Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Original Research Article

A comparative study in the Indian patients of geographic atrophy for the efficacy and safety for the AREDS 2 Formula, the combination of Vitamin C, Copper, Zeaxanthin, Zinc, Lutein, and Vitamin E, with the combination of L-Glutathione, Lutein (contains Zeaxanthin) and Astaxanthin

Lalit Pawaskar[1]*, **Amit Sharma**[1], **Mayuresh Kiran**[2]

[1]*Jagannath University, Jaipur, Rajasthan, India*
[2]*Centaur Pharmaceuticals Pvt. Ltd, Mumbai, Maharashtra, India*

ARTICLE INFO

Article history:
Received 09-09-2023
Accepted 21-10-2023
Available online 29-12-2023

Keywords:
Vitamin C
Vitamin E
Lutein
Zeaxanthin
Zinc
Copper
Astaxanthin
L-Glutathione
Efficacy and safety

ABSTRACT

Background: Geographic atrophy (GA) is the main reason of blindness in people above 60 years. During this study, the efficacy and safety of two different combinations including Investigational product 1 (IP-1) combination of Vitamin C, Copper, Lutein, Zinc, Zeaxanthin, and Vitamin E vs Investigational product (IP-2) combination of Lutein (which contains Zeaxanthin), L-Glutathione and Astaxanthin was compared in for the indication of GA.

Methods: On day 30, 180, and 365 all the recruited clinical trial subjects were required to visit the clinical trial site, with day 0 serving as the baseline visit. Patients assigned to IP-1 were categorized as group C patients, whereas those assigned to IP-2 were categorized as group D patients. Visual acuity (VA), vision-related quality of life (VRQOL), and the vision impairment questionnaire (VIQ) were used as efficacy assessment measures. Based on the patients' reported adverse events, a safety assessment was done.

Results: Statistically significant increase was not found in patients randomized to IP-1 in VA (p=0.6229) and VRQOL (p=0.1772) and no statistically significant reduction in VIQ score (p = 0.2503). In patients randomized to IP-2, there was statistically significant increase in VA (p<0.0001), statistically significant reduction in VRQOL (p=0.0036) and no significant increase in VIQ (p=0.5993). In both groups there was statistically significant difference in VA (p=0.0134) and VRQOL (p=0.0045) and no statistically significant difference in VIQ (p=0.2787).

Conclusion: IP-1 was more effective than IP-2 in terms of maintaining VA (p=0.0134) and VRQOL (p=0.0045), however there was no statistically significant difference in the effectiveness of the two products for VIQ (p=0.2787) in patients of GA.

1. Introduction

Geographic atrophy (GA) is a persistent, multifactorial phenomenon distinguished by the development of numerous atrophic lesions in the fovea centralis of the macula. GA is regarded as the late-stage of dry age related macular degeneration (AMD), severely impairing vision and ultimately resulting in a slow, permanent loss of visual ability.[1] Given that the macula is the principal structure impacted, the primary manifestation of GA entails the presence of distorted central vision, which exhibits a progressive deterioration as time elapses. In the context of GA, a prominent stationary region of dark or grey pigmentation (known as the central scotoma) manifests at

* *Corresponding author*.
E-mail address: lalitpawaskar@gmail.com (L. Pawaskar).

https://doi.org/10.18231/j.ijceo.2023.105

the fovea centralis (central region of retina) within the eye. Impaired visual perception including challenges in reading, facial recognition, and driving as well as decreased visual acuity, compromised adaptation to varying light conditions, diminished depth perception, reduced contrast sensitivity (resulting in images appearing whitewashed), defective colour vision and difficulties in viewing objects in low light environments are additional symptoms associated with GA.[2] Optical coherence tomography, color fundus photography and fundus autofluorescence are just a few of the diagnostic techniques available for GA.[3]

