Title: NITRIC OXIDE INCREASING NUTRITIONAL SUPPLEMENTS AND METHODS

Abstract: The inventive concepts disclosed herein relate to nutritional supplements and, more particularly, but not by way of limitation, to nitric oxide increasing nutritional supplements and methods.
NITRIC OXIDE INCREASING NUTRITIONAL SUPPLEMENTS AND METHODS

BACKGROUND

1. Field of Inventive Concepts

[0001] The inventive concepts disclosed herein relate to nutritional supplements and, more particularly, but not by way of limitation, to nitric oxide increasing nutritional supplements and methods.

2. Brief Description of Related Art

[0002] Nitric oxide biology has received a large amount of attention in recent years by researchers, scientists, and the general public. Nitric oxide (NO) is a gas with the chemical formula NO and functions as an important biological signaling molecule in mammals, including humans. Dr. Nobel Murad first identified a biologic role of nitric oxide from his nitroglycerine work although he did not elucidate the functional biologic benefits of the NO molecule. Today, some effects of the biological action of nitric oxide are better known and familiar to many people. Nitroglycerin, for example, releases nitric oxide to open/widen blood vessels and open up arteries in mammalian hearts and alleviate heart pain. In this application, nitric oxide plays a role in cardiac and neurotransmitter regulation by binding to the heme group of a key enzyme. Nitric oxide is characterized as a redox-active signaling molecule. More recent research is extending the health related benefits of this redox-active signaling molecule and further elucidating the mechanics and chemistry of transfer mechanisms for how a nitric oxide group is transferred to hemoglobin and the mechanics of vascular relaxation. There is a lot to learn about the biochemical role of nitrogen in the atmosphere, in the soil, and its chemical
presence in plants and animals as food sources with regard to its conversion into nitric oxide biochemical redox-active entities.

[0003] As stated in the original studies done by Alfred Nobel, the biochemical pathway involving nitrogen-based entities, and specifically NO, and its effects in mammalian bodies and tissues is the basis of much research. In addition to research to better understand the role of nitric oxide with blood flow and circulation, there is other research regarding the role of nitric oxide in skincare as well as in many other medical and lifestyle related non-medical fields. One particular example relates to human and animal reproduction. Low intakes of nitrogen-based nutrition from plant food grown on nutrition poor soils correlates with poor reproductive success. In addition to the NO heart health benefit, the vascular benefit from NO in blood flow supports improved reproductive benefits reflected in the success of Viagra® and other similar formulations/medications. NO is increased in the body and causes widening of the blood vessels which enables better blood flow. This is to re-emphasize how NO, being a communication/signaling molecule, needs to be available at levels sufficient to enhance blood flow and open the circulation in a region that is specifically targeted by the medication.

[0004] Every nutrient has a specific tissue or family of tissues that it functions on, or functions within, for biochemical stimulation. We can say that the intake of certain heart medicines, such as nitroglycerine as a source of active NO, promotes vascular blood flow throughout a person's entire body; however, its primary benefit would be on a person's heart, when that person had a heart pain problem relievable by NO. Another good example is that people who are in the early stage of dementia can slow down the deterioration of their intellectual faculties by regular intake of Viagra® or similar NO-increasing medications.
This leads up to nitrogen metabolism and how nitrogen in the atmosphere is converted into useful forms in plants and animals. It was once presumed that nitrogen in the atmosphere is basically in the Earth, since 78% of the atmosphere is made up of nitrogen. Through nitrogen fixation by a few bacterial species, plants assimilate nitrogen from the soil and conserve nitrogen in many biochemical forms in the plant structure and seeds. Humans and other animals, in turn, consume the plants and seeds, and thus receive the nutrition and health benefits of plant-stored nitrogen.

There are two main mechanisms by which human beings and other mammals obtain NO, the first being by absorption via the salivary glands of NO produced by symbiotic bacteria living inside the mouth, and the second being via endothelium production. Once NO is produced or introduced in the endothelium, it causes the smooth muscle tissue surrounding blood vessels to relax which leads to increased circulation.

However, as a person ages, particularly above forty, the NO production by the endothelium decreases significantly often leading to NO deficiencies in persons over forty years old. The absorption via the salivary glands of NO produced by symbiotic bacteria living inside the mouth is not affected to such a degree by the aging of the person and therefore its importance increases with age.

Some prior art nutritional supplements aim to increase NO levels by providing one or more building blocks used by the endothelium to produce NO, such as ascorbic acid (vitamin C), L-arginine, and L-lysine. Such prior art nutritional supplements have limited utility in persons over 40 due to the decline of endothelium production of NO described above.
To that end, a need exists in the prior art for a nutritional supplement that increases tissue levels of NO and to methods of increasing the tissue levels of NO in humans and other mammals. It is to such a nutritional supplement and methods of increasing NO tissue levels that the inventive concepts disclosed herein are directed.

**DETAILED DESCRIPTION**

Before explaining at least one embodiment of the inventive concepts disclosed herein in detail, it is to be understood that the inventive concepts are not limited in their application to the details of construction and the arrangement of the components or steps or methodologies set forth in the following description or illustrated in the drawings. The inventive concepts disclosed herein are capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting in any way.

All patents, published patent applications, and non-patent publications mentioned in the specification are indicative of the level of skill of those skilled in the art to which the inventive concepts disclosed herein pertain. All patents, published patent applications, and non-patent publications referenced in any portion of this application are herein expressly incorporated by reference in their entirety to the same extent as if each individual patent or publication was specifically and individually expressly set forth herein.

As utilized in accordance with the present disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings.
The use of the word "a" or "an" when used in conjunction with the term "comprising" in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more," "at least one," and "one or more than one."

The use of the term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and "and/or."

Throughout this disclosure, the term "about" is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects. Further, the term "about" is intended to include not only the exact amount or value qualified by the term, but also some slight variations due to manufacturing tolerances, measuring error, observer error, decay or other reactions of chemical substances over time, impurities, and combinations thereof, for example.

The use of the term "at least one" will be understood to include one as well as any quantity more than one, including but not limited to, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, etc. The term "at least one" may extend up to 100 or 1000 or more, depending on the term to which it is attached. In addition, the quantities of 100/1000 are not to be considered limiting, as higher limits may also produce satisfactory results. In addition, the use of the term "at least one of X, Y and Z" will be understood to include X alone, Y alone, and Z alone, as well as any combination of X, Y and Z.

Further, as used herein, any reference to "one embodiment" or "an embodiment" means that a particular element, feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment.
The appearances of the phrase "in one embodiment" in various places in the specification are not necessarily all referring to the same embodiment.

[0018] As used herein, "patient," "person," or "organism" may refer to a living organism, a dead organism, a synthetic anatomical model, a cadaver, an animal model, a virtual computer model, a human being, an animal, a living cell or tissue culture, and combinations thereof, for example.

[0019] As used in this specification and claims, the words "comprising" (and any form of comprising such as "comprise" and "comprises"), "having" (and any form of having such as "have" and "has"), "including" (and any form of including such as "includes" and "include") or "containing" (and any form of containing such as "contains" and "contain") are inclusive or open-ended and do not exclude additional, unrecited elements or method steps.

[0020] The term "combinations thereof as used herein refers to all permutations and combinations of the listed items preceding the term. For example, "A, B, C, and combinations thereof is intended to include at least one of A, B, C, AB, AC, BC, or ABC and, if order is important in a particular context, also BA, CA, CB, CBA, BCA, ACB, BAC, or CAB. Continuing with this example, expressly included are combinations that contain repeats of one or more item or term such as BB, AAA, MB, BBC, AAABCCCC, CBAAAA, CABABB, and so forth. The skilled artisan will understand that typically there is no limit on the number of items or terms in any combination unless otherwise apparent from the context.

[0021] In the following detailed description of embodiments of the inventive concepts disclosed herein, numerous specific details are set forth in order to provide a more thorough understanding of the inventive concepts. However, it will be apparent to one of ordinary skill in the art that the inventive concepts disclosed
herein may be practiced without these specific details. In other instances, well-known features have not been described in detail or have been incorporated by reference to avoid unnecessarily complicating the instant disclosure.

[0022] Broadly, an exemplary embodiment of a nutritional supplement according to the inventive concepts disclosed herein may include one or more of the following ingredients, in various relative amounts (e.g., percent by weight, percent by volume, ml, mg, g), combinations, extracts, solutions, powders, liquid, solids, and with or without other ingredients as will be described herein.

