US 20220008357A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2022/0008357 A1**

Stringham (43) **Pub. Date: Jan. 13, 2022**

(54) **EYE HEALTH SUPPLEMENT WITH CURCUMIN**

(71) Applicant: **QH Holdings (Oregon), Inc.**, Eugene, OR (US)

(72) Inventor: **James Stringham**, Eugene, OR (US)

(21) Appl. No.: **17/448,513**

(22) Filed: **Sep. 22, 2021**

Related U.S. Application Data

(63) Continuation of application No. 16/282,025, filed on Feb. 21, 2019, now Pat. No. 11,141,386.

(60) Provisional application No. 62/786,270, filed on Dec. 28, 2018.

Publication Classification

(51) **Int. Cl.**

A61K 31/065	(2006.01)
A61K 31/202	(2006.01)
A61K 33/30	(2006.01)
A61K 35/644	(2006.01)
A61K 36/28	(2006.01)
A61K 35/60	(2006.01)
A61P 27/02	(2006.01)
A61K 31/341	(2006.01)
A61K 36/48	(2006.01)
A61K 31/355	(2006.01)
A61K 47/42	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/065*** (2013.01); ***A61K 31/202*** (2013.01); ***A61K 33/30*** (2013.01); ***A61K 35/644*** (2013.01); ***A61K 36/28*** (2013.01); ***A61K 47/42*** (2013.01); ***A61P 27/02*** (2018.01); ***A61K 31/341*** (2013.01); ***A61K 36/48*** (2013.01); ***A61K 31/355*** (2013.01); ***A61K 35/60*** (2013.01)

(57) **ABSTRACT**

An eye health supplement and methods of using the eye health supplement are disclosed.

EYE HEALTH SUPPLEMENT WITH CURCUMIN

CROSS-REFERENCE TO RELATED APPLICATION

[0001] The present application is a Continuation of U.S. patent application Ser. No. 16/282,025, entitled "EYE HEALTH SUPPLEMENT WITH CURCUMIN" and filed on Feb. 21, 2019. U.S. patent application Ser. No. 16/282,025 claims priority to U.S. Provisional Application No. 62/786,270, filed Dec. 28, 2018. The entire contents of the above-identified applications are hereby incorporated by reference for all purposes.

FIELD

[0002] This disclosure concerns embodiments of an eye health supplement dosage form and methods of use.

SUMMARY

[0003] Embodiments of an eye health supplement dosage form and methods of using the eye health supplement dosage form are disclosed.

[0004] In some embodiments, the eye health supplement dosage form includes 1 part by weight zeaxanthin, 1-20 parts by weight lutein, 4-70 parts by weight vitamin E, 0.8-15 parts by weight zinc, 6-100 parts by weight curcumin, and 6-100 parts by weight omega-3 oils providing 3-50 parts by weight docosahexaenoic acid (DHA) and 3-50 parts by weight eicosapentaenoic acid (EPA). In certain embodiments, the eye health supplement dosage form includes 1-4 mg zeaxanthin, 5-20 mg lutein, 16.75-67 mg vitamin E, 3.75-15 mg zinc, 25-100 mg curcumin; and 25-100 mg omega-3 oils comprising 12.5-50 mg DHA and 12.5-50 mg EPA.

[0005] In any of the above embodiments, the eye health supplement dosage form may further comprise fish oil, gelatin, glycerin, sunflower oil, yellow beeswax, water, carob, or any combination thereof. In some embodiments, the eye health supplement dosage form consists essentially of, or consists of, zeaxanthin, lutein, vitamin E, zinc, curcumin, DHA, EPA, fish oil, glycerin, sunflower oil, yellow beeswax, water, and carob. In certain embodiments, the eye health supplement dosage form consists essentially of, or consists of, 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin; 25 mg DHA, 25 mg EPA, fish oil, gelatin, glycerin, sunflower oil, yellow beeswax, water, and carob.

[0006] In any of the above embodiments, the zinc may be provided by zinc gluconate. In any of the above embodiments, the eye health supplement dosage form may not comprise resveratrol. In some embodiments, the eye health supplement dosage form is a softgel.

[0007] In some embodiments, a method of supporting eye health includes administering to a subject a dose of an eye health supplement dosage form as disclosed herein, wherein the dose is effective to support eye health. Administering may be performed daily.