As we age, drusen particles build up in the subretinal region area between Bruch Membrane and Retinal Pigment Epithelium. These particles are visually evident as yellowish spots located at the posterior part of the retina.[4] Increased levels of oxidative stress are brought on by the occurrence of environmental risk factors and the accumulation of drusen. This leads to negative effects on the retinal pigment epithelium (RPE) layer, thickening of the Bruch's membrane, photoreceptor cells, and the choriocapillaris. This phenomenon gives rise to persistent inflammation in the macula initiating the degenerative process.[5,6] If the condition of GA is not medically addressed, it might result in irreversible vision loss.[7]

The incidence and trends of Geographic Atrophy (GA) were examined in a study by the Asian Eye Epidemiology Consortium (AEEC). It was revealed that GA had a higher prevalence in South Asia, as shown by studies conducted in India and Nepal.[8] According to a N. Likhar et al., in the Indian population, the prevalence of GA varies from 1.4% to 3.1%. The highest prevalence was found in South India (3.1%), while the lowest prevalence was found in west India of 1.4%.[9] At now, there exists a dearth of effective treatments for GA. However, some dietary nutraceuticals, in conjunction with antioxidants, can be used to decelerate the advancement of this condition.[1,10]

Oxidative stress is one of the major concern responsible for the deterioration of ocular structures in GA. Given the significance of antioxidants in cellular defence against oxidative stress, it is plausible to consider the potential utility of antioxidant therapy in mitigating disease progression and safeguarding visual function in cases of GA. Consequently, the utilisation of micronutrients possessing significant antioxidant capacity holds potential as a promising preventative and therapeutic approach for GA and AMD. This includes the addition of nutrients including Zinc, Copper, Vitamin E, Vitamin C, and Carotenoids like Lutein, Zeaxanthin, and Astaxanthin, which have been used to treat GA to slow the progression of the condition.[10]

Vitamin C and Vitamin E have a significant part in the process of neutralising free radicals that are present inside the retina. The aqueous phase containing Vitamin C and the lipid phase containing Vitamin E undergo a direct reaction to effectively counteract the presence of free radicals, namely hydroxyl, alkoxy, and lipid peroxyl radicals. The reaction results in the formation of water, alcohol, and lipid hydroperoxides, respectively.[11,12] Both Zinc and Copper are crucial for the survival of retinal cells and for the proper functioning of antioxidant enzymes.[13] In addition to possessing antioxidant properties, Lutein and Zeaxanthin are known to exert a significant influence on the visual performance of individuals with AMD due to their ability to filter blue light.[14] Glutathione is known for its antioxidative characteristics, as it is capable of effectively eliminating reactive oxygen species.[15] Astaxanthin is a carotenoid compound that exhibits a red pigment. Anti-inflammatory, Antioxidant anti-proliferative, and anti-apoptotic effects are only a few of its many scientific attributes. Hence, it exhibits superior antioxidant efficacy in comparison to alternative Carotenoids, namely α-Carotene, Lycopene, Lutein and β-Carotene.[16]

There are various combinations available in Indian market for the medical management of GA but out of them the clinical trial data is available for the combination of Vitamin C, Vitamin E, Lutein, Zeaxanthin, Zinc, and Copper which is referred as AREDS2 combination and for this article it was referred as an investigational product 1 (IP-1) and the combination of Astaxanthin, L-Glutathione and Lutein (which contains Zeaxanthin) is widely used for the medical management of GA which was referred in this article as investigational product 2 (IP-2). The current study was conducted to compare the efficacy and safety of IP-1 and IP-2 as for IP-1 though the clinical trial data is available but it is not of Indian patients and for IP-2 there was no clinical trial data available as per the best knowledge so the comparative clinical efficacy and safety data was generated from this clinical trial.

2. Materials and Methods

The study was conducted to compare the efficacy and safety of IP-1 and IP-2. The study specifically focused on patients with GA. The cohort of individuals receiving the IP-1 were designated as group C patients, while those receiving the IP-2 were designated as group D patients.

