

A close-up, monochromatic blue-tinted photograph of a person's face, focusing on the eye. The eye is light-colored and looking slightly to the right. The skin texture is visible.

EYEMUSE™

—

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Easier on the eyes/Relief in sight: Postbiotics improve eye health from the inside out

Viewed in hindsight's charitable gaze, the past few years might stand as a masterclass in how to make do amidst chaos. And one of the more surprising lessons the course offered suggests that living life in front of a screen—if not on one—actually has its merits.

How so? Consider the number of personal and professional relationships that might've atrophied or never even emerged had videoconferencing not bridged the physical gaps that pandemic restrictions opened.

Or consider how many educations would've ground to a halt absent the pivot to virtual learning—an imperfect substitute for school, to be sure, but a fallback that preserved some semblance of structure for teachers, families, and students.

Nielsen research found that 82% of global consumers escaped the drudgery of peak lockdown by playing video games or watching video-game content



Or consider that online gaming not only got an obligatory bounce from COVID-19 but gave a boost to its housebound fans, too. To wit: Nielsen research found that 82% of global consumers escaped the drudgery of peak lockdown by playing video games or watching video-game content¹—a diversion that proves what a refuge the wired world can be.

Up-and-coming concern

But if ever the phrase “too much of a good thing” applied to a phenomenon, it applies now to the astronomical amount of time we spend staring at glowing screens.

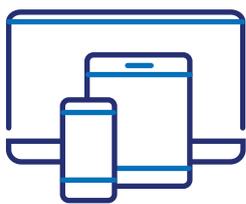
Even with lockdowns over, Nielsen reports that Americans still while away upwards of 13 hours per day engaging with TVs, phones, tablets, computers, and other allied devices², and one clear consequence of all that screen time has been a gradual deterioration of eye health.

Screen-related eye symptoms—often experienced as fatigue, strain, sensitivity, blurriness, or even muscle aches and weariness—fuel more than 10 million visits to the eye doctor annually³,

making them so common as to warrant their own “diagnosis”: computer vision syndrome, or CVS.

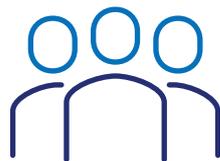
This collection of complaints isn’t just sending consumers to ophthalmologists’ offices, either; it’s sending them to supplement shelves, where they’re purchasing eye-health products to the tune of \$889 million in current domestic sales⁴, according to Nutrition Business Journal.

All of which makes good sense to Maria Stanieich, marketing manager, Kyowa Hakko USA. “The focus on eye fatigue is an up-and-coming concern,” she says, “and as long as screens mediate modern life, it’ll continue to be.”



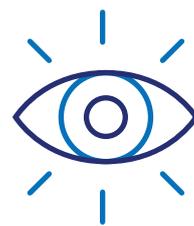
13+ HOURS

of screen time per day



10M DOCTOR

visits for eye fatigue



14.6% INCREASE

in eye health supplement sales

Non-stop video conferencing, endless smartphone scrolling, and the rise in gaming are taking a toll on our eyes. Consumers are turning to supplements to address their concerns.

Got tired eyes?

More and more adults are likely to face eye strain and fatigue with the continued increase of digital devices. It is estimated that computer-related eye fatigue is responsible for upwards of 10M visits to the eye doctor. From gamers to working professionals, everyone can benefit from EYEMUSE™, a clinically-researched postbiotic to support eye health.



For Gamers

Gamers are spending 14 hrs a week playing video games, up from 12 hrs a week in 2018. With increasing numbers of individuals playing games, EYEMUSE™ is the perfect ingredient to help gamers continue their relentless pursuit of leveling up. EYEMUSE™ may help gamers:

- Support eye health
- Promote healthy eye function
- In vitro studies suggest EYEMUSE™ may help filter blue light



For Multitaskers

It seems like nowadays all of us are wearing multiple hats. From teaching to working, we are running from one video conference to another. We're becoming more reliant on technology to help us stay on task. With 50% of the day in front of digital devices, EYEMUSE™ may help multitaskers:

- Reduce tired eyes
- Reduce eye fatigue caused by digital stress
- Reduce stiffness of the waist/shoulders associated with eye fatigue