[0008] In some embodiments, the dose comprises 4 mg zeaxanthin, 20 mg lutein, 67 mg vitamin E, 15 mg zinc, 100 mg curcumin, 50 mg DHA, and 50 mg EPA. In certain embodiments, administering comprises orally administering two eye health supplement dosage forms to the subject, each eye health supplement dosage form comprising 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin, 25 mg DHA, and 25 mg EPA.

[0009] In any of the above embodiments, supporting eye health may comprise supporting a healthy retina, supporting visual performance, or a combination thereof. Supporting a healthy retina may include supporting a macular pigment density of at least 0.60 over a period of time. Supporting visual performance may comprise any one or more of, or all of, (i) supporting visual processing speed, (ii) supporting the ability of the subject's eyes to recover from glare, and/or (iii) supporting contrast sensitivity.

DETAILED DESCRIPTION

[0010] A healthy retina, including the macula, is an important part of the eye for vision throughout life. The retina, including the macula, is constantly under stress. As they age, many people develop significant problems that impact their vision.

[0011] Embodiments of the disclosed eye health supplement, when administered to a subject, support eye health. In some embodiments, the eye health supplement supports a healthy retina and/or visual performance. In certain embodiments, the eye health supplement supports eye health of a subject exposed to blue light. For example, embodiments of the eye health supplement may support macular density (e.g., lutein and zeaxanthin pigment density), support visual performance in low light conditions, support the ability of the subject's eyes to recover from glare, and/or support contrast sensitivity.

I. Definitions and Abbreviations

[0012] The following explanations of terms and abbreviations are provided to better describe the present disclosure and to guide those of ordinary skill in the art in the practice of the present disclosure. As used herein, "comprising" means "including" and the singular forms "a" or "an" or "the" include plural references unless the context clearly dictates otherwise. The term "or" refers to a single element of stated alternative elements or a combination of two or more elements, unless the context clearly indicates otherwise. In addition, the term "and/or" when used in this document is to be construed to include the conjunctive "and", the disjunctive "or", and both "and" and "or". Also, the terms "includes" and "has" have the same meaning as "comprises" and the terms "including" and "having" have the same meaning as "comprising".

[0013] Unless explained otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. The materials, methods, and examples are illustrative only and not intended to be limiting. Other features of the disclosure are apparent from the following detailed description and the claims.

[0014] The disclosure of numerical ranges should be understood as referring to each discrete point within the range, inclusive of endpoints, unless otherwise noted. Unless otherwise indicated, all numbers expressing quantities of components as used in the specification or claims are to be understood as encompassing variations up to ±5% relative to the stated value. When the disclosure states

"substantially equal to," the following value encompasses variations up to ±2% relative to the stated value. When the disclosure states "equal to," the following value encompasses variations up to ±1% relative to the stated value.

[0015] Although there are alternatives for various components, parameters, operating conditions, etc. set forth herein, that does not mean that those alternatives are necessarily equivalent and/or perform equally well. Nor does it mean that the alternatives are listed in a preferred order unless stated otherwise.

[0016] Definitions of common terms in chemistry may be found in Richard J. Lewis, Sr. (ed.), *Hawley's Condensed Chemical Dictionary*, published by John Wiley & Sons, Inc., 2016 (ISBN 978-1-118-13515-0).

[0017] In order to facilitate review of the various embodiments of the disclosure, the following explanations of specific terms are provided:

[0018] Administering: Administration by any route to a subject (e.g., a human). As used herein, administration typically but not necessarily refers to oral administration.

[0019] Consisting essentially of: The term "consisting essentially of" means that the eye health supplement does not contain any active components other than those recited, and contains no more than trace amounts (e.g., <1 wt %) of additional non-active components.

[0020] Consisting of: The term "consisting of" excludes all components not specified except for impurities ordinarily associated therewith.

[0021] Curcumin: A compound produced by some plants, such as turmeric; also known as (1E, 6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione, diferuloylmethane, natural yellow 3, or turmeric yellow.

[0022] Dosage form: A form suitable for administration to a subject, e.g., a softgel, tablet, capsule, or the like. The dosage forms of the claims can be broken up into sub-dosage form which together comprise or consist essentially of the components that add up to the dosage form.

[0023] Effective dose: An amount sufficient to provide and/or support a beneficial effect to a subject or a given percentage of subjects.

[0024] Omega-3 oil: A polyunsaturated fatty acid characterized by a double bond three atoms away from the terminal methyl group. The three primary omega-3 oils in human physiology are α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). ALA is found in plant oils. EPA and DHA are commonly found in marine oils and are obtained from fish, fish oils, squid oils, and krill oil.

