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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

OMNIACTIVE HEALTH TECHNOLOGIES, INC., **Plaintiff,** **v.** **KEMIN INDUSTRIES, INC.,** **Defendant.**	**Civil Action No. _____** **COMPLAINT FOR DECLARATORY JUDGMENT** **(Filed Electronically)**

Plaintiff OmniActive Health Technologies, Inc. ("OmniActive") hereby pleads the following claims for Declaratory Judgment against Defendant Kemin Industries, Inc. ("Kemin"), and alleges as follows:

NATURE OF THE ACTION

1. OmniActive seeks a declaration under 28 U.S.C. §§ 2201 and 2202 that its products do not infringe United States Patent Nos. 8,815,955 ("the '955 Patent") and 9,226,940 ("the '940 Patent") (collectively, the "Patents-in-Suit").

PARTIES

2. Plaintiff OmniActive Health Technologies, Inc. is a Delaware corporation, with its principal place of business at 67 East Park Place, Suite 500, Morristown, NJ 07960.

OmniActive is an innovator and global leader in the business of supplying ingredients to the food, beverage, and supplements industries.

3. On information and belief, Defendant Kemin is a company organized and existing under the laws of the State of Iowa, with its principal place of business at 2100 Maury Street, Des Moines, Iowa 50317.

SUBJECT MATTER JURISDICTION

4. This action for a declaratory judgment arises under the United States patent laws, Title 35, U.S. Code, including but not limited to 35 U.S.C. § 271. Therefore, this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a) and 15 U.S.C. § 1121. These claims are also brought pursuant to the Federal Declaratory Judgments Act, 28 U.S.C. §§ 2201 and 2202 with respect to an actual controversy within this Court's jurisdiction.

5. Beginning on or around July 2016, Kemin directed correspondence to OmniActive related to the claims recited in this Complaint. On July 29, 2016, OmniActive received a letter, dated July 20, 2016, from Kemin demanding that OmniActive immediately cease and desist from specific marketing activities. Kemin identified the '955 Patent and '940 Patent as the bases for its demands in this letter. Kemin's communication with OmniActive demonstrates its intent to enforce the '955 Patent and '940 Patent against OmniActive.

6. OmniActive contends that it does not infringe the '955 Patent and the '940 Patent.

7. As a result of Kemin's conduct, there is a "case or actual controversy" between the parties under the Declaratory Judgment Act, 28 U.S.C. § 2201, and jurisdiction is proper in this Court.

8. This Court also has subject matter jurisdiction pursuant to 28 U.S.C. § 1332(a)(1) because OmniActive and Kemin are citizens of different states and the amount in controversy exceeds $75,000.

PERSONAL JURISDICTION AND VENUE

9. Kemin is subject to jurisdiction in New Jersey because, *inter alia*, the events giving rise to this action, as detailed above and below, occurred in the State of New Jersey.

10. Upon information and belief, Kemin makes, markets, and sells a product known as FloraGLO® Lutein. *See* Ex. A.

11. Upon information and belief, Kemin also makes, markets, and sells a product known as ZeaONE® Zeaxanthin. *See* Ex. B, at 2.

12. Kemin has stated that the '940 Patent covers the use of FloraGLO® Lutein and ZeaOne® Zeaxanthin. *See id.* Specifically, Kemin has stated that "[the '940 patent] specifically covers products containing ocular antioxidants including lutein and zeaxanthin employed to protect the eye from light-induced damage, particularly the damage caused by the blue wavelengths of light." *Id.* In addition, Kemin has previously stated that "Kemin intends to vigorously defend and enforce its intellectual property and related rights." *See* Ex. C, at 1.

13. Upon information and belief, Kemin maintains an exclusive strategic partnership with DSM Nutritional Products, Inc. ("DSM") related to, *inter alia*, FloraGLO® Lutein and ZeaOne® Zeaxanthin (distributed by DSM as OPTISHARP® Natural).

14. DSM has a large innovation center in Parsippany, New Jersey. *See* Ex. D, at 1. New Jersey is the US headquarters of DSM's nutritional products business. *See id*.

15. Upon information and belief, under Kemin's agreement with DSM, DSM is Kemin's exclusive distributor, partner, and licensee for FloraGLO® Lutein. *See* Ex. A, at 1-2.

DSM's website states that "FloraGLO® lutein is . . . manufactured by Kemin Health and formulated by DSM as part of an exclusive strategic alliance." Ex. E, at 1. Upon information and belief, Kemin has granted to DSM an exclusive trademark license regarding the FloraGLO® trademark. *Id.*

16. Upon information and belief, under Kemin's agreement with DSM, DSM is also Kemin's exclusive distributor, partner, and licensee for ZeaONE® Zeaxanthin (also branded as OPTISHARP). Kemin has stated that under this agreement, "DSM will serve as Kemin Industries' exclusive and global zeaxanthin distributor for human nutrition, and Kemin will act as DSM's exclusive supplier of naturally-sourced zeaxanthin crystalline material. DSM will also invest in high performance product form innovations for dietary supplement and food applications." *See* Ex. F, at 1. OPTISHARP® is a trademark of DSM. *Id.* Upon information and belief, Kemin has licensed the OPTISHARP® mark from DSM.

17. Upon information and belief, DSM is an exclusive licensee of the '955 Patent and the '940 Patent. As of June 2009, Kemin has publicly stated that DSM is the "sole sublicensee" of FloraGLO® Lutein under certain patent rights, and that it has granted DSM "an exclusive basis to market purified lutein extracted from marigolds." *See* Ex. C, at 1.

18. Upon information and belief, Kemin has extensively sold and marketed FloraGLO® Lutein and ZeaONE® Zeaxanthin through its distributor DSM in the state of New Jersey and gained substantial revenue therefrom.

19. Upon information and belief, Kemin's exclusive agreement(s) with New Jersey-based DSM grant Kemin the right to exercise control over DSM's sales and/or marketing activities.

20. As detailed above, Kemin sent a cease and desist demand to OmniActive's office in New Jersey. *See* Ex. I. OmniActive received the letter on July 29, 2016. Kemin identified the '955 Patent and the '940 Patent as the grounds for Kemin's demands in the letter. Ex. I, at 1.

21. Venue is proper in this forum pursuant to 28 U.S.C. § 1391(b) because a substantial part of the events giving rise to the claims in this Complaint occurred in this forum.

THE PATENTS-IN-SUIT

A. The '955 Patent

22. The '955 Patent was issued to named inventor Richard Roberts on August 26, 2014. The '955 Patent is titled "Methods of Treating Ocular Disorders."

23. A copy of the '955 Patent is attached as Exhibit G.

24. Upon information and belief, the '955 Patent is assigned to Kemin.

B. The '940 Patent

25. The '940 Patent, titled " Methods of Treating Ocular Disorders," issued to named inventor Richard Roberts on January 5, 2016. The '940 Patent is titled "Methods of Treating Ocular Disorders."

26. A copy of the '940 Patent is attached as Exhibit H.

27. Upon information and belief, the '940 Patent is assigned to Kemin.

FACTUAL BACKGROUND

28. As recounted in the foregoing paragraphs, Kemin has engaged in conduct demonstrating its intent to enforce the '940 Patent and '955 Patent against OmniActive by sending communications to OmniActive demanding that OmniActive cease and desist certain marketing activities. More specifically, on July 29, 2016, OmniActive received a letter dated

July 20, 2016 from Kemin demanding that OmniActive immediately cease and desist from specific marketing activities. Kemin identified the '955 Patent and '940 Patent as the bases for its demands in this letter. *See* Ex. I, at 1.

29. As recounted in the foregoing paragraph, Kemin has confirmed its ability and willingness to file suit against OmniActive for infringement of the '955 Patent and '940 Patent and has threatened to bring suit against OmniActive for infringement of the '955 Patent and '940 Patent. *See id*. at 1-2.

30. As recounted in the foregoing paragraphs, Kemin partners with DSM, a company with a U.S. headquarters and an innovation center in Parsippany, New Jersey, to distribute and commercialize its FloraGLO® Lutein and ZeaONE® Zeaxanthin products. *See* Ex. D, at 1; Ex. E, at 1; Ex. F, at 1.

31. According to a Kemin press release, the '940 Patent covers the use of both FloraGLO® and ZeaONE®. *See* Ex. B, at 2.

32. According to another Kemin press release, "[i]n 2008, Kemin and DSM joined forces working under an exclusive strategic alliance. Kemin supplies FloraGLO Lutein exclusively through DSM, which globally commercializes FloraGLO Lutein products through distributors and directly to customers." *See* Ex. A, at 1.

33. As recounted in the foregoing paragraphs, OmniActive has not infringed, and does not infringe, any claims of the '955 Patent and the '940 Patent.

34. As recounted in the foregoing paragraphs, Kemin's accusations against OmniActive implicate OmniActive's Lutemax 2020® product and a case or controversy exists as to whether OmniActive infringes one or more claims of the '940 Patent and the '955 Patent.

Accordingly, a substantial controversy exists between the parties which is of sufficient immediacy and reality to warrant declaratory relief.

COUNT I
(Declaratory Judgment of Non-infringement of the '955 Patent)

35. OmniActive restates, realleges, and incorporates by reference all foregoing paragraphs of this Complaint as if set forth here in their entirety.

36. OmniActive does not infringe, whether directly or indirectly, any valid and enforceable claim of the '955 Patent.

37. As a result of the acts described in the foregoing paragraphs, there exists a substantial controversy of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

38. A judicial declaration is necessary and appropriate at this time so that OmniActive may ascertain its rights and duties regarding the '955 Patent. Absent such a declaration, Kemin will continue to threaten OmniActive with assertion of the '955 Patent against OmniActive and therefore cause OmniActive irreparable injury and damage. OmniActive has no other adequate remedy at law.

39. This is an exceptional case under 35 U.S.C. § 285, entitling OmniActive to an award of its attorneys' fees incurred in connection with this action.

COUNT II
(Declaratory Judgment of Non-infringement of the '940 Patent)

40. OmniActive restates, realleges, and incorporates by reference all foregoing paragraphs of this Complaint as if set forth here in their entirety.

41. OmniActive does not infringe, whether directly or indirectly, any valid and enforceable claim of the '940 Patent.

42. As a result of the acts described in the foregoing paragraphs, there exists a substantial controversy of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

43. A judicial declaration is necessary and appropriate at this time so that OmniActive may ascertain its rights and duties regarding the '940 Patent. Absent such a declaration, Kemin will continue to threaten OmniActive with assertion of the '940 Patent against OmniActive and thereby cause OmniActive irreparable injury and damage. OmniActive has no other adequate remedy at law.

44. This is an exceptional case under 35 U.S.C. § 285, entitling OmniActive to an award of its attorneys' fees incurred in connection with this action.

REQUEST FOR RELIEF

WHEREFORE, OmniActive respectfully requests the following relief:

A. A Judgment be entered that OmniActive has not infringed the '955 Patent;

B. A Judgment be entered that OmniActive has not infringed the '940 Patent;

C. A Judgment be entered in OmniActive's favor that this case is exceptional and awarding OmniActive its attorneys' fees and costs under 35 U.S.C. § 285; and

D. Such further and other relief as this Court may deem just and proper.

Dated: August 15, 2016

By: s/ Charles M. Lizza

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CERTIFICATION PURSUANT TO L. CIV. R. 11.2

I hereby certify that, to the best of my knowledge, this matter is not the subject of any other action pending in any court or of any pending arbitration or administrative proceeding.

Dated: August 15, 2016

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EXHIBIT A

KEMIN INSPIRED MOLECULAR SOLUTIONS™

Technical Literature

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FLORAGLO® LUTEIN: SEE THE DIFFERENCE

Samanta Maci

KEY CONCLUSIONS

- *FloraGLO® Lutein is a brand of purified lutein produced according to a proprietary manufacturing process, naturally contains zeaxanthin, does not contain lutein esters, zeaxanthin esters or synthetic carotenoids.*
- *FloraGLO Lutein is trusted: it is the most clinically researched lutein brand and is the lutein ingredient used in the AREDS2 Study. FloraGLO Lutein is the lutein ingredient used by the leading ocular supplement brands worldwide.*
- *FloraGLO Lutein provides efficient formulations, confirmed stability and shelf life, a critical factor to quality.*
- *FloraGLO Lutein is proven: it is absorbed by the body and has been shown to improve eye and skin health.*
- *The FloraGLO Lutein branding program offers customers Marketing, Regulatory and Technical support that extends around the globe.*

INTRODUCTION

There is a growing body of evidence that lutein, a non-pro-vitamin A carotenoid pigment naturally found in plants, plays an important role in human health.
The rationale for the protective role of lutein in the body stems from the ability of this carotenoid to: 1) filter harmful short-wavelengths of visible light (i.e. blue light), 2) function as antioxidant and 3) stabilize membrane integrity. These biological functions allow lutein to reduce the number of free radicals generated in the body directly by filtering blue light filter, or indirectly by working as an antioxidant.
Lutein can exist in nature in its true “free” form (“lutein” or “free lutein”) or bound to fatty acids (lutein esters). Lutein is not synthesized by the body and thus must be ingested as part of the diet in order for it to be utilized. Dark green leafy vegetables like spinach and kale are the richest sources of lutein, and its isomer zeaxanthin, but other foods such as corn or eggs also provide these carotenoids. It is estimated that 93% of total daily intake of lutein and zeaxanthin is present as free forms while only about 7% is present in the esterified form [1]. The unesterified form of lutein and zeaxanthin is the only form directly absorbed by the human body and found in the human serum [2]. Lutein and zeaxanthin are deposited in almost all the structures of the eye and are selectively concentrated in the *macula lutea*, the region of the retina responsible for central vision. The skin is the second largest repository of lutein in the body [3-5].

Due to its specific deposition in the eye and skin and its reported protective role, lutein is believed to play an important role in reducing light-induced oxidative damage in the eye and skin, the only two organs directly exposed to light.

The daily lutein and zeaxanthin intake in the industrialized world is quite low, averaging between 1-2.5 mg/day in the USA [6] and between 0.45-4 mg/day in EU [7-9]. Although there is no recommended daily intake for lutein and zeaxanthin, many intervention trials support the intake of at least 10 mg lutein for increasing plasma concentration, macular pigment accumulation, improvements in visual function and protection of the skin from environmental hazards [10-15].

FloraGLO® Lutein is a branded lutein ingredient manufactured by Kemin Foods L.C. It naturally contains both lutein and zeaxanthin and is intended for inclusion in food supplements or as a food ingredient for use in foods and beverages to increase the dietary intake of total lutein and zeaxanthin.

In 2008, Kemin and DSM joined forces working under an exclusive strategic alliance. Kemin supplies FloraGLO Lutein exclusively through DSM, which globally commercializes FloraGLO Lutein products through distributors and directly to

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customers. Under this collaboration, customers and consumers benefit from the combination of DSM's strengths: global reach, unique formulation technology and broad product portfolio, and Kemin's strengths: lutein expertise, intellectual property, technical know-how and market development experience.

YOUR SOURCE FOR PEACE OF MIND

FloraGLO Lutein is more than just the original source of purified lutein commercialized worldwide. It is your source for peace of mind:

- Proprietary Manufacturing process[1] and uncompromised quality guarantee:
  - FloraGLO Lutein is a brand of purified lutein that naturally contains zeaxanthin, does not contain esterified lutein or zeaxanthin or synthetic carotenoids.
  - The petals of the flowers of *Tagetes erecta* (marigold) are the starting material of the quality controlled Food Grade Marigold Oleoresin used to manufacture FloraGLO Crystalline Lutein under Kemin's proprietary, manufacturing process.
  - FloraGLO Lutein provides assurances of supply chain management including traceability down to the seeds and fields used to grow the marigold flowers. Good Agricultural Practices (GAP) are used by to grow and harvest the flowers. The use of pesticides, antioxidants and solvents is tightly controlled to ensure that the marigold oleoresin is consistently a quality food grade material.
  - FloraGLO Crystalline Lutein is of U.S. origin and manufactured in compliance with US FDA's current Food Good Manufacturing Practices (CGMPs). At the end of 2009 Kemin received a certification of compliance from NSF® to its NSF/ANSI Standard 173, Section 8, which is based upon the U.S. Food and Drug Administration (FDA) Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements, 21 C.F.R. Part 1108111.
  - FloraGLO Lutein has been the subject of quality review by the United States Pharmacopoeia (USP).

- Customer Focus and Efficient Formulation:
  - FloraGLO Lutein is available in different product forms and concentrations making it suitable for inclusion in many different types of functional foods and food supplement formulations. Similar flexibility can be found in delivery forms for topical applications.
  - The excellent flowability and uniform particle size of the dry forms make formulation convenient. FloraGLO Lutein dry product forms utilize DSM's Actilease® technology to offer superior stability, greater nutrient absorption or bioavailability, and very low extrusion losses. The end result is a premium FloraGLO product form that provides cost savings for the customer and enables them to cost-effectively produce quality nutritional products.
  - FloraGLO Lutein has a confirmed stability and shelf life, a critical factor to quality. Stability analyses, performed in both the ingredient and the finished products, ensure that our customers' finished products meet their label claim throughout shelf life.
- Confirmed safety and World Friendly™ regulatory status provide customers the ability to quickly enter key global markets:
  - FloraGLO Lutein has been the subject of safety reviews by the Food and Drug Administration (FDA) in its Generally Recognized as Safe (GRAS) process and the globally recognized World Health Organization Joint Food Expert Committee on Food Additives (JECFA). JECFA, after reviewing the FloraGLO Lutein specifications, determined an acceptable daily intake (ADI) level for lutein of 2 mg/day per kg of body weight. The European

[1] FloraGLO Lutein's innovative purification process is patent protected in the European Union, Canada, Mexico, Japan and other countries worldwide.

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Food Safety Authority (EFSA) Panel taking a more conservative approach determined an ADI for lutein of 1mg/day per Kg of body weight[16]. These ADIs do not apply to other lutein products not in compliance with the specifications set by JECFA.

