin.

Ethanol extraction: 12g sample in 250 ml 100% ethanol, 5 hours in Soxhlet apparatus.
50% acetone extraction and 75% ethanol extraction: 2 g sample in 20 ml solvent at ambient temperature and filtration through 45 micron filter.

Water content of the Jiaogulan samples ranged from 3.79 to 7.57 g/100 g sample. Dietary fiber content ranged from 0.6 g/g to 0.24 g/g sample. Selenium content ranged from 1.7 mg/kg to 0.94 mg/kg.

According to a specific embodiment, the active ingredient or combination thereof includes a gypenoside. Some specific gypenosides include, but are not limited to CP-1-6.

According to a specific embodiment, the active ingredient or combination thereof includes a volatile compound, e.g., malonic acid, benzyl-O-beta-D-glucopyranoside, lutein, vomifoliol, palmitic acid, linoleic acid.

According to a specific embodiment, the active ingredient or combination thereof includes a phytosterol, e.g., stigmasterol, ergostane.

According to a specific embodiment, the active ingredient or combination thereof includes a flavenoid, e.g., Kaempferol, quercetin, rutin.

According to a specific embodiment, the active ingredient or combination thereof includes a phenolic compound.

According to a specific embodiment, the active ingredient or combination thereof includes a mineral, e.g., potassium, calcium, magnesium, phosphorus, aluminum, iron, sodium, boron, zinc, cadmium, selenium.

According to a specific embodiment, the active ingredient or combination thereof includes a vitamin, e.g., vitamin D, vitamin A and vitamin C.

According to a specific embodiment, a methanol or ethanol extract is performed, e.g., ethanol concentration is 100 or 75%; 5 hours in Soxhlet apparatus, or 50% acetone extraction and 75% ethanol extraction: 2 g sample in 20 ml solvent at ambient temperature and filtration through 45 micron filter. Other extraction procedures include, but are not limited to, those described in Yantao et al. 2016 Chi Med 11:43, which is hereby incorporated by reference in its entirety.

According to another embodiment, the plant part is leaf.

Also contemplated herein are plants of the genus *Gynostemma*.

Origanum Syriacum

According to a specific embodiment, the plants of this species include flavones, monoterpenoids and monoterpenes. Over 60 different compounds have been identified, with the primary ones being carvacrol and thymol ranging to over 80%, while lesser abundant compounds include p-cymene, γ -terpinene, caryophyllene, spathulenol, germacrene-D, β -fenchyl alcohol and δ -terpineol.

The table below shows a profile of the organic compounds identified in *Origanum* extract through fractional distillation:

Profile of the organic compounds found in the fractions analyzed.

Compound Boiling Point °C	Code	% de Relative Area				Unoil	Ooil
		F1	F2	F3	F4		

5	α -thujene	150–152	MH1	5.03	0.389	ND	ND	1.74
	α -pinene	156	MH2	3.01	ND	ND	ND	1.07
	β -myrcene	166–168	MH3	11.62	6.93	1.08	ND	5.50
	Phellandrene	172	MH4	1.32	1.00	ND	ND	0.72
	α -terpinene	174	MH5	8.91	8.32	2.90	ND	5.57
10	<i>o</i> -cymene	174	MH6	47.96	53.97	38.14	1.31	0.973
	Limonene	175	MH7	2.29	2.71	1.25	ND	1.58
	1,8-cineole	177	MO1	1.51	1.77	2.74	ND	1.53
	γ -terpinene	181–183	MH8	15.59	24.43	40.57	1.40	0.94
	Thymol	232	MO2	ND	ND	ND	5.08	3.77
15	Carvacrol	237–238	MO3	ND	ND	4.58	60.03	64.31
	Trans-caryophyllene	268	SeH1	ND	ND	2.97	18.96	13.78
	α -humulene	276	SeH2	ND	ND	0.34	6.16	8.36
	Monoterpene hydrocarbons (MH)			95.73	97.75	83.94	2.71	1.91
	Monoterpene oxygenated (MO)			1.51	1.77	7.32	65.11	68.08
20	Sesquiterpene hydrocarbons (SeH)			ND	ND	3.31	25.12	22.14
	Total identified components			97.24	99.52	94.57	92.94	92.13

Oregano essential oil (Ooil) was obtained through the steam entrainment method and the oil fractions through a fractional distillation system. The first fraction started to distill at a temperature of 82 °C and the last fraction distilling at 140 °C, finally undistilled oil (Unoil) was obtained. At the end of the process, five fractions named Fraction 1 (F1), Fraction 2 (F2), Fraction 3 (F3), Fraction 4 (F4), and undistilled oil (Unoil) were obtained.

When Origanum extract was analyzed on HPLC, a variety of phenolic compounds were identified:

Phenolic compounds determined by the HPLC method in *O. vulgare* ssp. *vulgare* extract.

Compounds	[M – H] [–] , m/z	Retention Time (tr), min	UV Detection	MS Detection	Concentration (mg/g)
Gentisic acid	153	3.69 ± 0.04	NO	YES	<0.02
Chlorogenic acid	353	6.43 ± 0.05	YES	YES	2.10 ± 0.14
<i>p</i> -Coumaric acid	163	9.48 ± 0.08	NO	YES	<0.02
Hyperoside	463	18.60 ± 0.12	YES	YES	1.05 ± 0.03
Isoquercitrin	463	20.29 ± 0.10	YES	YES	0.71 ± 0.19
Rutin	609	20.76 ± 0.15	YES	YES	0.64 ± 0.15
Rosmarinic acid	360	21.80 ± 0.10	YES	YES	12.83 ± 2.19
Quercitrin	447	23.64 ± 0.13	YES	YES	0.50 ± 0.08
Quercetin	301	27.55 ± 0.15	NO	YES	<0.02
Luteolin	285	29.64 ± 0.19	YES	YES	0.10 ± 0.04

Values are the mean ± SD (n = 3).

Total polyphenol content and antioxidant activity of *O. vulgare* ssp. *vulgare* extract.

Sample	TPC (mg GAE/ g)	Flavonoid (mg RE/g)	Caffeic Acids (mg CAE/g)	CUPRAC (μ M TE/g)	FRAP (μ M TE/g)	SO Scavenging (μ M TE/g)
<i>O. vulgare</i>	94.69 $\pm$ 4.03	38.46 $\pm$ 3.54	29.92 $\pm$ 1.08	1284 $\pm$ 66	794.40 $\pm$ 25.80	44.00 $\pm$ 0.56

Each value is the mean $\pm$ SD of three independent measurements. TPC, total polyphenols content; SO, superoxide; GAE, gallic acid equivalents; RE, rutin equivalents; CAE, caffeic acid equivalents; TE, Trolox equivalents.

5 Also contemplated herein are plants of the genus *Origanum*.

Origanum is a genus of herbaceous perennials and subshrubs in the family Lamiaceae, native to Europe, North Africa, and much of temperate Asia, where they are found in open or mountainous habitats. A few species also naturalized in scattered locations in North America and other regions.

10 The plants have strongly aromatic leaves and abundant tubular flowers with long-lasting coloured bracts. The genus includes the important group of culinary herbs: marjoram (*Origanum majorana*) and oregano (*Origanum vulgare*).

Examples include, but are not limited to:

Origanum acutidens (Hand.-Mazz.) Ietsw. - Turkey, Iraq

15 *Origanum* $\times$ *adanense* Baser & H.Duman - Turkey (*O. bargyli* $\times$ *O. laevigatum*)

Origanum $\times$ *adonidis* Mouterde - Lebanon (*O. libanoticum* $\times$ *O. syriacum* subsp. *bevanii*)

Origanum akhdarensense Ietsw. & Boulos - Cyrenaica region of eastern Libya

Origanum amanum Post - Hatay region of Turkey

Origanum $\times$ *barbarae* Bornm. - Lebanon (*O. ehrenbergii* $\times$ *O. syriacum* subsp. *bevanii*)

20 *Origanum bargyli* Mouterde - Turkey, Syria

Origanum bilgeri P.H.Davis - Antalya region of Turkey

Origanum boissieri Ietsw. - Turkey

Origanum calcaratum Juss. - Greece

Origanum compactum Benth. - Spain, Morocco

25 *Origanum cordifolium* (Montbret & Aucher ex Benth.) Vogel - Cyprus

Origanum cyrenaicum Bég. & Vacc. - Cyrenaica region of eastern Libya

Origanum dayi Post - Israel

Origanum dictamnus L. – hop marjoram, Cretan dittany, dittany of Crete - endemic to Crete

30 *Origanum* $\times$ *dolichosiphon* P.H.Davis - Seyhan region of Turkey (*O. amanum* $\times$ *O. laevigatum*)

- Origanum ehrenbergii* Boiss. - Lebanon
- Origanum elongatum* (Bonnet) Emb. & Maire - Morocco
- Origanum floribundum* Munby - Algeria
- Origanum* × *haradjanii* Rech.f. - Turkey (*O. laevigatum* × *O. syriacum* subsp. *bevanii*)
- 5 *Origanum haussknechtii* Boiss. - Turkey
- Origanum husnucan-baseri* H.Duman, Aytac & A.Duran - Turkey
- Origanum hypericifolium* O.Schwarz & P.H.Davis - Turkey
- Origanum* × *intercedens* Rech.f. - Greece, Turkey (*O. onites* × *O. vulgare* subsp. *hirtum*)
- Origanum* × *intermedium* P.H.Davis - Denizli region of Turkey (*O. onites* × *O. sipyleum*)
- 10 *Origanum isthmicum* Danin - Sinai
- Origanum jordanicum* Danin & Kunne - Jordan
- Origanum laevigatum* Boiss. - Turkey, Syria, Cyprus
- Origanum leptocladum* Boiss. - Turkey
- Origanum libanoticum* Boiss. - Lebanon
- 15 *Origanum majorana* L. – (sweet) marjoram - Turkey, Cyprus; naturalized in scattered locations in Europe, North Africa, North + South America
- Origanum* × *lirium* Heldr. ex Halácsy - Greece (*O. scabrum* × *O. vulgare* subsp. *hirtum*)
- Origanum* × *majoricum* Cambess. – hardy sweet marjoram - Spain including Balearic Islands (*O. majorana* × *O. vulgare* subsp. *virens*)
- 20 *Origanum microphyllum* (Benth.) Vogel - Crete
- Origanum* × *minoanum* P.H.Davis - Crete (*O. microphyllum* × *O. vulgare* subsp. *hirtum*)
- Origanum minutiflorum* O.Schwarz & P.H.Davis - Turkey
- Origanum munzureense* Kit Tan & Sorger - Turkey
- Origanum* × *nebrodense* Tineo ex Lojac - Sicily (*O. majorana* × *O. vulgare* subsp. *viridulum*)
- 25 *Origanum onites* L. - Greece, Turkey, Sicily
- Origanum* × *pabotii* Mousterde - Syria (*O. bargyli* × *O. syriacum* subsp. *bevanii*)
- Origanum pampaninii* (Brullo & Furnari) Ietsw - Cyrenaica region of eastern Libya
- Origanum petraeum* Danin - Jordan
- 30 *Origanum punonense* Danin - Jordan
- Origanum ramonense* Danin - Israel
- Origanum rotundifolium* Boiss. - Turkey, Caucasus
- Origanum saccatum* P.H.Davis - Turkey

Origanum scabrum Boiss. & Heldr. in P.E.Boissier - Greece

Origanum sipyleum L. -Turkey, Greek Islands

Origanum solymicum P.H.Davis - Antalya region of Turkey

Origanum symes Carlström - Islands of the Aegean Sea

5 *Origanum syriacum* L. - Turkey, Cyprus, Syria, Lebanon, Jordan, Palestine, Israel, Sinai, Saudi Arabia

Origanum vetteri Briq. & Barbey - Crete

Origanum vogelii Greuter & Burdet - Turkey

10 *Origanum vulgare* L. - oregano - Europe, North Africa, temperate Asia (Iran, Siberia, Central Asia, China, etc.); naturalized in parts of North America, New Zealand, Venezuela.