[0025] Softgel: An oral dosage form, typically comprising a gelatin-based shell surrounding a liquid fill.

[0026] Subject: As used herein, the term "subject" refers to a mammal, particularly a human.

[0027] Vitamin E: The term vitamin E, as used herein, is synonymous with d-alpha tocopherol. Vitamin E may be measured in milligrams or international units (IU), where 1 IU is the biological equivalent of 0.67 mg d-alpha tocopherol.

II. Eye Health Supplement Dosage Form

[0028] Embodiments of the disclosed eye health supplement dosage form include zeaxanthin, lutein, vitamin E, zinc, curcumin, and omega-3 oils, the omega-3 oils providing docosaheaenoic acid (DHA) and eicosapentaenoic acid (EPA). The zinc may be provided by zinc gluconate. In some embodiments, the eye health supplement dosage form does not comprise resveratrol.

[0029] In any of the above embodiments, the eye health supplement dosage form may comprise 1 part by weight zeaxanthin, 1-20 parts by weight lutein, 4-70 parts by weight vitamin E, 0.8-15 parts by weight zinc, 6-100 parts by weight curcumin, and 6-100 parts by weight omega-3 oils providing 3-50 parts by weight docosahexaenoic acid (DHA) and 3-50 parts by weight eicosapentaenoic acid (EPA). In one embodiment, the eye health supplement dosage form comprises 1 part by weight zeaxanthin, 1-15 parts by weight lutein, 4-50 parts by weight vitamin E, 1-10 parts by weight zinc, 10-50 parts by weight curcumin, and 10-50 parts by weight omega-3 oils providing 5-25 parts by weight docosahexaenoic acid DHA and 5-25 parts by weight EPA. In another embodiment, the eye health supplement dosage form comprises 1 part by weight zeaxanthin, 1-10 parts by weight lutein, 10-25 parts by weight vitamin E, 1-5 parts by weight zinc, 20-30 parts by weight curcumin, and 20-30 parts by weight omega-3 oils providing 10-15 parts by weight docosahexaenoic acid DHA and 10-15 parts by weight EPA. In still another embodiment, the eye health supplement dosage form comprises 1 part by weight zeaxanthin, 5 parts by weight lutein, 16.75 parts by weight vitamin E, 3.75 parts by weight zinc, 25 parts by weight curcumin, and 25 parts by weight omega-3 oils providing 12.5 parts by weight docosahexaenoic acid DHA and 12.5 parts by weight EPA. In yet another embodiment, the eye health supplement dosage form comprises the following components in amounts substantially equal to, or equal to, 1 part by weight zeaxanthin, 5 parts by weight lutein, 16.75 parts by weight vitamin E, 3.75 parts by weight zinc, 25 parts by weight curcumin, and 25 parts by weight omega-3 oils providing 12.5 parts by weight docosahexaenoic acid DHA and 12.5 parts by weight EPA.

[0030] In any of the above embodiments, the eye health supplement dosage form may comprise 1-4 mg zeaxanthin, 5-20 mg lutein, 16.75-67 mg vitamin E, 3.75-15 mg zinc, 25-100 mg curcumin; and 25-100 mg omega-3 oils comprising 12.5-50 mg DHA and 12.5-50 mg EPA. In one embodiment, the eye health supplement dosage form comprises 1-3 mg zeaxanthin, 8-12 mg lutein, 25-40 mg vitamin E, 5-10 mg zinc, 40-60 mg curcumin; and 40-60 mg omega-3 oils comprising 20-30 mg DHA and 20-30 mg EPA. In another embodiment, the eye health supplement dosage form comprises 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin; 25 mg DHA and 25 mg EPA. In some examples, the amounts are substantially equal to, or equal to, 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin; 25 mg DHA and 25 mg EPA.

[0031] In any of the above embodiments, the eye health supplement dosage form may further comprise fish oil, gelatin, glycerin, sunflower oil, yellow beeswax, water, carob, or any combination thereof In some embodiments, the eye health supplement dosage form consists essentially of, or consists of, zeaxanthin, lutein, vitamin E, zinc, curcumin, DHA, EPA, fish oil, glycerin, sunflower oil, yellow beeswax, water, and carob. In certain embodiments, the eye health supplement dosage form consists essentially of, or consists of, 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin; 25 mg DHA, 25 mg EPA, fish oil, gelatin, glycerin, sunflower oil, yellow beeswax, water, and

carob. In certain embodiments, the eye health supplement dosage form consists essentially of, or consists of, the following components in amounts substantially equal to, or equal to, 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin; 25 mg DHA, 25 mg EPA, plus fish oil, gelatin, glycerin, sunflower oil, yellow beeswax, water, and carob.