- The French Agency for Food Safety (AFSSA) in conjunction with the General Directorate for Competitive Policy, Consumer Affairs, and Fraud Control (DGCCRF) has also reviewed the specifications and safety of FloraGLO Lutein and approved it as food supplement active ingredient.
- FloraGLO Lutein is an ingredient for use in dietary supplements in the US and for conventional foods. Its GRAS status allows manufacturers to add FloraGLO Lutein to a variety of conventional food and beverages at specified inclusion levels in the US market. Additionally, Kemin received a letter of Non-Objection from the FDA to the use of FloraGLO Lutein 20% Safflower Oil as an ingredient in term infant formula at a maximum level of 250 µg/l.
- FloraGLO Lutein can be used as nutritional ingredient in food supplements and conventional foods in the European Union and is not considered a novel food. Food supplement with daily dosages up to 20 mg FloraGLO Lutein per day can be found in the EU market.
- FloraGLO Lutein is suitable for use in many other countries worldwide (e.g. Canada, Brazil, Japan, China, Taiwan, Korea, Australia) where it can be used in conventional foods and/or food supplements.

- Worldwide Marketing, Regulatory and Technical Support:
  - The FloraGLO Lutein branding program offers customers support that extends around the globe. This partnerships includes:
    - Customers formulation assistance, validated analytical methods, customer laboratory support;
    - Scientific training of sales force, regulatory affairs and quality support;
    - Participation as speakers in trade, scientific and medical conferences and meetings;
    - Support of advertising campaigns, joint development of literature and promotional materials;
    - The sharing of information about health professionals' and consumers' product requirements and preferences that is obtained through surveys commissioned by Kemin and conducted by specialized well-known market research specialized companies.

TRUSTED AND PROVEN

Researchers choose FloraGLO Lutein. In fact, FloraGLO Lutein is the most clinically researched lutein ingredient brand [2]. A comprehensive review of the scientific literature reporting the research on human health in which an exogenous source of lutein was used as the test product, FloraGLO Lutein was chosen more often than any other commercially available brand of lutein or lutein esters, and more often than any synthetic source of lutein or any one food source. FloraGLO Lutein was the lutein ingredient used in the AREDS2 study.

- FloraGLO Lutein is proven to be absorbed by the body:
  - FloraGLO Lutein is a purified form of free lutein, chemically identical to the lutein found in abundance in the diet.
  - A pharmacokinetic study conducted in healthy volunteers has clearly demonstrated that lutein from FloraGLO Lutein is absorbed unmodified by the body and circulates in bloodstream [17].
  - Several intervention trials have confirmed that FloraGLO Lutein supplementation significantly increases serum levels of lutein and zeaxanthin vs placebo in young and old subjects [18-21]. Additionally FloraGLO Lutein

[2] Kemin Foods L.C. Internal Memorandum based on Pubmed search.

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absorption is not impaired in the elderly [22].

- FloraGLO Lutein has been shown to help improve eye health:
  - Intervention studies confirm that the supplementation with 10 mg FloraGLO Lutein or more results in significant and sustained increased macular pigment optical density (MPOD) in both subjects with ocular diseases and healthy subjects [10, 23, 24].
  - The daily administration of 10-15 mg of FloraGLO Lutein over a 6 to 12 month period improved visual and macular function in patients suffering from AMD [10-12, 24, 25].
  - FloraGLO Lutein was the source of lutein chosen by the investigators of the AREDS2 study, sponsored by the National Eye Institute of the National Institutes of Health in USA., The AREDS2 study supports the daily supplementation with 10 mg FloraGLO lutein and 2 mg zeaxanthin in reducing the progression to advanced AMD by 10%[26, 27].
  - FloraGLO Lutein was additionally used in a recent research showing that the daily administration of 10 mg lutein or more, alone or in combination with 2 mg zeaxanthin, improves contrast acuity and reduces glare disability and photostress recovery time in healthy young adults[14, 28].
  - FloraGLO Lutein is the lutein ingredient used in the leading ocular supplement brands worldwide.

- FloraGLO Lutein has been shown to help improve skin health:
  - The administration of FloraGLO Lutein together with other carotenoids and antioxidants has been shown to be effective against free radical-induced damage in human skin, including that associated with UV light, and resulted in direct improvements in skin density, hydration and elasticity [29].
  - FloraGLO Lutein administered orally (10 mg lutein/day), topically (50 ppm twice daily) or in combination as the only treatment for skin health, significantly improved five important parameters of skin health (skin hydration, skin elasticity, skin lipids, skin lipid peroxidation, and skin photoprotective activity) in comparison to placebo ingested and/or topically applied [15].

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EXHIBIT B

Company

News (/en/north-america/company/news-events/news)

Press Releases (/en/north-america/company/news-events/press-releases)

Events (/en/north-america/company/news-events/events)

Media Center (/en/north-america/company/news-events/media-center)

FLORAGLO® LEGACY CONTINUES WITH NEW BLUE LIGHT PROTECTION PATENT. ROYALTY-FREE LICENSE PROVIDES 'HUGE MARKET OPPORTUNITY.'

July 12, 2016

Des Moines, Iowa – July 12, 2016 – The United States Patent and Trademark Office has issued Kemin Industries a patent (U.S. Patent No. 9,226,940 B2) for the role of its products, FloraGLO® Lutein and ZeaONE® Zeaxanthin (distributed by DSM as OPTISHARP® Natural), in protecting individuals with three common ocular disorders from blue light or light-induced damage.

Kemin's patent allows vitamin and dietary supplement manufacturers using FloraGLO® and/or ZeaONE® to position their products for blue light protection. The patent specifically covers products containing ocular antioxidants including lutein and zeaxanthin employed to protect the eye from light-induced damage, particularly the damage caused by the blue wavelengths of light. The patent targets individuals with presbyopia, hyperopia or astigmatism. In these three conditions, blue wavelengths of light are focused directly onto the macula, creating a higher risk for ocular damage.

Blue light impacts the majority of adults ages 45 and older who have presbyopia, commonly known as age-related farsightedness.[1]

"Because of the widespread prevalence of presbyopia, this patent opens the door for FloraGLO® and OPTISHARP® Natural customers to make blue light eye protection claims when targeting consumers 45 years and older," said Dr. Richard Roberts, patent inventor and principal manager of scientific affairs and technical services for the Human Nutrition and Health division of Kemin.

Nearly every source of light—whether natural or artificial—emits harmful blue wavelengths of light. The growing prevalence of digital devices like computers, tablets and smartphones is exposing individuals to more blue light than ever before. Over half of Americans use digital devices more than five hours a day and 70% use two or more devices at the same time.

In addition to blue light from digital devices, the use of the light emitting diode (LED) in indoor lighting is another growing source of blue light exposure. LED bulbs contain 35% blue light levels as compared to 3% levels in traditional incandescent bulbs. In North America alone, LED lighting made up a $4.8 billion market in 2012 and is expected to make up a $42 billion market by 2019.

As blue light levels and sources continue to grow, children are especially vulnerable to the effects. Blue light exposure is especially concerning for infants and young children, as nearly every child is born with hyperopia, commonly known as farsightedness. Because of the condition, they are at a higher risk for blue light and light-induced damage as their eyes develop.

"Children are exposed to blue light more than ever before. Believe it or not, greater than half of American children use digital devices two or more hours a day," said Heather Richardson, vision platform senior product manager at for the Human Nutrition and Health division of Kemin. "Our patent can help customers address this growing concern and develop blue light protection products for kids."

"We are pleased to be able to offer a royalty-free license of our patent to customers who are interested in marketing blue light protection products to adults 45+ and children ages 0-2," said Anita Norian, president of the Human Nutrition and Health division of Kemin. "It is clear this will be a huge market opportunity for our customers as the concern of blue light exposure and consumer awareness grows."

Rooted in science with unparalleled efficacy and safety, the FloraGLO® name is synonymous with lutein excellence. For the past 20 years, FloraGLO® has been a pioneer for lutein science and discovery. Kemin's blue light patent is just another example of FloraGLO® setting the gold standard for the lutein market, and building new opportunities in the lutein marketplace.

For more information on FloraGLO®, visit www.floraglo.com (https://www.kemin.com/en/north-america/products/floraglo-lutein).

ZeaONE® is marketed as OPTISHARP® Natural in North America. OPTISHARP® Natural is made with patented ZeaONE™ from Kemin. ZeaONE is a ® trademark of Kemin Industries, Inc. and is licensed under U.S. Patent Numbers 6,748,351, 7,575,766, and 7,033,622. OPTISHARP® Natural is a registered trademark of DSM Nutritional Products.

Kemin® – Inspired Molecular Solutions™

Kemin (www.kemin.com (https://www.kemin.com/)) provides "inspired molecular solutions" specifically developed to provide nutrition and health benefits for humans and animals. Committed to feed and food safety, Kemin maintains top-of-the-line manufacturing facilities where approximately 500 specialty ingredients are made for the global feed and food industries as well as the health, nutrition and beauty markets. A privately held, family-owned and operated company, Kemin has nearly 2,000 employees and operates in 90 countries with manufacturing facilities in Belgium, Brazil, China, India, Italy, Singapore, South Africa and the United States.

For media inquiries, please contact:

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References:

Source document KHMKTC-022-000357-R

Back to articles (/en/north-america/company/news-events/press-releases)

EXHIBIT C

Patent Reissued Including New Claims for Kemin Health's FloraGLO® Lutein

June 11, 2009 08:00 AM Eastern Daylight Time

DES MOINES, Iowa--(BUSINESS WIRE)--Kemin Health is pleased to announce that Notices of Allowance have been issued by the United States Patent Office for claims 1-20 and two new claims 21 and 22 of U.S. Patent 5,382,714. The Notices of Allowance are in response to two recent decisions from the Board of Patent Appeals and Interferences of the U.S. PTO, where the Board agreed with Kemin's position in the reissue applications the company filed on the '714 Patent. The Board, in its review, also granted Kemin two additional claims

The reissue applications contain claims covering (1) a lutein composition comprising (a) at least about 90% lutein having been extracted and purified from plant extracts which contain 10% or less of non-lutein carotenoids, (b) no traces of toxic chemicals that would render the lutein composition unsuitable for human consumption, and (c) significantly less than about 10% of non-lutein carotenoids obtained by purification of said plant extracts as well as (2) a method for providing such lutein compositions to humans

Kemin believes the reissue presumptively gives DSM Nutritional Products, Inc. ("DSM"), our sole sublicensee of FloraGLO lutein under the patent, an exclusive basis in the US to market purified lutein extracted from marigolds (at the above-recited concentration) that does not contain toxic chemicals above levels that would make it unsuitable for human consumption

Since 1995, Kemin Health's FloraGLO lutein has been protected in the US by the '714 patent, along with additional patent rights in the US and worldwide. "The patent reissue significantly strengthens our intellectual property and will help further to protect the FloraGLO market and the business of our FloraGLO customers," said Rodney Ausich, president of Kemin Health. "Kemin intends to vigorously defend and enforce its intellectual property and related rights."

FloraGLO Lutein is the world's first and leading patented, purified lutein (floraglolutein.com). The ingredient is used extensively in supplements, in foods and beverages and most recently, in infant formula throughout the world. Derived from marigolds, FloraGLO Lutein is distributed worldwide for its beneficial effects on eye health and function, skin health, and as an antioxidant.

Kemin® – Inspired Molecular Solutions™

Founded in 1961, Kemin Industries, Inc. (www.kemin.com) provides health and nutritional solutions to the agrifoods, food ingredients, pet food and human health and pharmaceutical industries. Kemin operates in more than 60 countries with manufacturing facilities in Belgium, Brazil, China, India, Singapore, South Africa, Thailand and the United States.

Kemin Health, a division of Kemin Industries Inc., develops, manufactures and markets specialty ingredients with healthful benefits for the dietary supplement and functional food and beverage markets. Specific to the nutraceutical industry, Kemin Health is credited with successfully commercializing lutein and significantly developing the eye supplement category under the FloraGLO® lutein brand, the leading brand sold worldwide.

Contacts

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EXHIBIT D

NUTRA ingredients-usa.com

Breaking News on Supplements, Health & Nutrition - North America

DSM opens state-of-the-art innovation center in Parsippany, NJ

By Elaine Watson, 23-May-2011

Related topics: Suppliers

DSM has opened a new multi-million-dollar state-of-the-art nutrition innovation center in Parsippany, New Jersey, at the US headquarters of its Nutritional Products business.

The center, which is staffed by more than 100 applications specialists and technical marketing experts in food, beverage, dietary supplement and personal care, includes laboratories, pilot plants and sensory analysis facilities enabling DSM to work far more closely with customers at every stage of the product development process.

The facility will enable DSM to optimize production processes, improve quality, test new ingredients and develop novel finished product concepts, from sports nutrition bars with zeaxanthin and lutein to enhance visual performance to chocolates or beverages laced with green tea extracts, resveratrol and vitamin E for beauty-from-within.

But it would also help the firm build closer relationships with customers, who are increasingly working with DSM at the earliest stages of product concept development, DSM Nutritional Products North America president Jim Hamilton told journalists during a preview of the new center last week.

"Increasingly we're doing our own market research to understand where consumers are heading and combining that insight with our science and applications expertise to help customers get innovative products to market more quickly."

Metabolic health, mental performance and fitness/wellness

While the US dietary supplements market continued to grow throughout the recession, the functional food and drink market had not weathered the storm so well, with a steady drop in the number of new products launched in 2008-10, accepted market segment head for infant nutrition and medical foods Anthony Palmieri.

However, big branded manufacturers were still looking at functional foods because genuine innovation would always be a differentiator, stressed Todd Sitkowski, senior marketing manager.

"I still think most people want to get their nutrition from food not pills."

For consumers, the hot areas were metabolic health, fitness and wellness, and mental performance, said Jean-Claude Tritsch, director, global technical marketing.

"We are involving our customers from the very beginning, right at the concept stage, starting with health benefits rather than ingredients."

Visual performance and sports nutrition

Customers visiting the innovation center could see a raft of new concepts in all of the above areas, including new bars targeting an emerging area in sports nutrition, said senior marketing manager Aparna Parikh.

While visual performance might sound niche from a functional foods perspective, DSM had recently pitched concepts featuring Kemin's FloraGlo lutein and DSM's OptiSharp zeaxanthin for enhanced contrast, glare tolerance and recovery to major food and beverage manufacturers as well as dietary supplements companies, she said.

"This is an emerging area in sports nutrition. If you're playing sports in the sunshine, being able to tolerate and recover from glare and see the ball more clearly at pace and from a distance can make a big difference.

"It's not something you would just eat once before a baseball game, you'd need to take it regularly."

Battling the bulge

New product concepts on show at Parsippany featuring appetite-busting palm and oat oil emulsion Fabuless were also garnering interest, claimed dietary supplements marketing director Lynda Doyle.

"Fabuless has been doing very well, and more products should be launching this year. To date, most of the launches have been in one shot products or stick packs but we're working on solutions for bars and other products."

Meanwhile, a new powdered formulation for partner Provexis' Fruitflow tomato-extract was expected to launch in second half of this year, while a raft of new concepts – and new ingredients – were also being investigated in the mental function arena, said Tritsch. *"Cognition is particularly hot, right now, and we're got new products in internal pipeline beyond DHA and B vitamins."*

Although the firm did not provide a precise definition of what constituted a 'new' product, 20 percent of its revenues were expected to be from innovation/new products by 2020, said Doyle.

"We have bought or invested in companies in order to access new ingredients but we are also doing a lot of work internally on new ingredients and have a huge database of compounds and molecules from natural sources that we're looking at across multiple health platforms."

Formulation and applications expertise

While DSM spent a whopping €424m on R&D in 2010 (5.2 percent of net sales), much of which went into new ingredient discovery and development, the investment in the innovation center at Parsippany reflected an increasing commitment to differentiate itself in the market through its formulation and applications expertise, he said.

"A key part of the value we add is in blending, formulation, from how to add [fat-soluble] *vitamin E to a beverage without it going cloudy or how to add vitamin A to sugar and retain stability to how to improve the bioavailability of iron."*

Major branded customers in the food and drink world were also turning to DSM because of its expertise in quality and sustainability, said Hamilton.

"If you have a brand and you are interested in quality and innovation, you will be interested in us. You can never buy back your reputation with the money you save on cheap ingredients."

Meanwhile, sustainability and the desire for 'cleaner' labels and natural ingredients was "*becoming more and more part of the conversation we're having with customers and end consumer*s", he said.

For more details about the facilities at the new innovation center at Parsippany, look out for our photo gallery, which will be published later this week.

EXHIBIT E

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

DSM in Food, Beverages & Dietary Supplements

FloraGLO® Lutein

Lutein is a yellow pigment found in many plants – particularly the marigold.

FloraGLO® lutein is the most clinically researched lutein brand worldwide - manufactured by Kemin Health and formulated by DSM as part of an exclusive strategic alliance.

Lutein is a structural isomer that belongs to the carotenoid family. Carotenoids are synthesized by plants for coloration and absorption of light.

Of the 600-plus carotenoids found in nature, only lutein and zeaxanthin and their metabolites are located in macula of the eye, where they are found in the highest concentration anywhere in the human body - suggesting an important biological role for these molecules.

FloraGLO® is a registered trademark of Kemin Industries, Inc.

Key benefits

Lutein absorbs blue light and acts as 'internal sunglasses' that may reduce photochemical damage caused by short-wavelength visible light.

Consuming lutein – though green leafy vegetables or dietary supplements – increases Macular Pigment Optical Density (MPOD) in human eyes; which in turn decreases the risk of Age-related Macular Degeneration (AMD).

Age-related Macular degeneration (AMD)

AMD is a disease of the central retina that generally affects people aged over 55. Causes include environmental factors (nutrition, UV light exposure), risk factors (aging, hypertension, and smoking) and genetic predispositions.

Lutein (together with zeaxanthin) has a well-founded biologic rational including its high density in the macula, ability to filter short-wavelength light, and protection from free radical formation in the macula. A growing body of research indicates that high intake of lutein and zeaxanthin may play a role in lowering the risk of AMD – the most common cause of blindness in the elderly in the western world.

Visual Performance

Visual Performance is all about how well we see fine details; distinguish between different objects (contrast); and recover sight after a flash of bright light. Emerging evidence points to the role lutein and zeaxanthin play in visual performance. They form a filter (macula pigment) over the part of the retina responsible for detailed vision.

This filter blocks out blue light and haze from strong light – which increases the eyes' tolerance to bright lights. Supplementation with the macular pigments has the potential to improve vision in our daily lives, particularly when our eyes are challenged by intense light such as glare from the sun, a camera flash, or blinding headlights at night.

Skin Health

Recent human studies demonstrate that lutein also has skin health benefits, providing protection from the harmful effects of sunlight and enhancing skin hydration and elasticity.