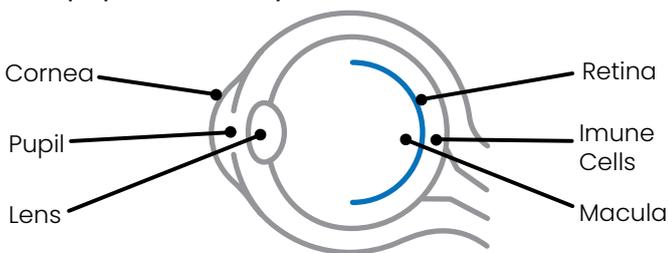
For Young Professionals

To stay ahead in the ever-increasing competitive world, it requires constant improvement to your craft. From virtual learning to digital conferences, today's young professionals are always on. EYEMUSE™ may help young professionals:

- Reduce eye fatigue
- Help filter blue light (suggested by in vitro studies)
- Suppress cellular markers associated with eye fatigue

In a bad light

The reason eye fatigue is such a concern in modern life lies in the high-energy, low-wavelength blue light digital screens emit. That light passes through the eye's cornea and lens to reach the retina, a metabolically active⁵ tissue at the eye's rear that contains millions of specialized cells, including ganglion and photoreceptor cells, which convert light into visual signals that travel to the brain to become sight, as well as retinal immune cells that help protect eyes.



Modern eyes need that protection, as the continual streams of

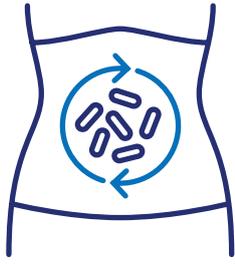
blue light washing over them are precisely what set off such common ocular complaints as the aforementioned CVS in the short term and an increased risk for cataracts, dry eyes, age-related macular degeneration, even inhibited melatonin secretion and increased adrenocortical hormone production—both of which diminish sleep quality—over the long term.⁶

“A healthy immune response helps ameliorate these problems,” Stanieich notes. So when researchers from the Kirin Group—parent company of Kyowa Hakko Bio—discovered that an ingredient derived from inactivated probiotic bacteria may actually improve ocular immunity, she declares, “They knew they were onto something big. And that something big was EYEMUSE.”

Gut-eye-immune connection

EYEMUSE is a postbiotic, which is an emerging class of products comprising—per the official definition set out by the International Scientific Association for Probiotics and Prebiotics (ISAPP)—“a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.”

More specifically, EYEMUSE is a heat-treated preparation of *Lacticaseibacillus paracasei* KW3110 (*L. paracasei* KW3110), a proprietary strain of lactic-acid bacteria with recognized benefits around gut health. And while heat treatment renders the *L. paracasei* KW3110 in EYEMUSE inactive and nonviable, it doesn't render EYEMUSE itself without benefit.



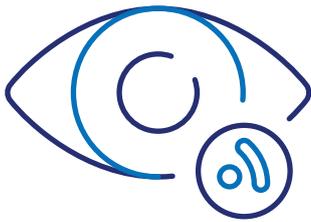
What is *Lacticaseibacillus paracasei*?

L. paracasei is a commonly used lactic acid bacteria for the fermentation of dairy products and has benefits for gut health.



What are postbiotics?

Postbiotics are defined as the preparation of inanimate microorganisms and/or their components that confers a health benefit on the host. EYEMUSE, a heat-treated probiotic, is classified as a postbiotic. Postbiotics, in general, have a superior stability profile compared to probiotics.



What is EYEMUSE™?

EYEMUSE™ is heat-treated *Lacticaseibacillus paracasei* KW3110, the only strain in the world that has been clinically researched to support eye health and reduce eye fatigue.

In fact, the close relationship between postbiotics and probiotics raised intriguing questions for Kirin Group researchers. Namely, the researchers asked themselves this: If we know that 1) probiotics contribute to a robust immune response as constituents of a healthy microbiome, and that 2)

the gut, which houses most of the microbiome, also houses roughly 70% of the immune system, might 3) a postbiotic like EYEMUSE leverage that gut-immune connection to confer immune benefits of its own, and to overworked eyes, in particular?