[0023] Further, in some exemplary embodiments, one or more of the ingredients described herein may be omitted while in other exemplary embodiments the active substances or chemicals in one or more of the ingredients described herein may be substituted for that ingredient, or may be added to the ingredient to achieve a desired amount of the active substances or chemicals of the respective ingredient.

[0024] An ingredient for a nutritional supplement according to an exemplary embodiment of the inventive concepts disclosed herein is *Salvia officinalis*. *Salvia officinalis* is commonly known as sage although it has many other common names such as common sage, garden sage, golden sage, kitchen sage, true sage, culinary sage, Dalmatian sage, and broadleaf sage, for example. Sage is a perennial, evergreen shrub with woody stems, grayish leaves, and blue to purple flowers. Sage is a member of the family *Lamiaceae* and is native to the Mediterranean region though it has been naturalized to many places throughout the world. Sage has been broadly used to treat conditions of heart, skin, and brain throughout our history. Sage may help improve the nitric oxide level for better circulations in a person's brain, heart, skin, and reproduction system and may lead to benefits for the person's
overall wellbeing. In conclusion, *Salvia officinalis* can work well internally and externally and can be taken orally, for example. Other species of *Salvia* that may be used alone or in combinations with one another with exemplary embodiments of the inventive concepts disclosed herein include *Salvia elegans*, *Salvia leucantha*, and *Salvia miltiorrhiza*.

[0025] In one exemplary embodiment of the inventive concepts disclosed herein, the amount of *Salvia officinalis* per dose of a nutritional supplement may vary from about 0 mg to about 600 mg. Further, in some exemplary embodiments used herein, the amount of *Salvia officinalis* per dose may exceed about 600 mg and may vary from about 0 mg to about 1500 mg. Further, in some exemplary embodiments of the inventive concepts disclosed herein, the amount of *Salvia officinalis* per each serving of a nutritional supplement may exceed 1500 mg.

[0026] Another nutritional supplement ingredient that may be combined with *Salvia officinalis* according to an exemplary embodiment of the inventive concepts disclosed herein is Elderberry. Elderberry (*Sambucus nigra*) particularly focuses on our immune system to work more efficiently. *Sambucus nigra* is most commonly called Elder, Elderberry, Black Elder, European Elder, European Elderberry, European Black Elderberry, Common Elder, or Elder Bush when distinction from other species of *Sambucus* is needed. *Sambucus nigra* is a deciduous shrub or small tree. There are several closely related species that are similar and that may be used along with, or as a substitute for, *Sambucus nigra* in some exemplary embodiments of the inventive concepts disclosed herein such as *Sambucus mexicana*, subspecies *cabadensis*, subspecies *caerulea*, and various combinations thereof.
In some exemplary embodiment of the inventive concepts disclosed herein, a nutritional supplement may include Elderberry extract standardized to include about 6% anthocyanins (plant pigments) in an amount of between about 0 mg and about 600 mg per dose. Further, in some exemplary embodiments, a nutritional supplement may include Elderberry extract standardized to include about 6% anthocyanins (plant pigments) in an amount of between about 0 mg and about 1500 mg per dose, while in other embodiments, the amount of Elderberry extract standardized to include about 6% anthocyanins may exceed 1500 mg per dose, for example. Further, in some embodiments of the inventive concepts disclosed herein, the amount of anthocyanins included in the standardized Elderberry extract may vary from about 0% to about 15%, and the amount of such standardized Elderberry extract may be varied accordingly, as will be appreciated by persons of ordinary skill in the art.

Another exemplary ingredient that may be combined with *Salvia officinalis* and *Sambucus nigra* in a nutritional supplement according to an exemplary embodiment of the inventive concepts disclosed herein is apple. Apple, or *Malus domestica*, may function to increases NO production. As will be understood by a person of ordinary skill in the art, one or more than one of the more than 7,500 cultivars of *Malus domestica* may be implemented with the inventive concepts disclosed herein. Further, in some embodiments, other species or subspecies may be used instead of, or in addition to, *Malus domestica*, such as *Malus sieversii*, for example. Nitrogen is primarily stored in the region of an apple's skin and enters into our body in its nitrite form which may later be converted to NO in the stomach, for example.
Malus domestica fruit skin standardized to include from about 0% to about 50% polyphenols may be used in an exemplary embodiment of a nutritional supplement in amounts varying from about 0 mg to about 120 mg per dose. It is to be understood that in some embodiments of the inventive concepts disclosed herein, the amount of polyphenols in the Malus domestica fruit skin may vary from about 50% to about 100%, from about 0% to about 100%, from about 25% to about 75%, and combinations thereof, for example. Further, in some exemplary embodiments, the amount of Malus domestica fruit skin per dose may exceed 120 mg and may vary from about 0 mg to about 300 mg depending on the amount of polyphenols present, for example.

Another exemplary ingredient that may be combined with Salvia officinalis, Sambucus nigra, and Malus domestica in a nutritional supplement according to an exemplary embodiment of the inventive concepts disclosed herein is Black Currant. Black Currant (Ribes nigrum, also known as Phalsa or Falsa) has been extensively studied for everything vascular and it offers a higher concentration of NO. Some ingredients in the remedies focus on macro-vascular health, the heart and the major heart vessels around it, while the nitrogen in the Black Currant may also have a positive impact in the smaller blood vessels. For example, diabetic retinopathy is a condition relating to the age-related macular degeneration. In some cases, the poor circulation of small blood vessels in one's eyes eventually leads to vision loss. The intake of Black Currant not only helps increase the nitric oxide level in our heart, brain, and reproduction system but also in our blood vessels of eyes and ears. In some exemplary embodiments, Black Currant seeds, from the fruit itself, may be used to maintain and/or increase NO blood levels. It is to be understood that in some exemplary embodiments of the inventive concepts disclosed herein, one or
more other species or subspecies from the genus *Ribes* may be implemented instead of or in addition to *R. nigrum*, such as *Ribes nigrum* var. *sibiricum*, *Ribes cyathiforme*, *Ribes nigrum* forma *chlorocarpum*, and various combinations thereof.

[0031] In some exemplary embodiments, Black Currant extract standardized to include from about 0% to about 15% anthocyanins and may be used in an amount varying from about 0 mg to about 100 mg per dose of a nutritional supplement according to the inventive concepts disclosed herein. It is to be understood that in some embodiments, the Black Currant extract may be standardized to include an amount of anthocyanins which may vary from about 0% to about 45%, and the amount of Black Currant extract per dose of nutritional supplement may vary from about 100 mg to about 250 mg, and combinations thereof, for example.

[0032] Chaste berry (*Vitex agnus-castus*) is another ingredient that may be combined with *Salvia officinalis*, *Sambucus nigra*, *Malus domestica*, and *Ribes nigrum* in some exemplary embodiments of the inventive concepts disclosed herein. *Vitex agnus-castus* is also called Vitex, Chaste Tree, Chaste berry, Abraham’s balm, or Monk’s pepper. It was once understood as an anti-Viagra®. However, chaste berry has similar benefits and impact as other NO-inducing berries in the family. Its tissue-specific focus is on the hormone center of the human brain, primarily on the HPA axis (hypothalamic-pituitary-adrenal axis). It may turn off the effect of stress in our circulatory system and may turn up the effect of oxytocin. Oxytocin is a hormone which is released when people fall in love, or when a woman has a baby, and it also helps us recognize patterns better. For example, a higher level of oxytocin may improve our ability to recall numbers and recognize faces and names. Chaste berry is not necessarily targeting our reproduction system but it may deliver NO to the
region of our brain that deals with the oxytocin production and also hormone production.

[0033] In some exemplary embodiments, chaste berry fruit extract standardized to include from about 0% to about 0.3% casticin (or other casticin-type flavonoids) and may be used in an amount varying from about 0 mg to about 40 mg per dose of a nutritional supplement according to the inventive concepts disclosed herein. Further, in some embodiments, the chaste berry fruit extract may be standardized to include casticin which may vary from about 0% to about 0.75% casticin, and the amount of chaste berry fruit extract per dose of the nutritional supplement may exceed 40 mg and may vary between about 0 mg and about 100 mg, and combinations thereof, for example.