2.1. Inclusion and Exclusion criteria

Based on the predetermined criteria for study inclusion, participants with geographic atrophy (not involving fovea deformities) in either the right eye, left eye or both eyes, geographic atrophy (non-foveal) in one eye, were selected for recruitment. The clinical trial subjects for this study were required to be 50 years of age or older, male or female, able to swallow pills or capsules with water, and have vision in both eyes that was at least 20/200 in both eyes. Moreover, the participants were obligated to exhibit compliance with the set study protocol. The study exclusion

criteria included, patients with exudative AMD; patients with retinal abnormalities other than AMD; patient with history of diabetic retinopathy or presence of haemorrhage in the vitreous chamber or RPE detachment or macular hole; patient with IOP ≥26 mmHg; patients allergic to IP-1 and/or IP-2; patients who follow the study procedure mentioned in the protocol, patient with any disease with a poor 1 year survival prognosis were excluded from the study.

2.2. Study intervention

IP-1 was a fixed-dose combination of vitamins and minerals that contained fixed dose combination of 250 mg of Vitamin C, 40 mg of Zinc, 5 mg of Lutein, 1 mg of Zeaxanthin, 1 mg of Copper, and 200 IU of Vitamin E per capsule. IP-2 was the fixed dose combination of 6 mg of Astaxanthin, 5 mg of L-Glutathione, and 3.2 mg of Lutein (contains 256 mcg of Zeaxanthin) per capsule.

2.3. Study procedure

According to the inclusion and exclusion criteria, patients were recruited. On days 180 and 365, efficacy was evaluated. On day 0, baseline efficacy was determined. A safety evaluation was performed on day 30, 180, and 365. Patients were randomized to group C (patients treated with IP-1) or group D (patients treated with IP-2) by simple randomization method. At each clinical trial site 30 patients were recruited out of which 15 were randomized to each group. Similarly patients were recruited at 5 clinical trial sites. In group C, patients were asked to take 2 capsules per day with food with 12 hrs interval of IP-1. In group D, patients were asked to take a tablet per day of IP-2.

2.4. Concomitant therapy

Patients instructed of not to take any concomitant therapy containing Zinc, Lutein, Astaxanthin, Zeaxanthin, Glutathione, Copper, Vitamin E or Vitamin C but there were no objections to any other therapy.

2.5. Efficacy assessment

The primary efficacy assessment was made by evaluating the visual acuity (VA) in each eye at visit 1 (day 0), 3 (day 180) and 4 (day 365). The secondary efficacy assessment included the vision related quality of life (VRQOL) and visual impairment questionnaire (VIQ) score at visit 1, 3 and 4. Snellen chart was used to measure the VA. On a scale of 0 to 10, subjects were asked to rate their overall vision-related quality of life. Loss of vision was designated as 0, while 1, 2 was designated as very poor VRQOL; 3, 4 was designated as poor VRQOL; 5, 6 was designated as average VRQOL; 7, 8 was designated as good VRQOL and 9, 10 was designated as very good VRQOL. In the efficacy assessment parameter; VIQ score patients were asked questions and for the same they asked to answer the same as either no difficulty at all, a little difficulty, moderate difficulty, extreme difficulty or stopped doing this due to insufficient vision and accordingly recorded the score as 0, 1, 2, 3 or 4 respectively and by adding up the score of all 10 questions which are mentioned below, the visual impairment questionnaire score for the visit was calculated. These efficacy assessment parameter, "visual impairment questionnaire score" were evaluated on visit 1, 3 and 4 by asking 10 questions including difficulty while reading ordinary newspapers print; difficulty while working or following hobbies which requires close vision including but not limited to sewing, cooking, or any other household work; difficulty while finding out anything on a crowded shell; difficulty while reading names of shops or reading the street signs; difficulty while walking down stairs, or in dim light or at night time; difficulty while noticing objects off to the side walking; difficulty while watching movies on television; difficulty while shaving or styling your hair or putting on makeup; difficulty watching TV/Computer/Laptops and difficulty while reading messages or dialing number on mobile phone.