According to a specific embodiment, the active ingredient or combination thereof includes an organic compound component of *Origanum* extract.

According to a specific embodiment, the active ingredient or combination thereof is selected from the group consisting of α -thujene α -pinene, β -myrcene, Phellandrene, α -terpinene, o-cymene, Limonene, 1,8-cineole, γ -terpinene, Thymol, Carvacrol, Trans-caryophyllene and α -humulene.

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According to a specific embodiment, the active ingredient or combination thereof includes a monoterpene hydrocarbon, an oxygenated monoterpene and a sesquiterpene hydrocarbon.

20 According to a specific embodiment, the active ingredient or combination thereof includes a phenolic compound, e.g., gentisic acid, chlorogenic acid, *p*-coumaric acid, hyperoside, isoquercitrin, rutin, rosmarinic acid, quercitrin, quercetin and luteolin.

According to a specific embodiment, the active ingredient or combination thereof includes a mineral, e.g., potassium, calcium, magnesium, phosphorus, aluminum, iron, sodium, boron, zinc, cadmium, selenium.

25

Sesame

Sesame seeds contain thelignans, sesamol, sesamin, pinorelinol andlaricresinol. Insoluble 11S globulin and soluble 2S albumin, conventionally termed α -globulin and β -globulin, are the two major storage proteins and constitute 80–90% of total seed proteins in sesame. Comparison of amino acid composition indicated that they are substantially less hydrophobic than the known oleosins, and thus should not be aggregated multimers of oleosins. The results of immuno-recognition to sesame proteins reveals that these three polypeptides are unique proteins gathered in oil bodies, accompanying oleosins and

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triacylglycerols, during the active assembly of the organelles in maturing seeds. The phospholipid, oleic and linoleic acids, chlorophyll and sesamol, sesamol and γ -tocopherol are found. 10 compounds [2-furfurylthiol, 2-phenylethylthiol, 2-methoxyphenol, 4-hydroxy-2, 5-dimethyl-3[2H]-furanone, 2-pentylpyridine, 2-ethyl-3,5-dimethylpyrazine, acetylpyrazine, [E,E]-2,4-decadienal, 2-acetyl-1-pyrroline and 4-vinyl-2-methoxy-phenol] are quantified. On the basis of high OAVs in oil, especially 2-acetyl-1-pyrroline [roasty], 2-furfurylthiol [coffee-like], 2-phenylethylthiol [rubbery] and 4-hydroxy-2,5-dimethyl-3[2H]-furanone [caramel-like] are elucidated as important contributors to the overall roasty, sulphury odour of the crushed sesame material. The structures of novel sesaminol glucosides isolated from sesame seed are determined to be sesaminol 2'-O- β -d-glucopyranoside, sesaminol 2'-O- β -d-glucopyranosyl [1 $\rightarrow$ 2]-O- β -d-glucopyranoside and sesaminol 2'-O- β -d-glucopyranosyl [1 $\rightarrow$ 2]-O-[β -d-glucopyranosyl [1 $\rightarrow$ 6]]-[β -d-glucopyranoside. Also minor sesame lignans such as -(7S,8'R,8R)-acuminatolide piperitol and pinoresinol (as mentioned).

Also contemplated herein are plants of the genus *Sesamum*.

Examples include, but are not limited to:

- Sesamum abbreviatum* Merxm.
- Sesamum alatum* Thonn.
- Sesamum angolense* Welw.
- Sesamum biapiculatum* De Wild.
- Sesamum calycinum* Welw.
- Sesamum capense* Burm. f.
- Sesamum digitaloides* Welw. ex Schinz
- Sesamum gracile* Endl.
- Sesamum hopkinsii* Suess.
- Sesamum indicum* L.
- Sesamum lamiifolium* Engl.
- Sesamum latifolium* J.B. Gillett
- Sesamum lepidotum* Schinz
- Sesamum macranthum* Oliv.
- Sesamum marlothii* Engl.
- Sesamum mombazense* De Wild. & T.Durand
- Sesamum parviflorum* Seidenst.

Sesamum pedalioides Welw. ex Hiern

Sesamum radiatum Schumach. & Thonn.

Sesamum rigidum Peyr.

Sesamum rostratum Hochst.

5 *Sesamum sabulosum* A.Chev.

Sesamum schinzianum Asch.

Sesamum somalense Chiov.

Sesamum thonneri De Wild. & T. Durand

Sesamum triphyllum Welw. ex Asch.

10 Plants that contain Lignan according to some embodiments of the invention include a wide variety of plant foods, including seeds (flax, pumpkin, sunflower, poppy, sesame), whole grains (rye, oats, barley), bran (wheat, oat, rye), beans, fruit (particularly berries), and vegetables (Broccoli and curly kale are rich sources of lignans. Other vegetables such as white and red cabbage, Brussels sprouts, cauliflower, carrots, green and red sweet
15 peppers are also good sources).

Additional plants that contain Sesamin include but are limited to *Eleutherococcus senticosus*.

Thus, any combination of the above plants is contemplated including 2, 3, 4, 5, 6, 7 of the plants. According to another embodiment, a combination of extracts or fractions
20 including 2, 3, 4, 5, 6, 7 of the different plants.

Examples include, but are not limited to, *Nigella sativa*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

25 *Nigella sativa*, *Thymus capitatus*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

30 *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Sesamum indicum* and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum*.

Nigella sativa, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

5 *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Satujera thymbra*, *Sesamum indicum* and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Sesamum indicum* and *Rhus coriaria*.

10 *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, and *Rhus coriaria*.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satujera thymbra*.

Nigella sativa, *Thymus capitatus*.

Nigella sativa, *Thymus vulgaris*.

15 *Nigella sativa*, *Origanum syriacum*.

Nigella sativa, *Thymbra spicata*.

Nigella sativa, *Satujera thymbra*.

Nigella sativa, *Sesamum indicum*.

Nigella sativa, *Rhus coriaria*.

20 Also contemplated are various combinations without *Nigella sativa*.

According to another embodiment, a combination of active ingredients e.g., thymoquinone, carvacrol, thymol; thymoquinone, carvacrol; thymoquinone, thymol; carvacrol, thymol.

Nigella sativa, *Thymus capitatus*, *Thymus vulgaris*.

25 *Nigella sativa*, *Thymus vulgaris*, *Origanum syriacum*.

Nigella sativa, *Origanum syriacum*, *Thymbra spicata*.

Nigella sativa, *Thymbra spicata*, *Satujera thymbra*.

Nigella sativa, *Satujera thymbra*, *Sesamum indicum* *Rhus coriaria*.

30 According to some embodiments the plants and active ingredients thereof are listed in the Table below.

Origanum Syriacum	Carvacrol thymol
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Thymus Capitatus	Carvacrol p-cymene γ-terpinene β-caryophyllene
Thymus Vulgaris	Thymol
Thymbra Spicata	Carvacrol γ-terpinene p-cymene
Satureja Thymbra	γ-terpinene p-cymene carvacrol thymol
Sumac	Tannin
Sesame	Lignans Seasamolin Seasamin Pinoresinol Lariciresinol
Nigella sativa	Thymoquinone

Other embodiments, which comprise any of the *Nigella sativa*, *Thymus capitatus*, *Thymus vulgaris*, *Origanum syriacum*, *Thymbra spicata*, *Satureja thymbra*, *Sesamum indicum*, *Rhus coriaria*, *Panax ginseng* and *Gynostemma pentaphyllum* plants or genera thereof in combinations of 2, 3, 4, 5, 6, 7 and 8 plants are contemplated herein.

Any of the compositions (i.e., plant part, extract thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof) described herein can be used for the treatment of inflammation.

In some embodiments of the present invention there is provided compositions or food supplements comprising Bromelain or pineapple extracts comprising Bromelain.

In some embodiments of the present invention there is provided compositions or food supplements comprising tryptophan, analogs of tryptophan or extract of plant containing tryptophan such as sesame or oregano.

In some embodiments of the present invention there is provided method, vaccine, pharmaceutical composition, composition or food supplement *further including* "Beduin Tea" comprising at least 3 of dried thyme dried sage cardamom pods cinnamon stick black tea Habuk and Marmaraya

The term “treating” refers to inhibiting, preventing or arresting the development of regression of a pathology. Those of skill in the art will understand that various methodologies and assays can be used to assess the development of a pathology, and similarly, various methodologies and assays may be used to assess the reduction, remission or regression of a pathology.

As used herein, the term “preventing” refers to keeping a disease, disorder or condition from occurring in a subject who may be at risk for-, or predisposed to the disease, but has not yet been diagnosed as having the disease.

As used herein, the term “subject” includes mammals, preferably human beings at any age which suffer from the pathology. Preferably, this term encompasses individuals who are at risk to develop the pathology.

As used herein “inflammation” refers to a part of the complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants,^[1] and is a protective response involving immune cells, blood vessels, and molecular mediators. The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and initiate tissue repair.

The five classical signs of inflammation are heat, pain, redness, swelling, and loss of function. Inflammation is a generic response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen. Too little inflammation could lead to progressive tissue destruction by the harmful stimulus (e.g. bacteria) and compromise the survival of the organism. In contrast, chronic inflammation is associated with various diseases, such as hay fever, periodontal disease, atherosclerosis, and osteoarthritis.