Probiotic strains have long shown benefits for gut & immune health. Recent research by the Kirin group has shown that a proprietary postbiotic, heat-treated *Lacticaseibacillus paracasei* KW3110, also known as EYEMUSE™, has benefits for eye health by working on immune cells within the eye.

EYEMUSE to the test

The researchers set out to answer these questions in studies involving cell cultures, animal models, and human subjects, and the results have proven impressive.

For example, in one study published in 2018, Kirin researchers found that of the 62 human subjects with eye fatigue who participated in the study's eight-week randomized, double-blind, placebo-controlled clinical trial arm, those who received EYEMUSE experienced greater reductions in shoulder and waist stiffness—both symptoms of eye fatigue—than did those receiving the placebo.⁷

Later that same year, the researchers published another study in the same journal investigating EYEMUSE's mechanism of action, reporting that not only did the postbiotic induce production of the anti-inflammatory cytokine interleukin-10 (IL-10) by activating macrophage cells in vitro, but it also significantly increased IL-10 gene expression in intestinal immune tissues in vivo.⁸

"This matters," explains Danielle Citrolo, PharmD, vice president of scientific and regulatory affairs, Kyowa Hakko USA, "because excessive light exposure degenerates the eye's photoreceptor cells via an inflammatory response—leading us to surmise that anti-inflammatory

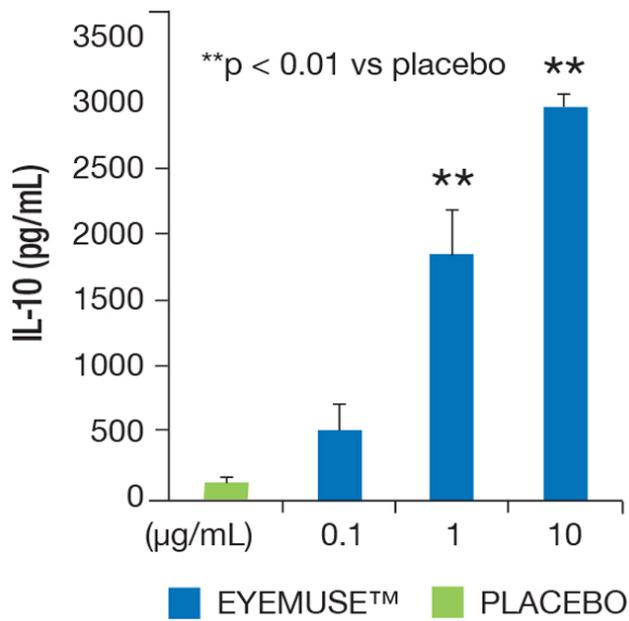
agents like EYEMUSE might help stanch the course of photoreceptor degeneration. And, indeed, EYEMUSE tamps down inflammation by triggering regulatory cytokine induction, supporting a balanced immune response and promoting healthy eye function."

Even more recently, Kirin researchers conducted an eight-week, randomized, double-blind, placebo-controlled parallel-group study involving 88 healthy subjects, using critical flicker frequency (CFF)—the threshold at which the eyes cease distinguishing between a flickering light and a steady one—as a measure of eye fatigue.

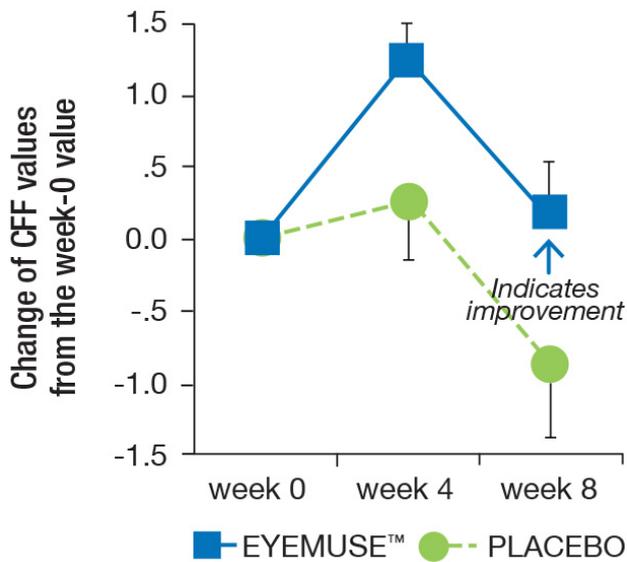
Those who received EYEMUSE experienced greater reductions in shoulder and waist stiffness—both symptoms of eye fatigue—than did those receiving the placebo

