**CASE REPORT**

**Improved Visual Acuity and Retinal Integrity with Resveratrol Based Supplementation in Patients with Macular Degeneration**

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**Abstract**

These case reports evaluate oral supplementation with a resveratrol based red wine supplement, containing vitamin D3 and labile iron binding inositol hexaphosphate. We appraised function Visual Acuity (VA) and Structure Domain Optical Coherence Tomography (SDOCT) in 3 geriatric patients with atrophic AMD, without clinical alternatives. One female and two males (ages 96, 84, and 85 respectively) were treated under compassionate care guidelines and prescribed Longevinex® (a resveratrol based oral supplement), on a case-by-case-basis. Snellen VA was measured at every visit and photos/SDOCT were also taken to document and track retinal changes. Persistent enhancement is noted on follow up for all patients, continuing for several years for the 96-year-old, thus far. Low dose, low molecular weight nutraceutical molecules can render benefits in the aged with atrophic AMD. Improvement of subjective visual function and retinal integrity is consistent with our previous published reports, as well as reports across several medical disciplines, on the effectiveness of supplementation with a resveratrol-based nutraceutical. This account supports restoration of photoreceptor/RPE function, when other measures have been exhausted by a retinal specialist.

**Keywords**

Age related Macular Degeneration (AMD), Retinal Pigment Epithelium (RPE), Resveratrol (RV), Epigenetics

**Introduction**

Age Related Macular Degeneration (AMD) is the leading cause of vision loss in aging western societies, accounting for half of patients attending blind rehabilitation facilities. AMD eventually results in both loss of reading and driving vision, with resultant loss of geriatric independence [1]. It is most commonly characterized by degeneration of the retina with accumulation of waste called retinal drusen, thickening of Bruch’s membrane as well as retinal and Choriocapillaris circulatory atrophy [2].

Resveratrol (RV), the medicinal component found in red wine, was discovered in the 1940s. It was later found to have broad-spectrum anti-cancer, anti-cardiovascular disease, and anti-inflammatory properties [3]. This weak antioxidant is concentrated in red wine via fermentation, from grapes grown under stressful conditions of northern latitude, high altitude, and cold temperature. RV works through a process known as hormesis - the upregulation of endogenous antioxidant protective systems [4].

RV is a small molecular weight, polyphenol phytoalexin, able to transit all cells, similar to allicin found in garlic. RV sparked interest in the world of medicine because of the French Paradox, where consumption of red wine showed positive health benefits of decreasing cardiac mortality in a smoking population consuming fatty foods, as shown by the Melbourne Collaborative Research Study [5,6]. With its comprehensive suite of biological actions, we have also observed healing effects in the human retina, in short and long-time periods [7]. Quite recently, we demonstrated stabilization/improvement of the dark adaptation curve, in AMD patients,
Longevinex® is an RV matrix of small molecular weight epigenetically active molecules having the ability to cross the blood aqueous and blood-retina barrier. The combination of a low dose Trans RV (100 mg), red wine polyphenols, 25 mg quercetin, fisetin as well as 1200 IU vitamin D3, and 17 mg rice bran IP6, has been shown to be synergistic. Additionally, this brand of RV was chosen due to its published safety profile. Patients returned for periodic eye examinations where Snellen visual acuity retinal macula spectral domain optical coherence tomography (Cirrus Model 4000, Carl Zeiss Meditec, (Dublin, CA USA) and OptoVue RTVue (Fremont, CA) were used to document retinal health change. Color fundus photographs were taken for Case 1 and Case 2 using an OPTOS Wide field camera (Sydney, Australia).

Case 1

A 96-year-old Caucasian female veteran presented to our clinic with her son with complaints of progressively decreasing vision at both distance and near OS > OD for many years secondary to both exudative and non-exudative AMD. She was diagnosed with atrophic AMD and moderately severe nuclear-cortical cataract and 20/150 Snellen visual acuity in her right eye (OD). She was diagnosed with exudative AMD status post 10+ intravitreal anti vascular endothelial growth factor (anti-VEGF) injections. She also has a prosthetic intraocular lens in her left eye and light perception only (OS).