Applications

Actilease for better absorption

We provide FloraGLO® Lutein in various forms. All products provide excellent flowability and uniform particle size for ease of formulation. ForaGLO® also offers superior stability, greater nutrient absorption and very low extrusion losses. This means lower overages, smaller tablets and higher yields, saving time and money. FloraGLO® beadlet product forms use special Actilease® technology developed to maximize nutrient absorption and optimize bioavailability.

FloraGLO® product forms:

20% liquid for soft gelatine capsules
5% and 10% beadlets for tablets, hard-shell capsules, effervescents and fortification of beverages, bars and other selected foods.

Hear their stories

Professional athletes are convinced of the visual performance benefits of lutein and zeaxanthin.

Disclaimer

HEALTH · NUTRITION · MATERIALS

EXHIBIT F

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

Back to press releases

Kemin and DSM expand partnership to include natural zeaxanthin

Kaiseraugst, CH, 01 Oct 2014 10:00 CEST

Companies partner to offer naturally-sourced zeaxanthin and lutein for important health benefits

Kemin and DSM are pleased to announce the launch of OPTISHARP™ Natural brand of zeaxanthin. Kemin, pioneer of FloraGLO® Lutein, and DSM, creator of OPTISHARP Zeaxanthin, are expanding their longtime lutein partnership to deliver high-quality, naturally-sourced zeaxanthin. OPTISHARP Natural, made from Kemin Industries' ZeaONE™ brand of zeaxanthin, offers important benefits for eye health, cognition and skin health.

"*This is a real win for both our customers*," said Anita Norian, Kemin president of the human nutrition and health division. "*Kemin and DSM have been partners in the global carotenoid market since the late 1990s, and further collaboration will only maximize the exceptional quality and service both organizations' customers have come to know*."

This partnership combines the sound science, research, marketing and technical support of Kemin and DSM. Under the agreement, DSM will serve as Kemin Industries' exclusive and global zeaxanthin distributor for human nutrition, and Kemin will act as DSM's exclusive supplier of naturally-sourced zeaxanthin crystalline material. DSM will also invest in high performance product form innovations for dietary supplement and food applications.

The zeaxanthin ingredients will be marketed under DSM's OPTISHARP brand as *OPTISHARP Natural*. *OPTISHARP Natural* is formulated from hybrid marigold flowers that are protected under patent rights licensed exclusively by Kemin and provide the same free-form of zeaxanthin found in most fruits and vegetables.

"*We are excited about this new collaboration that solidifies both organizations' positions as leaders in the eye health market, facilitating further development for both lutein and zeaxanthin*," said Norian. "*Customers will be offered easy-to-use, convenient formulations that combine the two complementary ingredients, lutein and zeaxanthin*."

"*As a leading provider of zeaxanthin, DSM is pleased to expand its relationship with Kemin and offer an additional 'natural' choice as part of our existing OPTISHARP portfolio*," said Will Black, DSM vice president of marketing for human nutrition & health, North America. "*There is a significant and comprehensive body of evidence supporting the positive effects of lutein and zeaxanthin on eye health*

and visual function, both through the protection of specific eye tissues and by increasing visual performance. We continue to support further clinical research to reinforce the scientific basis for the positive impact of lutein and zeaxanthin on eye health, as well as the benefits that zeaxanthin provides for cognition and skin health in its role as an antioxidant."

OPTISHARP Natural will be featured at Supply Side West in Las Vegas on Oct. 8-10. Both teams will be promoting sales of FloraGLO Lutein and *OPTISHARP Natural* in order to offer customers the convenience of both forms from a single source and to provide DSM customers with a naturally-sourced, quality zeaxanthin backed by both Kemin and DSM.

HEALTH · NUTRITION · MATERIALS

EXHIBIT G

US008815955B2

(12) **United States Patent**
Roberts

(10) **Patent No.: US 8,815,955 B2**
(45) **Date of Patent: Aug. 26, 2014**

(54) **METHOD OF TREATING OCULAR DISORDERS**

(75) Inventor: **Richard Roberts**, Johnston, IA (US)

(73) Assignee: **Kemin Industries, Inc.**, Des Moines, IA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 207 days.

(21) Appl. No.: **13/238,939**

(22) Filed: **Sep. 21, 2011**

(65) **Prior Publication Data**

US 2012/0070422 A1 Mar. 22, 2012

Related U.S. Application Data

(60) Provisional application No. 61/384,958, filed on Sep. 21, 2010.

(51) **Int. Cl.**

A61K 31/07	(2006.01)
A61K 31/34	(2006.01)
A61K 31/355	(2006.01)
A61K 31/35	(2006.01)
A61K 33/24	(2006.01)
A61K 36/00	(2006.01)

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

USPC **514/725**; 514/474; 514/458; 514/734; 424/617; 424/725

(58) **Field of Classification Search**

USPC 514/725, 474, 458, 734; 424/617, 725

See application file for complete search history.

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(Continued)

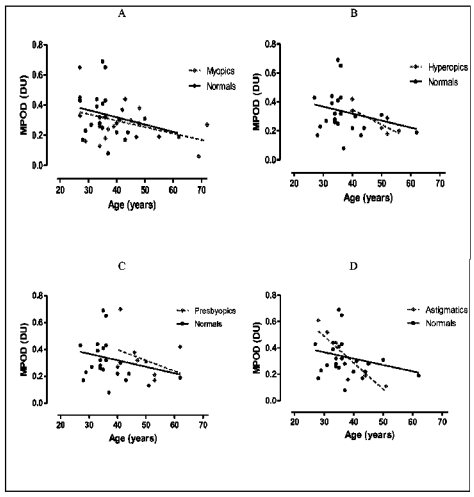
Primary Examiner — Rosanne Kosson

(74) *Attorney, Agent, or Firm* — Davis, Brown, Koehn, Shors & Roberts, P.C.; Kent A. Herink

(57) **ABSTRACT**

A method wherein subjects having or at risk for having hyperopia, presbyopia or astigmatism are administered a composition having an effective amount of ocular antioxidants, including specifically macular pigments, to prevent, treat, or delay the onset of age-related macular degeneration (AMD).

13 Claims, 4 Drawing Sheets



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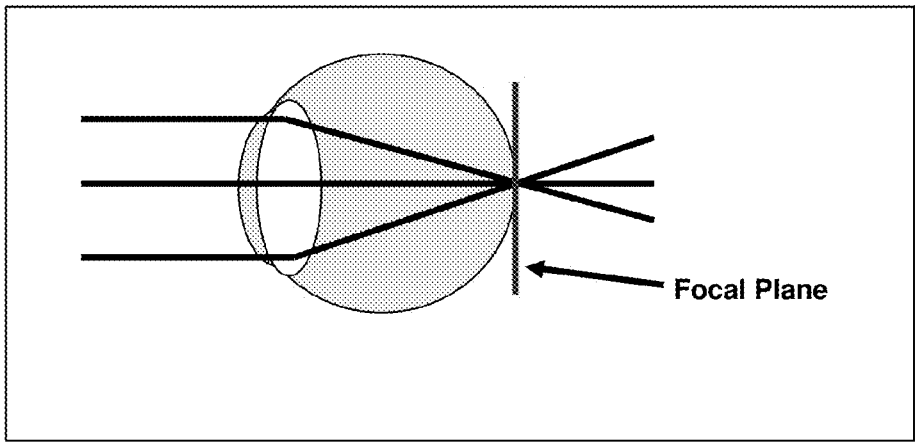


FIG. 1

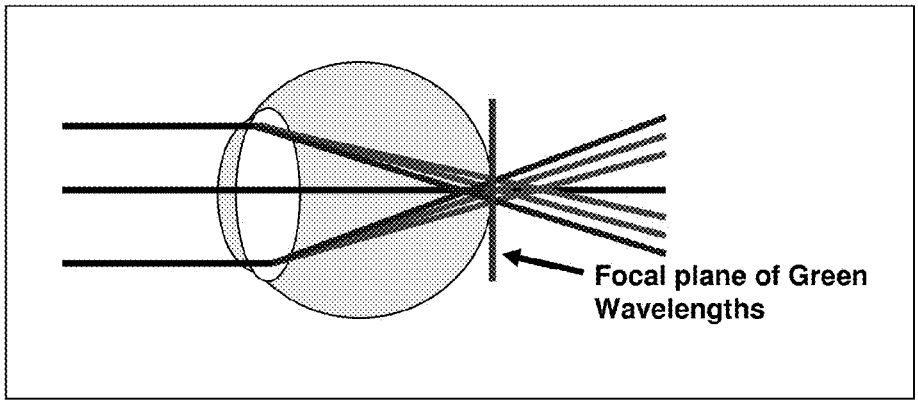


FIG. 2

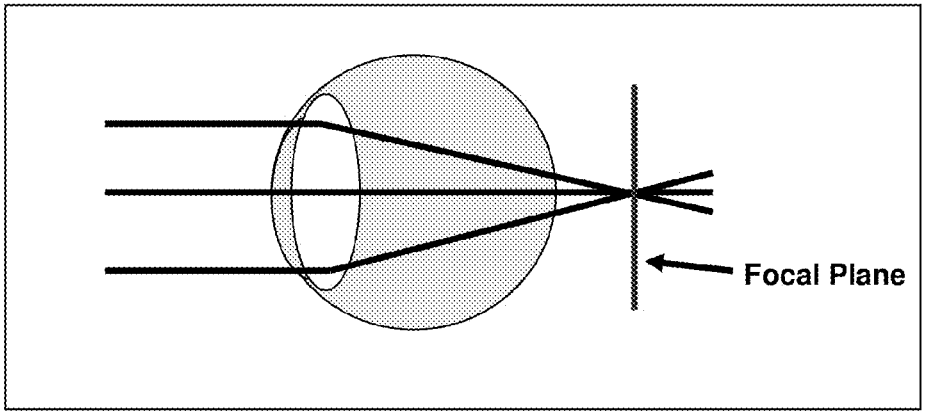


FIG. 3

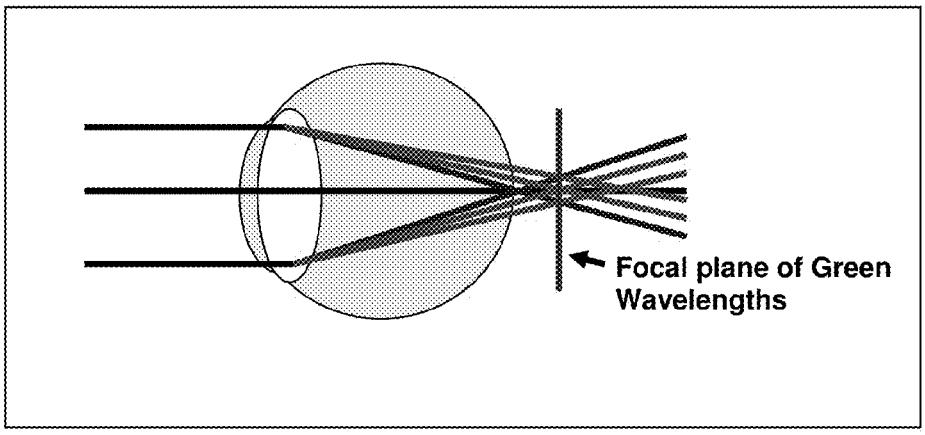


FIG. 4

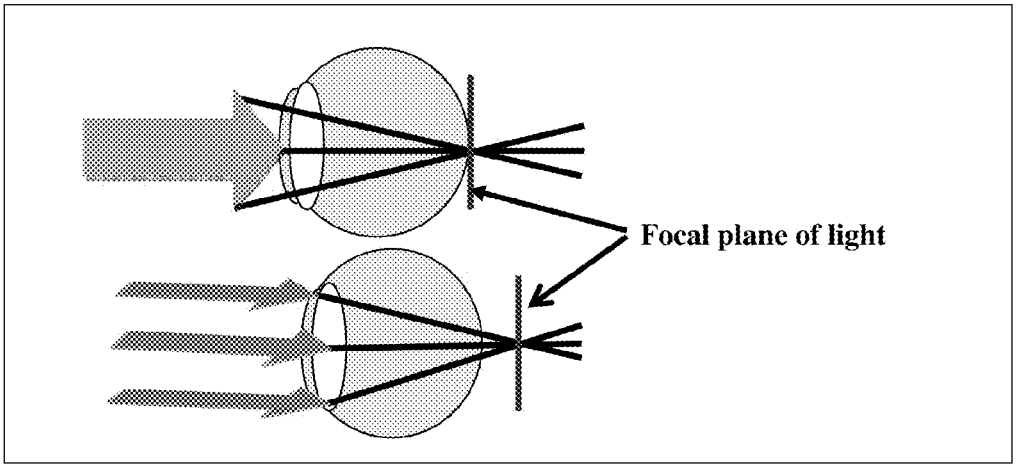
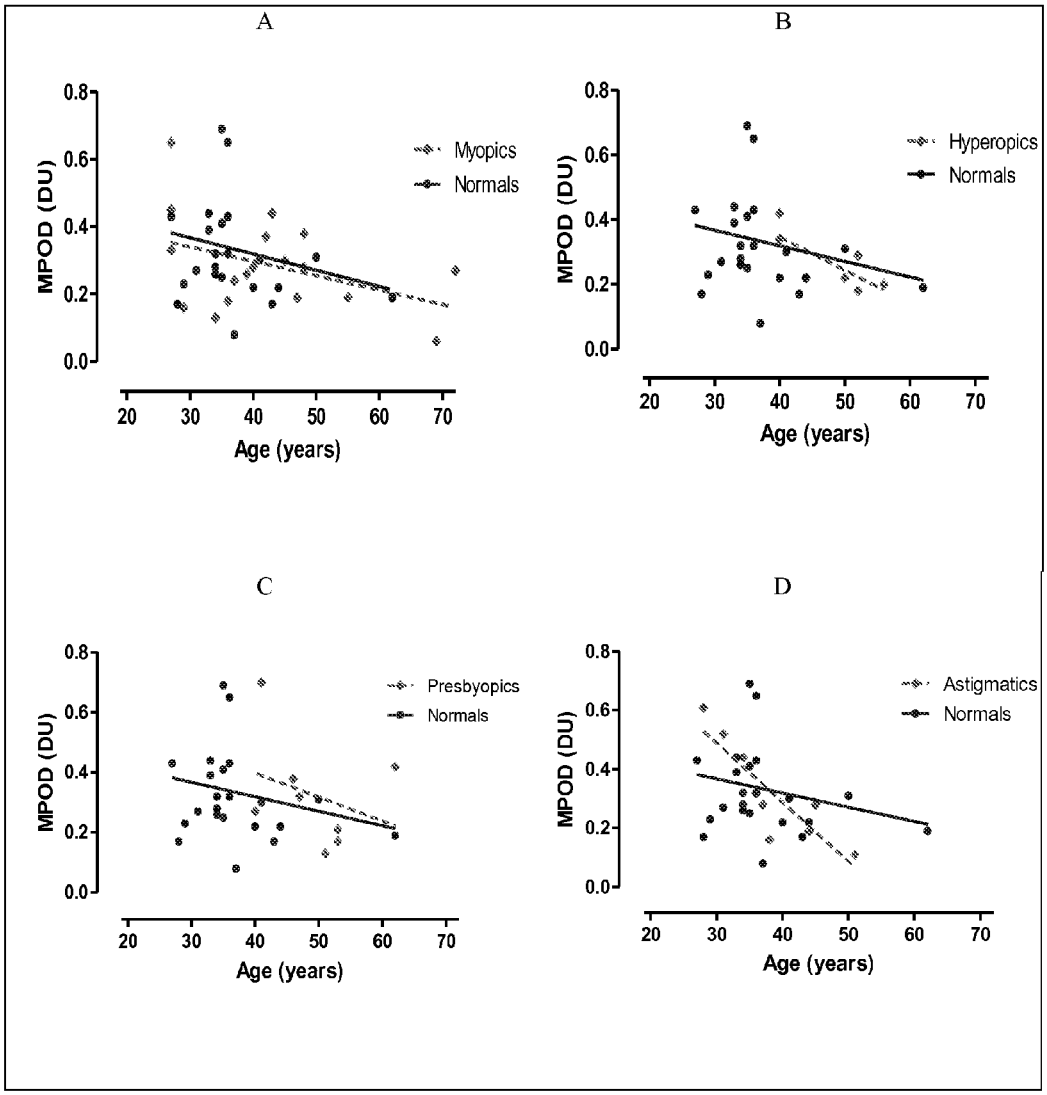


FIG. 5


A
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MPOD (DU)
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Myopics
Normals
Hyperopics
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Presbyopics
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Astigmatics
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FIG. 6

METHOD OF TREATING OCULAR DISORDERS

This application claims priority to U.S. Patent Application Ser. No. 61/384,958, filed Sep. 21, 2010, which is incorporated herein by this reference.

BACKGROUND OF THE INVENTION

The present invention relates generally to a method of early diagnosis and treatment of ocular disorders and, more specifically, to the early diagnosis of subjects at risk for age-related macular degeneration and the administration of ocular antioxidants to subjects having hyperopia, presbyopia or astigmatism.

Hyperopia, presbyopia, and astigmatism are visual or ocular disorders that affect a significant percentage of the human population worldwide.

Age-related macular degeneration (AMD) is a disease associated with aging that gradually destroys sharp, central vision. The disease attacks the macula, the central area of the retina that allows a person to see fine detail. Individuals can lose all but the outermost peripheral vision, leaving dim images or black holes at the center of vision. AMD is a leading cause of vision loss and legal blindness in adults over 60 in the United States. An inverse relationship exists between the incidence of AMD and the amount of macular pigments, principally lutein and zeaxanthin, in the macula.

SUMMARY OF THE INVENTION

The present invention consists of the administration to subjects having or at risk for having hyperopia, presbyopia or astigmatism with a composition having a therapeutically effective amount of ocular antioxidants, including specifically macular pigments, to prevent, treat, or delay the onset of AMD. The invention also consists of a method for the early diagnosis of subjects at increased risk of developing AMD consisting of the existence or risk for the existence of hyperopia, presbyopia or astigmatism.

The composition may also include antioxidant compounds include vitamins A, C, E, and other vitamins exhibiting antioxidant activity; beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin; zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems; natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, and the like; and synthetic antioxidants including BHT, BHA, BTHQ, or any synthetic analog of the natural antioxidants.