[0032] In any of the foregoing embodiments, the zinc may be provided by zinc gluconate. In any of the foregoing embodiments, the lutein may be present as free lutein. In some embodiments, the lutein and zeaxanthin are provided by Lutemax 2020® marigold extract (OmniActive Health Technologies, Morristown, N.J.), an extract providing lutein and both zeaxanthin isomers (R,R and R,S [meso]-zeaxanthin) at a 5:1 ratio by mass.

[0033] In any of the foregoing embodiments, the dosage form may be a softgel, a capsule (e.g., a sealed hard capsule), or a tablet. In some embodiments, the dosage form is a softgel. Softgels typically comprise a gelatin-based shell surrounding a liquid fill. Thus, in some embodiments, the dosage form comprises a gelatin-based shell surrounding a liquid fill comprising, consisting essentially of, or consisting of zeaxanthin, lutein, vitamin E, zinc, curcumin, DHA, EPA, fish oil, glycerin, sunflower oil, yellow beeswax, water, and carob. The gelatin-based shell may comprise gelatin, water, a plasticizer, and optionally an opacifier and/or a colorant.

III. Methods of Use

[0034] Embodiments of a method for supporting eye health comprise administering to a subject a dose of an eye health supplement dosage form as disclosed herein, wherein the dose is effective to support eye health. In some embodiments, the effective dose comprises 2-8 mg zeaxanthin, 10-40 mg lutein, 33.5-134 mg vitamin E, 7.5-30 mg zinc, 50-200 mg curcumin; and 50-200 mg omega-3 oils comprising 25-100 mg DHA and 25-100 mg EPA. In one embodiment, the effective dose comprises 3-5 mg zeaxanthin, 15-25 mg lutein, 50-76 mg vitamin E, 10-20mg zinc, 72-125 mg curcumin; and 80-120 mg omega-3 oils comprising 40-60 mg DHA and 40-60 mg EPA. In another embodiment, the effective dose comprises 4 mg zeaxanthin, 20 mg lutein, 67 mg vitamin E, 15 mg zinc, 100 mg curcumin, 50 mg DHA, and 50 mg EPA. In another embodiment, the effective dose comprises the following components in amounts substantially equal to, or equal to, 4 mg zeaxanthin, 20 mg lutein, 67 mg vitamin E, 15 mg zinc, 100 mg curcumin, 50 mg DHA, and 50 mg EPA. In any of the foregoing embodiments, the zinc may be provided by zinc gluconate.

[0035] Administration may be by any suitable route, although in most instances the dosage form is orally administered. In some embodiments, the dose is administered daily. The dose may be administered once daily, or the dose may be broken into two or more sub-doses administered throughout the day. For example, one half of the dose may be administered at a first time and the second half of the dose may be administered at a subsequent time.

[0036] In some embodiments, each dosage form includes less than the effective dose, and more than one dosage form can be taken by the subject. For example, in certain embodiments, each dosage form includes half of the effective dosage, and the subject takes two dosage forms in a day. In such embodiments, each eye health supplement dosage form comprises 1-4 mg zeaxanthin, 5-20 mg lutein, 16.75-134 mg vitamin E, 3.75-15 mg zinc, 25-100 mg curcumin; and 25-100 mg omega-3 oils comprising 12.5-50 mg DHA and 12.5-50 mg EPA. In certain embodiments, each eye health supplement dosage form comprises 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin, 25 mg DHA, and 25 mg EPA. In certain embodiments, administering comprises orally administering two eye health supplement dosage forms to the subject, each eye health supplement dosage form comprising 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin, 25 mg DHA, and 25 mg EPA. In some examples, the amounts are substantially equal to, or equal to, 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin, 25 mg DHA, and 25 mg EPA. In any of the foregoing embodiments, the zinc may be provided by zinc gluconate.