[0034] Grape or Vitis vinifera may also be combined with Salvia officinalis, Sambucus nigra, Malus domestica, Ribes nigrum, and Vitex agnus-castus as a NO-inducing ingredient of a nutritional supplement in some exemplary embodiments of the inventive concepts disclosed herein. We commonly use it for wine production. The earlier studies of NO-related health benefits began with wine, and new discoveries about red wine continue and emphasize that it is consumed in moderation. Like apple, the nitrogen may be stored in the region of the skin of Vitis vinifera. Red wine grape has more hydrogen in its skin than white grapes and goes into our wine.

[0035] In some exemplary embodiments, grape skin extract standardized to include from about 0% to about 30% polyphenols and may be used in an amount varying from about 0 mg to about 100 mg per dose of a nutritional supplement according to the inventive concepts disclosed herein. Further, in some embodiments, the grape skin extract may be standardized to include an amount of polyphenols
varying from about 30% to about 75%, varying from about 75% to about 100%, or varying from about 30% to about 100%, and the amount of grape skin extract per dose may be varied from about 100 mg to about 250 mg, and combinations thereof, for example.

[0036] Another ingredient that may be combined with Salvia officinalis, Sambucus nigra, Malus domestica, Ribes nigrum, Vitex agnus-castus, and Vitis vinifera according to exemplary embodiments of the inventive concepts disclosed herein is Hawthorn Berry, or Crataegus oxycantha which has been historically used to strengthen human hearts. Other species or subspecies may be implemented with the inventive concepts disclosed herein such as Crataegus monogyna, for example. One or more of the many related species or subspecies may be implemented in some exemplary embodiments of the inventive concepts disclosed herein such as Crataegus aemula (Rome Hawthorn), Crataegus aestivalis (May Hawthorn), Crataegus altaica (Altai Hawthorn), Crataegus ambigua (Russian Hawthorn), Crataegus ambitiosa (Grand Rapids Hawthorn), Crataegus anamesa (Fort Bend Hawthorn), Crataegus ancisa (Mississippi Hawthorn), Crataegus annosa (Phoenix City Hawthorn), Crataegus apiomorpha (Fort Sheridan Hawthorn), Crataegus aprica (Sunny Hawthorn), Crataegus arborea (Montgomery Hawthorn), Crataegus arcana (Carolina Hawthorn), Crataegus ater (Nashville Hawthorn), Crataegus austromontana (Valley Head Hawthorn), Crataegus azarolus (Azarole Hawthorn), Crataegus berberifolia, Crataegus biltmoreana, Crataegus boyntonii, Crataegus brachyacantha (Blueberry Haw), Crataegus calpodendron (Late Hawthorn), Crataegus canbyi, Crataegus chlorosarca, Crataegus chrysocarpa, Crataegus coccinea, Crataegus coccinioides, Crataegus collina, Crataegus columbiana, Crataegus compta, Crataegus crusgalli (Cockspur Thorn), Crataegus cuneata
(Japanese Hawthorn), Crataegus cupulifera, Crataegus dahurica, Crataegus douglasii (Black Hawthorn or Douglas hawthorn), Crataegus ellwangeriana, Crataegus erythropa, Crataegus flabellata, Crataegus flava (Yellow-fruited Hawthorn), Crataegus fontanesiana, Crataegus harbisonii, Crataegus heldreichii, Crataegus heterophylla (Various-leaved Hawthorn), Crataegus holmesiana, Crataegus hupehensis, Crataegus intricata (Thicket Hawthorn or Intricate Hawthorn), Crataegus iracunda, Crataegus jackii, Crataegus jonesae, Crataegus laevigata (Midland Hawthorn or English Hawthorn), Crataegus lepida, Crataegus macrosperma, Crataegus marshallii (Parsley-leaved Hawthorn), Crataegus maximowiczii, Crataegus mercerensis, Crataegus mexicana-tejocote, Crataegus mollis (Downy Hawthorn), Crataegus monogyna (Common Hawthorn), Crataegus nigra (Hungarian Hawthorn), Crataegus okanaganensis, Crataegus orientalis, Crataegus pedicellata (Scarlet Hawthorn), Crataegus pentagyna, Crataegus peregrina, Crataegus phaenopyrum (Washington Hawthorn), Crataegus phippsii, Crataegus pinnatifida (Chinese Hawthorn), Crataegus pruinosa (Frosted Hawthorn), Crataegus pulcherrima, Crataegus punctata (Dotted Hawthorn or White Hawthorn), Crataegus putnamiana, Crataegus pyncoloba, Crataegus rhipidophylla, Crataegus nvularis, Crataegus saligna, Crataegus sanguinea (Redhaw Hawthorn), Crataegus sargentii, Crataegus scabrida, Crataegus scabrifolia, Crataegus songarica, Crataegus spathulata (Littlehip Hawthorn), Crataegus submollis, Crataegus succulenta (Fleshy Hawthorn), Crataegus tanacetifolia, Crataegus tracyi, Crataegus triflora, Crataegus uniflora, Crataegus viridis (Green Hawthorn, including cultivar 'Winter King'), Crataegus visenda, Crataegus vulsa, Crataegus wattiana, Crataegus wilsonii. For example, people who take hawthorn berries may have better tolerance towards exercise. Hawthorn berry may target the functions of our heart, such as
congestive heart failure, and may allow our heart to work smarter and more efficiently. From our heart, its effects may move to the rest of our muscles.

[0037] In some exemplary embodiments, a nutritional supplement, according to the inventive concepts disclosed herein, may include Hawthorn berry concentrated to a ratio of about 4:1 (e.g., by concentration of vitamin C as compared with the original concentration of vitamin C) in an amount varying from about 0 mg to about 400 mg per dose. Further, in some exemplary embodiments, Hawthorn berry concentrate of different strength may be used such as from about 1:1 to about 5:1, and/or an amount varying from about 0 mg to about 1000 mg per dose may be used, and combinations thereof.

[0038] Another ingredient that may be combined with Salvia officinalis, Sambucus nigra, Malus domestica, Ribes nigrum, Vitex agnus-castus, Vitis vinifera, and Crataegus oxyacantha in some exemplary embodiments of the inventive concepts disclosed herein is Schisandra chinensis. Schisandra berry (Schisandra chinensis) is harvested in China and its literal name is "five flavor berry." Some studies have demonstrated its anti-depressant properties. Hawthorn is also another Chinese-adopted herb. Between these two, they may provide us with increased resistance to stress. Its primary effect may be to the hormone-regulating side of our brain and adrenal glands and, at the same time, it may be a beneficial effect to our cardiovascular system. It is to be understood that other Schisandra species such as Schisandra sphenanthera may be implemented instead of, or in addition to, Schisandra chinensis in some exemplary embodiments of the inventive concepts disclosed herein.

[0039] In some exemplary embodiments, a nutritional supplement may include an extract of Schisandra chinensis having a concentration of about 4:1 and in an
amount varying from about 0 mg to about 600 mg per dose. It is to be understood that in some exemplary embodiments of the inventive concepts disclosed herein, the concentration of the Schisandra chinensis extract may be varied from about 1:1 to about 5:1, for example, and the amount used may exceed 600 mg per dose as will be understood by persons of ordinary skill in the art.

[0040] As will be understood by persons of ordinary skill in the art, any portion of the ingredients described herein may be implemented with some exemplary embodiments of the inventive concepts disclosed herein including the entire plant and/or portions of the plant such as roots, bulbs, stalks, stems, bark, leaves, flowers, buds, fruits, seeds, shoots, sap, and combinations thereof. Further, one or more than one portion of one or more of the above ingredients, or the entire plants of one or more of the above ingredients, and combinations thereof, may be implemented with the inventive concepts disclosed herein, for example.

[0041] In some exemplary embodiments, a nutritional supplement according to the inventive concepts disclosed herein may include blending a powdered mixture of one or more ingredients, the powdered mixture having a particle size such that it may be passed through a 200-mesh, for example.

[0042] In an exemplary embodiment, a tablet form may be used for a nutritional supplement according to the inventive concepts disclosed herein. A tablet may include an amount of one or more of the active pharmaceutical ingredients (API) disclosed herein from about 0.1% to about 30% by weight, flavor/taste additives from about 0.1% to about 0.5% by weight, solubilizer (e.g., salts, buffers, cyclo-dextrin) as needed, entrainers/suspending agents (e.g., polyethylene glycol Mol. Wt. 100-600M) varying from about 40% to about 90% by weight, binders (e.g., hydroxy-propyl cellulose, Mg Stearate) from about 1% to about 5% by weight, dissolution/swelling
agents (e.g., sodium alginate, cyclodextrins, PEOs, inorganic salts NaCl, Na Citrate) from about 1% to about 10% by weight.