Inflammation can be classified as either *acute* or *chronic*. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues. A series of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged inflammation, known as *chronic inflammation*, leads to a

progressive shift in the type of cells present at the site of inflammation, such as mononuclear cells, and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.

As used herein “inflammatory disease” refers to a medical condition in which inflammation takes a role in onset or progression.

According to a specific embodiment, the inflammatory disease comprises an autoimmune disease.

According to a specific embodiment, the inflammatory disease comprises an acute inflammatory disease.

According to a specific embodiment, the inflammatory disease comprises a chronic inflammatory disease.

Inflammatory diseases - Include, but are not limited to, chronic inflammatory diseases and acute inflammatory diseases.

Inflammatory diseases associated with hypersensitivity

Examples of hypersensitivity include, but are not limited to, Type I hypersensitivity, Type II hypersensitivity, Type III hypersensitivity, Type IV hypersensitivity, immediate hypersensitivity, antibody mediated hypersensitivity, immune complex mediated hypersensitivity, T lymphocyte mediated hypersensitivity and DTH.

Type I or immediate hypersensitivity, such as asthma.

Type II hypersensitivity include, but are not limited to, rheumatoid diseases, psoriasis, rheumatoid autoimmune diseases, rheumatoid arthritis (Krenn V. *et al.*, *Histol Histopathol* 2000 Jul;15 (3):791), spondylitis, ankylosing spondylitis (Jan Voswinkel *et al.*, *Arthritis Res* 2001; 3 (3): 189), systemic diseases, systemic autoimmune diseases, systemic lupus erythematosus (Erikson J. *et al.*, *Immunol Res* 1998;17 (1-2):49), sclerosis, systemic sclerosis (Renaudineau Y. *et al.*, *Clin Diagn Lab Immunol.* 1999 Mar;6 (2):156); Chan OT. *et al.*, *Immunol Rev* 1999 Jun;169:107), glandular diseases, glandular autoimmune diseases, pancreatic autoimmune diseases, diabetes, Type I diabetes (Zimmet P. *Diabetes Res Clin Pract* 1996 Oct;34 Suppl:S125), thyroid diseases, autoimmune thyroid diseases, Graves’ disease (Orgiazzi J. *Endocrinol Metab Clin North Am* 2000 Jun;29 (2):339), thyroiditis, spontaneous autoimmune thyroiditis (Braley-Mullen H. and Yu S, *J Immunol* 2000 Dec 15;165 (12):7262), Hashimoto’s thyroiditis (Toyoda N. *et al.*, *Nippon Rinsho* 1999 Aug;57 (8):1810), myxedema, idiopathic myxedema (Mitsuma T. *Nippon Rinsho*. 1999 Aug;57 (8):1759); autoimmune reproductive diseases, ovarian diseases, ovarian

autoimmunity (Garza KM. *et al.*, J Reprod Immunol 1998 Feb;37 (2):87), autoimmune anti-sperm infertility (Diekman AB. *et al.*, Am J Reprod Immunol. 2000 Mar;43 (3):134), repeated fetal loss (Tincani A. *et al.*, Lupus 1998;7 Suppl 2:S107-9), neurodegenerative diseases, neurological diseases, neurological autoimmune diseases, multiple sclerosis

5 (Cross AH. *et al.*, J Neuroimmunol 2001 Jan 1;112 (1-2):1), Alzheimer's disease (Oron L. *et al.*, J Neural Transm Suppl. 1997;49:77), myasthenia gravis (Infante AJ. And Kraig E, Int Rev Immunol 1999;18 (1-2):83), motor neuropathies (Kornberg AJ. J Clin Neurosci. 2000 May;7 (3):191), Guillain-Barre syndrome, neuropathies and autoimmune neuropathies (Kusunoki S. Am J Med Sci. 2000 Apr;319 (4):234), myasthenic diseases,

10 Lambert-Eaton myasthenic syndrome (Takamori M. Am J Med Sci. 2000 Apr;319 (4):204), paraneoplastic neurological diseases, cerebellar atrophy, paraneoplastic cerebellar atrophy, non-paraneoplastic stiff man syndrome, cerebellar atrophies, progressive cerebellar atrophies, encephalitis, Rasmussen's encephalitis, amyotrophic lateral sclerosis, Sydeham chorea, Gilles de la Tourette syndrome, polyendocrinopathies, autoimmune

15 polyendocrinopathies (Antoine JC. and Honnorat J. Rev Neurol (Paris) 2000 Jan;156 (1):23); neuropathies, dysimmune neuropathies (Nobile-Orazio E. *et al.*, Electroencephalogr Clin Neurophysiol Suppl 1999;50:419); neuromyotonia, acquired neuromyotonia, arthrogryposis multiplex congenita (Vincent A. *et al.*, Ann N Y Acad Sci. 1998 May 13;841:482), cardiovascular diseases, cardiovascular autoimmune diseases,

20 atherosclerosis (Matsuura E. *et al.*, Lupus. 1998;7 Suppl 2:S135), myocardial infarction (Vaarala O. Lupus. 1998;7 Suppl 2:S132), thrombosis (Tincani A. *et al.*, Lupus 1998;7 Suppl 2:S107-9), granulomatosis, Wegener's granulomatosis, arteritis, Takayasu's arteritis and Kawasaki syndrome (Praprotnik S. *et al.*, Wien Klin Wochenschr 2000 Aug 25;112 (15-16):660); anti-factor VIII autoimmune disease (Lacroix-Desmazes S. *et al.*, Semin

25 Thromb Hemost.2000;26 (2):157); vasculitises, necrotizing small vessel vasculitises, microscopic polyangiitis, Churg and Strauss syndrome, glomerulonephritis, pauci-immune focal necrotizing glomerulonephritis, crescentic glomerulonephritis (Noel LH. Ann Med Interne (Paris). 2000 May;151 (3):178); antiphospholipid syndrome (Flamholz R. *et al.*, J Clin Apheresis 1999;14 (4):171); heart failure, agonist-like β -adrenoceptor antibodies in

30 heart failure (Wallukat G. *et al.*, Am J Cardiol. 1999 Jun 17;83 (12A):75H), thrombocytopenic purpura (Moccia F. Ann Ital Med Int. 1999 Apr-Jun;14 (2):114); hemolytic anemia, autoimmune hemolytic anemia (Efremov DG. *et al.*, Leuk Lymphoma 1998 Jan;28 (3-4):285), gastrointestinal diseases, autoimmune diseases of the

gastrointestinal tract, intestinal diseases, chronic inflammatory intestinal disease (Garcia Herola A. *et al.*, Gastroenterol Hepatol. 2000 Jan;23 (1):16), celiac disease (Landau YE. and Shoenfeld Y. Harefuah 2000 Jan 16;138 (2):122), autoimmune diseases of the musculature, myositis, autoimmune myositis, Sjogren's syndrome (Feist E. *et al.*, Int Arch
 5 Allergy Immunol 2000 Sep;123 (1):92); smooth muscle autoimmune disease (Zauli D. *et al.*, Biomed Pharmacother 1999 Jun;53 (5-6):234), hepatic diseases, hepatic autoimmune diseases, autoimmune hepatitis (Manns MP. J Hepatol 2000 Aug;33 (2):326) and primary biliary cirrhosis (Strassburg CP. *et al.*, Eur J Gastroenterol Hepatol. 1999 Jun;11 (6):595).

Type IV or T cell mediated hypersensitivity, include, but are not limited to,
 10 rheumatoid diseases, rheumatoid arthritis (Tisch R, McDevitt HO. Proc Natl Acad Sci U S A 1994 Jan 18;91 (2):437), systemic diseases, systemic autoimmune diseases, systemic lupus erythematosus (Datta SK., Lupus 1998;7 (9):591), glandular diseases, glandular autoimmune diseases, pancreatic diseases, pancreatic autoimmune diseases, Type 1 diabetes (Castano L. and Eisenbarth GS. Ann. Rev. Immunol. 8:647); thyroid diseases,
 15 autoimmune thyroid diseases, Graves' disease (Sakata S. *et al.*, Mol Cell Endocrinol 1993 Mar;92 (1):77); ovarian diseases (Garza KM. *et al.*, J Reprod Immunol 1998 Feb;37 (2):87), prostatitis, autoimmune prostatitis (Alexander RB. *et al.*, Urology 1997 Dec;50 (6):893), polyglandular syndrome, autoimmune polyglandular syndrome, Type I autoimmune polyglandular syndrome (Hara T. *et al.*, Blood. 1991 Mar 1;77 (5):1127),
 20 neurological diseases, autoimmune neurological diseases, multiple sclerosis, neuritis, optic neuritis (Soderstrom M. *et al.*, J Neurol Neurosurg Psychiatry 1994 May;57 (5):544), myasthenia gravis (Oshima M. *et al.*, Eur J Immunol 1990 Dec;20 (12):2563), stiff-man syndrome (Hiemstra HS. *et al.*, Proc Natl Acad Sci U S A 2001 Mar 27;98 (7):3988), cardiovascular diseases, cardiac autoimmunity in Chagas' disease (Cunha-Neto E. *et al.*, J
 25 Clin Invest 1996 Oct 15;98 (8):1709), autoimmune thrombocytopenic purpura (Semple JW. *et al.*, Blood 1996 May 15;87 (10):4245), anti-helper T lymphocyte autoimmunity (Caporossi AP. *et al.*, Viral Immunol 1998;11 (1):9), hemolytic anemia (Sallah S. *et al.*, Ann Hematol 1997 Mar;74 (3):139), hepatic diseases, hepatic autoimmune diseases, hepatitis, chronic active hepatitis (Franco A. *et al.*, Clin Immunol Immunopathol 1990
 30 Mar;54 (3):382), biliary cirrhosis, primary biliary cirrhosis (Jones DE. Clin Sci (Colch) 1996 Nov;91 (5):551), nephric diseases, nephric autoimmune diseases, nephritis, interstitial nephritis (Kelly CJ. J Am Soc Nephrol 1990 Aug;1 (2):140), connective tissue diseases, ear diseases, autoimmune connective tissue diseases, autoimmune ear disease

(Yoo TJ. *et al.*, Cell Immunol 1994 Aug;157 (1):249), disease of the inner ear (Gloddek B. *et al.*, Ann N Y Acad Sci 1997 Dec 29;830:266), skin diseases, cutaneous diseases, dermal diseases, bullous skin diseases, pemphigus vulgaris, bullous pemphigoid and pemphigus foliaceus.