Systemic history includes sciatica, osteoporosis, osteoarthritis, Chronic Obstructive Lung Disease (COPD), depression, and history of pulmonary embolism. The patient is currently taking Warfarin 2 mg once daily by mouth and Calcium carbonate with 1000 IU vitamin D3 once daily by mouth. The patient denies smoking, alco-
hol consumption, and illicit drug usage. She is ambulator-
y and responsive. The patient was monitored every six
months for thirty months (Baseline and 5 visits). Her son
accompanied her at each visit and confirmed changes in
his mother’s ‘activities of daily living’.

Case 2

An 85-year-old Caucasian male veteran presents to
our clinic for driver’s license renewal. He complains of
seeing “holes” in his vision, at distance while driving,
and at near while reading. The patient was diagnosed
with primary open angle glaucoma, non-exudative AMD
OS > OD and is pseudophakic (implant, post cataract
surgery) both eyes. Entrance best corrected visual ac-
uity was 20/50-2 OD, with the patient consistently missed
the 2\textsuperscript{nd} and 3\textsuperscript{rd} letter of the 5 letter Snellen VA line, and
20/50-2 OS, with the patient consistently missing the 3\textsuperscript{rd}
and 4\textsuperscript{th} letter. The resulting bilateral defect manifested
as a disabling binocular central foveal visual field defect.
A retinal photo was taken to document the appearance
of the retina at time of evaluation (Figure 1a).

Systemic history includes hypertension, hyperliped-
emia, thrombocytopenia, gout, chronic kidney disease
and hypothyroidism. Current medications: Latanoprost
ophthalmic drops daily, allopurinol 500 mg daily, Lisin-
opril 40 mg daily, pravastatin 80 mg one-half tablet by
mouth daily with evening meal and terazosin 5 mg cap-
sules once nightly by mouth.

Case 3

An 84-year-old Caucasian male veteran presented
initially with complaints of blurry vision distance and
near OU. He had difficulties driving as well as reading
standard newspaper text. He has a nuclear sclerotic
cataract OD and prosthetic intraocular lens OS without
secondary posterior subcapsular post-surgical opacifi-
cation. The patient also has a mild epiretinal membrane
(thickening of the internal limiting membrane of the
retina) and is a bilateral glaucoma suspect based upon
suspicous optic nerve cupping and increased intraocu-
lar pressure. Systemic history includes hypothyroidism.
He is currently using latanoprost 0.005% ophthalmic
drops daily, levothyroxine 0.088 mg two tablets daily by
mouth, vitamin B complex capsules every morning.

Results

Case 1

Gradual continued improvement of vision was not-
ed at each visit both objectively and subjectively in the
better seeing eye for all 3 cases. In Case 1, initial VA was
20/150 OD, Light Perception OS eventually improving
to 20/70 OD (3 lines improved) and 20/150 OS (now
form vision), 2.5 years after RV-based nutraceutical
treatment was prescribed (Figure 1b). However, there
were no changes in the Optomap® color photographs
(Figure 1c). S DOCT comparing initial visit with final visit
OD shows reformation to a normal foveal contour and a
decrease in signal scatter, suggesting improved RPE in-
tegrity (Figure 1d).

Case 2

OCT showed decreased signal scatter in the foveal
area (Figure 2a), indicative of RPE thickening. The initial
VA was 20/50 - 2 OD, OS. Final VA was 20/25 + 2 OD,
20/25 + 1 OS (3 lines better) (Figure 2b). The patient was
able to maintain his driver’s license.

Figure 1B: 96-year-old Caucasian female patient demonstrates drastic Snellen visual acuity improvement, right eye, from
20/150 to 20/70 from Jan-2014 to July-2016 using Longevinex Advantage® for thirty months. Supplementation was initiated after the first visit, but reduced to 50% dose by using Longevinex Advantage formulation containing only 50 mg RV (1 capsule Longevinex Advantage®), as patient reported being “over energized”.

Figure 1C: 96-year-old Caucasian female patient demonstrates drastic optical coherence tomography (OCT) improvement, right eye, from 20/150 to 20/70 from Jan-2014 to July-2016 using Longevinex Advantage® for thirty months.