The supplementation can take any desired form, including addition of the composition to food, beverages, and/or dietary supplement tablets, capsules, and other more esoteric delivery forms. Furthermore, the composition including ocular antioxidants can take any form, including but not limited to powders, beadlets, crystals, liquids, dispersions, and the like as long as it can be delivered to the body in a form and in amounts that can be absorbed and used by the body

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a graphical representation of the focal plane of visible light in a normal eye.

FIG. **2** is a graphical representation of focal plane for the chromatic wavelengths of visible light in the normal eye.

FIG. **3** is a graphical representation of focal plane for the visible light by the presbyopic/hyperopic eye.

FIG. **4** is a graphical representation of focal plane for the chromatic wavelengths of visible light in the presbyopic eye.

FIG. **5** is a graphical representation of the focal plane of light after passing through lens of a hyperopic, astigmatic eye; the two planes of light entering the eye in this figure are orthogonal (at 90°) to one another.

FIGS. **6**A-D are graphical representations of MPOD values as a function of age for different types of vision correction in comparison to subjects who exhibiting vision that has never required correction (i.e., normals).

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

As used herein, the terms "age-related macular degeneration" and "AMD" refer to a disease associated with aging that gradually destroys sharp, central vision. The disease attacks the macula, the central area of the retina that allows a person to see fine detail.

"Macular pigment" refers to a composition that includes carotenoids found in the macula of the eye, principally lutein and zeaxanthin.

"Ocular antioxidant" includes (a) vitamins A, C, E, and other vitamins exhibiting antioxidant activity; (b) beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin; (c) zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems; (d) natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, and the like; and (e) synthetic antioxidants including BHT, BHA, BTHQ, or any synthetic analog of the natural antioxidants.

As used herein, the term "therapeutically effective amount" refers to the amount/dose of a compound or pharmaceutical composition that is sufficient to produce an effective response (i.e., a biological or medical response of a tissue, system, animal or human sought by a researcher, medical doctor or other clinician) upon administration to a subject. The "therapeutically effective amount" will vary depending on inter alia the disease and its severity, and the age, weight, physical condition and responsiveness of the subject to be treated.

As used herein, the terms "treated" and "treating" refers to preventing or delaying the appearance of clinical symptoms of a disease or condition in a subject that may be afflicted with or predisposed to the disease or condition, but does not yet experience or display clinical or subclinical symptoms of the disease or condition. "Treating" also refers to inhibiting the disease or condition, i.e., arresting or reducing its development or at least one clinical or subclinical symptom thereof. "Treating" further refers to relieving the disease or condition, i.e., causing regression of the disease or condition or at least one of its clinical or subclinical symptoms. The benefit to a subject to be treated is either statistically significant or at least perceptible to the subject and/or the physician.

Hyperopia, or farsightedness, is a physical defect of the eye, primarily of genetic origin, in which the lateral axis of the eyeball (from cornea to posterior sclera) is too short or the lens of the eye exhibits insufficiently curvature for light to properly be focused upon the retina. This condition is normally easily detected through a routine eye examination and is readily corrected through the use of corrective lenses (surgery, glasses, or contact lenses).

Presbyopia, which is commonly confused with hyperopia, is an age-related visual disorder that affects virtually everyone to some extent. However, the degree of presbyopia varies between individuals. Although the exact cause of presbyopia

is not known, it is generally accepted that it is a result of 1) a hardening of the lens of the eye and/or 2) an inability of the lens to adequately change curvature under the influence of the ciliary muscles and the zonules. The result is an improper focus of the image upon the retina. Regardless of the cause of presbyopia, at about the age of 40, most individuals begin to notice that nearby objects appear to be blurred. These individuals complain that their arms are not long enough to accurately focus upon nearby objects, especially when reading, particularly when trying to focus upon small print such as labels and/or newspapers, or when manipulating small objects with their hands. Therefore, the hallmark of presbyopia is that adults find it increasingly difficult to focus upon objects that are near to them. Distance vision is normally unaffected. Prebyopia is a slowly progressing ocular disorder. This progressive loss of near vision is slow enough that individuals may not complain about it for a considerable period of time. This is because of two reasons: 1) there is a stigma associated with wearing corrective lenses, especially glasses when they have never worn glasses and 2) when the distance between the eye and a blurry object is increased, the blurry object may come into better focus, especially in early presbyopia. In this early stage, presbyopia can be corrected to normal or near-normal vision through the use magnifying lenses (commonly referred to as reading glasses, which can be purchased at most drugstores). However, over the decades as we age, presbyopia normally becomes progressively worse thereby making vision correction by corrective lenses or surgery a necessity in many individuals.

Astigmatism is a defect of either the cornea (corneal astigmatism) or the lens (lenticular astigmatism) of the eye in which there is an irregular curvature to one or both of these structures. Corneal astigmatism is the most common type. In normal vision, the curvature of both the cornea and the lens are symmetrical along their horizontal and vertical planes creating a curvature similar to that of the surface of a basketball. Although irregular astigmatism (i.e., irregular curvatures in both the horizontal and vertical planes simultaneously, commonly referred to as compound astigmatism; or mismatched curvatures in both the cornea and lens) is known to exist, it is considered to be rare. In the typical form of astigmatism, the curvature in one of these planes (horizontal or vertical) is steeper than the curvature in the other plane. Therefore, the surface through which the light must pass in order to reach the retina resembles that of a football with the long axis directed either along either the horizontal or vertical axis of the eye. Since light passing through these mismatched curvatures cannot be focused equally, the focal point of light striking the retina in the two planes is not equivalent. When the light impinging upon the retina from one plane is in focus, light in the other plane is not in focus. This results in a blurring or smudging of the visual image. Although astigmatism less than about 0.5 diopters is not considered as needing correction, astigmatism greater than 0.5 diopter generally results in noticeable visual impairment and thereby requires correction. Further complicating this issue, although light passing through the normally curved plane of the cornea is focused properly, light in the astigmatic plane can be focused hyperopically (focused behind the retina) or myopically (focused in front of the retina) depending upon the curvature of the cornea.

At birth, the prevalence and degree of astigmatism is very high and primarily of corneal origin as it is in adults. Fortunately the incidence rate of astigmatism decreases as children grow as a result of a flattening of the astigmatic curvature of the cornea. In the age range of about 6 years and early adulthood, the incidence of astigmatism does not change appreciably. Approximately 5% of people in this age group exhibit astigmatism and about 75% of them exhibit "with the rule" astigmatism (i.e., the steepest slope of cornea is oriented along the vertical meridian). After the age of about 45, not only does the incidence of astigmatism increase, but additionally the direction of astigmatic corneal curvature also appears to change. Adult astigmatism, which has been estimated to reach an incidence rate of 35%, is primarily "against the rule" (i.e., exhibiting the steepest slope of the cornea along the horizontal meridian). This change in the orientation of the corneal slope is believed to be a result of a reduction in tension of the eyelids upon the eyeball that typically occurs with aging.

Relationship between Ocular Defects, AMD, and Ocular Antioxidants

The relationship between hyperopia, presbyopia and astigmatism, Age-Related Macular Degeneration (AMD) and ocular antioxidants as described in this document, is based upon the known effects of the cornea and lens of the eye in relation to the focusing light of upon the retina; the available information on ocular disorders including AMD (the factors associated with their incidence; the effects of light upon the retina; and the reported effects of ocular antioxidants to reduce the potential damage induced in retinal tissues caused by that light, particularly the reported effect of ocular antioxidants in helping to reduce the progression of AMD). Although references have been found that tie some of these factors together as described in this document, no publications or references have been identified relating all of these factors in a unified manner. Therefore, some background is necessary to understand the relationship between these factors.

Multiple studies, particularly the Lutein Antioxidant Supplementation Trial (the LAST Study) conducted by Dr. Stuart Richer have produced results demonstrating that visual acuity, contrast sensitivity, and the amount of macular pigment in the human eye can be improved as a result of lutein and zeaxanthin supplementation or a combination of these xanthophylls with other antioxidants (Richer S, Stiles W, Statkute L, Pulido J, Frankowski J, Rudy D , Pei K, Tsipursky M, and Nyland J. (2004) Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: The Veterans LAST study (Lutein Antioxidant Supplementation Trial). *Optometry* 75:216-230). The LAST Study was conducted using a group of 90 patients with AMD over a time period of 12 months. The results show that the intake of xanthophylls with or without additional antioxidants increased visual parameters (visual acuity and contrast sensitivity) as well as helping retard progression of AMD in the test subjects. Even prior to the LAST study, the AREDS study (Age-Related Eye Disease Study Research Group. (2001) A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E and Beta Carotene for Age-Related Cataract and Vision Loss. AREDS Report No. 9. *Arch Ophthalmol.* 119:1439-1452) showed that the ingestion of a mixture of ocular antioxidants including vitamins A, C and E combined with beta-carotene, copper and zinc helps reduced the progression of AMD in subjects at risk for AMD or with early stages of this disease. Additionally, in a follow-up epidemiological analysis of data from the AREDS study, data gathered showed that the ingestion of lutein and zeaxanthin was related to a lower chance of progression of this ocular disease. Furthermore, the results of an epidemiological study conducted by Dr. Johanna Seddon at Harvard University (Seddon J, Ajani U, Sperduto R , Hiller R, Blair N, Burton T, Farber M, Gragoudas E, Haller J, Miller D,

Yannuzzi L , and Willett W. (1994) Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *JAMA* 272: 1413-1420) showed an inverse relationship between the incidence of AMD and the amounts of lutein and zeaxanthin ingested daily as part of the diet. These results along with a plethora of other results from in-vitro, ex-vivo, and animal and human studies support a definite relationship between the ingestion of ocular antioxidants and a reduction in the risk for the incidence and/or progression of AMD.

To understand the effects of antioxidants in the eye, it must be first understood that light entering the eye has potentially damaging effects upon the very ocular tissues that are responsible for vision. However, not all light impinged upon the eye enters the eye and not all wavelengths of light impinged upon the retina have potentially damaging effects. When light enters the human eye, the ultraviolet wavelengths are absorbed by the cornea and lens of the eye. This filtering of UV light effectively prohibits these potentially damaging wavelengths from reaching the retina. Upon passing through the lens, the visible wavelengths of light are focused upon the macular area of the retina. Of the wavelengths of visible light impinged upon the macula, the blue wavelengths are the shortest wavelength and exhibit the highest energy. Therefore, the blue wavelengths have the greatest potential to induce damage by absorption by photosensitizers and/or induction of free radicals. Although this theory of macular damage associated with the blue wavelengths of visible light has long been speculated, proof that these wavelengths actually damage retinal tissue has only recently been demonstrated in-vivo by Barker and coworkers (Barker F, Snodderly D, Johnson E, Shcalch W, Koepcke W, Gerss J, Neuringer M. (2011) Nutritional Manipulation of Primate Retinas, V: Effects of Lutein, Zeaxanthin, and n-3 Fatty Acids on Retinal Sensitivity to Blue-Light-Induced Damage. *Invest Ophthalmol Vis Sci.* 52:3934-3942).

In a normal eye, the focal length of the lens (the distance from the lens to the focal plane of the retina) accurately matches the axial length of the eye as depicted in FIG. **1**. In this focal process, the lens of the eye separates the wavebands of visible light in the same manner that a prism separates the wavelengths of light into its respective chromatic bands. Due to differences in the energy of these color bands, the lens is not able to focus each of these color bands at exactly the same distance. Therefore, the low energy red wavelengths are focused at the farthest distance from the lens and the high energy blue wavelengths are focused at the shortest distance from the lens. The green wavelengths are focused at an intermediate distance in comparison to the red and blue wavelengths. This chromatic separation of light is pictorially depicted in FIG. **2**. Assuming perfect functionality of the cornea and lens as well as an eyeball of normal dimensions, the red wavelengths of light are focused behind the retina of the eye as just described. The green wavelengths of light are focused upon the focal plane of the retina. The blue wavelengths of light are focused in front (actually short) of the retina.

This distance-related color focusing issue is probably a result of natural selection since the blue wavelengths are the most energetic and damaging waveband of visible light striking the retina as described above. The presence of the macular pigment, which is composed of lutein and zeaxanthin, is critically positioned in the macular retina of the human (and the primate) eye in order to absorb these blue wavelengths of light. This absorption of the blue wavelengths of visible light helps reduce the potential damage that this waveband of light might have upon the sensitive cells comprising the macula. Additionally, a recent publication describes how the absorption of the blue wavelengths of visible light by the macular pigment helps reduce chromatic aberration, often referred to as the "blue haze" effect in human vision (Wooten B, and Hammond B. (2002) Macular pigment: influences on visual acuity and visibility. *Prog Retinal and Eye Res.* 21: 225-240).

The issues associated with the relationship between presbyopia and hyperopia, AMD, and antioxidants as these visual disorders as manifested in the human eye are that light focused by the lens no longer falls onto the retina as described above for the normal eye. Instead the light is focused further back on the retina. Therefore, in the presbyopic or hyperopic eye, the chromatic bands of visible light are focused at a further distance from the lens. This implies that the light is focused similarly to that shown in FIG. **3**. This focal distance depends upon the degree of presbyopia/hyperopia. The greater the degree of presbyopia/hyperopia, the further behind the retina the light is focused.

Under presbyopic and hyperopic conditions, the chromatic separation of the wavelengths of visible light would cause the red and green wavelengths of light to be focused behind the retina and the blue wavelengths would be focused more close to or directly onto the retina. Focusing such potentially damaging light onto this sensitive retinal tissue will induce the generation of free radicals and reactive oxygen species in this tissue. These entities can cause considerable damage to the retinal cells in the macula, including damage to the photoreceptors and the retinal pigmented epithelium. Indeed, focusing increased amounts of the blue wavelengths of light upon these tissues, particularly over a period of time similar to that in which people notice the decreased ability to focus upon near objects caused by presbyopia, may initiate the cascade of damage that, over time, is known as AMD.

Despite broad acceptance among the ocular research community, macular pigment optical density (MPOD) is a relatively new concept amongst optometric and ophthalmologic communities that is gaining acceptance as a measure of the amounts of lutein and zeaxanthin in the macula of the living human eye as well as a marker of the health of the human eye. Healthy eyes contain higher levels of macular pigment thereby resulting in higher MPOD levels. This biomarker is being accepted because of the known properties of the macular pigment in absorbing the blue wavelengths of visible light, the antioxidant properties of constituents of the macular pigment, namely lutein and zeaxanthin, and the effects attributed to higher levels of macular pigment, namely reduction of chromatic aberration, increased glare tolerance/reduced glare recovery times, and better visual acuity (Richer, et al. 2004; Stringham J and Hammond B. (2007) The glare hypothesis of macular pigment function. *Optom Vis Sci.* 84: 858-864; Stringham J and Hammond B. (2008) Macular pigment and visual performance under glare conditions. *Optom Vis Sci.* 85: 82-88). Perhaps most importantly, it has been reported that approximately 46% of the population of the United States exhibits MPOD values that are in the low category (Stringham, et al., 2008). Furthermore, it is widely recognized that MPOD values decrease with age (Bernstein P, Delori F, Richer S, van Kuijk F, and Wenzel, A. (2010) The value of measurement of macular carotenoid pigment optical densities and distributions in age-related macular degeneration and other retinal disorders. *Vision Res* 50: 716-728). Therefore, the segment of the population with low MPOD values is believed to be more susceptible to damage induced by free radicals and reactive oxygen species in the macula caused by blue light exposure. Since such damage is suspected as being the basis upon which AMD develops, increasing MPOD values are being suggested as a way of reducing the risk for AMD

while simultaneously reducing vision related issues, especially amongst people with AMD or at risk for this disease.

Hyperopia/Presbyopia and AMD

The epidemiological literature contains conflicting reports of a relationship between hyperopia and AMD with one report indicating that people who exhibit hyperopia are more likely to get AMD in later life (Hyman L, Lillenfeld A, Ferris F, and Fine S. (1983) Senile macular degeneration: a case-control study. *Am J Epidemiol.* 18:213-227) and other reports indicated that such a relationship was weak at best (Maltzman B, Mulvhill M, and Greenbaum A. (1979) Senile macular degeneration and risk factors: a case-control study. *Ann Ophthalmol.* 11: 1197-1201; Eye Disease Case-Control Study Group. (1992) Risk factors for neovascular age-related macular degeneration. *Arch Ophthalmol.* 110: 1701-1708; Sandberg, M, Tolentinl M, Miller S, Berson E, and Gaudio A. (1993) Hyperopia and neovascularization in age-related macular degeneration. *Ophthalmol.* 100: 1009-1013; Boker T, Fang T, and Steinmetz R. (1993) Refractive error and choroidal perfusion characteristics in potential with choroidal neovascularization and age-related macular degeneration. *Ger J Ophthalmol.* 2:10-13; Wang J, Mitchell P, and Smith W. (1998) Refractive error and age-related maculopathy: the Blue Mountains Eye Study. *Invest Ophthalmol Vis Sci.* 39: 2167-2171). However, it must be noted that no clinical study has been conducted to confirm or refute the existence of such a relationship. Furthermore, no references have been found in the medical or scientific literature relating a potential increased incidence of AMD amongst individuals exhibiting presbyopia. However, data exists indicating that myopia (commonly referred to as nearsightedness) may indeed have the effect of helping to protect against AMD (Hirvela H, Luukinen H, Laara E, and Laatikainen L. (1996) Risk factors of age-related maculopathy in a population 70 years of age or older. *Ophthalmol.* 103: 871-877).

Although the reported protective relationship between myopia and protection against AMD can be easily rationalized based upon the fact that the blue wavelengths of light are focused at a significant distance in front of the retina in comparison to that of the normal eye, the link between hyperopia and an increased risk of AMD is somewhat more difficult to rationalize. Aside from people with very mild hyperopia, individuals who exhibit hyperopia are generally prescribed corrective lenses from an early age. Therefore, visual correction for hyperopia should limit the total amount of damage that might be induced in the retina by the blue light wavelengths impinging directly upon the retina. Therefore, unless the damage induced by the blue wavelengths of light in hyperopic individuals occurs very early in life (i.e., before the time of hyperopic correction) and such damage is dormant for many years (i.e., until the normal age of appearance of AMD which is accepted to be in the sixth to seventh decade of life), it is difficult to rationalize the link between normal hyperopia and AMD. There is always the chance the damage induced in undiagnosed childhood hyperopia is the link or at least an additional link between hyperopia and AMD. For this to be true, the damage induced by undiagnosed hyperopia would have to be undetectable for many years as just described. However, if this is the case, then this aspect of the relationship between hyperopia and AMD described in this work is considered to be covered by this document. However, in such an instance, there is a need for such individuals to be supplemented with ocular antioxidants across their entire life, not just in the mid- to later years of life. Despite that fact, ocular antioxidant supplementation in infants and children should still be considered to be important and advantageous to help reduce the possibility of AMD in later adulthood.