5 Examples of delayed type hypersensitivity include, but are not limited to, contact dermatitis and drug eruption.

 Examples of types of T lymphocyte mediating hypersensitivity include, but are not limited to, helper T lymphocytes and cytotoxic T lymphocytes.

 Examples of helper T lymphocyte-mediated hypersensitivity include, but are not
10 limited to, T_H1 lymphocyte mediated hypersensitivity and T_H2 lymphocyte mediated hypersensitivity.

Autoimmune diseases

 Include, but are not limited to, cardiovascular diseases, rheumatoid diseases, glandular diseases, gastrointestinal diseases, cutaneous diseases, hepatic diseases,
15 neurological diseases, muscular diseases, nephric diseases, diseases related to reproduction, connective tissue diseases and systemic diseases.

 Examples of autoimmune cardiovascular diseases include, but are not limited to atherosclerosis (Matsuura E. *et al.*, Lupus. 1998;7 Suppl 2:S135), myocardial infarction (Vaarala O. Lupus. 1998;7 Suppl 2:S132), thrombosis (Tincani A. *et al.*, Lupus 1998;7
20 Suppl 2:S107-9), Wegener's granulomatosis, Takayasu's arteritis, Kawasaki syndrome (Praprotnik S. *et al.*, Wien Klin Wochenschr 2000 Aug 25;112 (15-16):660), anti-factor VIII autoimmune disease (Lacroix-Desmazes S. *et al.*, Semin Thromb Hemost.2000;26 (2):157), necrotizing small vessel vasculitis, microscopic polyangiitis, Churg and Strauss syndrome, pauci-immune focal necrotizing and crescentic glomerulonephritis (Noel LH.
25 Ann Med Interne (Paris). 2000 May;151 (3):178), antiphospholipid syndrome (Flamholz R. *et al.*, J Clin Apheresis 1999;14 (4):171), antibody-induced heart failure (Wallukat G. *et al.*, Am J Cardiol. 1999 Jun 17;83 (12A):75H), thrombocytopenic purpura (Moccia F. Ann Ital Med Int. 1999 Apr-Jun;14 (2):114; Semple JW. *et al.*, Blood 1996 May 15;87 (10):4245), autoimmune hemolytic anemia (Efremov DG. *et al.*, Leuk Lymphoma 1998
30 Jan;28 (3-4):285; Sallah S. *et al.*, Ann Hematol 1997 Mar;74 (3):139), cardiac autoimmunity in Chagas' disease (Cunha-Neto E. *et al.*, J Clin Invest 1996 Oct 15;98 (8):1709) and anti-helper T lymphocyte autoimmunity (Caporossi AP. *et al.*, Viral Immunol 1998;11 (1):9).

Examples of autoimmune rheumatoid diseases include, but are not limited to rheumatoid arthritis (Krenn V. *et al.*, *Histol Histopathol* 2000 Jul;15 (3):791; Tisch R, McDevitt HO. *Proc Natl Acad Sci units S A* 1994 Jan 18;91 (2):437) and ankylosing spondylitis (Jan Voswinkel *et al.*, *Arthritis Res* 2001; 3 (3): 189).

5 Examples of autoimmune glandular diseases include, but are not limited to, pancreatic disease, Type I diabetes, thyroid disease, Graves' disease, thyroiditis, spontaneous autoimmune thyroiditis, Hashimoto's thyroiditis, idiopathic myxedema, ovarian autoimmunity, autoimmune anti-sperm infertility, autoimmune prostatitis and Type I autoimmune polyglandular syndrome. diseases include, but are not limited to
10 autoimmune diseases of the pancreas, Type 1 diabetes (Castano L. and Eisenbarth GS. *Ann. Rev. Immunol.* 8:647; Zimmet P. *Diabetes Res Clin Pract* 1996 Oct;34 Suppl:S125), autoimmune thyroid diseases, Graves' disease (Orgiazzi J. *Endocrinol Metab Clin North Am* 2000 Jun;29 (2):339; Sakata S. *et al.*, *Mol Cell Endocrinol* 1993 Mar;92 (1):77), spontaneous autoimmune thyroiditis (Braley-Mullen H. and Yu S, *J Immunol* 2000 Dec
15 15;165 (12):7262), Hashimoto's thyroiditis (Toyoda N. *et al.*, *Nippon Rinsho* 1999 Aug;57 (8):1810), idiopathic myxedema (Mitsuma T. *Nippon Rinsho.* 1999 Aug;57 (8):1759), ovarian autoimmunity (Garza KM. *et al.*, *J Reprod Immunol* 1998 Feb;37 (2):87), autoimmune anti-sperm infertility (Dickman AB. *et al.*, *Am J Reprod Immunol.* 2000 Mar;43 (3):134), autoimmune prostatitis (Alexander RB. *et al.*, *Urology* 1997 Dec;50
20 (6):893) and Type I autoimmune polyglandular syndrome (Hara T. *et al.*, *Blood.* 1991 Mar 1;77 (5):1127).

Examples of autoimmune gastrointestinal diseases include, but are not limited to, chronic inflammatory intestinal diseases (Garcia Herola A. *et al.*, *Gastroenterol Hepatol.* 2000 Jan;23 (1):16), celiac disease (Landau YE. and Shoenfeld Y. *Harefuah* 2000 Jan
25 16;138 (2):122), colitis, ileitis and Crohn's disease.

Examples of autoimmune cutaneous diseases include, but are not limited to, autoimmune bullous skin diseases, such as, but are not limited to, pemphigus vulgaris, bullous pemphigoid and pemphigus foliaceus.

Examples of autoimmune hepatic diseases include, but are not limited to, hepatitis, autoimmune chronic active hepatitis (Franco A. *et al.*, *Clin Immunol Immunopathol* 1990
30 Mar;54 (3):382), primary biliary cirrhosis (Jones DE. *Clin Sci (Colch)* 1996 Nov;91 (5):551; Strassburg CP. *et al.*, *Eur J Gastroenterol Hepatol.* 1999 Jun;11 (6):595) and autoimmune hepatitis (Manns MP. *J Hepatol* 2000 Aug;33 (2):326).

Examples of autoimmune neurological diseases include, but are not limited to, multiple sclerosis (Cross AH. *et al.*, J Neuroimmunol 2001 Jan 1;112 (1-2):1), Alzheimer's disease (Oron L. *et al.*, J Neural Transm Suppl. 1997;49:77), myasthenia gravis (Infante AJ. And Kraig E, Int Rev Immunol 1999;18 (1-2):83; Oshima M. *et al.*, Eur J Immunol 5 1990 Dec;20 (12):2563), neuropathies, motor neuropathies (Kornberg AJ. J Clin Neurosci. 2000 May;7 (3):191); Guillain-Barre syndrome and autoimmune neuropathies (Kusunoki S. Am J Med Sci. 2000 Apr;319 (4):234), myasthenia, Lambert-Eaton myasthenic syndrome (Takamori M. Am J Med Sci. 2000 Apr;319 (4):204); paraneoplastic neurological diseases, cerebellar atrophy, paraneoplastic cerebellar atrophy and stiff-man 10 syndrome (Hiemstra HS. *et al.*, Proc Natl Acad Sci units S A 2001 Mar 27;98 (7):3988); non-paraneoplastic stiff man syndrome, progressive cerebellar atrophies, encephalitis, Rasmussen's encephalitis, amyotrophic lateral sclerosis, Sydeham chorea, Gilles de la Tourette syndrome and autoimmune polyendocrinopathies (Antoine JC. and Honnorat J. Rev Neurol (Paris) 2000 Jan;156 (1):23); dysimmune neuropathies (Nobile-Orazio E. *et al.*, 15 Electroencephalogr Clin Neurophysiol Suppl 1999;50:419); acquired neuromyotonia, arthrogryposis multiplex congenita (Vincent A. *et al.*, Ann N Y Acad Sci. 1998 May 13;841:482), neuritis, optic neuritis (Soderstrom M. *et al.*, J Neurol Neurosurg Psychiatry 1994 May;57 (5):544) and neurodegenerative diseases.

Examples of autoimmune muscular diseases include, but are not limited to, 20 myositis, autoimmune myositis and primary Sjogren's syndrome (Feist E. *et al.*, Int Arch Allergy Immunol 2000 Sep;123 (1):92) and smooth muscle autoimmune disease (Zauli D. *et al.*, Biomed Pharmacother 1999 Jun;53 (5-6):234).

Examples of autoimmune nephric diseases include, but are not limited to, nephritis and autoimmune interstitial nephritis (Kelly CJ. J Am Soc Nephrol 1990 Aug;1 (2):140).

25 Examples of autoimmune diseases related to reproduction include, but are not limited to, repeated fetal loss (Tincani A. *et al.*, Lupus 1998;7 Suppl 2:S107-9).

Examples of autoimmune connective tissue diseases include, but are not limited to, ear diseases, autoimmune ear diseases (Yoo TJ. *et al.*, Cell Immunol 1994 Aug;157 (1):249) and autoimmune diseases of the inner ear (Gloddek B. *et al.*, Ann N Y Acad Sci 30 1997 Dec 29;830:266).

Examples of autoimmune systemic diseases include, but are not limited to, systemic lupus erythematosus (Erikson J. *et al.*, Immunol Res 1998;17 (1-2):49) and

systemic sclerosis (Renaudineau Y. *et al.*, Clin Diagn Lab Immunol. 1999 Mar;6 (2):156); Chan OT. *et al.*, Immunol Rev 1999 Jun;169:107).

Infectious diseases

Examples of infectious diseases include, but are not limited to, chronic infectious
5 diseases, subacute infectious diseases, acute infectious diseases, viral diseases, bacterial diseases, protozoan diseases, parasitic diseases, fungal diseases, mycoplasma diseases and prion diseases.

According to a specific embodiment, the inflammatory disease is not an infectious disease.

10 According to a specific embodiment, the inflammatory disease is not a viral disease.

According to a specific embodiment, the inflammatory disease is not a Coronavirus infection (e.g., COVID19).

According to a specific embodiment, the inflammatory disease comprises diabetes.

15 According to a specific embodiment, the diabetes comprises type I diabetes.

According to a specific embodiment, the diabetes comprises type II diabetes.

According to a specific embodiment, the diabetes comprises gestational diabetes.

Graft rejection diseases

Examples of diseases associated with transplantation of a graft include, but are not
20 limited to, graft rejection, chronic graft rejection, subacute graft rejection, hyperacute graft rejection, acute graft rejection and graft versus host disease.