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Figure 1D: 96-year-old Caucasian female patient demonstrates drastic spectral domain optical coherence tomography (OCT) improvement, right eye, from 20/150 to 20/70 from Jan-2014 to July-2016 using Longevinex Advantage® for thirty months.
Figure 1C: 96-year-old female Optomap widefield retinal photos (OD retina (left images) and OS eye (right images) of the posterior pole comparing the patient’s initial visit with the final visit 30 months later. No gross retinal changes are noted in the fundus photography even though the patient had continuous improved visual acuity and exhibited retinal remodeling on spectral domain optical coherence retinal imaging (SDOCT) (see Figure 1d).

Figure 1D: 96-year-old female patient shows significant improvement in OD visual acuity, along with rebuilding of the fovea to a normal concave contour during the course of 2 1/2 years while she was using Longevinex® Advantage at 50% daily dose. More SDOCT retinal uniformity is noted in the foveal region corresponding to the markedly improved visual acuity of the patient.
status [7]. Lastly, IP6 is a labile iron and copper binding
divalent mineral chelator derived from rice bran, and
also aids in DNA repair and decalcification of the Bruch’s
membrane [7]. In the cases presented thickening of the
RPE was observed, even though the tissue thins with
age. AMD furthermore exacerbates RPE thinning [9,10].
Taken together, these cases are suggestive of improve-
mant in retinal thickness and organization by resvera-
trol supplementation in helpless cases in patients when
treatment options have been exhausted.

**Conclusion**

Nutraceutical intervention administered in low dos-
es has the potential to render benefits to patients with
advanced atrophic AMD. Improvement of visual acuity
and retinal integrity is consistent with previous reports
on the effectiveness of RV-based supplementation even
in older AMD patients with advanced stages of the dis-
ease, for which few option remain. The oral supplement
typically affects both eyes, with the less advanced ret-
inai receiving the best enhancement in structure and

**Case 3**

Resolution of RPE disruption, more uniformity and
thickening of the RPE in the foveal area was noted on
OCT (and confirmed by our retinal specialist) (Figure
3a). Entrance VA was 20/60-1 OD, 20/50-2 OS. 1 lined of
VA improvement (20/40) was noted in the better see-
ing eye at 1 month (Figure 3b). The patient now has the
ability to read the newspaper clearly and has sufficient
a sufficient VA to pass his driver’s license test without a
ight restriction.

**Discussion**

The red wine polyphenols in the chosen combination
are phytonutrients of the polyphenolic class and asso-
ciated with disease prevention, due to their ability to
epigentically orchestrate helpful and harmful genes.
Vitamin D3 is a potent anti-inflammatory, decalcify-
ing agent, as well as a prohormone, for which several
studies have shown its synergism with RV as well as the
known association of Vitamin D deficiency with AMD

![Figure 2A: OCT 86-year-old SD OCT shows decreased signal scatter OD (the better seeing eye) in the foveal area, after Longevinex® supplementation which is indicative of RPE thickening. No changes were evident in his OS eye.](image)

![Figure 2B: Visual Acuity - Baseline versus follow up visual acuity in a 86-year-old male with atrophic AMD. Prominent improvement resulted after supplementation with a resveratrol-based nutraceutical supplement.](image)

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<td>OD</td>
<td>20/50-2 (missing 2nd and 3rd letter consistently)</td>
<td>20/25+2 (resolved bilateral scotomas)</td>
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<tr>
<td>OS</td>
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function. These cases suggest that even octogenarians with severe non-exudative AMD can have vision recovery after all medical resources have been exhausted by a retinal specialist. Yet today, we are left only with the limited set of nutrients from research conducted by the National Eye Institute, National Institute of Health USA [11]. Longevinex® has formally petitioned and been denied Fast Track evaluation by the US FDA [12]. Further research is warranted in order to prove the potential benefit of this nutraceutical supplement on advanced stages of macular degeneration in hopeless cases.

Acknowledgements

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Ethical Statement

Longevinex® was prescribed under compassionate care guidelines and informed consent was obtained in writing from the patient for the use of their health information.

References