2.6. Safety assessment

Adverse events reported by the patient or observed by the investigator were recorded and causality assessment was made. Using the WHO-UMC probability scale, the adverse event was categorized as drug- or non-drug-related. Until they were resolved, the adverse events were observed by the investigators.

3. Results

A total of 150 participants were enrolled in this study at 5 clinical trial site, of whom 75 were randomly assigned to each group. In group C, 71 patients (119 eyes) and in group D, total 69 patients (120 eyes) completed the study. The only patients completed the study were considered for the statistical analysis for the efficacy assessment. For safety assessment all the patients recruited for the study and whether completed or not completed the study were considered.

3.1. Efficacy assessment

Visual acuity (VA) was the primary efficacy assessment parameter. In Table 1 below we have mentioned the no. of patients where VA was maintained, worsened and improved.

Table 1: VA maintained, worsened and improved in group C and D patients

	Group C	**Group D**
VA maintained	103 eyes	49 eyes
VA worsened	16 eyes	71 eyes
VA improved	no eye	no eye

Prior to statistical analysis of the visual acuity findings, the value acquired from the visual acuity result was converted to the logMAR formula because, especially for lower acuities, converting decimal visual acuity to logMAR creates an overestimation of its true value. The formula logMAR=-Log(decimal acuity) was used to calculate the logMAR value.[17] In group C patients, mean LogMAR value was 0.2070 at baseline visit, 0.2068 at visit 3 and 0.2109 at visit 4. Increase in the logMAR value was not statistically significant as p=0.6229 and F=0.4740 when one way ANOVA method applied. In group D patients, mean LogMAR value was 0.2198 at baseline visit, increased to 0.2254 at visit 3 and further increased to 0.3037 at visit 4. Increase in the LogMAR value was statistically significant as the p <0.0001 and F =15.21 when one way ANOVA method was applied. There was statistically significant difference between both the groups as p=0.0134 and F= 4.336 when two-way ANOVA method was applied.

VRQOL was one of the secondary efficacy assessment parameter. In Table 2 below we have mentioned the no. of patients where VRQOL was maintained, worsened and improved.

Table 2: VRQOL maintained, worsened and improved in group C and D patients

	Group C	Group D
VRQOL maintained	71 eyes	44 eyes
VRQOL worsened	6 eyes	52 eyes
VRQOL improved	42 eyes	24 eyes

In group C patients, mean VRQOL value was 6.857 at baseline visit, increased to 7.092 at visit 3 and 7.272 at visit 4. Increase in the mean VRQOL value was not statistically significant as p=0.1772 and F= 1.739 when one way ANOVA method was applied. In group D patients, mean VRQOL value was 7.05 at baseline visit, 7.26 at visit 3 and 6.59 at visit 4. Reduction in the mean VRQOL value was statistically significant as p =0.0036 and F =5.730 when one way ANOVA method was applied. There was statistically significant difference between both the groups as p=0.0045 and F= 5.454 when two-way ANOVA method was applied.

VIQ was one of the secondary efficacy assessment parameter. In Table 3 below we have mentioned the no. of patients where VIQ score was maintained, worsened and improved.

Table 3: VIQ maintained, worsened and improved in group C and D patients

	Group C	Group D
VIQ maintained	24 patients	29 patients
VIQ worsened	6 patients	10 patients
VIQ improved	41 patients	30 patients

In group C patients, mean VIQ score was 16.6901 at baseline visit, reduced to 15.4507 at visit 3 and 14.2535 at visit 4. Reduction in the mean VIQ score was not statistically significant as p=0.2503 and F= 1.394 when one way ANOVA method was applied. In group D patients, mean VIQ score was 17.246 at baseline visit, 16.376 at visit 3 and 17.782 at visit 4. Reduction in the mean VIQ score was statistically significant as p =0.5993 and F =0.5133 when one way ANOVA method was applied. There was not statistically significant difference between both the groups as p=0.2787 and F= 1.282 when two-way ANOVA method was applied.