Allergic diseases

Examples of allergic diseases include, but are not limited to, asthma, hives, urticaria, pollen allergy, dust mite allergy, venom allergy, cosmetics allergy, latex allergy,
25 chemical allergy, drug allergy, insect bite allergy, animal dander allergy, stinging plant allergy, poison ivy allergy and food allergy.

Further examples of diseases with an inflammatory component include cholesterol disorders, hair loss, depression, hormonal disorders. It is further acknowledged herein that the compositions of the present invention are useful for treating and preventing
30 appendicitis.

There are three types of glycosylation disorders sorted by the type of alterations that are made to the glycosylation process: congenital alterations, acquired alterations and non-enzymatic acquired alterations.

1) Congenital alterations: Over 40 congenital disorders of glycosylation (CGDs) have been reported in humans.^[27] These can be divided into four groups: disorders of protein *N*-glycosylation, disorders of protein *O*-glycosylation, disorders of lipid glycosylation and disorders of other glycosylation pathways and of multiple glycosylation pathways. No effective treatment is known for any of these disorders. 80% of these affect the nervous system.^[citation needed]

<https://www.sciencedirect.com/science/article/pii/B9780444595652000447?via=ihub>

2) Acquired alterations: In this second group the main disorders are infectious diseases, autoimmune illnesses or cancer. In these cases, the changes in glycosylation are the cause of certain biological events. For example, in Rheumatoid Arthritis (RA), the body of the patient produces antibodies against the enzyme lymphocytes galactosyltransferase which inhibits the glycosylation of IgG. Therefore, the changes in the *N*-glycosylation produce the immunodeficiency involved in this illness. In this second group we can also find disorders caused by mutations on the enzymes that control the glycosylation of Notch proteins, such as Alagille syndrome.^[26]

Non-enzymatic acquired alterations: Non-enzymatic disorders, are also acquired, but they are due to the lack of enzymes that attach oligosaccharides to the protein. In this group the illnesses that stand out are Alzheimers disease and diabetes.^[28]

All these diseases are difficult to diagnose because they do not only affect one organ, they affect many of them and in different ways. As a consequence, they are also hard to treat. However, thanks to the many advances that have been made in next-generation sequencing, scientists can now understand better these disorders and have discovered new CDGs.^[29]

It is herein acknowledged that embodiments of the present invention are directed towards congenital disorders of glycosylation:

Congenital disorders of glycosylation (CDG) are genetic diseases due to defects in the synthesis or the attachment of the glycan moiety of glycoproteins and glycolipids.

- 5 They can be divided into four groups: disorders of protein N-glycosylation, disorders of protein O-glycosylation, disorders of lipid glycosylation, and disorders of other glycosylation pathways and of multiple glycosylation pathways. Of the more than 40 reported CDG, some 80% are neurological or have an important neurological component. By far the most common neurological CDG is phosphomannomutase 2
- 10 deficiency. Isoelectrofocusing of serum transferrin, the most widely used screening test, picks up only CDG associated with sialic acid deficiency of N-linked glycans. Predominant neurological signs and symptoms are psychomotor retardation, epilepsy, hypotonia, hyporeflexia, strabismus, retinitis pigmentosa, polyneuropathy, myopathy, and cerebellar hypotrophy/hypoplasia. All known neurological CDG have an
- 15 autosomal recessive inheritance except for IAP-CDG, an X-linked pure mental retardation syndrome. No curative or effective treatment is available for neurological CDG. Since at least 1% of the genome is involved in glycosylation, it is likely that the large majority of CDG is yet to be discovered. In 2008, a novel nomenclature was introduced using the gene symbol followed by -CDG, e.g., CDG-1a becomes PMM2-
- 20 CDG. CDG should be looked for in any unexplained neurological syndrome.

- 25 It is herein acknowledged that embodiments of the present invention are directed towards treatment of autoimmune diseases namely;

Achalasia

Addison's disease

Adult Still's disease

Agammaglobulinemia

Alopecia areata

Amyloidosis

5 Ankylosing spondylitis

Anti-GBM/Anti-TBM nephritis

Antiphospholipid syndrome

Autoimmune angioedema

Autoimmune dysautonomia

10 Autoimmune encephalomyelitis

Autoimmune hepatitis

Autoimmune inner ear disease (AIED)

Autoimmune myocarditis

Autoimmune oophoritis

15 Autoimmune orchitis

Autoimmune pancreatitis

Autoimmune retinopathy

Autoimmune urticaria

- Axonal & neuronal neuropathy (AMAN)
- Baló disease
- Behcet's disease
- Benign mucosal pemphigoid
- 5 Bullous pemphigoid
- Castleman disease (CD)
- Celiac disease
- Chagas disease
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- 10 Chronic recurrent multifocal osteomyelitis (CRMO)
- Churg-Strauss Syndrome (CSS) or Eosinophilic Granulomatosis (EGPA)
- Cicatricial pemphigoid
- Cogan's syndrome
- Cold agglutinin disease
- 15 Congenital heart block
- Coxsackie myocarditis
- CREST syndrome
- Crohn's disease

Dermatitis herpetiformis

Dermatomyositis

Devic's disease (neuromyelitis optica)

Discoid lupus

5 Dressler's syndrome

Endometriosis

Eosinophilic esophagitis (EoE)

Eosinophilic fasciitis

Erythema nodosum

10 Essential mixed cryoglobulinemia

Evans syndrome

Fibromyalgia

Fibrosing alveolitis

Giant cell arteritis (temporal arteritis)

15 Giant cell myocarditis

Glomerulonephritis

Goodpasture's syndrome

Granulomatosis with Polyangitis

Graves' disease

Guillain-Barre syndrome

Hashimoto's thyroiditis

Hemolytic anemia

5 Henoch-Schonlein purpura (HSP)

Herpes gestationis or pemphigoid gestationis (PG)

Hidradenitis Suppurativa (HS) (Acne Inversa)

Hypogammaglobulinemia

IgA Nephropathy

10 IgG4-related sclerosing disease

Immune thrombocytopenic purpura (ITP)

Inclusion body myositis (IBM)

Interstitial cystitis (IC)

Juvenile arthritis

15 Juvenile diabetes (Type 1 diabetes)

Juvenile myositis (JM)

Kawasaki disease

Lambert-Eaton syndrome

Leukocytoclastic vasculitis

Lichen planus

Lichen sclerosis

Ligneous conjunctivitis

5 Linear IgA disease (LAD)

Lupus

Lyme disease chronic

Meniere's disease

Microscopic polyangiitis (MPA)

10 Mixed connective tissue disease (MCTD)

Mooren's ulcer

Mucha-Habermann disease

Multifocal Motor Neuropathy (MMN) or MMNCB

Multiple sclerosis

15 Myasthenia gravis

Myositis

Narcolepsy

Neonatal Lupus

Neuromyelitis optica

Neutropenia

Ocular cicatricial pemphigoid

Optic neuritis

5 Palindromic rheumatism (PR)

PANDAS

Paraneoplastic cerebellar degeneration (PCD)

Paroxysmal nocturnal hemoglobinuria (PNH)

Parry Romberg syndrome

10 Pars planitis (peripheral uveitis)

Parsonage-Turner syndrome

Pemphigus

Peripheral neuropathy

Perivenous encephalomyelitis

15 Pernicious anemia (PA)

POEMS syndrome

Polvarteritis nodosa

Polyglandular syndromes type I, II, III

Polymyalgia rheumatica

Polymyositis

Postmyocardial infarction syndrome

Postpericardiotomy syndrome

5 Primary Biliary Cholangitis

Primary sclerosing cholangitis

Progesterone dermatitis

Psoriasis

Psoriatic arthritis

10 Pure red cell aplasia (PRCA)

Pvoderma gangrenosum

Ravnaud's phenomenon

Reactive Arthritis

Reflex sympathetic dystrophy

15 Relapsing polychondritis

Restless legs syndrome (RLS)

Retroperitoneal fibrosis

Rheumatic fever

Rheumatoid arthritis

Sarcoidosis

Schmidt syndrome

Scleritis

5 Scleroderma

Sjögren's syndrome

Sperm & testicular autoimmunity

Stiff person syndrome (SPS)

Subacute bacterial endocarditis (SBE)

10 Susac's syndrome

Sympathetic ophthalmia (SO)

Takayasu's arteritis

Temporal arteritis/Giant cell arteritis

Thrombocytopenic purpura (TTP)

15 Thyroid eye disease (TED)

Tolosa-Hunt syndrome (THS)

Transverse myelitis

Type 1 diabetes

Ulcerative colitis (UC)

Undifferentiated connective tissue disease (UCTD)

Uveitis

Vasculitis

5 Vitiligo

Vogt-Koyanagi-Harada Disease

It is herein acknowledged that embodiments of the present invention are directed towards Central nervous system diseases, such as those described below:

Neurodegeneration is the progressive loss of structure or function of neurons, including their death. Many neurodegenerative diseases—including amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, Alzheimer's disease, Huntington's disease, and prion diseases—occur as a result of neurodegenerative processes. Such diseases are incurable, resulting in progressive degeneration of neurons.^[1] As research progresses, many similarities appear that relate these diseases to one another on a sub-cellular level. Discovering these similarities offers hope for therapeutic advances that could ameliorate many diseases simultaneously. There are many parallels between different neurodegenerative disorders including atypical protein assemblies as well as induced cell death.^{[2][3]} Neurodegeneration can be found in many different levels of neuronal circuitry ranging from molecular to systemic.

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25 *Cancerous diseases*

Examples of cancer include but are not limited to carcinoma, lymphoma, blastoma, sarcoma, and leukemia. Particular examples of cancerous diseases but are not limited to: Myeloid leukemia such as Chronic myelogenous leukemia. Acute myelogenous leukemia with maturation. Acute promyelocytic leukemia, Acute nonlymphocytic leukemia with
5 increased basophils, Acute monocytic leukemia. Acute myelomonocytic leukemia with eosinophilia; Malignant lymphoma, such as Birkitt's Non-Hodgkin's; Lymphocytic leukemia, such as Acute lymphoblastic leukemia. Chronic lymphocytic leukemia; Myeloproliferative diseases, such as solid tumors Benign Meningioma, Mixed tumors of salivary gland, Colonic adenomas; Adenocarcinomas, such as Small cell lung cancer,
10 Kidney, Uterus, Prostate, Bladder, Ovary, Colon, Sarcomas, Liposarcoma, myxoid, Synovial sarcoma, Rhabdomyosarcoma (alveolar), Extraskelitel myxoid chondrosarcoma, Ewing's tumor; other include Testicular and ovarian dysgerminoma, Retinoblastoma, Wilms' tumor, Neuroblastoma, Malignant melanoma, Mesothelioma, breast, skin, prostate, and ovarian.