Additionally, there is always the possibility that damage induced by early childhood hyperopia and subsequently aggravated by presbyopia-induced damage is the actual link between the observed epidemiological relationship between hyperopia and AMD. Based upon the high metabolic activity exhibited by all cells of the human body in youth, it seems likely that any damage induced early in childhood should be readily repaired before the sixth decade of life. This should limit the importance of this link between childhood retinal light exposure, hyperopia, and AMD. Nonetheless, if this is the case, as stated above for the case of AMD resulting only from ocular damage induced by light upon the retina of the childhood hyperopic eye, supplementation of these individuals with ocular antioxidants throughout their lifetime should help reduce the incidence of AMD in late adulthood. This situation is considered to be covered within the relationships described in this document.

It is also possible that the relationship between hyperopia and AMD as described in the epidemiological literature is a result of presbyopia and not hyperopia. This is because it is virtually impossible to differentiate between these two ocular conditions upon a simple eye examination. Additionally, without a complete ocular history, an older person participating in an epidemiological study might not know the difference between these two conditions. Furthermore, no published studies in the epidemiological literature have provided any indication that they have questioned subjects about whether they have presbyopia as compared to hyperopia. Regardless, this issue is considered of little significance as it pertains to the relationship between ocular diseases and AMD since this document covers both hyperopia and presbyopia.

Returning to the original premise that presbyopia is the actual link between the damage observed in AMD, the age of onset of the potential damage caused by the presbyopic focus of blue light on the retina and the age of prevalence of ocular damage in AMD is logical. The prevalence of presbyopia increasing after the age of 40 and the age of diagnosis of AMD in the sixth to seventh decade allows a sufficient amount of time for the damage related to AMD to occur. Additionally, the effects of presbyopic changes upon the focal point of the damaging blue wavelengths of visible light upon the retina is consistent with the types of damage seen in AMD. Therefore, the initiation of dietary supplementation with ocular antioxidants at a much earlier age (in the early to mid-30s) than commonly undertaken in today's environment (in the mid- to late-50s) makes significant sense in order to help reduce AMD incidence in the elderly adult population. In fact, given the totality of the above potential links between early childhood damage caused by hyperopia and presbyopia in adulthood, it is probably most advisable to consider supplementation with ocular antioxidants throughout life, not just in later adulthood.

Astigmatism and AMD

The principles described above regarding the focusing of light upon the macula of the eye in hyperopia and presbyopia equally apply in the circumstances where people suffer from astigmatism except for the fact that, in the astigmatic eye, light can be focused correctly in the normal orthogonal plane of the eye and improperly focused in the astigmatic plane as shown in FIG. **5** for a hyperopic astigmatic eye. In this example, light in the vertical plane is in focus at the retina whereas light in the horizontal plane is focus hyperopically (i.e., behind the plane of the retina). Similar to the case shown in FIG. **5**, when the light entering the horizontal plane is separated prismatically into its component color wavebands, the blue wavelengths are focused directly upon the retina. These damaging blue wavelengths are capable of inducing

significant damage upon the macular tissues which can result in AMD over the years as discussed previously. However, the damage noted may not encompass the entire macular area. Instead, because light in one plane is more focused upon the retina, the damage potential in presbyopics may be more to the central retina such as is found in choroidal neovascularization whereas the damage potential in astigmatics may be either more confined to the peripheral macular area such as found in geographic atrophy or more diffuse encompassing the central and peripheral retinal areas. This is not to imply that these two forms of AMD cannot be induced in either presbyopics or astigmatics but instead the focal properties of the eye exhibiting these conditions may be more likely to result in these forms of AMD.

As in the case of presbyopia, astigmatism increases with age and this condition is not readily noticed by people, particularly in the elderly, because astigmatism causes vision to be blurred or fuzzy but not completely out of focus (Gudmundsdorrir E, Jonasson F, Jonsson V, Stefansson E, Sasaki H, Sasaki K, and the Iceland-Japan Co-Working Group. (2000) "With the rule" astigmatism in not the rule in the elderly. *Acta Ophthalmol Scand.* 78:642-646). This finding implies that the need for correction for astigmatism can potentially exist for some time before it becomes serious enough to cause people to go their doctor to seek correction. The lag time between the existence of astigmatism and its correction means that the macula of the astigmatic eye is exposed to ever greater amounts of blue light exposure and potential damage.

Studies Demonstrating the Need for Macular Antioxidants in Presbyopia, Hyperopia, and Astigmatism

As described above, the presence and relative amounts of the two principle antioxidants found in the macula, namely lutein and zeaxanthin, can be assessed by measurement of Macular Pigment Optical Density (MPOD). Additionally, as described above, it is known that MPOD declines with age which makes older people even more susceptible to AMD. Although MPOD values are a measure of only the amount of macular pigment (lutein and zeaxanthin) present in the eye, they are not the only antioxidants present in ocular tissues. However, because ocular antioxidants are derived from the same types of foods that macular pigment are obtained from, it is easy to hypothesize that people with low MPOD values also exhibit low levels of other ocular antioxidants. Such a hypothesis is also consistent with the published results (Bernstein, et al., 2010). Therefore, it is important to maintain high levels of macular pigment.

A study was conducted in which MPOD values were measured in a large, multi-ethnic population using an auto-fluorescence imaging instrument (Sharifzadeh M, Bernstein P, Gellermann W. (2006) Nonmydriatic fluorescence-based quantitative imaging of human macular pigment distributions. *J Opt Soc Am A: Optics and Image Sci Vis.* 23: 2373-2387). In total, 241 subjects volunteered for MPOD testing and values were obtained for 224 subjects. Of this total database, subjects were asked about their history of vision correction. Only subjects with and without a self-reported history of vision correction were included in the following analysis. Of the total number of subjects available, twenty-three indicated that their vision had never required any type of correction. These subjects were classified as the normal subject database. Eight subjects indicated that they had been diagnosed with only presbyopia, seven had been diagnosed with only hyperopia, nine had been diagnosed with only astigmatism, and an additional eighteen had been diagnosed with only myopia. The MPOD values were plotted as a function of subject age for the four types of visual disorders as shown in FIG. **6**. FIG. **6**A compares subjects with myopia to normals; **6**B compares subjects with hyperopia with normals; **6**C compares subjects with presbyopia to normals; and **6**D compares subjects with astigmatism to normals.

As can be seen from the data in FIG. **6**A, subjects with myopia do not show any appreciable difference in the rate of decline in MPOD as a function of age when compared to the rate of decline in MPOD with age in subjects who had vision that never required any correction. Similar comparisons of MPOD values with age in subjects who have had their vision corrected for hyperopia (FIG. **6**B), presbyopia (FIG. **6**C), or astigmatism (FIG. **6**D) indicate a steeper decline in MPOD over the age range, especially subjects with astigmatic correction. Although a decline in MPOD values with age is not in itself an indicator of a predisposition for age-related macular degeneration, it definitely indicates an increased risk factor since studies have indicated that people with lower MPOD values are at greater risk for AMD (Bernstein, et al., 2010). Given the fact that presbyopia, and astigmatism are ocular conditions that occur with increasing frequency amongst people above the age of 40, this decline definitely indicates a need for supplementation with ocular antioxidants including lutein and zeaxanthin in people exhibiting these ocular disorders in order to reduce the potential damage to ocular tissues brought about by an increase exposure to blue light damage which could lead to AMD.

SUMMARY

The principles behind the relationships between MPOD values, blue light damage to ocular tissues, and the risk for AMD are based upon known data. They represent the cumulative blue light-induced damage from oxidative processes that occur in retinal tissues of the human eye that has been related to increased likelihood of AMD. Although the amount of cumulative damage required to elicit AMD is not known, it is known that ocular antioxidants are important in reducing the potential of such damage.

Based upon the data presented, eyes exhibiting hyperopia, presbyopia, and/or astigmatism exhibit a decline in MPOD values with age that is greater than in myopic eyes as well as eyes that have never required visual correction. This increased rate of decline in MPOD with age renders eyes with hyperopia, presbyopia, and/or astigmatism at greater risk for AMD. It is also possible that a combination of astigmatism with either hyperopia or presbyopia could result in an even higher risk of AMD than any one of the ocular conditions by itself. Therefore, such combination of ocular conditions are included in the present invention.

Supplementation of eyes with macular antioxidants, including but not limited to vitamins A, C, E, and other vitamins exhibiting antioxidant activity; beta-carotene and other carotenoids including lutein, zeaxanthin, retinoids, retinal, retinaldehyde, and meso-zeaxanthin; zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems, natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercetin, anthocyanins, anthocyanidins, etc.; and the synthetic antioxidants including BHT, BHA, BTHQ that increase ocular antioxidant levels will reduce the risk of blue light-induced damage to retinal tissues.

The cumulative damage theory of AMD is consistent with the onset of hyperopia or astigmatism regardless of age. Additionally, it is consistent with the onset of presbyopia, and adult onset astigmatism, both of which are reported to increase at about the age of 40. The slow progression of the ocular damage associated with AMD is consistent with rate of pro-

gression of presbyopia and/or adult-onset astigmatism. Such damage is probably compounded by the reluctance of people to wear any type of vision correction for presbyopia or astigmatism as well as the inability of people to take action on such visual changes until vision has deteriorated significantly.

The methods of the present invention are consistent with the knowledge that people with high levels of macular pigment are less likely to suffer from AMD. They are also consistent with the knowledge that MPOD levels decline with age, especially amongst people with hyperopia, presbyopic, and/or astigmatism. The presence of high levels of macular pigment may reduce the probability that people with hyperopia, presbyopia, and/or astigmatism would incur less blue light-induced retinal tissue damage than people with lower MPOD levels might incur. This is because the known blue light-absorbing capability and/or antioxidant capacity of the xanthophylls (lutein and zeaxanthin) comprising the macular pigment and the presence of other ocular antioxidants. These properties help limit the blue light-induced damage.

The methods of the present invention are not meant to cover damage that might be induced in the eye as a result of other ocular conditions/diseases that might also result in AMD, including but not limited to inherited conditions (a genetic component) or damage from other forms of retinopathies aside from AMD. Instead, the methods address the link between hyperopia, presbyopia, and/or astigmatism and AMD as well as the beneficial effect of ocular antioxidant supplementation upon reducing the risk associated with AMD. Supplementation with ocular antioxidants, as described above, is not limited to the xanthophylls that comprise the macular pigment. Ocular antioxidants as described above include vitamins A (1 to 150 IU/kg Body Weight (BW)/day), C (0.05 to 15 mg/kg BW/day), E (0.02 to 5 mg/kg BW/day), and other vitamins exhibiting antioxidant activity (0.01 to 500 mg/kg BW/day); lutein, zeaxanthin, beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin (0.0001 to 2 mg/kg BW/day); zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems (0.0001 to 5 mg/kg BW/day), natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, etc. (0.001 to 75 mg/kg BW/day); and the synthetic antioxidants including BHT, BHA, BTHQ (0.001 to 15 mg/kg BW/day), or any synthetic analog of the natural antioxidants. Additionally, any combination of these ocular antioxidants may be used. The amounts described above pertain to a suggested dosage for an individual weighing approximately 150 pounds (approximately 70 kg). The relationships described are also not limited by the form of deliver of the above described materials and includes food, beverages, and/or dietary supplement tablets, capsules, and other more esoteric delivery forms. Furthermore, the ocular antioxidants can take any form, including but not limited to powders, beadlets, crystals, liquids, dispersions, and the like as long as it can be delivered to the body in a form and in amounts that can be absorbed and used by the body.

Even though the components and activity of the carotenoids comprising the macular pigment are described above in relation to reducing the potential damage associated with a relationship between hyperopia, presbyopia, and/or astigmatism and AMD, these relationships are not restricted to the activity of these xanthophylls. The relationships described also do not preclude the use of other antioxidants and associated molecules individually or in combinations that might reduce the oxidative damage associated with hyperopic-, presbyopic-, and/or astigmatic-induced AMD.

The foregoing description and drawings comprise illustrative embodiments of the present inventions. The foregoing embodiments and the methods described herein may vary based on the ability, experience, and preference of those skilled in the art. Merely listing the steps of the method in a certain order does not constitute any limitation on the order of the steps of the method. The foregoing description and drawings merely explain and illustrate the invention, and the invention is not limited thereto, except insofar as the claims are so limited. Those skilled in the art that have the disclosure before them will be able to make modifications and variations therein without departing from the scope of the invention.

What is claimed is:

1. A method of treating the increased age-related macular degeneration present in a subject having age-related macular degeneration and either hyperopia or astigmatism, relative to the age-related macular degeneration present in a subject having age-related macular degeneration but neither hyperopia nor astigmatism, comprising administering to the subject having the macular degeneration and either the hyperopia or astigmatism a composition comprising a therapeutically effective amount of one or more ocular antioxidants.

2. The method of claim **1**, wherein said ocular antioxidant is selected from the group consisting of antioxidant vitamins, carotenoids, antioxidant minerals, natural antioxidant extracts and synthetic antioxidants.

3. The method of claim **2**, wherein said antioxidant vitamin is selected from the list consisting of vitamins A, C, and E.

4. The method of claim **2**, wherein said carotenoid is selected from the list consisting of lutein, zeaxanthin, beta-carotene, retinoids, retinal, retinaldehyde, and meso-zeaxanthin.

5. The method of claim **2**, wherein said antioxidant mineral is selected from the list consisting of zinc, copper, and selenium.

6. The method of claim **2**, wherein said natural extract is selected from the list consisting of polyphenols, quercitin, anthocyanins, and anthocyanidins.

7. The method of claim **2**, wherein said synthetic antioxidant is selected from the list consisting of BHT, BHA, and BTHQ.

8. The method of claim **2**, wherein said therapeutically effective amount of said antioxidant vitamin is between 0.02 (1 IU) and 15 mg (150 IU) per kilogram of body weight of said subject per day.

9. The method of claim **2**, wherein said therapeutically effective amount of said carotenoid is between 0.0001 and 2 mg per kilogram of body weight of said subject per day.

10. The method of claim **2**, wherein said therapeutically effective amount of said antioxidant mineral is between 0.0001 and 5 mg per kilogram of body weight of said subject per day.

11. The method of claim **2**, wherein said therapeutically effective amount of said synthetic antioxidant is between 0.001 and 15 mg per kilogram of body weight of said subject per day.

12. The method of claim **2**, wherein said therapeutically effective amount of said natural extract is between 0.0001 and 20 mg per kilogram of body weight of said subject per day.

13. The method of claim **2**, wherein said therapeutically effective amount of said synthetic antioxidant is between 0.0001 and 20 mg per kilogram of body weight of said subject per day.

* * * * *

EXHIBIT H

US009226940B2

(12) **United States Patent**
Roberts

(10) **Patent No.: US 9,226,940 B2**
(45) **Date of Patent: Jan. 5, 2016**

(54) **METHOD OF TREATING OCULAR DISORDERS**

(71) Applicant: **Kemin Industries, Inc.**, Des Moines, IA (US)

(72) Inventor: **Richard Roberts**, Johnston, IA (US)

(73) Assignee: **Kemin Industries, Inc.**, Des Moines, IA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/307,684**

(22) Filed: **Jun. 18, 2014**

(65) **Prior Publication Data**

US 2014/0302169 A1 Oct. 9, 2014

Related U.S. Application Data

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(60) Provisional application No. 61/384,958, filed on Sep. 21, 2010.

(51) **Int. Cl.**

A61K 33/34	(2006.01)
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A61K 31/05	(2006.01)
A61K 31/07	(2006.01)
A61K 31/11	(2006.01)
A61K 31/353	(2006.01)
A61K 31/355	(2006.01)
A61K 31/375	(2006.01)
A61K 45/06	(2006.01)
A61K 31/085	(2006.01)
A61K 31/352	(2006.01)
A61K 33/04	(2006.01)
A61K 33/30	(2006.01)

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

CPC ***A61K 33/34*** (2013.01); ***A61K 31/00*** (2013.01); ***A61K 31/015*** (2013.01); ***A61K 31/047*** (2013.01); ***A61K 31/05*** (2013.01); ***A61K 31/07*** (2013.01); ***A61K 31/085*** (2013.01); ***A61K 31/11*** (2013.01); ***A61K 31/352*** (2013.01); ***A61K 31/353*** (2013.01); ***A61K 31/355*** (2013.01); ***A61K 31/375*** (2013.01); ***A61K 33/04*** (2013.01); ***A61K 33/30*** (2013.01); ***A61K 45/06*** (2013.01)

(58) **Field of Classification Search**

IPC A61K 31/07,8/687, 8/347

See application file for complete search history.

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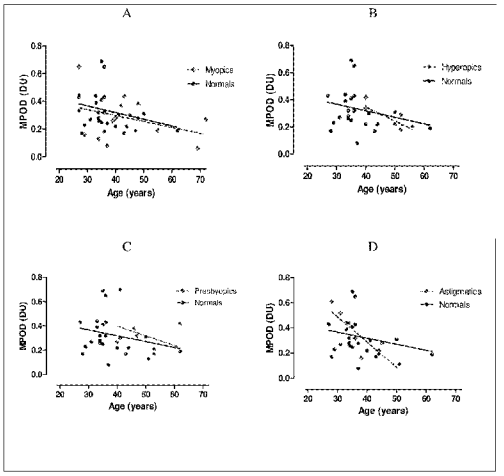
(57) **ABSTRACT**

A method wherein subjects having or at risk for having hyperopia, presbyopia or astigmatism are administered a composition having an effective amount of ocular antioxidants, including specifically macular pigments, to prevent, treat, or delay the onset of age-related macular degeneration (AMD).