[0043] In an exemplary embodiment, a tablet form of a nutritional supplement according to the inventive concepts disclosed herein may include an amount of one or more of the API disclosed herein from about 0.1% to about 75% by weight, flavor/taste additives from about 0.1% to about 1.5% by weight, solubilizer (e.g., salts, buffers, cyclo-dextrin) as needed, entrainers/suspending agents (e.g., polyethylene glycol Mol. Wt. 100-600M) varying from about 40% to about 90% by weight, binders (e.g., hydroxy-propyl cellulose, Mg Stearate) from about 1% to about 15% by weight, dissolution/swelling agents (e.g., sodium alginate, cyclodextrins, PEOs, inorganic salts NaCl, Na Citrate) from about 1% to about 25% by weight.

[0044] The tablet form of the nutritional supplement may be formed by particle sizes exclusion 200-mesh, blending, and die compression to produce stable tablets with targeted hardness, friability, disintegration dissolution, taste, and texture properties against specific product design specifications, for example.

[0045] In an exemplary embodiment, a nutritional supplement according to the inventive concepts disclosed herein may be implemented in a syrup form, which may include an amount of one or more of the API disclosed herein from about 0.1% to about 3% by weight, one or more flavoring agent from about 0.1% to about 2% by weight, buffer (e.g., sodium citrate/citric acid) from about 1% to about 7% by weight, sucrose (or other suitable high intensity sweeteners) from about 1% to about 60% by weight, suspending agents (e.g., hydroxyl propyl cellulose, Polyethylene glycol, oleic acid) from about 1% to about 10% by weight, water from about 10% to about 70% by weight, and preservatives (e.g., EDTA, potassium sorbate) from about 0.1% to about 1% by weight.
In some exemplary embodiments, a syrup form of a nutritional supplement according to the inventive concepts disclosed herein may include an amount of one or more of the API disclosed herein from about 0.1% to about 7.5% by weight, one or more flavoring agent from about 0.1% to about 5% by weight, buffer (e.g., sodium citrate/citric acid) from about 1% to about 15% by weight, sucrose (or other suitable sweetener) from about 1% to about 60% by weight, suspending agent (e.g., hydroxyl propyl cellulose, Polyethylene glycol, oleic acid) from about 1% to about 10% by weight, water from about 10% to about 70% by weight, and preservatives (e.g., EDTA, potassium sorbate) from about 0.1% to about 1% by weight.

The syrup form of a nutritional supplement according to some embodiments may be formulated by suspending active powder in a mixture of water and the remaining ingredients to form an emulsion with controlled stirring/agitation which may then be diluted to target concentration as desired, for example.

In some exemplary embodiments, the NO levels in a patient may be measured prior to and/or at a certain time after administering an NO increasing supplement according to the inventive concepts disclosed herein. For example, the level of NO in a patient's blood, tissue, or saliva may be measured by any suitable method. In one exemplary embodiment, a saliva NO level of less than about 20 \( \mu \text{mol/L} \) may be considered depleted. A saliva NO level of between about 20 \( \mu \text{mol/L} \) and about 100 pmol/L may be considered low. A saliva NO level of between about 100 pmol/L and about 300 pmol/L may be considered normal, and a saliva NO level of above about 300 \( \mu \text{mol/L} \) may be considered optimal. Saliva NO levels may be measured via a test strip, for example, such as a test strips of the type currently sold as Nitric Oxide Diagnostics™ test strips by NeoGenis Laboratories, Inc., 248 Addie
Roy Road, Suite B-201, Austin, Texas, 78746, and may be measured in the morning on an empty stomach about 15 minutes after taking an NO increasing supplement according to the inventive concepts disclosed herein, about 2 or about 3 hours after taking an NO increasing supplement according to the inventive concepts disclosed herein, or at any time, regardless of when, if at all, an NO increasing supplement according to the inventive concepts disclosed herein was taken by the patient. The blood, tissue, or saliva NO levels of a patient may be measured by any other suitable method, procedure, or device as will be appreciated by a person of ordinary skill in the art having the benefit of the instant disclosure.

In some exemplary embodiments, an NO increasing supplement according to the inventive concepts disclosed herein may increase the blood, tissue, and/or saliva NO levels of a patient to between about 20 pmol/L and about 100 pmol/L, to between about 100 pmol/L and about 300 μmol/L, to above about 300 pmol/L, and including any ranges and sub-ranges between about 20 pmol/L and about 350 pmol/L. Such increased blood, tissue, and/or saliva NO levels may be measured about 15 minutes, between about 2 and about 3 hours, or at any desired time after taking an NO increasing supplement according to the inventive concepts disclosed herein, for example.

Examples of other nutritional ingredients which are herbal or natural extracts and which may be incorporated with the inventive concepts disclosed herein include one or more, and various combinations and permutations of aaron's rod (verbascum thapsus), abelmoschus moschatus, abrus precatorius, absinthe, abuta, acacia, acacia Senegal, acai, acemannan, acerola, achicoria, achillea millefolium, achiote, ackee, aconite, aconitum napellus, acorus calamus L, actaea racemosa L, actinidia chinensis, actinidia deliciosa, adam's needle, adelfa, adrue, aegle
marmelos, aesculus hippocastanum L., african wild potato, agathosma betulina, agave americana, agave sisalana, agrimonia eupatoria, agrimonia odorata, agrimonia procera, agrimony, agropyron repens, aguacate, alanine, albahaca morada, albarraz, alchemilla vulgaris, alcusa, alder, alfalfa, algarrobo, algin, alizarin, alkanet tinctoria, allium cepa, allium sativum, allium ursinum, allspice, almendra amarga, almendra dulce, aloe, aloe barbadensis, aloe ferox, aloe vera, alpine cranberry, alpinia galanga, alpinia officinarum, althaea officinalis, aluminum phosphate, amanita muscaria, amaranth, amargo, ambrette (abelmoschus moschatus), american aloe, american hellebore, american pawpaw, american pennyroyal, american scullcap, american valerian, american white water lily, american yew, aminobenzoic acid, amla fruit, ammi visnaga, ammonum, anacardium occidentale, ananas comosus, ananas sativus, anapsos, anchusa, andiroba, andrographis paniculata, anemone acutiloba, angelica sinensis, angel's trumpet, angostura trifoliata, anis estrellado, annatto, annona muricata, annual mugwort, annual wormwood, antelaea azadirachta, anthemis grandiflorum, anthemis nobilis, anthozoa, antineoplastones, antineoplastons, AFA (aphanizomenon flos-aquae), apis cerana, apis mellifera, apium graveolens, apocynum cannabinum, apple cider vinegar, apricot, arachis hypogaea, arbre fricassee, arbutin, arcilla, arctium lappa, arctium majus, arctostaphylos, arctostaphylos uva-ursi, areca catechu L., arecoline, aristolochia, armeniaca vulgaris, armoracia rusticana, arnica montana, arrowroot, arsenicum album, artemisia absinthium, artemisia annua, artemisia vulgaris, arthospira plantensis, artichoke, artocarpus heterophyllus, arundinaria japonica, asafoetida, asarabacca, asarum, asclepias tuberosa, ascophyllum nodosum, ashwagandha, asian ginseng, asimina americana, asimina triloba, asophyllum nodosum, aspalathus linearis, asparagus, asparagus officinalis, aspen, asperula
odorata, asperula olorosa, astaxanthin, astaxantina, asthma weed, astragalo, astragalus, astragalus membranaceus, atropa belladonna, australian tea tree oil, autumn crocus, aveloz, avena extract, avocado, and azadirachta indica.

Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more and various combinations and permutations of ba ji tian, babassu, baccharis genistelloides, baccharis trimera, baccharis triptera, bacopa, bacopa monnieri, bael fruit, baikal skullcap, ballota nigra, balm of gilead, balsam herb, bamboo, bantu tulip, banxia houpo tang, baptisia australis, barbados cherry, barberry, bardana, barosma betulina, bay leaf, bayberry, bear's garlic, bearberry, bedstraw, bee pollen, beeswax, beet, bejunco de cerca, belcho (ephedra sinica), belladona, bellis perennis, bentonite, berberina, berberine, berberis aristata, berberis vulgaris, bergamot oil, β-vulgaris, betel nut, betony, betula spp., bifidobacteria, bilberry, biminne, bing gan tang, birch sugar, birthwort, bishop's weed, bismuth, bitter almond, bitter aloe, bitter ash, bitter gourd, bitter melon, bitter orange, bitter wood, bitterroot, bixa orellana, biznaga, black bryony, black cohosh, black currant, black haw, black horehound, black mulberry, black mustard oil, black pepper, black seed, black tea, blackberry, black cherry, black walnut, bladderwrack, blessed thistle, blighia sapida, bloodroot, blue cohosh, blue flag root, blue rocket (aconite), blueberry, blue-green algae, bluperum, boldo, boneset, borage seed oil, boragara officinalis, borsforis, boswelia carterii, boswellia sacra, boswellia serrata, bovine cartilage, boxwood, brahmi, brassica campestris oil, brassica nigra, brassica oleracea, brazilian vetiver, bromelain, broom corn, brugmansia, bryonia, b-sitosterol, buchu, buckhorn plantain, buckshorn plantain, buckthorn, buckwheat, bugleweed, bulbous buttercup,
bupleurum, burdock, butanediol, butcher's broom, butterbur, and buxus sempervirens.

Yet further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of L, cabbage rose, cactus prickly pear, cajeput oil, calaguala, calamus, calcitriol, calendula, California jimson weed, California poppy, calophyllum inophyllum L, calostro bovino, camellia sinensis, campesterol, camphor, Canadian hemp, cancer weed, cannabis sativa, canola oil, cantharis, capsella bursapastoris, capsicum, carapa ssp., caraway, caraway oil, carbohydrate supplement, cardamom, cardamomo, cardo bendito, cardo lechero, carica papaya, carnitine, carnosine, carob, carotene, carqueja (baccharis genistelloides), carrageenan, carrot, carthamus tinctorius, cascara sagrada, cashew, castana de indias, castor oil, castor seed, caterpillar fungus, catha edulis, catnip, cat's claw, cat's hair, catuaba, caulophyllum thalictroides, cayenne, cebada, cebolla albarrana, cedar leaf oil, celandine, cemphire, centaurea benedicta, centaurea cyanus, centella asiatica, century plant (agave americanan), cephaelis ipecacuanha, ceratonia asiatica, ceratonia siliqua, cervus elaphus, cervus nippon, cetyl myristoleate, ceylon citronella, chamaemulum nobile, chamomile, chaparral, chasteberry, chaste tree, chelidonium majus, chenopodium quina, chenopodium vulvaria, chewing tobacco, chia, chickweed, chicory, chili pepper, China rose, Chinese angelica, Chinese boxthorn, Chinese foxglove, Chinese gelatin, Chinese ginger, Chinese ginseng, Chinese matrimony vine, Chinese star anise, Chinese wormwood, chintul, chirayata, chitosan, chlorella, Cholestin®, chrysanthemum, chrysanthemum vulgare, chrysin, chrysopogon spp., cichorium intybus, cicuta virosa, cider vinegar, cimicifuga racemosa, cinnamomum aromaticum, cinnamon, cissampelos pareira, citrillus
colocynthis, citronella grass, citrulline, citrus aurantifolia, citrus aurantium, citrus bergamia, citrus naringine, citrus paradisi, citrus reticulata, claviceps purpurea, clavo de olor, cloud mushroom, clove, club moss, cnidium monnieri, cobalamin, coca, coccinia indica, cochlearia armoracia, cocklebur, coconut oil, codonopsis, coenzyme Q10, coenzyme R, cohosh azul, cohosh negro, cola nut, colchicum, coleus forskohlii, coltsfoot, colubrina arborescens, comfrey, commifora mukul, commiphora molmol, commiphora myrrha, condurango, cone flower, conium maculatum, consuelda, copaiba balsam, copaifera officinalis, coptis formula, coral calcium, cordyceps sinensis, coriolius mushroom, coriolius versicolor, corn poppy, corn silk, corn sugar gum, cornflower, cornus spp., corydalis, corylus avellana, corynanthe yohimbi, costmary, cottonseed oil, cottonwood, couch grass, cow parsley, cowbane, cowhage, cowslip (primula veris), crab's eye, cramp bark, cranberry, cranesbill, Crataegus, cumin, creosote bush, cucurbita pepo, cupressus sempervirens, curcuma domestica, curcuma longa, curcumin, curly dock, cusparia febrifuga, cusparia trifoliata, cuspidatum, custard apple, cyamopsis tetragonolobus, cyanocobalamin, cymbopogon spp., cynara scolymus, cyperus articulatus, cypress, cypripedium acaule, cypripedium calceolus, cystadane, and cytisus scoparius.

[0053] Other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of daio-kanzo-to, daisy, damiana, dandelion, dangshen (or danshen), date palm, datura meteoides, datura sauveolens, datura stramonium, datura wrightii, daucus carota, deadly nightshade, deanol, deer velvet, desert parsley, devil's claw, devil's club, di huang, diente de leon, diet, macrobiotic, dietary fiber, dietary saccharides, digitalis, dill, dioscorea communis, dioscorea villosa L., diviner's sage, dogwood, dolichos pruriens, dolomite, dong quai, D-
pantothenic acid, D-phenylalanine, dromaius novaehollandiae, drosera, dumontiaceae, and dutchman's pipe.

[0054] Yet further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of eastern hemlock, echinacea, echinacea angustifolia, echinacea purpurea, echium, elderberry, elecampane, electro colloidal silver, elemental iron, elettaria cardamomum, eleusine indica, elletaria cardamomum, elymus repens, emu oil, enebrina, English chamomile, English ivy, English walnut, English yew, ephedra, EGCG (Epigallocatechin gallate), epilobium angustifolium, epilobium parviflorum, epimedium grandiflorum, equinacea, equisetum arvense L, ergocalciferol, eriodictyon californicum, erythroxylum vacciniifolium, eschscholzia californica, escobia negra, espirulina, Essiac®, estevia, eucalyptus oil, euforbia, eufrasia, eugenia aromatica, eupatorium perfoliatum, euphorbia, euphorbiaceae, euphrasia officinalis, European cranberry, euterpe oleracea, evening primrose oil, evodia rutecarpa, and eyebright.

[0055] Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of fagopyrum esculentum, fennel (foeniculum vulgare mill.), fenugreek, fermented milk, ferula assafoetida, feverfew, fucus carica, fucus inspida, fig, filipendula ulmaria, fireweed, flaxseed and flaxseed oil, fleet phospho-soda, fleet enema, Flor-Essence®, fly agaric, fo-ti, foxglove, fragaria, fragaria vesca, frambuesa, frangula purshiana, frankincense, fraxinus, French rose, friar's cap, fructus barbarum, fucus vesiculosus, and fuzheng jiedu tang.

[0056] More examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various
combinations and permutations of gallic acid, galanga, galanthus, galipea officinalis, galium odoratum, gallium aparine, gambierdiscus toxicus, ganoderma lucidum, garcinia cambogia, garcinia mangostana, garcinia, acido hydroxicitrico, garlic, garra del diablo (harpagophytum procumbens), gelatin, gelidiella acerosa, gelsemium, genistein, gentian, gentian violet, geranium maculatum, German chamomile, germander, germanio, germanium, germanium sesquioxide, germinated barley foodstuffs, giant knotweed, gimnema, gentian, ginger, ginkgo, ginseng, glechoma hederacea, globe artichoke, glycine soja, glycyrrhiza glabra, gobi, goji, goldenrod, goldenseal, goniopora spp., goosegrass, gossypol, gotu kola, gotu kola y fraccion triterpenica total de lacentella asiatica (TTFCA), you qi (Chinese wolfberry), gramilla, granada, grape seed extract, grapefruit, grass pea, graviola, greater celandine, greater galangal, green hellebore, green tea, griffonia, grifola frondosa, grindelia, grindelia camporum, ground ivy, guar gum, guarana, guayule, guelder rose, guggals, guggul, gum acacia, gum arabic, gumweed, guru nut, gymnema sylvestre, and gynostemma pentaphyllum.