15 According to a specific embodiment, the cancer is a non-solid tumor, e.g., blood/hematologic cancer.

According to a specific embodiment, the inflammatory disease is not a solid tumor.

The composition of matter comprising the component(s) (a plant species or genus thereof-derived component selected from the group consisting of a plant part, extract
20 thereof, fraction thereof, active ingredient thereof, synthetic analog thereof, mimetic thereof or combination thereof, wherein said component is capable of treating inflammation) of the present invention can be administered to the subject *per se*, or in a pharmaceutical composition where it is mixed with suitable carriers or excipients.

As used herein a "pharmaceutical composition" refers to a preparation of one or
25 more of the active ingredients described herein with other chemical components such as physiologically suitable carriers and excipients. The purpose of a pharmaceutical composition is to facilitate administration of a compound to an organism.

Herein the term "active ingredient" refers to the composition of matter comprising the components accountable for the biological effect.

30 Hereinafter, the phrases "physiologically acceptable carrier" and "pharmaceutically acceptable carrier" which may be interchangeably used refer to a carrier or a diluent that does not cause significant irritation to an organism and does not abrogate the biological

activity and properties of the administered compound. An adjuvant is included under these phrases.

Herein the term "excipient" refers to an inert substance added to a pharmaceutical composition to further facilitate administration of an active ingredient. Examples, without
5 limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils and polyethylene glycols.

Techniques for formulation and administration of drugs may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition, which is incorporated herein by reference.

10 Suitable routes of administration may, for example, include oral, rectal, transmucosal, especially transnasal, intestinal or parenteral delivery, including intramuscular, subcutaneous and intramedullary injections as well as intrathecal, direct intraventricular, intracardiac, e.g., into the right or left ventricular cavity, into the common coronary artery, intravenous, intraperitoneal, intranasal, or intrapulmonary or intraocular
15 injections.

In various exemplary embodiments of the invention, the composition is provided as a pharmaceutical or dietary supplement dosage form suitable for oral administration. Dosage forms suitable for oral administration include tablets, soft capsules, hard capsules, pills, granules, powders, emulsions, suspensions, sprays, syrups and pellets. In various
20 other embodiments of the invention, the composition is provided as a pharmaceutical dosage form suitable for parenteral administration such as liquid formulations for administration as drops or by injection, or as solid or semisolid dosage forms for suppositories.

Conventional approaches for drug delivery to the central nervous system (CNS)
25 include: neurosurgical strategies (e.g., intracerebral injection or intracerebroventricular infusion); molecular manipulation of the agent (e.g., production of a chimeric fusion protein that comprises a transport polypeptide that has an affinity for an endothelial cell surface molecule in combination with an agent that is itself incapable of crossing the BBB) in an attempt to exploit one of the endogenous transport pathways of the BBB; pharmacological strategies designed to increase the lipid solubility of an agent (e.g.,
30 conjugation of water-soluble agents to lipid or cholesterol carriers); and the transitory disruption of the integrity of the BBB by hyperosmotic disruption (resulting from the infusion of a mannitol solution into the carotid artery or the use of a biologically active

agent such as an angiotensin polypeptide). However, each of these strategies has limitations, such as the inherent risks associated with an invasive surgical procedure, a size limitation imposed by a limitation inherent in the endogenous transport systems, potentially undesirable biological side effects associated with the systemic administration
5 of a chimeric molecule comprised of a carrier motif that could be active outside of the CNS, and the possible risk of brain damage within regions of the brain where the BBB is disrupted, which renders it a suboptimal delivery method.

Alternately, one may administer the pharmaceutical composition in a local rather than systemic manner, for example, via injection of the pharmaceutical composition
10 directly into a tissue region of a patient.

Pharmaceutical compositions of some embodiments of the invention may be manufactured by processes well known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

15 Pharmaceutical compositions for use in accordance with some embodiments of the invention thus may be formulated in conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries, which facilitate processing of the active ingredients into preparations which, can be used pharmaceutically. Proper formulation is dependent upon the route of administration chosen.

20 For injection, the active ingredients of the pharmaceutical composition may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological salt buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

25 For oral administration, the pharmaceutical composition can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the pharmaceutical composition to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for oral ingestion by a patient. Pharmacological preparations for oral use can be made using a solid
30 excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat

starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carbomethylcellulose; and/or physiologically acceptable polymers such as polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, titanium dioxide, lacquer solutions and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical compositions which can be used orally, include push-fit capsules made of gelatin as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules may contain the active ingredients in admixture with filler such as lactose, binders such as starches, lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active ingredients may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for the chosen route of administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

In specific embodiments, the components and/or compositions of the invention are provided in form suitable for administration by inhalation or nasal administration.

For administration by nasal inhalation, the active ingredients for use according to some embodiments of the invention are conveniently delivered in the form of an aerosol spray presentation from a pressurized pack or a nebulizer with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane or carbon dioxide. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin for use in a dispenser may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The pharmaceutical composition described herein may be formulated for parenteral administration, e.g., by bolus injection or continuous infusion. Formulations for injection

may be presented in unit dosage form, e.g., in ampoules or in multidose containers with optionally, an added preservative. The compositions may be suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

5 Pharmaceutical compositions for parenteral administration include aqueous solutions of the active preparation in water-soluble form. Additionally, suspensions of the active ingredients may be prepared as appropriate oily or water based injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acids esters such as ethyl oleate, triglycerides or liposomes. Aqueous
10 injection suspensions may contain substances, which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the active ingredients to allow for the preparation of highly concentrated solutions.

 Alternatively, the active ingredient may be in powder form for constitution with a
15 suitable vehicle, e.g., sterile, pyrogen-free water based solution, before use.

 The pharmaceutical composition of some embodiments of the invention may also be formulated in rectal compositions such as suppositories or retention enemas, using, e.g., conventional suppository bases such as cocoa butter or other glycerides.

 Pharmaceutical compositions suitable for use in context of some embodiments of
20 the invention include compositions wherein the active ingredients are contained in an amount effective to achieve the intended purpose. More specifically, a therapeutically effective amount means an amount of active ingredients (composition of matter comprising the components accountable for the biological effect) effective to prevent, alleviate or ameliorate symptoms or progress of a disorder (e.g. inflammatory disease) or prolong the
25 survival of the subject being treated.

 Determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

 For example, any in vivo or in vitro method of evaluating the severity of the inflammation or related symptoms may be employed.

30 For any preparation used in the methods of the invention, the therapeutically effective amount or dose can be estimated initially from in vitro and cell culture assays. For example, a dose can be formulated in animal models to achieve a desired concentration or titer. Such information can be used to more accurately determine useful doses in

humans. Description of some relevant animal models for inflammatory diseases and autoimmune diseases are provided infra.

Toxicity and therapeutic efficacy of the active ingredients described herein can be determined by standard pharmaceutical procedures in vitro, in cell cultures or experimental
5 animals. The data obtained from these in vitro and cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage may vary depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g., Fingl, et al., 1975, in "The
10 Pharmacological Basis of Therapeutics", Ch. 1 p.1).

Dosage amount and interval may be adjusted individually to provide the active ingredient at a sufficient amount to induce or suppress the biological effect (minimal effective concentration, MEC). The MEC will vary for each preparation, but can be estimated from in vitro data. Dosages necessary to achieve the MEC will depend on
15 individual characteristics and route of administration. Detection assays can be used to determine plasma concentrations.

Depending on the severity and responsiveness of the condition to be treated, dosing can be of a single or a plurality of administrations, with course of treatment lasting from several days to several weeks or until cure is effected or diminution of the disease state is
20 achieved.

The amount of a composition to be administered will, of course, be dependent on the subject being treated, the severity of the affliction, the manner of administration, the judgment of the prescribing physician, etc.

25

Systemic Lupus Erythematosus (SLE)

The New Zealand Black (NZB) and the New Zealand White (NZW) mouse, (NZB × NZW)F1, is a spontaneous model which develops a lupus-like disease.

Multiple Sclerosis

30 For example, experimental autoimmune encephalomyelitis (EAE) has been widely used as a model of multiple sclerosis. In this model, spinal cord homogenate or a protein derivative such as myelin basic protein is injected with a mixture of potent immunostimulants, most commonly in mice from the SJL strain.

Diabetes

Five animal models of spontaneous diabetes are mainly preferred for studying autoimmune diabetes: the NOD mouse, the diabetes-prone BB rat, the LETL rat, the KDP rat and the LEW-iddm rat. NOD mouse and BB rat are the most widely used.

5 Rheumatoid Arthritis

Animal models have been used extensively in studies of rheumatoid arthritis pathogenesis. Despite the inherent limitations of all animal models, several rodent models have significantly progressed our understanding of the fundamental mechanisms underpinning rheumatoid arthritis and contributed to several current major advances in
10 treatment. These models include the induced arthritis models such as collagen-induced arthritis, collagen-antibody-induced arthritis, zymosan-induced arthritis, and the methylated BSA model, and the genetically manipulated or spontaneous arthritis models such as the TNF-alpha-transgenic mouse, K/BxN mouse, and the Skg mouse.

Crohn's disease (CD) and Ulcerative Colitis (UC)

15 Dextran sulfate sodium

Dextran sulfate sodium (DSS) is a polyanionic derivative of dextran with a chemical formula of $(C_6H_7 Na_3O_{14}S_3)_n$. DSS is most commonly administered in the drinking water for peroral treatment of the animals with the compound. The concentration of the compound which is often used is 3%. An inflammatory response is initiated by DSS
20 in wild-type animals which starts distally after about 5 days and is limited to the colonic mucosa. It is still not well understood how DSS starts the inflammation in the colon. However, a recent study investigating DSS both *in vitro* and *in vivo* revealed that DSS has a direct effect on the inner mucus layer, leading to bacterial penetration of this layer before any inflammatory signs could be seen. Thus, it can be concluded that a loss of the inner
25 colon mucus layer is the initial episode leading to bacterial penetration and ultimately, the development of an inflammatory response.

2, 4, 6-trinitrobenzene sulfonic acid

Trinitrobenzene sulfonic acid (TNBS) is an oxidizing Nitroaryl compound which is administered intrarectally in animals to induce IBD. It causes induction of colonic damage
30 which leads to necrotic regions associated with inflammatory areas. High myeloperoxidase activity causes damage mainly characterized by neutrophilic infiltration into the colonic tissue. An increase in the mucosal permeability is a result of the damage to the colonic epithelium and interstitium. TNBS may cause a decrease in the mucosal hydrophobicity by

interacting with the phospholipids present on the surface of the colonic mucosa. This decreased hydrophobicity is believed to contribute to TNBS-induced inflammation of the colon. TNBS causes necrosis and deep tissue damage which mimics the transmural involvement of CD; hence, it may be preferred to be a better experimental model of CD rather than UC.