[0037] Zeaxanthin and lutein can be obtained from dietary sources, such as dark-green leafy vegetables, eggs, carrots, sweet potatoes, dried fruit, citrus fruit, green peas, green beans, romaine lettuce, Brussel sprouts, bell peppers, grapes, squash, and corn. However, zeaxanthin and lutein supplementation has been shown to exhibit a beneficial effect on ocular health, particularly as a subject ages. Zeaxanthin and lutein are present in the macula and supplementation may support or even increase macular pigment optical density and/or promote enhanced visual health and performance, which is indicative of good retinal health. A third carotenoid, meso-zeaxanthin is a non-dietary carotenoid that is also present in the macula. Meso-zeaxanthin is produced in the retina from lutein by isomerization. Zeaxanthin and lutein supplementation also been shown to increase visual processing speed as macular pigment density is augmented. Zeaxanthin and lutein supplementation also has been shown to improve visual recovery from glare and to improve visual performance in low light. These features may be attributed at least in part to the spectral properties of zeaxanthin and lutein, which absorb short-wavelength (blue) light (e.g., light having a wavelength within a range of 380-550 nm). Additionally, zeaxanthin and lutein supplementation has been correlated with a reduced risk of age-related macular degeneration (AMD).

[0038] Omega-3 oils, particularly DHA and EPA, enhance the bioavailability of lutein and zeaxanthin, as well as the bioavailability of vitamin E. DHA also provides essential structural components of the retina. Vitamin E, DHA, and lutein have been shown to work in concert by aggregating together in neural membranes, and interacting to promote healthy tissue and function.

[0039] Zinc plays a role in maintaining normal ocular function, and is present in high concentrations in ocular tissue, particularly in the retina and choroid. Curcumin is the main component of the spice turmeric (*Curcuma longa*). Curcumin has an appreciable anti-inflammatory effect in the eye, thereby supporting eye health.

[0040] Researchers with the Age-Related Eye Disease Study (AREDS) reported in 2001 that a formulation including 500 mg vitamin C, 400 international units of vitamin E, 15 mg beta-carotene, 80 mg zinc as zinc oxide, and 2 mg copper as cupric oxide could reduce the risk of developing advanced age-related macular degeneration (AMD). In 2006, the original AREDS formulation was modified to omit beta-carotene, and add 10 mg lutein, 2 mg zeaxanthin, and 1000 mg of omega-3 fatty acids (350 mg DHA and 650 mg EPA. The revised formulation is known as AREDS2.

[0041] In some embodiments, a dose of the eye health supplement dosage form disclosed herein includes greater amounts of zeaxanthin and/or lutein than a dose of the AREDS2 formulation. For example, where a dose of the AREDS2 formulation includes 2 mg zeaxanthin and 10 mg lutein, a dose of the disclosed eye health supplement dosage form may include 4 mg zeaxanthin and 20 mg lutein, thereby providing superior results in supporting eye health. The superior results may be more pronounced in older subjects, such as subjects over the age of 30, over the age of 40 over the age of 50, or over the age of 60. Older subjects may experience reduced bioavailability of zeaxanthin and/or lutein from supplements, resulting in decreased absorption in the subject's serum and/or eye.

[0042] In some embodiments, administering to a subject a dose of an eye health supplement dosage form as disclosed herein supports eye health. Supporting eye health may comprise supporting a healthy retina, supporting visual performance, or a combination thereof.

[0043] Supporting a healthy retina includes supporting macular density over a period of time, such as a period of several days, weeks, months, or even years. Macular density refers to macular pigment density. Macular pigment is a pigmented spot in the center of the retina. The macular pigment comprises lutein and zeaxanthin. The macular pigment protects the macula from harmful blue light and helps maintain macular function. The thickness or density of the macular pigment varies amongst individuals and can change over time. In particular, macular pigment density may decrease as a subject ages. Low macular density is a known risk factor for AMD. A low macular density also may reduce visual processing speed. Studies have shown that macular density also is related to glare disability and photostress recovery (Stringham et al., *Optom Vis Sci* 2008, 85:82-88). Macular pigment optical density (MPOD) may be measured, for example, using dual wavelength autofluorescence imaging, scanning laser ophthalmoscopy, resonance Raman spectroscopy, or heterochromatic flicker photometry technology. The MPOD score is based on a scale from 0 to 1. A low MPOD score may be defined as a score of from 0-0.2, a mid-range is an MPOD score from 0.21-0.44, and an MPOD score greater than 0.45 is considered to be a high density. A score below 0.45 indicates an increased risk of developing AMD. Based on visual performance data, an MPOD of at least 0.60 is desirable (Stringham et al., *ARVO Meeting Abstracts Apr.* 22, 2011, 52:3638). Some studies have shown that MPOD may peak at 45-50 years of age, followed by a gradual decrease as a subject ages, particular after the age of 60 (see, e.g., Lima et al., *Clinical Ophthalmology* 2013, 7:685-690). Stringham et al. demonstrated that MPOD may be increased with lutein and zeaxanthin supplementation (Stringham et al., *Optom Vis Sci* 2008, 85:82-88). Effects of curcumin may be assessed, at least in part, by measuring serum inflammatory cytokine levels (e.g., IL-6, TNF-α, and IL-1β), by a suitable method such as enzyme-linked immunosorbent assay (ELISA).