The results showed that EYEMUSE significantly reduced eye fatigue in subjects in the study's treatment arm, Citrolo says, adding that "the team also showed that EYEMUSE applied to mouse macrophages in vitro produced significantly higher levels of IL-10 as compared to other lactic-acid strains."⁹

In vitro IL-10 induction with EYEMUSE™ 1

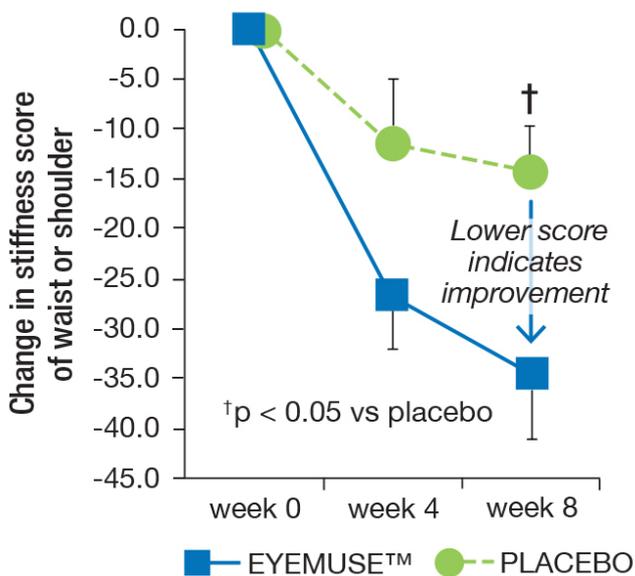


EYEMUSE™ stimulates immune cells that induce regulatory cytokine to promote healthy eye function.



EYEMUSE™ significantly reduced eye fatigue.

Reduction of shoulder/waist stiffness score



EYEMUSE™ has been shown to reduce ocular discomfort, stiffness in the waist and/or shoulder, and ocular fatigue sensation.

Broad audience...

“These studies are just the start of what we’re learning about EYEMUSE’s potential,” Stanieich states. “But even at this early stage, it’s hard to deny that a lot of tired eyes could benefit from its actions.”

Take those aforementioned gamers. “Gamers today are bona fide athletes,” she argues, “and eye strain can sideline them just as much as a hamstring tear can sideline a sprinter. So, like any other athlete, they need safe anti-inflammatory ingredients that keep their bodies in working order and their competitive edge sharp.”

Gamers today are bona fide athletes and eye strain can sideline them just as much as a hamstring tear can sideline a sprinter.

Equally competitive are contemporary professionals. No matter their field or position, “They’re under constant pressure always to be ‘on,’” Stanieich observes.



“These are the go-getters taking online courses to improve their marketability, or attending digital conferences in time zones across the globe. And that means they’re staring at screens day and night, and their eyes pay the price. We believe EYEMUSE can help.”

Then there’s the rest of us. “You don’t need to be a high-powered professional or serious gamer to be a multitasker,” Stanieich points out. “So, with more of us leaning on technology to get ‘stuff’ done, we’re spending at least half the day—literally, more than 50% of our time—in front of a digital device. We feel this in our eyes, our muscles, our focus—and we need safe, effective, natural products like EYEMUSE to provide relief.”



...Broad applications

Those qualities—safety, efficacy, a clean label free of additives, colors, flavors, or preservatives—don't just endear EYEMUSE to discerning consumers; they're valuable to brands looking for formulation-friendly ingredients that address today's wellness concerns.



Even better, as a postbiotic, EYEMUSE offers on-the-ground functional and operational benefits in production and in finished applications. As Citrolo notes, "Probiotics are great, but they've got their limitations." As living organisms, they have to remain alive in the finished product to deliver their purported benefits to consumers. That usually imposes storage requirements like refrigeration, can limit formulation options, or can mean a shorter effective shelf life.

"Because EYEMUSE is a postbiotic," Citrolo explains, "the probiotic strain it's made from is already heat-treated and inactivated.