TNBS-induced colitis models have helped to be an important source for generating vital information about the cytokines involved in the human IBD. It has also helped in shaping the therapy regimens of the human disease.

Oxazolone colitis

Intrarectal administration of the hapten compound oxazolone along with ethanol in animals causes acute colitis. Oxazolone leads to acute superficial mucosal inflammation in the distal part of colon. There is colonic infiltration by lymphocytes and neutrophils along with associated edema in lamina propria. There is type helper 2 (Th2) cell-mediated immune response with an elevation in the production of interleukins. This animal model is distinguished from TNBS-induced colitis by the presence of Th2-mediated response instead of Th1 found in the TNBS model.

Acetic acid-induced colitis

Administration of diluted acetic acid through the rectal route is another method to induce colitis in rodents. The treatment with acetic acid causes colonic mucosal damage which leads to a condition similar to UC.^[10] MacPherson and Pfeiffer were the first ones to demonstrate this model where they administered 10%–50% acetic acid intrarectally to the rat for 10 s, followed by flushing the lumen three times with saline. Acetic acid caused diffuse colitis in a dose-dependent manner in these rodents, with histopathological features including ulceration of the distal colon and crypt abnormalities. The latest practice utilizing 4% acetic acid for 15–30 s.^[13] The low cost of the chemical as well as the ease of administration are few advantages of acetic acid-induced colitis model. The epithelial injury induced by acetic acid is not immunological in the first 24 h. Thus, drugs which target the immune responses should be evaluated after 24 h of induction.

Salmonella-induced colitis

Salmonella typhimurium and *Salmonella* Dublin are Gram-negative bacteria that can cause foodborne intestinal diseases. Direct administration of *S. typhimurium* to mice orally causes a systemic infection that may resemble the picture of intestinal inflammation after pretreatment with oral antibiotics. The pretreatment helps to disturb the normal

bacterial microflora causing high growth of *S. typhimurium* within 1 day. The intestinal inflammation caused by such colonization has histopathological characteristics which are similar to the human UC in terms of epithelial crypt damage and infiltration of neutrophils. The induction of colitis causes the systemic infection within 5–7 days of infection.

5 Adherent-invasive *Escherichia coli*

Adherent-invasive *Escherichia coli* (AIEC) could adhere to the epithelial cells of both small and large intestine with equal affinity.^[15] However, AIEC infection cannot induce colitis on its own. During the entire course of AIEC infection, colonic inflammation is induced in animal models using the infection along with low-dose DSS administration to
10 cause mild epithelial damage. Disruption of the intestinal microflora, including the probiotic biofilm, is caused by certain antibiotics which lead to the development of an ideal environment for the opportunistic AIEC to adhere to and invade IECs and macrophages. The changes induced by this model closely resemble the human UC.

Adoptive transfer models of colitis

15 The adoptive transfer model includes the process of transferring T-cells or immune tissue from one mouse into an adoptive host leading to the development of colitis. The various donors and hosts which have been used include:

- CD4+ T-cells transferred into severe combined immunodeficiency (SCID) mice;
- hsp60-specific CD8+ T-lymphocytes into T-cell receptor –/– or SCID mice;
- 20 CD4+ CD25-T-cells into SCID mice.

The adoptive models are well-characterized models of chronic colitis induced by disturbing the T-cell homeostasis. These models are particularly useful in understanding how different T-cell populations might contribute to the pathogenesis of IBD as they rely on the transfer of T cells.

25 Genetic models of colitis

The advancement in the genetic technologies has resulted in the development of multiple genes whose variants may be related to elevated predisposition to IBD. Tools such as genome-wide association study have recognized susceptibility genes. The various murine models containing relevant genetic variants, or those incorporating these newly
30 identified variants, have been used to further explore the genetic contribution to colitis.

Compositions of some embodiments of the invention may, if desired, be presented in a pack or dispenser device, such as an FDA approved kit, which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example,

comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. The pack or dispenser may also be accommodated by a notice associated with the container in a form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals, which
5 notice is reflective of approval by the agency of the form of the compositions or human or veterinary administration. Such notice, for example, may be of labeling approved by the U.S. Food and Drug Administration for prescription drugs or of an approved product insert. Compositions comprising a preparation of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and
10 labeled for treatment of an indicated condition, as is further detailed above.

In another embodiment, the invention provides a nutritional or dietary compositions in the form of foods or beverages, which comprise the component(s) described herein. These foods or beverages comprise various exemplary embodiments of the inventive compositions. These foods or beverages can be prepared or provided as cereals, baby
15 foods, healthy foods, or food for specified health uses such as solid food like chocolate or nutritional bars, semisolid food like cream or jam, or gel; and also as beverages. Specific and non-limiting examples of such food or beverage items include refreshing beverages, lactic acid bacteria beverages, drops, candies, chewing gum, chocolate, gummy candy, yoghurts, ice creams, puddings, soft adzuki bean jellies, jellies, cookies and the like.

20 The plant-derived component or components of the present invention can be administered with other medications to increase therapeutic bioavailability, boost therapeutic efficacy, and minimize side effects.

Anti inflammatory drugs that can be administered in combination with the compositions of some embodiments of the invention include NSAIDS and steroids such as
25 corticosteroids. Examples of anti-inflammatory drugs include, but are not limited to, Alclofenac; Alclometasone Dipropionate; Algestone Acetonide; Alpha Amylase; Amcinafal; Amcinafide; Amfenac Sodium; Amiprilose Hydrochloride; Anakinra; Anirolac; Anitrazafen; Apazone; Balsalazide Disodium; Bendazac; Benoxaprofen; Benzydamine Hydrochloride; Bromelains; Broperamole; Budesonide; Carprofen;
30 Cicloprofen; Cintazone; Cliprofen; Clobetasol Propionate; Clobetasone Butyrate; Clopirac; Cloticasone Propionate; Cormethasone Acetate; Cortodoxone; Deflazacort; Desonide; Desoximetasone; Dexamethasone Dipropionate; Diclofenac Potassium; Diclofenac Sodium; Diflorasone Diacetate; Diflumidone Sodium; Diflunisal; Difluprednate; Diftalone;

Dimethyl Sulfoxide; Drocinonide; Endrysone; Enlimomab; Enolicam Sodium; Epirizole; Etodolac; Etofenamate; Felbinac; Fenamole; Fenbufen; Fenclofenac; Fenclorac; Fendosal; Fenpipalzone; Fentiazac; Flazalone; Fluazacort; Flufenamic Acid; Flumizole; Flunisolid Acetate; Flunixin; Flunixin Meglumine; Fluocortin Butyl; Fluorometholone Acetate; 5 Fluquazone; Flurbiprofen; Fluretofen; Fluticasone Propionate; Furaprofen; Furobufen; Halcinonide; Halobetasol Propionate; Halopredone Acetate; Ibufenac; Ibuprofen; Ibuprofen Aluminum; Ibuprofen Piconol; Ilonidap; Indomethacin; Indomethacin Sodium; Indoprofen; Indoxole; Intrazole; Isoflupredone Acetate; Isoxepac; Isoxicam; Ketoprofen; Lofemizole Hydrochloride; Lomoxicam; Loteprednol Etabonate; Meclofenamate Sodium; 10 Meclofenamic Acid; Meclorison Dibutyrate; Mefenamic Acid; Mesalamine; Meseclazone; Methylprednisolone Suleptanate; Momiflumate; Nabumetone; Naproxen; Naproxen Sodium; Naproxol; Nimazone; Olsalazine Sodium; Orgotein; Orpanoxin; Oxaprozin; Oxyphenbutazone; Paranyline Hydrochloride; Pentosan Polysulfate Sodium; Phenbutazone Sodium Glycerate; Pirfenidone; Piroxicam; Piroxicam Cinnamate; 15 Piroxicam Olamine; Pirprofen; Prednazate; Prifelone; Prodolic Acid; Proquazone; Proxazole; Proxazole Citrate; Rimexolone; Romazarit; Salcolex; Salsalate; Sanguinarium Chloride; Seclazone; Sermetacin; Sudoxicam; Sulindac; Suprofen; Talmetacin; Talniflumate; Talosalate; Tebufelone; Tenidap; Tenidap Sodium; Tenoxicam; Tesicam; Tesimide; Tetrydamine; Tiopinac; Tixocortol Pivalate; Tolmetin; Tolmetin 20 Sodium; Triclonide; Triflumidate; Zidometacin; Zomepirac Sodium.

As used herein the term "about" refers to $\pm 10\%$.

The terms "comprises", "comprising", "includes", "including", "having" and their conjugates mean "including but not limited to".

The term "consisting of" means "including and limited to".

25 The term "consisting essentially of" means that the composition, method or structure may include additional ingredients, steps and/or parts, but only if the additional ingredients, steps and/or parts do not materially alter the basic and novel characteristics of the claimed composition, method or structure.

30 As used herein, the singular form "a", "an" and "the" include plural references unless the context clearly dictates otherwise. For example, the term "a compound" or "at least one compound" may include a plurality of compounds, including mixtures thereof.

Throughout this application, various embodiments of this invention may be presented in a range format. It should be understood that the description in range format is

merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be
5 considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 3, 4, 5, and 6. This applies regardless of the breadth of the range.

Whenever a numerical range is indicated herein, it is meant to include any cited numeral (fractional or integral) within the indicated range. The phrases "ranging/ranges
10 between" a first indicate number and a second indicate number and "ranging/ranges from" a first indicate number "to" a second indicate number are used herein interchangeably and are meant to include the first and second indicated numbers and all the fractional and integral numerals therebetween.

As used herein the term "method" refers to manners, means, techniques and
15 procedures for accomplishing a given task including, but not limited to, those manners, means, techniques and procedures either known to, or readily developed from known manners, means, techniques and procedures by practitioners of the chemical, pharmacological, biological, biochemical and medical arts.