[0044] Supporting visual performance may include (i) supporting visual processing speed, (ii) supporting the ability of the subject's eyes to recover from glare, (iii) supporting contrast sensitivity, or (iv) any combination of (i), (ii), and (iii). In some embodiments, the eye health supplemental dosage form is administered to a subject who is exposed to blue light. Even in the absence of ocular disease, many older adults have difficulty seeing under low illumination including a loss of steady-state light sensitivity and a delay in rod-mediated dark adaptation; older adults also may experience delayed glare recovery (see, e.g., Owsley, *Annu Rev Vis Sci* 2016, 2:255-271; Babizhayev, *Ophthalmic Res* 2003, 35:19-25; Haegerstrom-Portnoy et al., *Optometry and Vis Sci* 1999, 76(3):141-158). Low luminance visual acuity may be assessed, for example, with a SKILL card (Haegerstrom-Portnoy et al., *Invest. Ophthalmol Vis Sci* 1997, 38:207-218). Glare recovery may be assessed, for example, having a subject view the glare source of the Berkley Glare test (Bailey, *Optom Vis Sci* 1991, 68:911-917) for one minute, followed by assessing visual acuity based on the time required for the subject to read the line two lines larger than the subject's previously assessed SKILL dark chart acuity (Haegerstrom-Portnoy et al., *Optometry and Vis Sci* 1999, 76(3):141-158). Photostress, or glare recovery, and/or contrast sensitivity also may be assessed with an 8 cycle/degree, 15% contrast Gabor patch target after each of five successive exposures to intense LED lights (Stringham et al., *Eye and Vision* 2016 3:30). Stringham et al. demonstrated that MPOD may be increased with lutein and zeaxanthin supplementation, with concomitant improvements in disability glare threshold and photostress recovery (Stringham et al., *Optom Vis Sci* 2008, 85:82-88; Stringham et al., *Eye and Vision* 2016 3:30). Visual processing speed may be assessed by determining the critical flicker fusion threshold (Hammond et al., *Ophthalmic Physiol Opt* 2005, 25(4):315-319).

[0045] In some embodiments, administering to a subject a dose of an eye health supplement dosage form as disclosed herein, particularly when the subject is administered doses of the eye health supplement dosage form over a period of time, supports a healthy retina, e.g., by supporting macular density. For example, the macular density may remain substantially stable (e.g., varying by less than 10% relative to an initial macular pigment density) over a period of days, weeks, months, or years, or may decrease at a slower rate compared to the macular density of a subject that has not been administered the eye health supplement dosage form or compared to a rate of macular density decrease in the subject prior to receiving the eye health supplement dosage form.

[0046] In some embodiments, administering to a subject a dose of an eye health supplement dosage form as disclosed herein, particularly when the subject is administered doses of the eye health supplement dosage form over a period of time, supports visual performance. A subject receiving doses of the eye health supplement dosage form, particularly over a period of several days, weeks, months, or years, may experience greater and/or more stable visual performance, as evidenced by increased visual acuity and/or decreased eye discomfort, in low-light conditions such as in dimly-lit areas or at nighttime, relative to the subject's visual performance prior to receiving the eye health supplement dosage form or compared to a similar subject (e.g., similar age, same gender, similar general health) did not receive the eye health supplement dosage form. Alternatively, the subject's visual performance in low-light conditions may show greater stability over a period of days, weeks, months, or years, compared to a similar subject who did not receive the eye health supplement dosage form or relative to the subject's own visual performance prior to receiving the eye health supplement dosage form. A subject receiving doses of the eye health supplement dosage form, particularly over a period of several days, weeks, months, or years, also may report an increased ability of the eyes to recover from glare, such as

glare attributable to blue light, relative to the subject's ability to recover from glare prior to receiving the eye health supplement dosage form.