13 Claims, 4 Drawing Sheets



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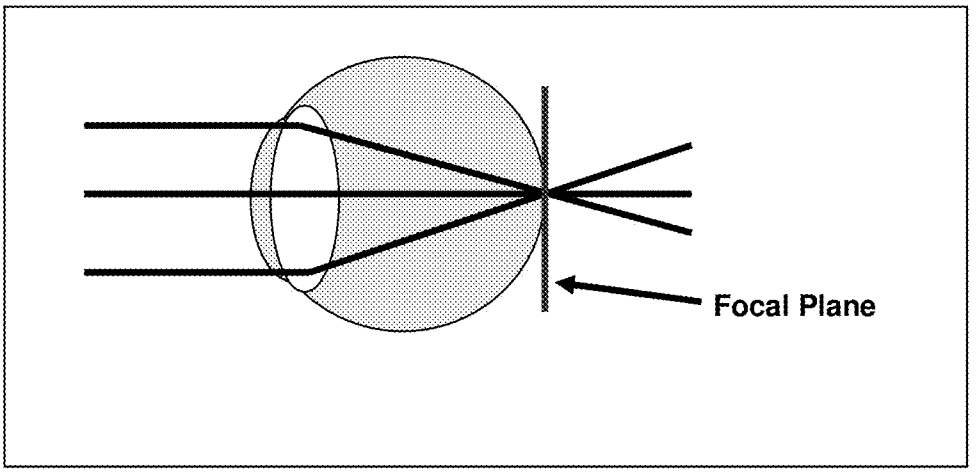

FIG. 1

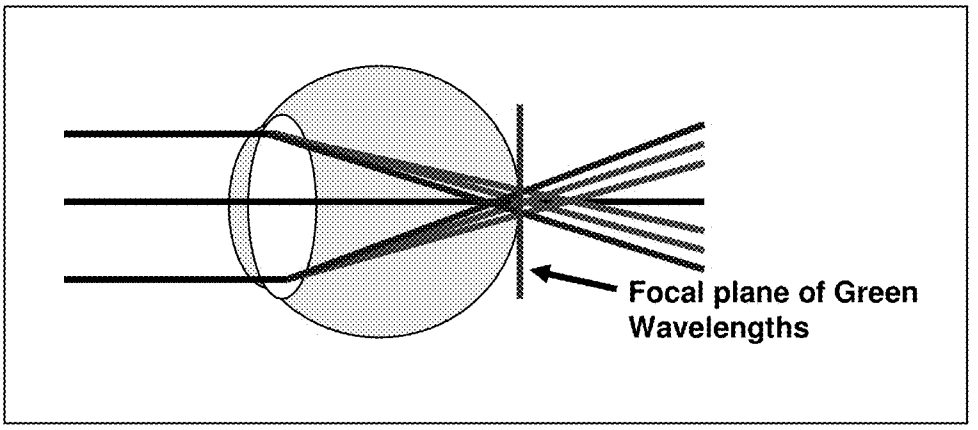

FIG. 2

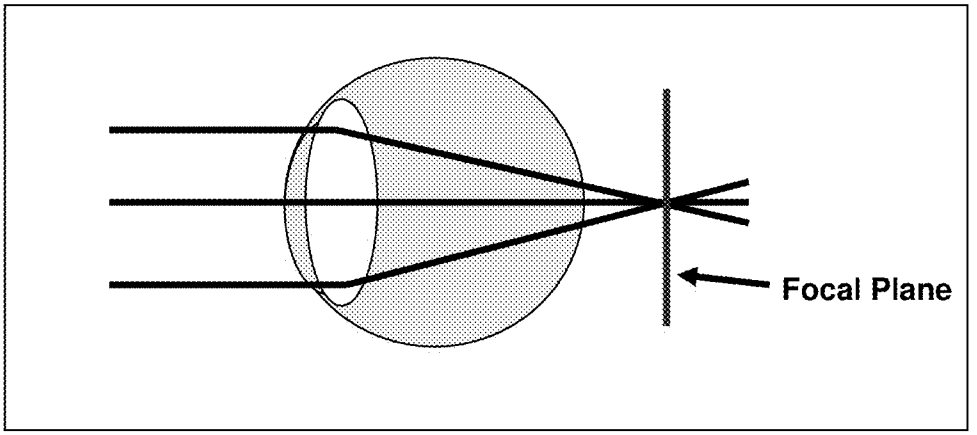

FIG. 3

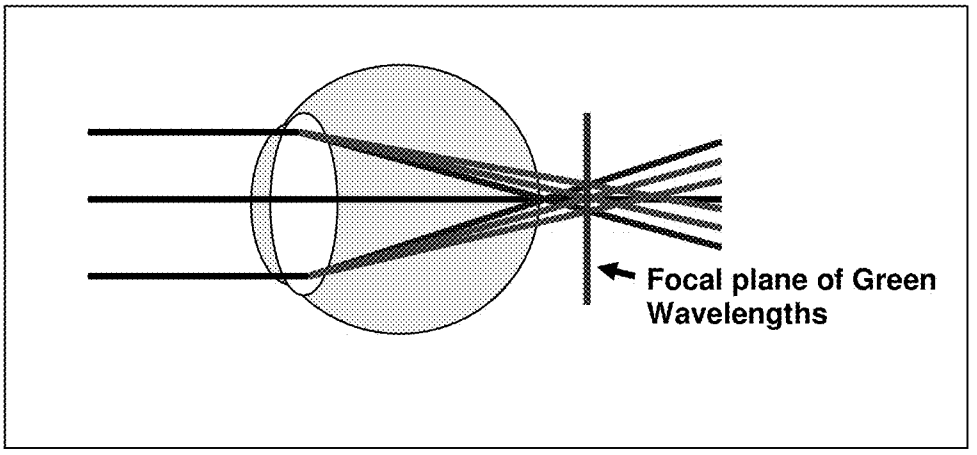

FIG. 4

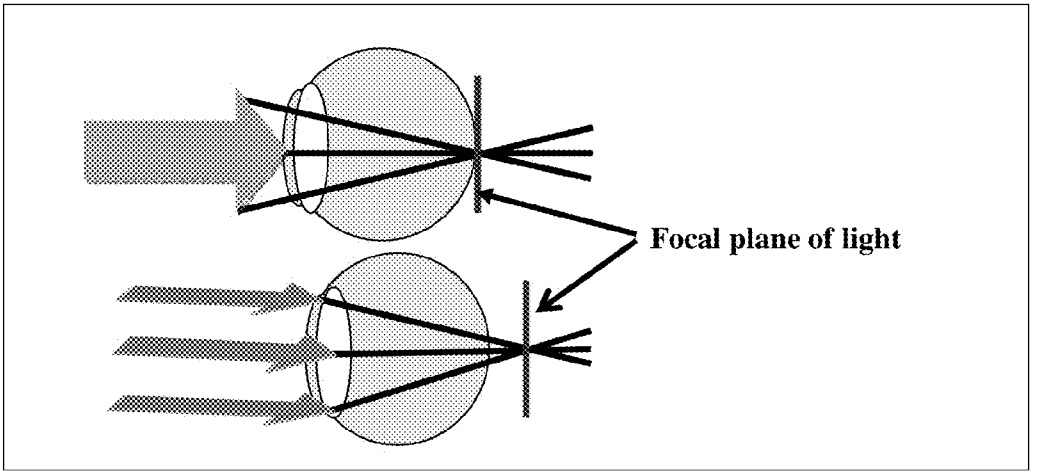

FIG. 5

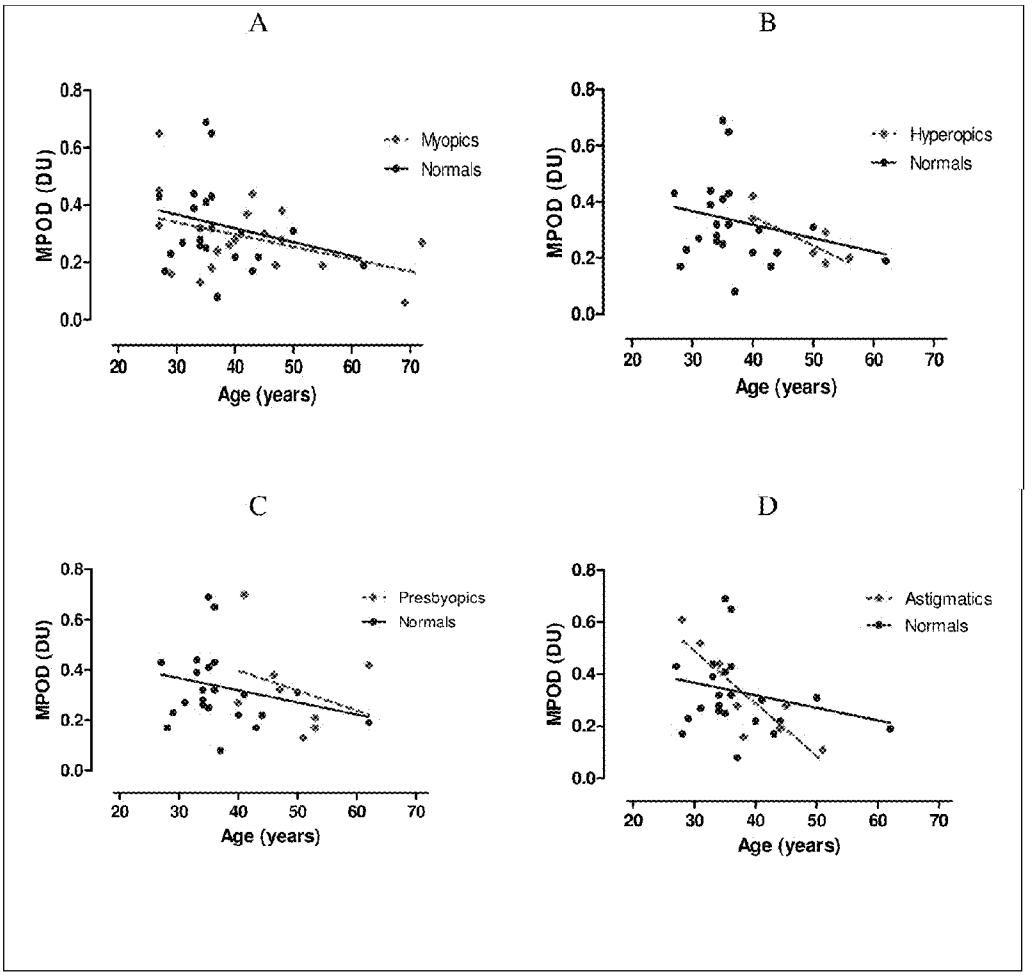
A
B
C
D
MPOD (DU)
Age (years)
Myopics
Normals
Hyperopics
Normals
Presbyopics
Normals
Astigmatics
Normals
0.0
0.2
0.4
0.6
0.8
20
30
40
50
60
70

FIG. 6

METHOD OF TREATING OCULAR DISORDERS

METHOD OF TREATING OCULAR DISORDERS

This application is a divisional application of U.S. patent application Ser. No. 13/238,939, filed on Sep. 21, 2011, which claims priority to U.S. patent application Ser. No. 61/384,958, filed Sep. 21, 2010, and incorporates the same herein in its entirety, by this reference.

BACKGROUND OF THE INVENTION

The present invention relates generally to a method of early diagnosis and treatment of ocular disorders and, more specifically, to the early diagnosis of subjects at risk for age-related macular degeneration and the administration of ocular antioxidants to subjects having hyperopia, presbyopia or astigmatism.

Hyperopia, presbyopia, and astigmatism are visual or ocular disorders that affect a significant percentage of the human population worldwide.

Age-related macular degeneration (AMD) is a disease associated with aging that gradually destroys sharp, central vision. The disease attacks the macula, the central area of the retina that allows a person to see fine detail. Individuals can lose all but the outermost peripheral vision, leaving dim images or black holes at the center of vision. AMD is a leading cause of vision loss and legal blindness in adults over 60 in the United States. An inverse relationship exists between the incidence of AMD and the amount of macular pigments, principally lutein and zeaxanthin, in the macula.

SUMMARY OF THE INVENTION

The present invention consists of the administration to subjects having or at risk for having hyperopia, presbyopia or astigmatism with a composition having a therapeutically effective amount of ocular antioxidants, including specifically macular pigments, to prevent, treat, or delay the onset of AMD. The invention also consists of a method for the early diagnosis of subjects at increased risk of developing AMD consisting of the existence or risk for the existence of hyperopia, presbyopia or astigmatism.

The composition may also include antioxidant compounds include vitamins A, C, E, and other vitamins exhibiting antioxidant activity; beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin; zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems; natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, and the like; and synthetic antioxidants including BHT, BHA, BTHQ, or any synthetic analog of the natural antioxidants.

The supplementation can take any desired form, including addition of the composition to food, beverages, and/or dietary supplement tablets, capsules, and other more esoteric delivery forms. Furthermore, the composition including ocular antioxidants can take any form, including but not limited to powders, beadlets, crystals, liquids, dispersions, and the like as long as it can be delivered to the body in a form and in amounts that can be absorbed and used by the body

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a graphical representation of the focal plane of visible light in a normal eye.

FIG. **2** is a graphical representation of focal plane for the chromatic wavelengths of visible light in the normal eye.

FIG. **3** is a graphical representation of focal plane for the visible light by the presbyopic/hyperopic eye.

FIG. **4** is a graphical representation of focal plane for the chromatic wavelengths of visible light in the presbyopic eye.

FIG. **5** is a graphical representation of the focal plane of light after passing through lens of a hyperopic, astigmatic eye; the two planes of light entering the eye in this figure are orthogonal (at 90°) to one another.

FIGS. **6**A-D are graphical representations of MPOD values as a function of age for different types of vision correction in comparison to subjects who exhibiting vision that has never required correction (i.e., normals).

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

As used herein, the terms "age-related macular degeneration" and "AMD" refer to a disease associated with aging that gradually destroys sharp, central vision. The disease attacks the macula, the central area of the retina that allows a person to see fine detail.

"Macular pigment" refers to a composition that includes carotenoids found in the macula of the eye, principally lutein and zeaxanthin.

"Ocular antioxidant" includes (a) vitamins A, C, E, and other vitamins exhibiting antioxidant activity; (b) beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin; (c) zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems; (d) natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, and the like; and (e) synthetic antioxidants including BHT, BHA, BTHQ, or any synthetic analog of the natural antioxidants.

As used herein, the term "therapeutically effective amount" refers to the amount/dose of a compound or pharmaceutical composition that is sufficient to produce an effective response (i.e., a biological or medical response of a tissue, system, animal or human sought by a researcher, medical doctor or other clinician) upon administration to a subject. The "therapeutically effective amount" will vary depending on inter alia the disease and its severity, and the age, weight, physical condition and responsiveness of the subject to be treated.

As used herein, the terms "treated" and "treating" refers to preventing or delaying the appearance of clinical symptoms of a disease or condition in a subject that may be afflicted with or predisposed to the disease or condition, but does not yet experience or display clinical or subclinical symptoms of the disease or condition. "Treating" also refers to inhibiting the disease or condition, i.e., arresting or reducing its development or at least one clinical or subclinical symptom thereof. "Treating" further refers to relieving the disease or condition, i.e., causing regression of the disease or condition or at least one of its clinical or subclinical symptoms. The benefit to a subject to be treated is either statistically significant or at least perceptible to the subject and/or the physician.

Hyperopia, or farsightedness, is a physical defect of the eye, primarily of genetic origin, in which the lateral axis of the eyeball (from cornea to posterior sclera) is too short or the lens of the eye exhibits insufficiently curvature for light to properly be focused upon the retina. This condition is normally easily detected through a routine eye examination and is readily corrected through the use of corrective lenses (surgery, glasses, or contact lenses).

Presbyopia, which is commonly confused with hyperopia, is an age-related visual disorder that affects virtually everyone to some extent. However, the degree of presbyopia varies between individuals. Although the exact cause of presbyopia is not known, it is generally accepted that it is a result of 1) a hardening of the lens of the eye and/or 2) an inability of the lens to adequately change curvature under the influence of the ciliary muscles and the zonules. The result is an improper focus of the image upon the retina. Regardless of the cause of presbyopia, at about the age of 40, most individuals begin to notice that nearby objects appear to be blurred. These individuals complain that their arms are not long enough to accurately focus upon nearby objects, especially when reading, particularly when trying to focus upon small print such as labels and/or newspapers, or when manipulating small objects with their hands. Therefore, the hallmark of presbyopia is that adults find it increasingly difficult to focus upon objects that are near to them. Distance vision is normally unaffected. Prebyopia is a slowly progressing ocular disorder. This progressive loss of near vision is slow enough that individuals may not complain about it for a considerable period of time. This is because of two reasons: 1) there is a stigma associated with wearing corrective lenses, especially glasses when they have never worn glasses and 2) when the distance between the eye and a blurry object is increased, the blurry object may come into better focus, especially in early presbyopia. In this early stage, presbyopia can be corrected to normal or near-normal vision through the use magnifying lenses (commonly referred to as reading glasses, which can be purchased at most drugstores). However, over the decades as we age, presbyopia normally becomes progressively worse thereby making vision correction by corrective lenses or surgery a necessity in many individuals.

Astigmatism is a defect of either the cornea (corneal astigmatism) or the lens (lenticular astigmatism) of the eye in which there is an irregular curvature to one or both of these structures. Corneal astigmatism is the most common type. In normal vision, the curvature of both the cornea and the lens are symmetrical along their horizontal and vertical planes creating a curvature similar to that of the surface of a basketball. Although irregular astigmatism (i.e., irregular curvatures in both the horizontal and vertical planes simultaneously, commonly referred to as compound astigmatism; or mismatched curvatures in both the cornea and lens) is known to exist, it is considered to be rare. In the typical form of astigmatism, the curvature in one of these planes (horizontal or vertical) is steeper than the curvature in the other plane. Therefore, the surface through which the light must pass in order to reach the retina resembles that of a football with the long axis directed either along either the horizontal or vertical axis of the eye. Since light passing through these mismatched curvatures cannot be focused equally, the focal point of light striking the retina in the two planes is not equivalent. When the light impinging upon the retina from one plane is in focus, light in the other plane is not in focus. This results in a blurring or smudging of the visual image. Although astigmatism less than about 0.5 diopters is not considered as needing correction, astigmatism greater than 0.5 diopter generally results in noticeable visual impairment and thereby requires correction. Further complicating this issue, although light passing through the normally curved plane of the cornea is focused properly, light in the astigmatic plane can be focused hyperopically (focused behind the retina) or myopically (focused in front of the retina) depending upon the curvature of the cornea.