Yet further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of hamamelis, hange koboku-to, haritaki, harpagophytum procumbens, hashish, hawthorn, hazelnut, hedeoma pulegioides L., hedera helix, helianthus annuus, hellebore, hemlock, hemp seed oil, hepatica, heracleum maximum, hesperidin, hibiscus, hiedra terrestre, hierba carmin, hierba de cabra en celo (epimedium grandiflorum), hierba de limon (lemon grass), hierba de san juan (hypericum perforatum L), hierba de trigo (triticum aestivum), high bush cranberry, hippophae rhamnoides, holy basil, hochu-ekki-to, honey, honeysuckle, hongo maitake, hoodia gordonii, hordeum vulgare, horehound, horny goat weed,
More examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of ignacia (or ignatia), illicium verum, impatiens biflora, impatiens pallida, Indian bael, Indian barberry, Indian fig, Indian licorice, Indian mulberry, Indian poke, Indian snakeroot, Indian tobacco, inula campana, inula helenium, ipecac, ipomoea orizabensis, ipriflavone, iris versicolor, isatis indigotica, iscador, isphagula, and ivy.

Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of jackfruit, Jamaican quassia, Japanese yew, Japanese sophora, jasmine, jengibre, jequirity, jervine alkaloids, jewelweed, jianpi wenshen recipe, jiaogulan, jimson weed, jointed flatsedge, jojoba, joshua tree, juglans regia, and juniper.

Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of Kan Jang®, karaya gum, karkada, katuka, kale, kava (piper methysticum), kefir, kelp, khat (catha edulis), khella (ammi visnaga, also known as khellin), kinetin, kiwi, kiwifruit, klamath weed, kola nut, Korean red ginseng, krebiozen, krestin, krill oil, and kudzu.
Yet other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of Labrador tea, lactalbumin, lactobacillus acidophilus, lactobacillus casei, lactobacillus GG, lactobacillus plantarum, lactobacillus reuteri, lactobacillus sporogenes, lactobacilo acidil-filo, lactoferrin, ladies mantle, lady's slipper, laetrile, lagerstroeim speciosa L, larch arabinogalactan, larix, larrea divaricata, larrea tridentata, lathyurus, laurus nobilis, laurus persea, lavender, lecithin, ledum groenlandicum, ledum latifolium, ledum palustre, legume, lei gong teng, lemon balm, lemongrass, lentinan, lentinula edodes, lentinus edodes, lentisco, leonurus cardica, lepidium meyenii, lepidium peruvianum chacc-n, lesser celandine, lesser galangal, lessertia frutescens, levisticum officinale, levoglutam ide, lichen, licorice, lignans, ligustrum, lime, lime flower, linden, lingonberry, linseed oil, linum usitatissimum, lipase, lirio azul, lirio de agua blanco (nymphaea odorata), liverwort, L-norvaline, lobelia inflata, locust bean, lomatium, lomatium dissectum, long pepper, lonicera spp., lophosphora spp., lophosphora williamsii, lorenzo's oil, lotus, lousewort, lovage, lucky nut, lupulo, lutein, luteinai, lycopersicon esculentum, lycopodium clavatum, lycopodium serrat a, lycopus americanus, lycopus europaeus, lycopus lucidus, lycopus virginicus, and lysichiton americanu.

Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of ma huang, maca (lepidium peruvianum chacon), macrobiotic diet, madagascar jewel, madder (rubia tinctorum), maeng lak kha, magic mint, magnolia, magnolia and pinelliae formula, mahonia, maidenhair tree, maitake mushroom, malpighia glabra, malpighia glabra, malpighia punicifolia, malus sylvestris, malta malvavisco, mangaresa, mandarin, mangosteen, manto de nuestra
Yet further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of narrowleaf plantain, nasturtium officinale, neem, nelumbo nucifera, neovastat, nepeta cataria, nerium oleander, nettle, nexrutine, nicotiana glauca, nicotiana tabacum, nigella sativa, noni (morinda citrifolia), nopal, northern prickly ash, norvaline, nuez de betel (areca catechu L), nutmeg, nux vomica, and nymphaea odorata.

Other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of oak bark, oak moss, oat beta-glucan, oat bran/straw, oat, ocimum basilicum, ocimum sanctum L, Oenothera biennis L, okra, old man's beard, olea europaea, oleander, olibanum, olive leaf, olive oil, olmo
Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of Pacific yew, pagoda tree, palm oil, palma enana americana (serenoa repens), pamabrom, panax ginseng, papaver rhoeas, parietaria officinalis, parsley, parsnip, parthenium argentatum, parthenolide, pasiflora, passion flower, pastinaca, pastinaca sativa, pau d'arco, paullinia cupana, pausinystalia yohimbe, PC-SPES, peanut oil, pectin, pedicularis, pedra hume caá (myrcia salicifolia), pellitory-of-the-wall, pencil tree, pennyroyal (mentha pulegium), peony, peppermint, peppermint oil, perilla frutescens, periwinkle, persea americana, petadolex, petasita, petasites hybridus, petty spurge, peumus boldus, peyote, phaseolamin (white kidney bean), phaseolus vulgaris varieties, phoenix dactylifera, phoradendron leucarpum, phyllanthus, physalis somnifera, phyto-1, Phytolacca americana, picraena excelsa, picrasma excelsa, picrorhiza kurroa, pill-bearing spurge, pimenta dioica, pimpinella anisum, pine bark extract, pine pollen, pinus maritima, pinus palustris, piper methysticum, piper nigrum, pistacia lentiscus, plant stanol ester, plantago coronopus, plantago isphagula, plantago lanceolata, plantago ovata, pleurisy, podophyllum hexandrum, podophyllum peltatum, poinsettia, poison ivy, poke root, pokeweed, poleo americano, policosanol, polygonum cuspidatum, polygonum multiflorum, polypodium leucotomos extract and anapsos, pomegranate, populus, poppy, precatory bean, prickly ash, prickly pear cactus, primula officinalis, primula veris, probeta, promensil, propagermanium, propolis, prunella vulgaris, prunus africanum, prunus amygdalus, prunus amygdalus dulcis, prunus armeniaca,
prunus armeniaca L., psyllium, ptychopetalum olacoides, pueraria lobata, pueraria montana var., puerarin, Puerto Rican cherry, pulegone, Pulsatilla, pumpkin, pumpkin seed oil, punica granatum, purple viper bugloss, pycnogenol, pygeum bark, pyres communis, and pyruvate.

[0066] Yet other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of qing hao, qinghao, qinghaosu, quack grass, quaker bonnet, quaker buttons, quaking aspen, quassia, queen anne's lace, queen of fruits (mangosteen fruts), queen of the meadow, queen's crape myrtle, quercus alba, quercus cortex, quercus marina, quick-in-the-hand (jewelweed), quimsa-kuchu, quinoa, quinsu-cucho, and quitch grass.

[0067] Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of rabdosia rubescens, radium weed, radix angelica sinensis, ranunculus bulbosus, ranunculus ficaria, rapeseed oil, raspberry, rauvolfia serpentine, red algae, red clover, red palm oil, red sorrell, red stinkwood, red yeast rice, regaliz, rehmannia, rehmannia glutinosa, reina de los prados (spiraea ulmaria), reishi mushroom, rennet, rhamnus purshiana, rheum officinale, rheum palmatum, rhodiola, rhodiola rosea, rhododendron tomentosum, rhubarb, rhus tox, ribes nigrum, rice bran oil, ricola, roble bianco, roman chamomile, romero, rooibos, rosa canina, rosary pea, rose haw, rose hip, rose laurel, roselle, rosemary, rosmarinus officinalis L., royal jelly, rhubarb, rubus fruticosus, rubus idaeus, rubus villosus, ruibarbo, rumalon, rumex crispus, ruscus aculeatus, ruta graveolens, rutin, and rye grass.