[0047] Advantageously, the increased amounts of zeaxanthin and lutein present in the disclosed eye health supplement dosage forms relative to the AREDS2 formulation may provide faster and/or enhanced benefits to the subject, such as a more stable macular pigment density, a greater increase in macular pigment density, a more stable visual processing speed, improved visual processing speed, a more stable contrast sensitivity, an improved contrast sensitivity, a more stable ability to recover from glare, and/or an increased ability to recover from glare, compared to a similar subject that receives the AREDS2 formulation or to a similar subject that does not receive an eye health supplement. The subject also may experience a more stable or increased macular pigment density and/or a more stable or improved visual performance relative to the subject's own macular pigment density and/or visual performance prior to receiving one or more doses of the disclosed eye health supplement dosage forms.

IV. Methods of Making

[0048] Methods of making softgel, hard capsule, and tablet dosage forms are known in the art. Processes for making softgel capsule shells, hard capsules, and tablets are known. See, e.g., Aulton, M., *Aulton's Pharmaceutics: The Design & Manufacture of Medicines,* 527-533 (Kevin M G Taylor, Ed., 3rd Ed., 2001). In some embodiments, the dosage form is a softgel made by a rotary die process involving continuous formation of a heat seal between two ribbons of gelatin to form a soft capsule shell while simultaneously filling the shell with a fill formulation. The gelatin composition for the shell may further include a plasticizer (e.g., glycerol, sorbitol, propylene glycol, or the like) and/or a colorant. In certain embodiments, the process of making the softgel may further include applying a coating to the softgel. For example, an enteric coating may be applied to a softgel as is known to those skilled in the art.

[0049] Typically, the fill formulation is a liquid at the manufacturing temperature. The fill formulation comprises zeaxanthin, lutein, vitamin E, zinc, curcumin, and omega-3 oils, the omega-3 oils providing docosaheaenoic acid (DHA) and eicosapentaenoic acid (EPA). In some embodiments, the fill formulation comprises, consists essentially of, or consists of, zeaxanthin, lutein, vitamin E, zinc, curcumin, omega-3 oils comprising DHA and EPA, fish oil, glycerin, sunflower oil, yellow beeswax, water, and carob.

V. EXAMPLES

Example 1

Effects of Xanthophyll Supplementation With and Without Curcumin on Inflammation, Visual Performance, Eye Strain, and Eye Fatigue

[0050] The purpose of this proposed study is to determine effects of an eye health supplement containing lutein, zeaxanthin, EPA, and DHA, but with or without 100 mg of curcumin. Outcomes to be addressed include macular pigment optical density (MPOD), visual processing speed, inflammatory cytokine levels (e.g., IL-6, TNF-α, and IL-β) and contrast sensitivity.

[0051] Methods: Healthy adults (e.g., adults aged 25-49 yrs.) will be recruited to participate in this placebo-controlled comparison trial. The placebo group will ingest daily a pill that contains only sunflower oil. The treatment groups will be asked to ingest daily a pill containing 24 mg of lutein and zeaxanthin, 150 mg of EPA/DHA, and either no curcumin or 100 mg curcumin.

[0052] Measures of eye strain and eye fatigue will be assessed via questionnaire. MPOD will be assessed via heterochromatic flicker photometry. Serum inflammatory parameters will be assessed via enzyme-linked immunosorbent assay (ELISA).

[0053] Results: It is expected that, at baseline, MPOD will be correlated significantly with all visual performance measures. In terms of the intervention, it is expected that those in the curcumin group will exhibit similar results in terms of visual performance and MPOD augmentation as the other nutrient supplementation group, but have significantly lower serum inflammatory levels, and perhaps report lower eye strain and eye fatigue. We also expect that both treatment groups will improve significantly for all parameters versus placebo.

[0054] In view of the many possible embodiments to which the principles of the disclosed invention may be applied, it should be recognized that the illustrated embodiments, as described in the claims, which form a portion of this disclosure, are only desirable examples of the invention and should not be taken as limiting the scope of the invention. Rather, the scope of the invention is defined by the following claims, which are incorporated into this specification and form a portion of this disclosure. I therefore claim as my invention all that comes within the scope and spirit of these claims.

