

Ophthalmic Wearable Devices for Color Blindness Management

Ahmed E. Salih,* Mohamed Elsherif, Murad Ali, Nader Vahdati, Ali K. Yetisen, and Haider Butt*

Color vision deficiency (CVD) or color blindness is an ocular disorder that hinders the patients from distinguishing shades of certain colors. Color blind patients are often not considered for critical occupations (e.g., military, police) and cannot differentiate colors in public places or media (i.e., watching TV). The most common form of color blindness is red-green, which is a result of either a missing or defective red or green photoreceptor cone. Since no cure for this disorder exists, sufferers opt for methods to enhance their color perception. The products and methods that have been developed to aid CVD patients are discussed. These technologies include contemporary work on gene therapy, tinted glasses, lenses, optoelectronic glasses, and advanced features developed on smartphones and computers. Among these wearables, tinted glasses, developed by companies such as Enchroma, are the most widely used by CVD patients.

1. Introduction

Color vision deficiency (CVD) is an ocular disorder that prevents perceiving and distinguishing certain colors. Color blindness usually refers to CVD, since total color blindness, in which only greyscale vision is possible, is very rare. This ocular disease can either be acquired or congenital.^[1] Congenital CVD is present from birth, affects both eyes, and decreases perception of the entire view. On the contrary, acquired CVD affects either a single eye or both eyes and reduces perception in limited regions of the individual's

view.^[1a] As inherited CVD is more common than acquired,^[2] CVD types discussed in this paper along with the management methods are for congenital CVD. Most common congenital CVD is inherited in the X-Chromosome and affects one in 12 males (8%) and one in 200 females (0.5%).^[3] Moreover, in some populations, prevalence of CVD in males has reached to near 15%.^[4]


CVD patients find difficulties in their day-to-day chores which involve distinguishing colors of similar shades. In a study done to assess the complications that CVD sufferers endure, it was concluded that patients cannot perceive colors when they do chores such as cooking and watching TV.^[5] Some patients also said that they prefer driving

during daytime as it is difficult to distinguish traffic lights and road sign colors at night.^[5] CVD patients are also restricted from careers that require normal color vision like engineering, aviation, military services, marine services, firefighting, and pharmacy.^[6] Doctors and medical students who suffer from CVD, find difficulties in identifying body color changes due to a wide range of conditions like cyanosis, jaundice, and rashes. They also experience problems distinguishing blood and urine test strips.^[7] CVD sufferers in the medical field made more mistakes than normal color-sighted individuals.^[7b,8] Moreover, high school studies show that there is no correlation between intelligence and color blindness, but there is a negative correlation between success and color blindness.^[9] This demonstrates that students are struggling to perceive and comprehend the information presented to them, due to their conditions.

Moreover, CVD patients cannot enjoy various forms of entertainment. **Figure 1** demonstrates how a normal color vision individual views football games and other day-to-day materials in contrast to how CVD patients view them. CVD football players reported their slower reaction time in games where teams' shirts were red and green.^[10] Organizations like Union of European Football Association (UEFA) and English Football Association (FA) have worked to produce color blind guidance booklets to help spread awareness.^[11] American football viewers were also furious with "Color Rush Campaign" designed to celebrate the league's first game in colors. CVD viewers were not able to distinguish between the two teams, wearing red and green kits.^[12]

A. E. Salih, M. Elsherif, M. Ali, Dr. N. Vahdati, Dr. H. Butt
Department of Mechanical Engineering
Khalifa University of Science and Technology
Abu Dhabi 127788, UAE
E-mail: ahmed.salih@ku.ac.ae; haider.butt@ku.ac.ae

Dr. A. K. Yetisen
Department of Chemical Engineering
Imperial College London
London SW7 2AZ, UK

 The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/admt.201901134>.

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2. Color Vision Deficiency: Types and Diagnosis

Human color vision begins with light perception by photoreceptor cells called cones.^[3b,13] There are three types of cone photoreceptors cells: short (S) cones, medium (M) cones, and long (L) cones, which are commonly referred to as blue, green, and red cells, respectively.^[3a,b,14] The S, M, and L cones have peak spectral sensitivity at 440, 540, and 560 nm, respectively. In normal color vision, all three cones are present and function according to their activation peaks.^[3b,14b] The combined signal from the three photoreceptor cones is analyzed by the brain, and the color is observed.

Normal human color vision is trichromatic.^[14c,15] Congenital CVD is caused by either a missing or faulty photoreceptor cones. The three different levels of CVDs are anomalous trichromacy, dichromacy, and monochromacy.^[3a,b,5,14] In anomalous trichromacy, one of the photoreceptor cones is defective. Anomalous trichromacy is divided to protanomaly (defective red cone), deuteranomaly (defective green cone), and tritanomaly (defective blue cone). In dichromacy, one of the photoreceptors is completely missing. Dichromacy is also divided into protanopia (missing red cone), deuteranopia (missing green cone), and tritanopia (missing blue cone).^[3a,14c,15] Monochromacy, rarest form of CVD, involves the loss of at least two photoreceptor cones. Monochromats are either totally color blind (achromatopsia) or have only blue cone.^[14c] **Figure 2a** shows how individuals with different CVDs perceive a picture. **Figure 2b** shows the sensitivity spectra of the normal human color vision and most common CVDs. **Table 1** shows the prevalence of the different types of CVDs.^[3a,14c,16] The most prevalent types of CVD are protans (protanopia and protanomaly) and deutans (deuteranopia and deuteranomaly) (Table 1). Protans and deutans are usually referred to as “red-green color blindness,” while tritans (tritanopia and tritanomaly) are classified as “blue-yellow color blindness.”^[3a]