[0068] Other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various
combinations and permutations of sabal serrulata, sabila, saccaromyces cerevisiae, 
saccharomyces boulardii, saccharomyces thermophilus, safflower, sage, saiboku-to, 
saiko-keishi-to, Salba®, salix alba, salix spp., salvia divinorum, salvia hispanica, 
salvia lavandulaefolia, salvia lavandulifolia, salvia miltiorrhiza, salvia officinalis, 
samambaia, sambucus nigra, sandalwood, sanguinaria canadensis, sanguinarine, 
santalum album, sarsaparilla, sassafras, saiboku-to, saiko-keishi-to, Salba®, 
secalce cereale, secretin, seer sage, sehydrin, sea cucumber, selagine, senna, serine, serenoa 
repens, sesame oil, seso vegetal, shakuyaku-kanzo-to, shallot, shark cartilage, 
sheng dihuang, shepherd's purse, shepherd's purse, shiitake mushroom, shikonin, 
sho seiryu to, sho-saiko-to, shuang huang lian, Siamese ginger, silka deer, silver 
birch, silver protein, silymarin, simmondsia chinensis, sisal, skunk cabbage, slippery 
elm, smilax spp., smokeless tobacco, snakeroot, snowball bush, soja, solidago 
virgaurea, sophora, sorghum vulgare, sorrel, sour cherry, sour orange juice, soy, soy 
bean extract, soy bran, soy protein, soy sprouts, soybean oil, sparteine, spinach, 
spirulina, stachys betonica, stachys officinalis, star anise, stellaria media, 
sterculia urens, stevia, stickleburr, stinging nettle, stinking goosefoot, strychnos ignatii, strychnos nux-vomica, styrchnolobium japonicum, substance x, sulfato de 
condroitina, suma (pfaffia paniculata), sunflower seed oil, sutherlandia frutescens, 
swamp hellebore, sweet almond, sweet annie, sweet basil, sweet cherry, sweet 
orange, sweet root, sweet woodruff, sweet wormwood, sweetflag, Symphytum, 
Symphytum officinalis, and symprocarpus foetidus.
Further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of tadenan, tamanu, tamarind, tamarindus indica L., tamus communis, tanacetum parthenium, tanacetum vulgare, tangerine, tansy, taraxacum officinale, taurine, tea tree oil, tejo, terminalia, teucrium chamaedrys, theobroma cacao, thevetia peruviana, thuja occidentalis, thunder god vine, thyme (thymus vulgaris), tibetan goji berry, tilofofa, toki-shakuyaku-san, toxicodendron radicans (eastern poison ivy), tragacanth, tree tobacco, trembling aspen, tribulus terrestris, trichilia catigua, trierucate oil, trifolium pratense, trigonella foenum-graecum, trigonella foenum-graecum L. leguminosae, trimethylethanolamine, tripterygium wilfordii, triticum aestivum, tsuga canadensis, TTFCA (total triterpenic fraction of centella asiatica), tuftsin, tulsi holy basil, turkey tail mushroom, turmeric, turnera aphrodisiaca, turnera diffusa, turpentine oil, tussilago farfara, tylophora, and tylophora indica.

Other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of Ukrain™, ulmus rubra/ulmus fulva, umbrella arum, uncaria guianensis, uncaria tomentosa, urugina maritima, urtica dioica, usnea barbata, and uva ursi.

Yet other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of vaccinium angustifolium, vaccinium macrocarpon, vaccinium myrtillus anthocyanoside, vaccinium vitis-idaea, valerian, velvet deer antler, velvet flower, velvetleaf, veratrum viride, verbascum thapsus, verbena, vervain, vetchling, vetiver (chrysopogon zizanioides), viburnum opulus, viburnum
prunifolium, vinagre de sidra de manzana, vinca minor, vinpocetine, viper’s bugloss, Virginia’s herbal E-Tonic™, viscum album L, vitex agnus-castus, vitis vinifera, and vulvaria.

[0072] Yet further examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of wasabia japonica, water hemlock, watercress, wheatgrass, wheat bran/grass, wheat germ, wheat sprouts, whey protein, white horehound, white mallow, white oak, white pepper, white sandalwood, white tea, white water lily, wild arrach, wild carrot, wild cherry, wild ginger, wild indigo, wild marjoram, wild rosemary, wild yam, willow bark, witch hazel, withania somnifera, wintergreen, wood betony, wolfberry, and wormwood.

[0073] More examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of Xango®, xanthan gum, xanthomonas campestris, xhoba, xi yang shen, xi zhang hu huang lian, xian cao, xian ling pi, xianxao, xiao qing long tang, xiao-chai-hu-tang, xu ku cao, and xue zhi kang.

[0074] Other examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of yadake, yagona, yam, yamabushitake mushroom, yang-mei, yangona, yaqona, yarrow, yashti-madhu, yashti-madhuka, yavatikta, yege, yellow astringent, yellow bark, yellow beeswax, yellow beet, yellow broom, yellow dock, yellow ginseng, yellow horse, yellow Indian paint, yellow indigo, yellow jasmine, yellow oleander, yellow poppy, yellow puccoon, yellow root, yellow sandalwood, yellow saunders, yellow starwort, yemen myrrh, yerba dulce, yerba mate, yerba santa, yew, yi zhu, yin yang huo, yinhsing, yodo, yogaraj guggul gum
resin, yohimbe bark extract (pausinystalia yohimbe), yongona, yuan hu suo, yucca, yucca aloifolia, yucca angustifolia, yucca arborescens, yucca breifolia, yucca filamentosa, yucca glauca, yucca schidigera, yucca whipplei, and yun zhi.

[0075] Yet more examples of ingredients that may be implemented with the inventive concepts disclosed herein may include one or more, and various combinations and permutations of zanthoxylum americanum, zapatilia de dama, zeamays, Zemaphyte®, zingiber officinale roscoe, or ZMATM.

[0076] Examples of other nutritional ingredients that may be included with a nutritional supplement according to the inventive concepts disclosed herein may include one or more, and various combinations and permutations of 5-HTP (5-hydroxytryptophan), 7-keto-DHEA (dehydroepiandrosterone), acetate, acetyl-L-carnitine, AE-941, a-carotene, a-hydroxy acids, a-aminohydrocinnamic acid, a-ketoglutarate, a-galactosidase, a-linolenic acid, a-lipoic acid, a-tocopherol, SHA-10, androstenediol, androstenedione, arginine, aspartic acid (aspartate), ascorbic acid, β-alanine, β-alanyl-L-histidine, β-carotene, β-cryptoxanthin, β-D-fructofuranosidase, betadine, β-glucan, β-glycans, betaine, β-sitosterol, β-tocopherol, BMS-214778, calcium carbonate matrix, calcium phosphate, caprylic acid, canthaxanthin, CDP-choline, chelated calcium, cholecalciferol, choline, chondroitin sulfate, citicoline, citric acid, creatine, cryptoxanthin, cysteine, D-calcium pantothenate, dehydroepiandrosterone, delta-tocopherol, dextran-iron, DGL (deglycyrrhiziated licorice), EA (Dehydroepiandrosterone), dibencozide, dichloroacetate, dimethylglycine, dimethylsulfoxide, disodium disuccinate astaxanthin, D,L-phenylalanine, DMAE (Dimethylaminoethanol), D-mannose, DMSO (dimethyl sulfoxide), docosahexaenoic acid, docusate sodium, eburnamenine-14-carboxylic acid, EDTA (ethylenediamine tetraacetic acid), EFA (essential fatty acid), ellagic
acid, eicosapentaenoic acid, ferrous gluconate, ferrous sulfate, 5-hydroxytryptophan, flavonoid, folacin, folate, folic acid, forskolin, fructo-oligosaccharides, GABA (gamma-aminobutyric acid), galanthamine hydrobromide, y-carotene, y-linolenic acid, y-oryzanol, y-glutamylcysteinylglycine, y-tocopherol, glucosamine, glucosamine sulfate, glutamine, glutamic acid, glutathione, glycerol, glycerophosphocholine, glycine, histidine, HMB (B-hydroxy-p-methylbutyrate monohydrate), hydroxycobalamin, hydroxybutyric acid, hydroxyethylbutyrate, hydroxytryptophan, hyoscine butylbromide (scopolamine), hydroxylysine, hydroxyproline, hypoxanthine riboside, indole-3-carbinol, inosine, inositol hexanicotinate, inositol hexaphosphate, isoascorbic acid, isoflavones, isoleucine, lactic acid, L-arginine, L-ascorbic acid, L-asparagine, L-carnitine, L-Dopa, leucine, L-phenylalanine, L-tryptophan, luzindole, lycopene, lysine, malic acid, mesoglycan, methionine, methylcobalamin, methylguanidine acetic acid, methylsulfonylmethane, monounsaturated fatty acid, N-3 fatty acids, N-acetyl cysteine, N-acetyl D-glucosamine, N-acetyl-5-methoxytryptamine, N-acetylaspartic acid, NADH, niacin, nicotinamide adenine dinucleotide, nordihydroguaiaretic acid (NDGA), octacosanol, octanoic acid, oleuropein, omega-3 fatty acids, omega-6 fatty acids, omega-9 fatty acid, PABA (para-aminobenzoic acid), pangamic acid, pantethine, pantothenic acid, pantethanol, perillyl alcohol, PGGi-glucan, phenylacetate, phosphatidylcholine, phosphatidylserine, phytoestrogen, phytonadione, phytosterols, polyphenols, polysaccharide-K, polyunsaturated fatty acids, polyvinylpyrrolidone-iodine, potassium, potassium aspartate, potassium phosphate, povidone-iodine, pregnenolone, progesterone, provitamin a, pteroylglutamic acid, pyridoxine, pyridoxal-5-phosphate, quercetin, quercetin-3-rhamnoglucoside, quercetin-3-rutinoside, quinine, resveratrol, retinol, riboflavin, riboflavin-5-phosphate, salicin,
salicylate, SAM-e (S-adenosylmethionine), sitostanol, sitosterol, sitosterolins, sodium alginate, sodium ascorbate, sodium chloride, sodium ferric gluconate, sodium iodide, sodium phenylacetate, sodium phosphate, sorbic acid, stigmasterol, sulforaphane, synephrine, tannic acid, theanine, theobromine, thiamin, thiocystic acid, tocopherols, tocotrienols, triacylglycerol lipase, tricholine citrate (TRI), troxerutin, tryptophan, tyrosine, acetyl-L-tyrosine, ubidecarenone, ubiquinone, urosolic acid, usnic acid, valine, vitamin A, vitamin B1, vitamin B12, vitamin B2, vitamin B3, vitamin B5, vitamin B6, vitamin B9, vitamin Bx, vitamin C, vitamin D, vitamin D2, vitamin D3, vitamin E, vitamin G, vitamin H, vitamin K, vitamin M, vitamin 0, vitamin Q10, xylitol, or zeaxanthin.