3.2. Safety

Out of 75 patients of group C, total 4 episodes of adverse events were reported including 1 episode of hyperacidity, 2 episodes of belching and 1 episode of constipation. All the adverse events were of non-serious nature and no medical management was required to be provided to any of the patient. Out of 75 patients of group D, total 2 episodes of adverse events were reported including nausea and constipation. All the adverse events were of non-serious nature and no medical management was required to be provided to any of the patient.

4. Discussion

One of the most common causes of blindness among those over 65 years, worldwide is GA, an advanced stage of dry AMD.[18] GA can progress to permanent loss of central vision if not diagnosed or treated on time.[7] Although there is currently no effective treatment for GA, adopting a healthy lifestyle and improving one's diet may assist to delay the disease onset and progression.[19] Antioxidants have been widely used to reduce the effects of continuous oxidation on the retina. The present study compared the effectiveness and safety of IP-1 and IP-2 in GA patients.

Primary efficacy assessment parameter was VA and secondary were VRQOL and VIQ. VA was the primary efficacy assessment parameter. In group C patients, mean LogMAR value was 0.2070 at baseline visit which increased to 0.2109 at visit 4. Increase in the logMAR value was not statistically significant (p=0.6229). In group D patients, mean LogMAR value was 0.2198 at baseline visit which increased to 0.3037 at visit 4. Increase in the LogMAR value was statistically significant (p <0.0001). There was statistically significant difference between both the groups (p=0.0134). As there was no statistically significant increase in LogMAR value in group C patients but there was statistically significant increase in LogMAR value in group D patients and also there was statistically significant difference between both the groups which means that in group C patients the VA was better maintained compared to group D patients. VRQOL was one of the secondary

efficacy assessment parameter. In group C patients, mean VRQOL value was 6.857 at baseline visit which increased to 7.272 at visit 4. Increase in the mean VRQOL value was not statistically significant (p=0.1772). In group D patients, mean VRQOL value was 7.05 at baseline visit which reduced to 6.59 at visit 4. Reduction in the mean VRQOL value was statistically significant (p =0.0036). There was statistically significant difference between both the groups (p=0.0045). VRQOL was maintained in group C patients as there was no statistically significant increase but in group D patients there was statistically significant reduction and also there was statistically significant difference (p=0.0045) between both the groups which indicates that, there was VRQOL was better maintained in group C patients with IP-1 compared to group D patients with IP-2 where VRQOL was declined. VIQ was one of the secondary efficacy assessment parameter. In group C patients, mean VIQ score was 16.6901 at baseline visit, reduced to 14.2535 at visit 4. Reduction in the mean VIQ score was not statistically significant as p=0.2503. In group D patients, mean VIQ score was 17.246 at baseline visit and 17.782 at visit 4. Increase in the mean VIQ score was statistically significant as p=0.5993. There was no statistically significant difference between both the groups when two-way ANOVA method was applied as p=0.2787. These results indicate that vision related for daily activities was equivalently maintained in both the groups.

Below we have discussed one study of the similar nature which supports our research work. Intermediate-stage dry AMD patients were the clinical trial subjects of a double-blind, prospective, randomised, monocentric study conducted by M. Parravano et al. The duration of the clinical trial was of six months. Patients with AREDS category 3 or intermediate AMD, which was identified by drusen of at least 20/30 or better visual acuity, were recruited for the study. 15 patients were randomly assigned to the active treatment, combination of Lutein 20 mg, Zeaxanthin 4 mg, N-acetylcysteine 140 mg, Bromelain 250 GDU (80 mg), Vitamin B12 18 mg, Vitamin D3 800 IU, Alpha lipoic acid 140 mg, Rutin 157 mg, Vitamin C 160 mg, Zinc Oxide 16 mg, Vaccinum Myritillus (36%), Anthocyanosides. Similarly 15 patients were treated with the placebo. Fourteen patients from each cohort of 15 completed the research. Multifocal electrocardiogram (mfERG) to detect selectively the bioelectrical response originating from photoreceptor and biopolar cells and spectral domain optical coherence tomography (SD-OCT) for quantitative and qualitative assessment of retina and choroid were utilised to evaluate the efficacy. While retinal and choroidal SD-OCT parameters did not change significantly from baseline values, the mfERG response amplitude density recorded from the central macular areas in the active group increased significantly at the 6-month follow-up. There were no correlations found between functional and structural variations. At six months, in the placebo group, mf-ERG and SD-OCT parameters did not differ significantly. The pre-ganglionic components of the macula in the active group performed better after taking the nutraceutical supplement, but there were no concurrent changes to the retinal and choroidal ultrastructure. [20]