As used herein the term "viral entry mechanism" refers to viral proteins that
20 mediate entry into cells. The viral entry mechanism proteins include attachment proteins and other proteins that are required for entry of non-enveloped and enveloped viruses into cells. Different viruses use different entry proteins, however, both non-enveloped and enveloped viruses share the same two main steps and routes of virus entry; (1) attachment to cell-surface receptors (2) conformational changes of the viral entry proteins or the host-
25 cell receptors, the viral entry can occur either by penetration of the cell membrane (for non-enveloped viruses) or fusion (for enveloped viruses) to the cell membrane (see "Virus entry: molecular mechanisms and biomedical applications", Dimitrov, 2004)

When reference is made to particular sequence listings, such reference is to be
30 understood to also encompass sequences that substantially correspond to its complementary sequence as including minor sequence variations, resulting from, e.g., sequencing errors, cloning errors, or other alterations resulting in base substitution, base deletion or base addition, provided that the frequency of such variations is less than 1 in 50

nucleotides, alternatively, less than 1 in 100 nucleotides, alternatively, less than 1 in 200 nucleotides, alternatively, less than 1 in 500 nucleotides, alternatively, less than 1 in 1000 nucleotides, alternatively, less than 1 in 5,000 nucleotides, alternatively, less than 1 in 10,000 nucleotides.

5 It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination or as suitable in any other described embodiment of the invention.

10 Certain features described in the context of various embodiments are not to be considered essential features of those embodiments, unless the embodiment is inoperative without those elements.

Various embodiments and aspects of the present invention as delineated hereinabove and as claimed in the claims section below find experimental support in the

15 following examples.

EXAMPLES

Reference is now made to the following examples, which together with the above descriptions illustrate some embodiments of the invention in a non limiting fashion.

20

EXAMPLE 1

Case Report

A 34 years old pregnant woman diagnosed with gestational diabetes and treated with glutamin was administered daily with 5 ml sesame oil 100 % w/v (commencing on

25 September 23, 2020 for 4 days and then co-administered with 5 ml sesame oil 100 % w/v (Naissance) and 5 ml 100 % w/v Nigella sativa oil (Better Flex). During oil treatment glucamin was not administered.

Blood glucose levels (mg/dL) were determined at the indicated hours.

Results are shown below.

6 AM	11 AM	15 PM	21 PM	Date
172	154	122	97	10/9/2020
125	109	126	103	11/9/2020

101	88	106	95	12/9/2020
113	84	125	80	13/9/2020
94	90	134	125	14/9/2020
158	159	98	83	15/9/2020
148	ND	154	88	16/9/2020
99	124	90	77	17/9/2020
94	84	89	84	18/9/2020
ND	ND	109	74	21/9/2020
151	86	73	81	23/9/2020
166	154	89	85	24/9/2020
112	134	99	80	25/9/2020
126	112	94	90	26/9/2020
ND	ND	70	83	27/9/2020
91	136	74	80	28/9/2020
130	83	113	85	29/9/2020
116	92	104	82	30/9/2020
101	96	96	95	1/10/2020
ND	ND	151	78	2/10/2020

ND=Not determined

EXAMPLE 2 10/03/21

5

Reduction of Blood Glucose in a Canine Subject.

Tests were carried out on a canine subject before and after oral dosage of the composition of the present invention.

10

Bag Number: 178075 Sticker Number: 2114353

The referring physician: Dr. Ofer Israeli

Owner details: Simba

Animal details: Simba, dog, female

History / Physical examination / Other findings:

- 5 Type of test: Blood count and biochemistry

lab results (Appendix 1)

- 10 The treatment reduced blood glucose from 123 mg/dL to 64 mg/dL measured 2 weeks after beginning treatment

	BEFORE	AFTER	
Blood Glucose	123 mg/dL	64 mg/dL	
NEU#	3.17	5.47	
MONO	2.6	5.0	
MONO#	0.15	0.45	

- 15 Case report : reversal of alopecia and weight loss in a human subject.

A woman was treated with mixtures of the present invention with 8 drops per day over a period of 2-3 months resulting in the reversal of hair loss and weight loss of 4 kg.

20

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended

25 claims.

EXAMPLE 3

Assays for destroying viral entry mechanism proteins by plant components .

COVID – 19 serves as a model for viral entry mechanism attenuation and modification.

5 COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The cell membrane ACE-2 receptor is an attachment and entry site for SARS-CoV-2. The ACE-2 receptor is a type I transmembrane metallopeptidase with homology to ACE, an enzyme long-known to be a key player in the Renin-Angiotensin system (RAS) and a target for the treatment of hypertension. There is evidence that SARS-CoV-2 utilizes

10 ACE-2 as a cellular entry receptor. Zhou et al. showed that SARS-CoV-2 could use ACE-2 from humans, Chinese horseshoe bats, civet cats, and pigs to gain entry into ACE-2-expressing HeLa cells (See Zhou, P., Yang, XL., Wang, XG. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273 (2020)). The spike (S) protein of SARS-CoV-2, which plays a key role in the receptor recognition

15 and cell membrane fusion process, is composed of two subunits, S1 (120 kDa) and S2 (80 kDa). The S1 subunit contains a receptor-binding domain that recognizes and binds to the host receptor angiotensin-converting enzyme 2 (ACE-2). The S2 subunit mediates viral cell membrane fusion by forming a six-helical bundle via the two-heptad repeat domain (see Huang, Y., Yang, C., Xu, Xf. et al. Structural and functional properties of SARS-CoV-2 spike protein: potential antivirus drug development for COVID-19. Acta Pharmacol Sin 41, 1141–1149 (2020)). Interfering, attenuating, impairing the function of the S1 and S2 subunits will eventually lead to an attenuated, impaired and less infective virus.

VIRAL PROTEIN DIGESTION ASSAYS

25 The materials used in all the following viral protein digestion assays are disclosed in table 1.

Table 1

	Company	cat #
Recombinant SARS-CoV-2 S1 Subunit	RayBiotech	230-30161
Recombinant SARS-CoV-2 S2 Subunit	RayBiotech	230-30163
Recombinant SARS-CoV-2 Nucleocapsid	RayBiotech	230-30164
Proteinase K	Sigma	P4850
Instant Blue	Expedeon	ISB11
DMSO	SIGMA	D2650
Criterion™ TGX Stain-Free Precast Midi Gels 4-15%, 18 wells, 30µl	BIORAD	5671084
10X Tris/Glycine/SDS	BIORAD	161-0772
4X Laemmli Sample Buffer	BIORAD	1610747
B-Mercaptoethanol 14.2M	SIGMA	M3148
Precision protein standard	BIORAD	161-0373

Each of the tested plant based treatment was numbered as disclosed in table 2 and the tested combinations complexes were classified as disclosed in table 3

5 Table 2

Treatment No.	Name
1	Oregano Oil
2	Thyme Oil
3	Nigella Sativa
4	Sumac Oil
5	Sesame Oil
6	Olibanum Oil

Table 3

Complex A	Oils 1+2+3
Complex B	Oils 1+2+3+4
Complex C	Oils 1+2+3+4+5
Complex D	Oils 1+2+3+4+5+6

Oils mixtures were prepared by mixing equal amounts of each oil. The mix was then diluted 1:2 with DMSO, to acquire a solution of 50% DMSO, 50% Oil mix and the final reaction concentration was 5% oil mix, 5% DMSO.

For each assay reaction, 1µg protein per reaction was incubated with 3µl of the oil mixture at final reaction volume of 30µl. The reaction was incubated for 6 hours at 37°C.

Following incubation, the reaction was stopped by adding 10µl/reaction of sample buffer 4X and incubation 10 minutes at 72°C. Samples were then run in 4-15% TGX Criterion Gel (BIORAD) for 50 minutes at 200 Volt. Following run, the gel was incubated for 1 hour with Instant Blue reagent (Expedeon) and further washed with water until distinct bands were observed.

	No. #	Protein	Treatment	Incubation	µg/lane	Expected MW (kDa)
25	1	SARS-CoV-2 S1 Subunit	Non treated - control	W/O incubation	1 µg	120 kDa
	2		Positive control - Proteinase K	6 hours - 37°C		
	3		Complex B			
	4		Complex C			
	5		Complex D			
	6		Negative control - DMSO			
	7		Non treated - control	W/O incubation		
8	Non treated - control					
9	Positive control - Proteinase K					
10	Complex B					
11	Complex C					
12	Complex D					
30	13	Negative control - DMSO	6 hours - 37°C			
	14	Non treated - control				
	15	Non treated - control		W/O incubation	1 µg	55 kDa
	16	Positive control - Proteinase K				
	17	Complex B				
	18	Complex C				
	19	Complex D				
20	Non treated - control					
21	Non treated - control	6 hours - 37°C				
22	Complex B					
23	Complex C					
24	Complex D					

Densitometry of the SARS-CoV-2 S1 subunit, SARS-CoV-2 S2 subunit, SARS-CoV-2 and the Nucleocapsid protein assays disclose that although the Nucleocapsid protein underwent little to no digestion with either of the tested treatments as compared to the protein K
5 treatment the two SARS-CoV-2 subunits S1 and S2 underwent a substantial digestion (see figures 5-7 respectively).

To conclude, the viral protein digestion assay demonstrates that there is a significant digestion of the S1 and S2 subunits without destroying the Nucleocapsid protein.

Recombinant SARS-Cov-2 S1 subunit

10 Following incubation of the protein with a mix prepared from equal volumes from items 1+2+3+4 (complex B), a 26% reduction in the protein signal was observed.

Recombinant SARS-Cov-2 S2 subunit protein

Following incubation of the protein with a mix prepared from equal volumes from items 1+2+3+4 (complex B), a 19% reduction in the protein signal was observed.

15 Following incubation of the protein with a mix prepared from equal volumes from items 1+2+3+4+5 (complex C), a 27% reduction in the protein signal was observed

Following incubation of the protein with a mix prepared from equal volumes from items 1+2+3+4+5+6 (complex D), a 47% reduction in the protein signal was observed.

These significant digestion rates of both S1 and S2 subunits of the spike protein are likely
20 to result in the subsequent attenuation of the Coronavirus cell attachment and internalization mechanism. It is clear that attenuating a virus cell attachment and internalization mechanism, entry mechanism, disease levels and viral load can be reduced in an infected subject, or prevent an uninfected subject from getting infected. Subsequently, viral mediated or/and triggered inflammatory and viral mediated or/and triggered Diabetes
25 Mellitus (type 1 or type 2) occurrence may be reduced.

It is the intent of the applicant(s) that all publications, patents and patent applications referred to in this specification are to be incorporated in their entirety by
30 reference into the specification, as if each individual publication, patent or patent application was specifically and individually noted when referenced that it is to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as

prior art to the present invention. To the extent that section headings are used, they should not be construed as necessarily limiting. In addition, any priority document(s) of this application is/are hereby incorporated herein by reference in its/their entirety.