So EYEMUSE is stable and heat-resistant from start to finish, with no need to ensure survivability, and no need for refrigeration.

Formulating it into supplements like capsules, powders, and tablets is so much easier as a result."

Stanieich also stresses that "inactivated" doesn't equal "ineffective." In fact, brands can trumpet the ingredient's scientifically researched benefits via label claims addressing support for eye health, promotion of healthy eye function, reductions in daily eye fatigue, and attenuation of eye issues caused by electronics.

EYEMUSE offers on-the-ground functional and operational benefits in production and in finished applications

"Claims like this resonate with consumers," Stanieich maintains, "and for the obvious reason: Like it or not, we're stuck to our screens for the foreseeable future. As long as that's the case, there's going to be a need for ingredients like EYEMUSE that help us see our way toward healthier sight."

JUST THE FACTS

AN EYEMUSE Q&A WITH KYOWA HAKKO USA MARKETING MANAGER MARIA STANIEICH

What is a postbiotic?

Stanieich: A postbiotic is defined as “a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.” That’s the definition produced by the International Scientific Association for Probiotics and Prebiotics (ISAPP).

By this definition, a postbiotic must include some nonliving microbial biomass, whether that be whole microbial cells, or cellular components. In comparison, a key characteristic of a probiotic is that it must remain alive at the time of consumption to deliver its benefits.

This being said, Kyowa Hakko’s EYEMUSE—a heat-treated, and thus nonliving, strain of *Lacticaseibacillus paracasei* KW3110 bacteria—is a novel ingredient and the first postbiotic developed and marketed for eye health.

We’ve long known that probiotic bacterial strains demonstrate gut- and immune-health benefits, but recent research conducted by scientists at the Kirin Group shows that this particular proprietary postbiotic improves eye health via its action on immune cells within the eye.

What more can you tell us about the scientific evidence behind EYEMUSE’s mechanism of action in conferring eye-health benefits?

Stanieich: Recently published clinical trials show that EYEMUSE stimulates immune cells that produce regulatory cytokines—such as interleukin-10—that, in turn, support eye health.¹⁰ So by aiding the induction of regulatory cytokines and supporting a balanced immune response, EYEMUSE may help reduce eye fatigue and other ocular discomforts related to digital stress.¹¹

And indeed, a randomized, double-blind, placebo-controlled trial found that EYEMUSE significantly reduced eye fatigue as measured by critical flicker frequency in 88 healthy subjects over the course of eight weeks.

Researchers conducted another randomized, double-blind, placebo-controlled study on 62 healthy participants aged 35 to 45 who were experiencing eye fatigue. Over the study's eight-week duration, EYEMUSE appeared to reduce eye-fatigue symptoms like ocular discomfort, stiffness in the waist and shoulder, and sensations of ocular fatigue.¹²

What more should readers know about EYEMUSE, as well as its features and benefits?

Stanieich: To start, Kyowa Hakko makes EYEMUSE using a proprietary cultivation, separation, pasteurization and drying process, yielding an ingredient that's pure, allergen-free, and entirely of plant origin—in other words, vegetarian.

And as mentioned above, Kirin research shows that EYEMUSE, thanks to its immune-stimulating properties, has a positive effect on eye health.

With that sort of pedigree, brands should be eager to incorporate this unique health ingredient into dietary supplements—capsules, powders, tablets—whether for gamers, young professionals, or multitaskers like the rest of us. Anyone looking for eye-health support can benefit.

What claims can brands make regarding EYEMUSE and its benefits?