1. An eye health supplement dosage form, comprising:
- at least 4 mg zeaxanthin;
- at least 20 mg lutein;
- at least 16.75 mg vitamin E;
- at least 3.75 mg zinc, wherein zinc is provided by zinc gluconate;
- at least 25 mg curcumin; and
- at least 25 mg omega-3 oils providing 12.5 mg docosahexaenoic acid (DHA) and 12.5 mg eicosapentaenoic acid (EPA).

2. The eye health supplement dosage form of claim **1**, wherein the eye health supplement dosage form does not comprise resveratrol.

3. The eye health supplement dosage form of claim **1**, comprising:
- 1 part by weight zeaxanthin;
- 5 parts by weight lutein;
- 16.75 parts by weight vitamin E;
- 3.75 parts by weight zinc;
- 25 parts by weight curcumin; and
- 25 parts by weight omega-3 oils providing 12.5 parts by weight DHA and 12.5 parts by weight EPA.

4. The eye health supplement dosage form of claim **1**, further comprising fish oil, gelatin, sunflower oil, glycerin, yellow beeswax, water, carob, or any combination thereof.

5. The eye health supplement dosage form of claim **1**, wherein the lutein is present as free lutein.

6. The eye health supplement dosage form of claim **1**, wherein the dosage form is a softgel comprising one or more of gelatin, water, a plasticizer, an opacifer, and a colorant.

7. The eye health supplement dosage form of claim **1**, comprising:

4 mg Zeaxanthin;

20 mg lutein;

67 mg vitamin E;

15 mg zinc;

100 mg curcumin; and

50 mg docosahexaenoic acid (DHA) and 50 mg eicosapentaenoic acid (EPA).

8. The eye health supplement dosage form of claim **1**, wherein the eye health supplement dosage form comprises 120 mg of omega-3 oils.

9. A method of supporting eye health, comprising administering to a subject a dose of an eye health supplement dosage form according to claim **1**, wherein the dose is effective to support eye health.

10. The method of claim **9**, wherein administering comprises orally administering two eye health supplement dosage forms to the subject, each eye health supplement dosage form comprising 2 mg zeaxanthin, 10 mg lutein, 33.5 mg vitamin E, 7.5 mg zinc, 50 mg curcumin, 25 mg DHA, and 25 mg EPA.

11. A method for supporting eye health, comprising:

administering to a subject a dose of an eye health supplement dosage form, wherein the dose is effective to support eye health; wherein the eye health supplement dosage form comprises:

at least 4 mg zeaxanthin;

at least 20 mg lutein;

at least 16.75 mg vitamin E;

at least 3.75 mg zinc, wherein zinc is provided by zinc gluconate;

at least 25 mg curcumin;

at least 25 mg omega-3 oils providing 12.5 mg docosahexaenoic acid (DHA) and 12.5 mg eicosapentaenoic acid (EPA).

12. The method of claim **12**, wherein an effective dosage of the eye health supplement dosage form comprises:

2-8 mg zeaxanthin;

10-40 mg lutein;

33.5-134 mg vitamin E;

7.5-30 mg zinc;

50-200 mg curcumin; and

50-200 mg omega-3 oils.

13. The method of claim **12**, wherein the administering further comprises administering two or more sub-doses separately throughout a day.

14. The method of claim **12**, wherein administering occurs daily.

15. The method of claim **11**, wherein supporting eye health comprises supporting a healthy retina, supporting visual performance; or a combination thereof.

16. The method of claim **15**, wherein supporting a healthy retina comprises supporting a macular density of at least 0.60 over a period of time.

17. The method of claim **15**, wherein supporting visual performance comprises (i) supporting visual processing speed, (ii) supporting the ability of the subject's eyes to recover from glare, (iii) supporting contrast sensitivity, or (iv) any combination of (i), (ii), and (iii).

18. An eye health supplement, comprising:

an effective dosage comprising:

24 mg of lutein and zeaxanthin.

19. The eye health supplement of claim **18**, wherein the effective dosage comprises:

4 mg zeaxanthin;

20 mg lutein;

67 mg vitamin E;

15 mg zinc;

100 mg curcumin; and

120 mg of omega-3 oils providing 50 mg docosahexaenoic acid (DHA) and 50 mg eicosapentaenoic acid (EPA).

20. The eye health supplement of claim **18**, wherein the effective dosage is encapsulated in a softgel comprising a gelatin-based shell, the effective dosage further comprising vitamin E< zinc, curcumin, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), fish oil, glycerin, sunflower oil, yellow beeswax, water, and carob.

* * * * *