Though there were so many studies conducted before for the indication of dry AMD or GA but there was no comparative data for the efficacy and safety for IP-1 and IP-2 and this is the only study which gives data for the same.

5. Conclusion

From the results it was concluded that, in the patients treated with the IP-1, fixed-dose combination of vitamins and minerals that contained 250 mg of Vitamin C, 40 mg of Zinc, 5 mg of Lutein, 1 mg of Zeaxanthin, 1 mg of Copper, and 200 IU of Vitamin E per capsule in the dose of 1 capsule twice a day, the visual acuity was found to be maintained as there was no statistically significant increase (p=0.6229) in the logMAR value, the vision related quality of life was found to be maintained as there was no statistically significant increase (p=0.1772) in the vision related quality of life, visual functions required for the daily activities were also found to be maintained as there was no statistically significant reduction (p=0.2503) in the visual impairment questionnaire score.

In the group of patients treated with the investigational product 2, the fixed dose combination of 6 mg of Astaxanthin, 5 mg of L-Glutathione, and 3.2 mg of Lutein (contains 256 mcg of Zeaxanthin) per tablet once a day, visual acuity was not found to be maintained as there was statistically significant increase (p<0.0001) in the LogMAR value, vision related quality of life was found to be worsened as there was statistically significant reduction (p=0.0036) in the vision related quality of life and there was no statistically significant increase (p=0.5993) in the visual impairment questionnaire score so it was found that the visual functions required for daily activities were maintained.

During the comparative analysis it was found that there was statistically significant difference in visual acuity (p = 0.0134) and vision related quality of life (p=0.0045) but in visual impairment questionnaire score (p=0.2787) was not statistically significant difference. So, it was concluded that the IP-1 was more efficacious compared to IP-2 in maintaining the visual acuity and VRQOL whereas both the Investigational products were equivalently efficacious in maintaining the vision required for the daily activities.