At birth, the prevalence and degree of astigmatism is very high and primarily of corneal origin as it is in adults. Fortunately the incidence rate of astigmatism decreases as children grow as a result of a flattening of the astigmatic curvature of the cornea. In the age range of about 6 years and early adulthood, the incidence of astigmatism does not change appreciably. Approximately 5% of people in this age group exhibit astigmatism and about 75% of them exhibit "with the rule" astigmatism (i.e., the steepest slope of cornea is oriented along the vertical meridian). After the age of about 45, not only does the incidence of astigmatism increase, but additionally the direction of astigmatic corneal curvature also appears to change. Adult astigmatism, which has been estimated to reach an incidence rate of 35%, is primarily "against the rule" (i.e., exhibiting the steepest slope of the cornea along the horizontal meridian). This change in the orientation of the corneal slope is believed to be a result of a reduction in tension of the eyelids upon the eyeball that typically occurs with aging.

Relationship Between Ocular Defects, AMD, and Ocular Antioxidants

The relationship between hyperopia, presbyopia and astigmatism, Age-Related Macular Degeneration (AMD) and ocular antioxidants as described in this document, is based upon the known effects of the cornea and lens of the eye in relation to the focusing light of upon the retina; the available information on ocular disorders including AMD (the factors associated with their incidence; the effects of light upon the retina; and the reported effects of ocular antioxidants to reduce the potential damage induced in retinal tissues caused by that light, particularly the reported effect of ocular antioxidants in helping to reduce the progression of AMD). Although references have been found that tie some of these factors together as described in this document, no publications or references have been identified relating all of these factors in a unified manner. Therefore, some background is necessary to understand the relationship between these factors.

Multiple studies, particularly the Lutein Antioxidant Supplementation Trial (the LAST Study) conducted by Dr. Stuart Richer have produced results demonstrating that visual acuity, contrast sensitivity, and the amount of macular pigment in the human eye can be improved as a result of lutein and zeaxanthin supplementation or a combination of these xanthophylls with other antioxidants (Richer S, Stiles W, Statkute L, Pulido J, Frankowski J, Rudy D, Pei K, Tsipursky M, and Nyland J. (2004) Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: The Veterans LAST study (Lutein Antioxidant Supplementation Trial). *Optometry* 75:216-230). The LAST Study was conducted using a group of 90 patients with AMD over a time period of 12 months. The results show that the intake of xanthophylls with or without additional antioxidants increased visual parameters (visual acuity and contrast sensitivity) as well as helping retard progression of AMD in the test subjects. Even prior to the LAST study, the AREDS study (Age-Related Eye Disease Study Research Group. (2001) A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E and Beta Carotene for Age-Related Cataract and Vision Loss. AREDS Report No. 9. *Arch Ophthalmol.* 119:1439-1452) showed that the ingestion of a mixture of ocular antioxidants including vitamins A, C and E combined with beta-carotene, copper and zinc helps reduced the progression of AMD in subjects at risk for AMD or with early stages of this disease. Additionally, in a follow-up epidemiological analysis of data from the AREDS study, data gathered showed that the ingestion of lutein and zeaxanthin was related to a lower chance of pro-

gression of this ocular disease. Furthermore, the results of an epidemiological study conducted by Dr. Johanna Seddon at Harvard University (Seddon J, Ajani U, Sperduto R, Hiller R, Blair N, Burton T, Farber M, Gragoudas E, Haller J, Miller D, Yannuzzi L, and Willett W. (1994) Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *JAMA* 272: 1413-1420) showed an inverse relationship between the incidence of AMD and the amounts of lutein and zeaxanthin ingested daily as part of the diet. These results along with a plethora of other results from in-vitro, ex-vivo, and animal and human studies support a definite relationship between the ingestion of ocular antioxidants and a reduction in the risk for the incidence and/or progression of AMD.

To understand the effects of antioxidants in the eye, it must be first understood that light entering the eye has potentially damaging effects upon the very ocular tissues that are responsible for vision. However, not all light impinged upon the eye enters the eye and not all wavelengths of light impinged upon the retina have potentially damaging effects. When light enters the human eye, the ultraviolet wavelengths are absorbed by the cornea and lens of the eye. This filtering of UV light effectively prohibits these potentially damaging wavelengths from reaching the retina. Upon passing through the lens, the visible wavelengths of light are focused upon the macular area of the retina. Of the wavelengths of visible light impinged upon the macula, the blue wavelengths are the shortest wavelength and exhibit the highest energy. Therefore, the blue wavelengths have the greatest potential to induce damage by absorption by photosensitizers and/or induction of free radicals. Although this theory of macular damage associated with the blue wavelengths of visible light has long been speculated, proof that these wavelengths actually damage retinal tissue has only recently been demonstrated in-vivo by Barker and coworkers (Barker F, Snodderly D, Johnson E, Shcalch W, Koepcke W, Gerss J, Neuringer M. (2011) Nutritional Manipulation of Primate Retinas, V: Effects of Lutein, Zeaxanthin, and n-3 Fatty Acids on Retinal Sensitivity to Blue-Light-Induced Damage. *Invest Ophthalmol Vis Sci.* 52:3934-3942).

In a normal eye, the focal length of the lens (the distance from the lens to the focal plane of the retina) accurately matches the axial length of the eye as depicted in FIG. **1**. In this focal process, the lens of the eye separates the wavebands of visible light in the same manner that a prism separates the wavelengths of light into its respective chromatic bands. Due to differences in the energy of these color bands, the lens is not able to focus each of these color bands at exactly the same distance. Therefore, the low energy red wavelengths are focused at the farthest distance from the lens and the high energy blue wavelengths are focused at the shortest distance from the lens. The green wavelengths are focused at an intermediate distance in comparison to the red and blue wavelengths. This chromatic separation of light is pictorially depicted in FIG. **2**. Assuming perfect functionality of the cornea and lens as well as an eyeball of normal dimensions, the red wavelengths of light are focused behind the retina of the eye as just described. The green wavelengths of light are focused upon the focal plane of the retina. The blue wavelengths of light are focused in front (actually short) of the retina.

This distance-related color focusing issue is probably a result of natural selection since the blue wavelengths are the most energetic and damaging waveband of visible light striking the retina as described above. The presence of the macular pigment, which is composed of lutein and zeaxanthin, is critically positioned in the macular retina of the human (and the primate) eye in order to absorb these blue wavelengths of light. This absorption of the blue wavelengths of visible light helps reduce the potential damage that this waveband of light might have upon the sensitive cells comprising the macula. Additionally, a recent publication describes how the absorption of the blue wavelengths of visible light by the macular pigment helps reduce chromatic aberration, often referred to as the "blue haze" effect in human vision (Wooten B, and Hammond B. (2002) Macular pigment: influences on visual acuity and visibility. *Prog Retinal and Eye Res.* 21: 225-240).

The issues associated with the relationship between presbyopia and hyperopia, AMD, and antioxidants as these visual disorders as manifested in the human eye are that light focused by the lens no longer falls onto the retina as described above for the normal eye. Instead the light is focused further back on the retina. Therefore, in the presbyopic or hyperopic eye, the chromatic bands of visible light are focused at a further distance from the lens. This implies that the light is focused similarly to that shown in FIG. **3**. This focal distance depends upon the degree of presbyopia/hyperopia. The greater the degree of presbyopia/hyperopia, the further behind the retina the light is focused.

Under presbyopic and hyperopic conditions, the chromatic separation of the wavelengths of visible light would cause the red and green wavelengths of light to be focused behind the retina and the blue wavelengths would be focused more close to or directly onto the retina. Focusing such potentially damaging light onto this sensitive retinal tissue will induce the generation of free radicals and reactive oxygen species in this tissue. These entities can cause considerable damage to the retinal cells in the macula, including damage to the photoreceptors and the retinal pigmented epithelium. Indeed, focusing increased amounts of the blue wavelengths of light upon these tissues, particularly over a period of time similar to that in which people notice the decreased ability to focus upon near objects caused by presbyopia, may initiate the cascade of damage that, over time, is known as AMD.

Despite broad acceptance among the ocular research community, macular pigment optical density (MPOD) is a relatively new concept amongst optometric and ophthalmologic communities that is gaining acceptance as a measure of the amounts of lutein and zeaxanthin in the macula of the living human eye as well as a marker of the health of the human eye. Healthy eyes contain higher levels of macular pigment thereby resulting in higher MPOD levels. This biomarker is being accepted because of the known properties of the macular pigment in absorbing the blue wavelengths of visible light, the antioxidant properties of constituents of the macular pigment, namely lutein and zeaxanthin, and the effects attributed to higher levels of macular pigment, namely reduction of chromatic aberration, increased glare tolerance/reduced glare recovery times, and better visual acuity (Richer, et al. 2004; Stringham J and Hammond B. (2007) The glare hypothesis of macular pigment function. *Optom Vis Sci.* 84: 858-864; Stringham J and Hammond B. (2008) Macular pigment and visual performance under glare conditions. *Optom Vis Sci.* 85: 82-88). Perhaps most importantly, it has been reported that approximately 46% of the population of the United States exhibits MPOD values that are in the low category (Stringham, et al., 2008). Furthermore, it is widely recognized that MPOD values decrease with age (Bernstein P, Delori F, Richer S, van Kuijk F, and Wenzel, A. (2010) The value of measurement of macular carotenoid pigment optical densities and distributions in age-related macular degeneration and other retinal disorders. *Vision Res* 50: 716-728). Therefore, the segment of the population with low MPOD values is believed to be more susceptible to damage induced by free radicals and reactive oxygen species in the macula caused by

blue light exposure. Since such damage is suspected as being the basis upon which AMD develops, increasing MPOD values are being suggested as a way of reducing the risk for AMD while simultaneously reducing vision related issues, especially amongst people with AMD or at risk for this disease.

Hyperopia/Presbyopia and AMD

The epidemiological literature contains conflicting reports of a relationship between hyperopia and AMD with one report indicating that people who exhibit hyperopia are more likely to get AMD in later life (Hyman L, Lillenfeld A, Ferris F, and Fine S. (1983) Senile macular degeration: a case-control study. *Am J. Epidemiol.* 18:213-227) and other reports indicated that such a relationship was weak at best (Maltzman B, Mulvhill M, and Greenbaum A. (1979) Senile macular degeneration and risk factors: a case-control study. *Ann Ophthalmol.* 11: 1197-1201; Eye Disease Case-Control Study Group. (1992) Risk factors for neovascular age-related macular degeneration. *Arch Ophthalmol.* 110: 1701-1708; Sandberg, M, Tolentinl M, Miller S, Berson E, and Gaudio A. (1993) Hyperopia and neovascularization in age-related macular degeneration. *Ophthalmol.* 100: 1009-1013; Boker T, Fang T, and Steinmetz R. (1993) Refractive error and choroidal perfusion characteristics in potential with choroidal neovascularization and age-related macular degeneration. *Ger J. Ophthalmol.* 2:10-13; Wang J, Mitchell P, and Smith W. (1998) Refractive error and age-related maculopathy: the Blue Mountains Eye Study. *Invest Ophthalmol Vis Sci.* 39: 2167-2171). However, it must be noted that no clinical study has been conducted to confirm or refute the existence of such a relationship. Furthermore, no references have been found in the medical or scientific literature relating a potential increased incidence of AMD amongst individuals exhibiting presbyopia. However, data exists indicating that myopia (commonly referred to as nearsightedness) may indeed have the effect of helping to protect against AMD (Hirvela H, Luukinen H, Laara E, and Laatikainen L. (1996) Risk factors of age-related maculopathy in a population 70 years of age or older. *Ophthalmol.* 103: 871-877).

Although the reported protective relationship between myopia and protection against AMD can be easily rationalized based upon the fact that the blue wavelengths of light are focused at a significant distance in front of the retina in comparison to that of the normal eye, the link between hyperopia and an increased risk of AMD is somewhat more difficult to rationalize. Aside from people with very mild hyperopia, individuals who exhibit hyperopia are generally prescribed corrective lenses from an early age. Therefore, visual correction for hyperopia should limit the total amount of damage that might be induced in the retina by the blue light wavelengths impinging directly upon the retina. Therefore, unless the damage induced by the blue wavelengths of light in hyperopic individuals occurs very early in life (i.e., before the time of hyperopic correction) and such damage is dormant for many years (i.e., until the normal age of appearance of AMD which is accepted to be in the sixth to seventh decade of life), it is difficult to rationalize the link between normal hyperopia and AMD. There is always the chance the damage induced in undiagnosed childhood hyperopia is the link or at least an additional link between hyperopia and AMD. For this to be true, the damage induced by undiagnosed hyperopia would have to be undetectable for many years as just described. However, if this is the case, then this aspect of the relationship between hyperopia and AMD described in this work is considered to be covered by this document. However, in such an instance, there is a need for such individuals to be supplemented with ocular antioxidants across their entire life, not just in the mid- to later years of life. Despite that fact, ocular antioxidant supplementation in infants and children should still be considered to be important and advantageous to help reduce the possibility of AMD in later adulthood.

Additionally, there is always the possibility that damage induced by early childhood hyperopia and subsequently aggravated by presbyopia-induced damage is the actual link between the observed epidemiological relationship between hyperopia and AMD. Based upon the high metabolic activity exhibited by all cells of the human body in youth, it seems likely that any damage induced early in childhood should be readily repaired before the sixth decade of life. This should limit the importance of this link between childhood retinal light exposure, hyperopia, and AMD. Nonetheless, if this is the case, as stated above for the case of AMD resulting only from ocular damage induced by light upon the retina of the childhood hyperopic eye, supplementation of these individuals with ocular antioxidants throughout their lifetime should help reduce the incidence of AMD in late adulthood. This situation is considered to be covered within the relationships described in this document.

It is also possible that the relationship between hyperopia and AMD as described in the epidemiological literature is a result of presbyopia and not hyperopia. This is because it is virtually impossible to differentiate between these two ocular conditions upon a simple eye examination. Additionally, without a complete ocular history, an older person participating in an epidemiological study might not know the difference between these two conditions. Furthermore, no published studies in the epidemiological literature have provided any indication that they have questioned subjects about whether they have presbyopia as compared to hyperopia. Regardless, this issue is considered of little significance as it pertains to the relationship between ocular diseases and AMD since this document covers both hyperopia and presbyopia.

Returning to the original premise that presbyopia is the actual link between the damage observed in AMD, the age of onset of the potential damage caused by the presbyopic focus of blue light on the retina and the age of prevalence of ocular damage in AMD is logical. The prevalence of presbyopia increasing after the age of 40 and the age of diagnosis of AMD in the sixth to seventh decade allows a sufficient amount of time for the damage related to AMD to occur. Additionally, the effects of presbyopic changes upon the focal point of the damaging blue wavelengths of visible light upon the retina is consistent with the types of damage seen in AMD. Therefore, the initiation of dietary supplementation with ocular antioxidants at a much earlier age (in the early to mid-30s) than commonly undertaken in today's environment (in the mid- to late-50s) makes significant sense in order to help reduce AMD incidence in the elderly adult population. In fact, given the totality of the above potential links between early childhood damage caused by hyperopia and presbyopia in adulthood, it is probably most advisable to consider supplementation with ocular antioxidants throughout life, not just in later adulthood.

Astigmatism and AMD

The principles described above regarding the focusing of light upon the macula of the eye in hyperopia and presbyopia equally apply in the circumstances where people suffer from astigmatism except for the fact that, in the astigmatic eye, light can be focused correctly in the normal orthogonal plane of the eye and improperly focused in the astigmatic plane as shown in FIG. **5** for a hyperopic astigmatic eye. In this example, light in the vertical plane is in focus at the retina whereas light in the horizontal plane is focus hyperopically (i.e., behind the plane of the retina). Similar to the case shown in FIG. **5**, when the light entering the horizontal plane is

separated prismatically into its component color wavebands, the blue wavelengths are focused directly upon the retina. These damaging blue wavelengths are capable of inducing significant damage upon the macular tissues which can result in AMD over the years as discussed previously. However, the damage noted may not encompass the entire macular area. Instead, because light in one plane is more focused upon the retina, the damage potential in presbyopics may be more to the central retina such as is found in choroidal neovascularization whereas the damage potential in astigmatics may be either more confined to the peripheral macular area such as found in geographic atrophy or more diffuse encompassing the central and peripheral retinal areas. This is not to imply that these two forms of AMD cannot be induced in either presbyopics or astigmatics but instead the focal properties of the eye exhibiting these conditions may be more likely to result in these forms of AMD.

As in the case of presbyopia, astigmatism increases with age and this condition is not readily noticed by people, particularly in the elderly, because astigmatism causes vision to be blurred or fuzzy but not completely out of focus (Gudmundsdorrir E, Jonasson F, Jonsson V, Stefansson E, Sasaki H, Sasaki K, and the Iceland-Japan Co-Working Group. (2000) "With the rule" astigmatism in not the rule in the elderly. *Acta Ophthalmol Scand.* 78:642-646). This finding implies that the need for correction for astigmatism can potentially exist for some time before it becomes serious enough to cause people to go their doctor to seek correction. The lag time between the existence of astigmatism and its correction means that the macula of the astigmatic eye is exposed to ever greater amounts of blue light exposure and potential damage.

Studies Demonstrating the Need for Macular Antioxidants in Presbyopia, Hyperopia, and Astigmatism

As described above, the presence and relative amounts of the two principle antioxidants found in the macula, namely lutein and zeaxanthin, can be assessed by measurement of Macular Pigment Optical Density (MPOD). Additionally, as described above, it is known that MPOD declines with age which makes older people even more susceptible to AMD. Although MPOD values are a measure of only the amount of macular pigment (lutein and zeaxanthin) present in the eye, they are not the only antioxidants present in ocular tissues. However, because ocular antioxidants are derived from the same types of foods that macular pigment are obtained from, it is easy to hypothesize that people with low MPOD values also exhibit low levels of other ocular antioxidants. Such a hypothesis is also consistent with the published results (Bernstein, et al., 2010). Therefore, it is important to maintain high levels of macular pigment.