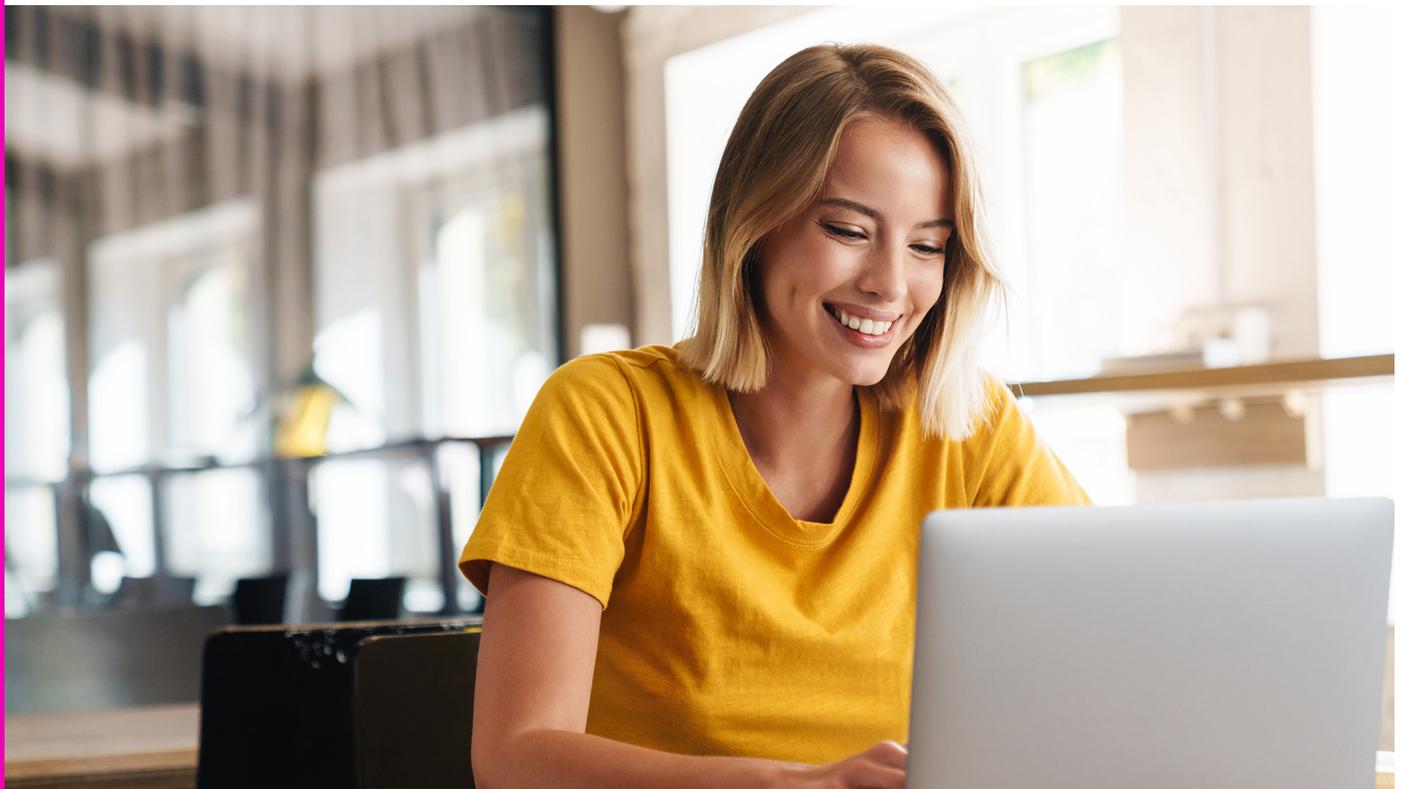
Stanieich: Based on a recommended daily dose of 50 mg, brands can claim that EYEMUSE supports eye health, promotes healthy eye function, may help reduce daily eye fatigue, may reduce eye fatigue caused by digital stress, may reduce eye fatigue caused by the use of electronics, may alleviate tired eyes, and may reduce stiffness of the waist or shoulders in individuals with severe eye fatigue.

And, as always, it's important to note that these statements have not been evaluated by the Food and Drug Administration, and that EYEMUSE is not intended to diagnose, treat, cure, or prevent any disease.

Given all of the above, why is EYEMUSE the right ingredient for right now?

Stanieich: Quite simply, EYEMUSE promotes healthy eye function and may improve eye fatigue and reduce waist and shoulder stiffness in those with severe eye fatigue.

EYEMUSE comes at a time when it's estimated that computer-related eye fatigue is responsible for upwards of 10 million visits to the eye doctor. So, with the eye-health market soaring, EYEMUSE is the clinically studied, branded ingredient that's ready to meet today's consumer-health needs today and going forward.




EYEMUSE™

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