As no significant adverse events or adverse events requiring medical management to resolve them were reported, both products were equally safe for the medical management of GA.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Khan H, Aziz AA, Sulahria H, Khan H, Ahmed A, Choudhry N, et al. Emerging Treatment Options for Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration. *Clin Ophthalmol*. 2023;17:321–7.
2. Boyer DS, Schmidt-Erfurth U, Campagne MVL, Henry EC, Brittain C. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. *Retina*. 2017;37(5):819–35.
3. Rickman CB, Farsiu S, Toth CA, Klingeborn M. Dry age-related macular degeneration: mechanisms, therapeutic targets, and imaging. *Invest Ophthalmol Vis Sci*. 2013;54(14):68–80.
4. Bonilha VL. Age and disease-related structural changes in the retinal pigment epithelium. *Clin Ophthalmol*. 2008;2(2):413–24.
5. Maurya M, Bora K, Blomfield AK, Pavlovich MC, Huang S, Liu CH, et al. Oxidative stress in retinal pigment epithelium degeneration: from pathogenesis to therapeutic targets in dry age-related macular degeneration. *Neural Regen Res*. 2023;18(10):2173–81.
6. Dong A, Xie B, Shen J, Yoshida T, Yokoi K, Hackett SF, et al. Oxidative stress promotes ocular neovascularization. *J Cell Physiol*. 2009;219(3):544–52.
7. Stahl A. The Diagnosis and Treatment of Age-Related Macular Degeneration. *Dtsch Arztebl Int*. 2020;117(29-30):513–20.
8. Rim TH, Kawasaki R, Tham YC, Kang SW, Ruamviboonsuk P, Bikbov MM, et al. Prevalence and Pattern of Geographic Atrophy in Asia: The Asian Eye Epidemiology Consortium. *Ophthalmology*. 2020;127(10):1371–81.
9. Likhar N, Mothe RK, Kanukula R, Shah C, Dang A. The prevalence of age-related Macular degeneration in Indian Population: a systematic review. 2015;18(3):180.
10. Kushwah N, Bora K, Maurya M, Pavlovich MC, Chen J. Oxidative Stress and Antioxidants in Age-Related Macular Degeneration. *Antioxidants (Basel)*. 2023;12(7):1379.
11. Kaźmierczak-Barańska J, Boguszewska K, Adamus-Grabicka A, Karwowski BT. Two Faces of Vitamin C-Antioxidative and Pro-Oxidative Agent. *Nutrients*. 2020;12(5):1501.
12. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacogn Rev*. 2010;4(8):118–26.
13. Wills NK, Ramanujam VMS, Kalariya N, Lewis JR, vanKuijk F. Copper and zinc distribution in the human retina: relationship to cadmium accumulation, age, and gender. *Exp Eye Res*. 2008;87(2):80–8.
14. Mrowicka M, Mrowicki J, Kucharska E, Majsterek I. Lutein and Zeaxanthin and Their Roles in Age-Related Macular Degeneration—Neurodegenerative Disease. *Nutrients*. 2022;14(4):827.
15. Kwon DH, Cha HJ, Lee H, Hong SH, Park C, Park SH, et al. Protective Effect of Glutathione against Oxidative Stress-induced Cytotoxicity in RAW 264.7 Macrophages through Activating the Nuclear Factor Erythroid 2-Related Factor-2/Heme Oxygenase-1 Pathway. *Antioxidants (Basel)*. 2019;8(4):82.
16. Nair A, Ahirwar A, Singh S, Lodhi R, Lodhi A, Rai A, et al. Astaxanthin as a King of Ketocarotenoids: Structure, Synthesis, Accumulation, Bioavailability and Antioxidant Properties. *Mar Drugs*. 2023;21(3):176.
17. Mataftsi A, Koutsimpogeorgos D, Brazitikos P, Ziakas N, Haidich AB. Is conversion of decimal visual acuity measurements to logMAR values reliable? *Graefes Arch Clin Exp Ophthalmol*. 2019;257(7):1513–7.
18. Waugh N, Loveman E, Colquitt J, Royle P, Yeong JL, Hoad G, et al. Introduction to age-related macular degeneration. In: Treatments for dry age-related macular degeneration and Stargardt disease: a systematic review. Southampton (UK): NIHR Journals Library; 2018.
19. Sacconi R, Corbelli E, Querques L, Bandello F, Querques G. A Review of Current and Future Management of Geographic Atrophy. Ophthalmol Ther. *Ophthalmol Ther*. 2017;6(1):69–77.
20. Parravano M, Tedeschi M, Manca D, Costanzo E, Renzo D, Giorno A, et al. Effects of Macuprev® Supplementation in age-related macular degeneration: A double-blind randomized morpho-functional study along 6 months of follow-up. *Adv Ther*. 2019;36(9):2493–505.

Author biography

Lalit Pawaskar, Research Scholar https://orcid.org/0000-0002-6437-3485

Amit Sharma, Professor https://orcid.org/0000-0002-1407-5228

Mayuresh Kiran, Vice President

Cite this article: Pawaskar L, Sharma A, Kiran M. A comparative study in the Indian patients of geographic atrophy for the efficacy and safety for the AREDS 2 Formula, the combination of Vitamin C, Copper, Zeaxanthin, Zinc, Lutein, and Vitamin E, with the combination of L-Glutathione, Lutein (contains Zeaxanthin) and Astaxanthin. *Indian J Clin Exp Ophthalmol* 2023;10(4):555-560.