A study was conducted in which MPOD values were measured in a large, multi-ethnic population using an auto-fluorescence imaging instrument (Sharifzadeh M, Bernstein P, Gellermann W. (2006) Nonmydriatic fluorescence-based quantitative imaging of human macular pigment distributions. *J Opt Soc Am A: Optics and Image Sci Vis.* 23: 2373-2387). In total, 241 subjects volunteered for MPOD testing and values were obtained for 224 subjects. Of this total database, subjects were asked about their history of vision correction. Only subjects with and without a self-reported history of vision correction were included in the following analysis. Of the total number of subjects available, twenty-three indicated that their vision had never required any type of correction. These subjects were classified as the normal subject database. Eight subjects indicated that they had been diagnosed with only presbyopia, seven had been diagnosed with only hyperopia, nine had been diagnosed with only astigmatism, and an additional eighteen had been diagnosed with only myopia. The MPOD values were plotted as a function of subject age for the four types of visual disorders as shown in FIG. **6**. FIG. **6**A compares subjects with myopia to normals; **6**B compares subjects with hyperopia with normals; **6**C compares subjects with presbyopia to normals; and **6**D compares subjects with astigmatism to normals.

As can be seen from the data in FIG. **6**A, subjects with myopia do not show any appreciable difference in the rate of decline in MPOD as a function of age when compared to the rate of decline in MPOD with age in subjects who had vision that never required any correction. Similar comparisons of MPOD values with age in subjects who have had their vision corrected for hyperopia (FIG. **6**B), presbyopia (FIG. **6**C), or astigmatism (FIG. **6**D) indicate a steeper decline in MPOD over the age range, especially subjects with astigmatic correction. Although a decline in MPOD values with age is not in itself an indicator of a predisposition for age-related macular degeneration, it definitely indicates an increased risk factor since studies have indicated that people with lower MPOD values are at greater risk for AMD (Bernstein, et al., 2010). Given the fact that presbyopia, and astigmatism are ocular conditions that occur with increasing frequency amongst people above the age of 40, this decline definitely indicates a need for supplementation with ocular antioxidants including lutein and zeaxanthin in people exhibiting these ocular disorders in order to reduce the potential damage to ocular tissues brought about by an increase exposure to blue light damage which could lead to AMD.

SUMMARY

The principles behind the relationships between MPOD values, blue light damage to ocular tissues, and the risk for AMD are based upon known data. They represent the cumulative blue light-induced damage from oxidative processes that occur in retinal tissues of the human eye that has been related to increased likelihood of AMD. Although the amount of cumulative damage required to elicit AMD is not known, it is known that ocular antioxidants are important in reducing the potential of such damage.

Based upon the data presented, eyes exhibiting hyperopia, presbyopia, and/or astigmatism exhibit a decline in MPOD values with age that is greater than in myopic eyes as well as eyes that have never required visual correction. This increased rate of decline in MPOD with age renders eyes with hyperopia, presbyopia, and/or astigmatism at greater risk for AMD. It is also possible that a combination of astigmatism with either hyperopia or presbyopia could result in an even higher risk of AMD than any one of the ocular conditions by itself. Therefore, such combination of ocular conditions are included in the present invention.

Supplementation of eyes with macular antioxidants, including but not limited to vitamins A, C, E, and other vitamins exhibiting antioxidant activity; beta-carotene and other carotenoids including lutein, zeaxanthin, retinoids, retinal, retinaldehyde, and meso-zeaxanthin; zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems, natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercetin, anthocyanins, anthocyanidins, etc.; and the synthetic antioxidants including BHT, BHA, BTHQ that increase ocular antioxidant levels will reduce the risk of blue light-induced damage to retinal tissues.

The cumulative damage theory of AMD is consistent with the onset of hyperopia or astigmatism regardless of age. Additionally, it is consistent with the onset of presbyopia, and adult

onset astigmatism, both of which are reported to increase at about the age of 40. The slow progression of the ocular damage associated with AMD is consistent with rate of progression of presbyopia and/or adult-onset astigmatism. Such damage is probably compounded by the reluctance of people to wear any type of vision correction for presbyopia or astigmatism as well as the inability of people to take action on such visual changes until vision has deteriorated significantly.

The methods of the present invention are consistent with the knowledge that people with high levels of macular pigment are less likely to suffer from AMD. They are also consistent with the knowledge that MPOD levels decline with age, especially amongst people with hyperopia, presbyopic, and/or astigmatism. The presence of high levels of macular pigment may reduce the probability that people with hyperopia, presbyopia, and/or astigmatism would incur less blue light-induced retinal tissue damage than people with lower MPOD levels might incur. This is because the known blue light-absorbing capability and/or antioxidant capacity of the xanthophylls (lutein and zeaxanthin) comprising the macular pigment and the presence of other ocular antioxidants. These properties help limit the blue light-induced damage.

The methods of the present invention are not meant to cover damage that might be induced in the eye as a result of other ocular conditions/diseases that might also result in AMD, including but not limited to inherited conditions (a genetic component) or damage from other forms of retinopathies aside from AMD. Instead, the methods address the link between hyperopia, presbyopia, and/or astigmatism and AMD as well as the beneficial effect of ocular antioxidant supplementation upon reducing the risk associated with AMD. Supplementation with ocular antioxidants, as described above, is not limited to the xanthophylls that comprise the macular pigment. Ocular antioxidants as described above include vitamins A (1 to 150 IU/kg Body Weight (BW)/day), C (0.05 to 15 mg/kg BW/day), E (0.02 to 5 mg/kg BW/day), and other vitamins exhibiting antioxidant activity (0.01 to 500 mg/kg BW/day); lutein, zeaxanthin, beta-carotene and other carotenoids including retinoids, retinal, retinaldehyde, and meso-zeaxanthin (0.0001 to 2 mg/kg BW/day); zinc, copper, selenium and other minerals that may be cofactors of antioxidant enzymes or systems (0.0001 to 5 mg/kg BW/day), natural extracts exhibiting antioxidant activity including but not limited to polyphenols, quercitin, anthocyanins, anthocyanidins, etc. (0.001 to 75 mg/kg BW/day); and the synthetic antioxidants including BHT, BHA, BTHQ (0.001 to 15 mg/kg BW/day), or any synthetic analog of the natural antioxidants. Additionally, any combination of these ocular antioxidants may be used. The amounts described above pertain to a suggested dosage for an individual weighing approximately 150 pounds (approximately 70 kg). The relationships described are also not limited by the form of deliver of the above described materials and includes food, beverages, and/or dietary supplement tablets, capsules, and other more esoteric delivery forms. Furthermore, the ocular antioxidants can take any form, including but not limited to powders, beadlets, crystals, liquids, dispersions, and the like as long as it can be delivered to the body in a form and in amounts that can be absorbed and used by the body.

Even though the components and activity of the carotenoids comprising the macular pigment are described above in relation to reducing the potential damage associated with a relationship between hyperopia, presbyopia, and/or astigmatism and AMD, these relationships are not restricted to the activity of these xanthophylls. The relationships described also do not preclude the use of other antioxidants and associated molecules individually or in combinations that might reduce the oxidative damage associated with hyperopic-, presbyopic-, and/or astigmatic-induced AMD.

The foregoing description and drawings comprise illustrative embodiments of the present inventions. The foregoing embodiments and the methods described herein may vary based on the ability, experience, and preference of those skilled in the art. Merely listing the steps of the method in a certain order does not constitute any limitation on the order of the steps of the method. The foregoing description and drawings merely explain and illustrate the invention, and the invention is not limited thereto, except insofar as the claims are so limited. Those skilled in the art that have the disclosure before them will be able to make modifications and variations therein without departing from the scope of the invention.

What is claimed is:

1. A method of reducing the increased blue and ultraviolet light damage to the retina of a subject having a condition that causes such blue or ultraviolet light to fall disproportionally on or in front of the retina relative to the blue and ultraviolet light damage present in a subject having no such condition, wherein the condition is presbyopia or hyperopia or astigmatism, comprising administering to the subject having such condition a composition comprising a therapeutically effective amount of one or more ocular antioxidants.

2. The method of claim **1**, wherein said ocular antioxidant is selected from the group consisting of antioxidant vitamins, carotenoids, antioxidant minerals, natural antioxidant extracts and synthetic antioxidants.

3. The method of claim **2**, wherein said antioxidant vitamin is selected from the list consisting of vitamins A, C, and E.

4. The method of claim **2**, wherein said carotenoid is selected from the list consisting of lutein, zeaxanthin, beta-carotene, retinoids, retinal, retinaldehyde, and meso-zeaxanthin.

5. The method of claim **2**, wherein said antioxidant mineral is selected from the list consisting of zinc, copper, and selenium.

6. The method of claim **2**, wherein said natural extract is selected from the list consisting of polyphenols, quercitin, anthocyanins, and anthocyanidins.

7. The method of claim **2**, wherein said synthetic antioxidant is selected from the list consisting of BHT, BHA, and BTHQ.

8. The method of claim **2**, wherein said therapeutically effective amount of said antioxidant vitamin is between 0.02 (1 IU) and 15 mg (150 IU) per kilogram of body weight of said subject per day.

9. The method of claim **2**, wherein said therapeutically effective amount of said carotenoid is between 0.0001 and 2 mg per kilogram of body weight of said subject per day.

10. The method of claim **2**, wherein said therapeutically effective amount of said antioxidant mineral is between 0.0001 and 5 mg per kilogram of body weight of said subject per day.

11. The method of claim **2**, wherein said therapeutically effective amount of said synthetic antioxidant is between 0.001 and 15 mg per kilogram of body weight of said subject per day.

12. The method of claim **2**, wherein said therapeutically effective amount of said natural extract is between 0.0001 and 20 mg per kilogram of body weight of said subject per day.

13. The method of claim **2**, wherein said therapeutically effective amount of said synthetic antioxidant is between 0.0001 and 20 mg per kilogram of body weight of said subject per day.

* * * * *

EXHIBIT I

DAVISBROWN LAW FIRM

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phone: 515-288-2500
Des Moines Office

July 20, 2016

OmniActive Health Technologies, Inc.
67 East Park Place, Suite 500
Morristown, NJ 07960

VIA CERTIFIED MAIL

Re: United States Patents No. 8,815,955 and 9,226,940

Dear Sir or Madam:

We represent Kemin Industries, Inc., ("Kemin") in matters relating to its intellectual property rights. Kemin is a leading innovator, manufacturer and seller of products which enhance nutrition and health for humans and animals.

We wanted to make you aware of the above-identified patents. These patents limit the marketing claims that can be made by sellers of ocular antioxidants. Specifically, these patents cover the marketing of products containing lutein and/or zeaxanthin to consumers with an increased risk of age-related macular degeneration with either hyperopia or astigmatism and such products to protect against blue or ultraviolet light damage to consumers with either persbyopia, hyperopia or astigmatism. Because all humans below the age of 4 have hyperopia and all humans over the age of 40 have presbyopia, these patents cover marketing claims directed to such age brackets.

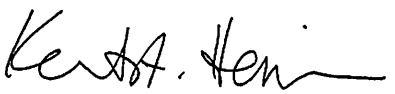
Accordingly, we demand that OmniActives immediately cease and desist from any such marketing, including specifically OmniActive's "What's Your B.L.U.E." marketing campaign and its marketing claims of Lutemax 2020® related to reducing blue and ultraviolet light damage, as set out in the attached materials and any similar materials, advertising or promotional activity. Please provide written confirmation that OmniActives will comply with this request by no later than August 2, 2016.

We trust that you will recognize the immediacy of our client's concerns and promptly take the actions requested so that this matter can be resolved quickly and amicably.

This letter does not contain a complete statement of Kemin's rights, claims, and remedies and shall not waive, affect, or impair any such rights, claims, and remedies.

Sincerely yours,

DAVIS, BROWN, KOEHN, SHORS & ROBERTS, P.C.



Kent A. Herink

Enclosures

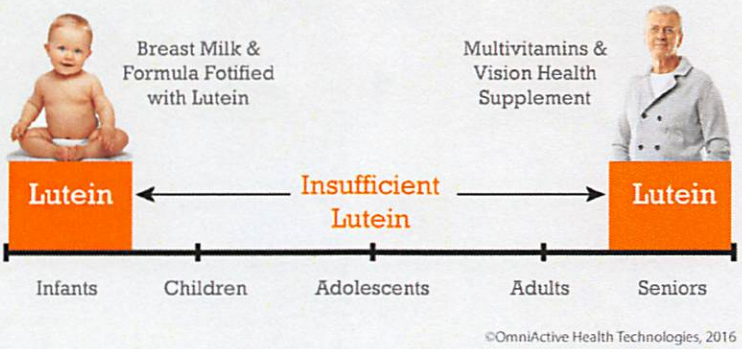
KAH/psl

cc: Elizabeth A. Nelson, General Counsel

Healthy eyes for a lifetime starts with the macular carotenoids

Of the more than 600 carotenoids found in nature, only lutein and zeaxanthin isomers—RR-zeaxanthin and RS (meso)-zeaxanthin—are located in the eye, specifically the macula. The macular carotenoids make up the macular pigment, and their deposition in the macula is highly specific: lutein is preferentially deposited in the peripheral macula, RR-zeaxanthin in the mid-peripheral macula and RS-zeaxanthin at the center of the macula —the region most susceptible to photo-oxidative damage. Acting as primary filters of high-energy blue light, lutein and zeaxanthin isomers support visual health and acuity by protecting against oxidative stress and inflammation.

gap in lutein intake



Lutein and zeaxanthin are not produced by the body and their specialized locations and functions emphasize the need to consume all three macular carotenoids through diet or supplementation. Lutein and RR-zeaxanthin are found in dark green leafy vegetables and yellow to orange fruits and vegetables, while RS-zeaxanthin is found in fish such as salmon, sardine and trout.

Given that the average US dietary intake of lutein and zeaxanthin is far below levels shown in research to be beneficial (less than 2 mg lutein and 0.5 mg zeaxanthin), supplementation may be a more viable approach to maintain optimal levels of all three macular carotenoids to support visual health.

Lutemax 2020

Envision the possibilities

Award-winning, globally-recognized Lutemax 2020 is a naturally-derived marigold extract providing all three macular carotenoids—lutein and enhanced levels of both zeaxanthin isomers (RR-and RS [meso]-zeaxanthin)—at the same 5:1 ratio as found in nature to optimally support eye health. This unique combination of lutein with zeaxanthin isomers makes Lutemax 2020 a convenient, cost effective way to boost the benefits of your eye health formulation.

- **Higher levels of zeaxanthin isomers than most commercial forms**
- **Manufactured under a fully vertically integrated supply chain**

- FDA-acknowledged GRAS notification
- Available in a variety of 100% vegetarian beadlets, oil suspensions and powder

To find out how to expand your sales in the growing eye health supplement market with Lutemax 2020

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OMNIACTIVE INTRODUCES WHAT'S YOUR B.L.U.E.? TO NATURAL PRODUCTS INDUSTRY MEMBERS AT ENGREDEA 2016

OMNIACTIVE INTRODUCES WHAT'S YOUR B.L.U.E.? TO NATURAL PRODUCTS INDUSTRY MEMBERS AT ENGREDEA 2016

OmniActive Health Technologies will be launching What's Your B.L.U.E.? (Blue Light User Exposer Campaign) at this year's Engredea (booth #544) in Anaheim, Calif. An extension of Lutein For Every Age, What's Your B.L.U.E.? is an exciting new initiative to educate consumers on high-energy blue light, its sources and ways to help protect healthy vision from its effects with the support of the macular carotenoids—lutein and zeaxanthin isomers (RR-zeaxanthin and RS [meso]-zeaxanthin). Natural products manufacturers and retailers are invited to OmniActive booth #544 to gauge their blue light user exposure.

More than ever before, our eyes are being bombarded by high-energy blue light sources including electronic devices such as televisions, tablets, smartphones and computers, as well as indoor lighting (CFL or LED), and even LED car headlights. High-energy blue light reaches deep into the eye and can harm the macula–the region of the eye responsible for the highest visual acuity and sharpness. Lutein and the zeaxanthin isomers are known as the "macular carotenoids" and support eye health by acting as powerful antioxidants and filtering high-energy blue light.

"Lutein For Every Age has brought something new to the show every year since its launch at Engredea 2013. It was only natural for us to have the official introduction of What's Your B.L.U.E.? at Engredea 2016," stated Lynda Doyle, Vice President of Global Marketing, OmniActive. "With ever increasing exposure to high-energy blue light sources, OmniActive proactively developed What's Your B.L.U.E.? to address the growing concerns surrounding the rapidly growing digital user demographic. In addition, we offer Lutemax 2020 – a scientifically substantiated, differentiated marigold extract providing all three macular carotenoids – lutein, RR- and RS (meso)-zeaxanthin – in a 5:1 ratio for optimal eye health support."

Representatives at the booth will also provide exclusive, one-on-one presentations on OmniLean, a scientifically validated ingredient that represents a new class of OmniActive ingredients called "metabolic synergizers." OmniLean targets multiple facets of weight management and metabolic markers. OmniActive will also discuss Lutemax 2020 Lutein with Enhanced Levels of Zeaxanthin Isomers, Lutemax Free Lutein and Lutein Esters, OmniXan RR-Zeaxanthin, Capsimax Capsicum Extract, CurcuWIN Curcumin with Enhanced Absorption and Gingever High Potency Ginger.

For more information on What's Your B.L.U.E.? and Lutein For Every Age, our innovative products and ingredient solutions, or to schedule an appointment with an OmniActive representative during Engredea, contact Lynda Doyle at l.doyle@omniactives.com or visit us at Engredea 2016 booth #544.

About Lutein For Every Age:

Aimed at natural products industry members, health care professionals and consumers, Lutein For Every Age raises awareness surrounding the importance of early and consistent lutein supplementation for helping maintain proper health over a lifetime. During the past year, OmniActive has enlisted a team of key opinion leaders and scientific experts, supported a variety of studies on the macular carotenoids, and launched two interactive,

innovative and scientifically validated for dietary supplementation, nutritional fortification, functional food/beverage, coloring, flavor enhancement and personal care applications. The company addresses complex challenges for customers in the dietary supplement, food and beverage space using technology-driven, sustainable solutions with application support within a global regulatory framework. Whether looking for a new ingredient to add to a finished product, or an ingredient solution to enhance an existing ingredient, you will find unmatched innovation at OmniActives.

Core products include carotenoids, plant extracts and specialty functional ingredients. OmniActives leverages international R&D strengths to deploy an array of state-of-the-art manufacturing technologies in extraction, purification, isolation and delivery of nutritional actives. The company's manufacturing operations are located at multiple sites in India and are cGMP and HACCP system compliant.

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