[0077] As will be understood by a person of ordinary skill in the art, a nutritional supplement composition according to the inventive concepts disclosed herein may be manufactured as a tablet, capsule, lozenge, dissolving strip, oral spray, tea, gelatin capsule, liquid capsule, hard candy, chewable pill, chewing gum, sublingual gel or tablet, intravenous fluid, injectable fluid, liquid, lyophilized powder, powder, crystalline, aerosol, liquid impregnated onto a dermal patch, ointment, or suppository, and combinations thereof, for example. The composition may be used as NO-increasing nutritional supplement, dietary supplement, food supplement, or as a food additive, and combinations thereof, for example.

[0078] For an example of preparing and administering physiologically acceptable nutritional supplements, see U.S. Publication No. 2002/0151592, the entire disclosure of which is hereby expressly incorporated herein by reference. For an example of incorporating nutritional supplements into caffeine-containing drinks such as energy drinks, see U.S. Publications No. 2006/0134300 and No. 2009/0155409, the entire disclosures of which are hereby expressly incorporated
herein by reference. For an example of NO-increasing supplement incorporating nitrates and/or nitrites which may be implemented with one or more of the ingredients according to the inventive concepts disclosed herein, see U.S. Publication No. 2010/0047344, the entire disclosure of which is hereby expressly incorporated herein by reference. For yet another example of delivery mechanisms that may be used with the inventive concepts disclosed herein, see U.S. Publication No. 2006/0110478, the entire disclosure of which is hereby expressly incorporated herein by reference.

[0079] In addition to oral dosage forms, the compositions of the inventive concepts disclosed herein may be administered to an organism by any available and effective delivery systems. Such delivery systems may include, but are not limited to, parenteral, transdermal, intranasal, intravenous, intramuscular, subdural, subcutaneous, sublingual, trans-mucosal, intra-arterial, intracardiac, or intradermal modes of administration in dosage unit formulations containing conventional nontoxic physiologically acceptable carriers, adjuvants, and vehicles as desired, such as a depot or a controlled release formulation, for example. Depending on the route of administration, the compositions of the inventive concepts disclosed herein may be formulated as a suppository, lotion, patch, or device (e.g., a sub-dermally implantable delivery device or an inhalation pump). The compositions may be optimized for particular types of delivery.

[0080] In some exemplary embodiments of the inventive concepts disclosed herein, the compositions may be delivered in an aerosol spray preparation from a pressurized pack, a nebulizer, or from a dry powder inhaler. The dosage can be determined by providing a valve to deliver a regulated amount of the compound in the case of a pressurized aerosol, for example.
Compositions for inhalation or insufflation may include solutions and suspensions in pharmaceutically acceptable, aqueous, or organic solvents, or mixtures thereof, and powders, for example. Compositions of the inventive concepts disclosed herein may be administered by any desired route for local effect, systemic effect, and combinations thereof. Solution, suspension, or powder compositions may be administered, for example, from medical devices that deliver the formulation in an appropriate manner such as intravenous drips, gastric tubes, or nasogastric tubes, for example.

Finally, nutritional supplement compositions according to the inventive concepts disclosed herein are not limited to nutritional supplements, but may also be used in pharmaceutical drugs or formularies to treat various conditions that may be beneficially affected by increasing NO concentrations in tissues, bodily fluids, and/or organs and organ systems such as blood, serum, capillaries, skeletal muscle, cardiac muscle, smooth muscle, endothelium, blood vessel walls, stomach, brain, spinal cord, spinal fluid, brain fluid, bone, bone marrow, salivary glands, saliva, lymph nodes, lymph, digestive tract, skin, and any other tissue, bodily fluid, and organ, and combinations thereof, for example.

From the above description, it is clear that the inventive concept disclosed herein is well adapted to carry out the objects and to attain the advantages mentioned herein as well as those inherent in the inventive concept. While presently preferred embodiments of the inventive concept have been described for purposes of this disclosure, it will be understood that numerous changes may be made which will readily suggest themselves to those skilled in the art and which are accomplished within the scope of the inventive concept disclosed and as defined in the appended claims.
What is claimed is:

1. A nitric oxide increasing composition, comprising one or more of: *Crataegus oxyacantha, Malus domestica, Ribes nigrum, Salvia officinalis, Sambucus nigra, Schisandra chinensis, Vitex agnus-castus, and Vitis vinifera.*

2. The composition of claim 2, wherein the composition comprises *Crataegus oxyacantha* and wherein the *Crataegus oxyacantha* is present in a dose of the composition in an amount less than about 1000 mg.

3. The composition of claim 1 or 2, wherein the composition comprises *Malus domestica* and wherein the *Malus domestica* is present in a dose of the composition in an amount less than about 300 mg.

4. The composition of any one of claims 1 to 3, wherein the composition comprises *Ribes nigrum* and wherein the *Ribes nigrum* is present in a dose of the composition in an amount less than about 250 mg.

5. The composition of any one of claims 1 to 4, wherein the composition comprises *Salvia officinalis* and wherein the *Salvia officinalis* is present in a dose of the composition in an amount less than about 1500 mg.

6. The composition of any one of claims 1 to 5, wherein the composition comprises *Sambucus nigra* and wherein the *Sambucus nigra* is present in a dose of the composition in an amount less than about 1500 mg.

7. The composition of any one of claims 1 to 6, wherein the composition comprises *Schisandra chinensis* and wherein the *Schisandra chinensis* is present in a dose of the composition in an amount less than about 600 mg.

8. The composition of any one of claims 1 to 7, wherein the composition comprises *Vitex agnus-castus* and wherein the *Vitex agnus-castus* is present in a dose of the composition in an amount less than about 100 mg.
9. The composition of any one of claims 1 to 8, wherein the composition comprises *Vitix vinifera* and wherein the *Vitix vinifera* is present in a dose of the composition in an amount less than about 250 mg.

10. The composition of any one of claims 1 to 9, wherein the composition is in the form of at least one of the group consisting of a tablet, capsule, lozenge, dissolving strip, oral spray, tea, gelatin capsule, hard candy, chewable pill, chewing gum, sublingual gel or tablet, intravenous fluid, injectable fluid, liquid, lyophilized powder, powder, crystalline aerosol, liquid impregnated onto a dermal patch, ointment, suppository, and combinations thereof.

11. The composition of claim 10, wherein the composition is in the form of a tablet, wherein the tablet further comprises at least one of a flavor additive, solubilizer, suspending agent, swelling agent, and combinations thereof.

12. A method for increasing nitric oxide levels in mammalian tissue, comprising administering the composition from any one of claims 1 to 11 to the mammal.

13. The method of claim 12, wherein the increased nitric oxide levels in mammalian tissue are in a range of from about 20 pmol/L to about 300 µmol/L.