Figure 2b shows that the sensitivity of the red cones is shifted towards shorter wavelengths in protanomaly, while the sensitivity of the green cones is shifted towards longer wavelengths in deuteranomaly. Therefore, when light at the wavelength of overlap is perceived by the eye, it activates both cones simultaneously.

People suffering from CVD are diagnosed in several ways. One of these methods is the use of pseudoisochromatic testing plates, which appear to be of a single color to individuals suffering from CVD.^[6b,17] The most common and widely available test is the Ishihara test. There are different versions from the Ishihara test, such as 10, 14, and 24 plate tests, but the 38-plate version is the one used in most studies.^[18] Ishihara is designed to identify only red-green color blindness. It cannot classify the patient as a protan or deutan, neither can it detect if the individual is a tritan.^[19] Other tests were developed to aid with classifying the latter, such as Hardy–Rand–Rittler (HRR), Farnsworth–Munsell (FM) 100 Hue, and Farnsworth D-15.^[17,19,20] HRR, like Ishihara, uses pseudoachromatic plates; however, it can diagnose people with all types of CVDs. In Farnsworth D-15 and FM 100 Hue, colored plates are arranged based on their hue and intensity. Patients suffering from CVD have difficulties in identifying



Ahmed E. Salih received his B.Sc. in mechanical engineering (High Honors) from the American University in Sharjah in 2018. He is currently pursuing his M.Sc. in mechanical engineering at Khalifa University. Ahmed's main area of interest is the development of hydrogel biosensors and smart contact lenses. He is currently working on developing nanocomposite contact lenses for color-blindness management.



Ali Yetisen is a senior lecturer in the Department of Chemical Engineering at Imperial College London. He was previously a Tosteson postdoctoral fellow at Harvard University. He holds a Ph.D. degree in chemical engineering and biotechnology from the University of Cambridge.



Haider Butt completed his M.Phil. in electrical engineering at the University of Cambridge in 2008, followed by a Ph.D. in nanophotonics in 2012. In 2013, he was appointed as a lecturer of Nanotechnology at the University of Birmingham, UK and was promoted to senior lecturer in 2016. He joined Khalifa University as an Associate Professor in mechanical engineering in 2019. He has earned international recognition for his research and leadership in the areas of nanophotonic sensors and healthcare technologies. His most pioneering works include glucose-sensing contact lenses, contact lenses for color-blind patients, and carbon-nanotube holograms.

the correct order of the plates.^[19,20b] Another method involves the usage of anomaloscopes. Anomaloscopes utilize control knobs to match two images in their color and brightness. The readings obtained from the control knobs indicate the type and degree of CVD. Although they are the most difficult to use, anomaloscopes provide accurate classification of all CVD conditions.^[20b]



Figure 1. Day-to-day activities and materials as perceived by individuals having a) normal color vision and b) CVD.

3. Management Technologies for Color Vision Deficiency

3.1. Gene Therapy

A cure for color blindness has not yet been developed; however, several attempts have been done to enhance the color vision of CVD patients. Of these attempts, Mancuso et al. evaluated gene therapy on two adult squirrel monkeys who were color blind since birth.^[21] The monkeys were specifically missing long wavelength visual photopigment, L-cones. Recombinant adeno-associated virus (rAAV), which modifies DNA sequences in cells, contained the L-cones gene and was fed through subretinal injections. For analysis of the experiment, monkeys were trained to do the Cambridge Colour Test. Prior to the treatment, monkeys were not able to discriminate between blue-green (490 nm) and red-violet (499 nm). Effects of L-cone gene injection were not observed till after 20 weeks postinjection. After repeating the test, monkeys have gained a trichromatic vision which remained stable for more than two years.^[21] The

investigators concluded that trichromacy can be achieved only by adding a third photoreceptor cone, which does not need to be in the early stages of the individual.

Another study was done by Alexander et al., which showed that it is possible to cure mice suffering from achromatopsia (i.e., partial or total color vision loss) using cone-targeted gene therapy.^[22] AAV along with red-green human opsin was used to target sequences in mouse cones. After two months, 19 out of 21 tested eyes responded positively to the therapy. Neural signals showed that mice adapted to the new input, and light-adapted electroretinogram signals were in the normal range.^[22] It is concluded that ideas from this study can help treat several CVDs that affect humans.

Moreover, Neitz et al. studied the effect of gene therapy in mice and compared them with nonhuman-primates.^[23] Post treatment results showed that red-green color vision in mice was very weak compared to humans with normal color vision and primates.^[23] Monkeys and mice were also tested using the Cambridge Colour Test. This proves that there are large differences in how mice and monkeys respond to the photoreceptor

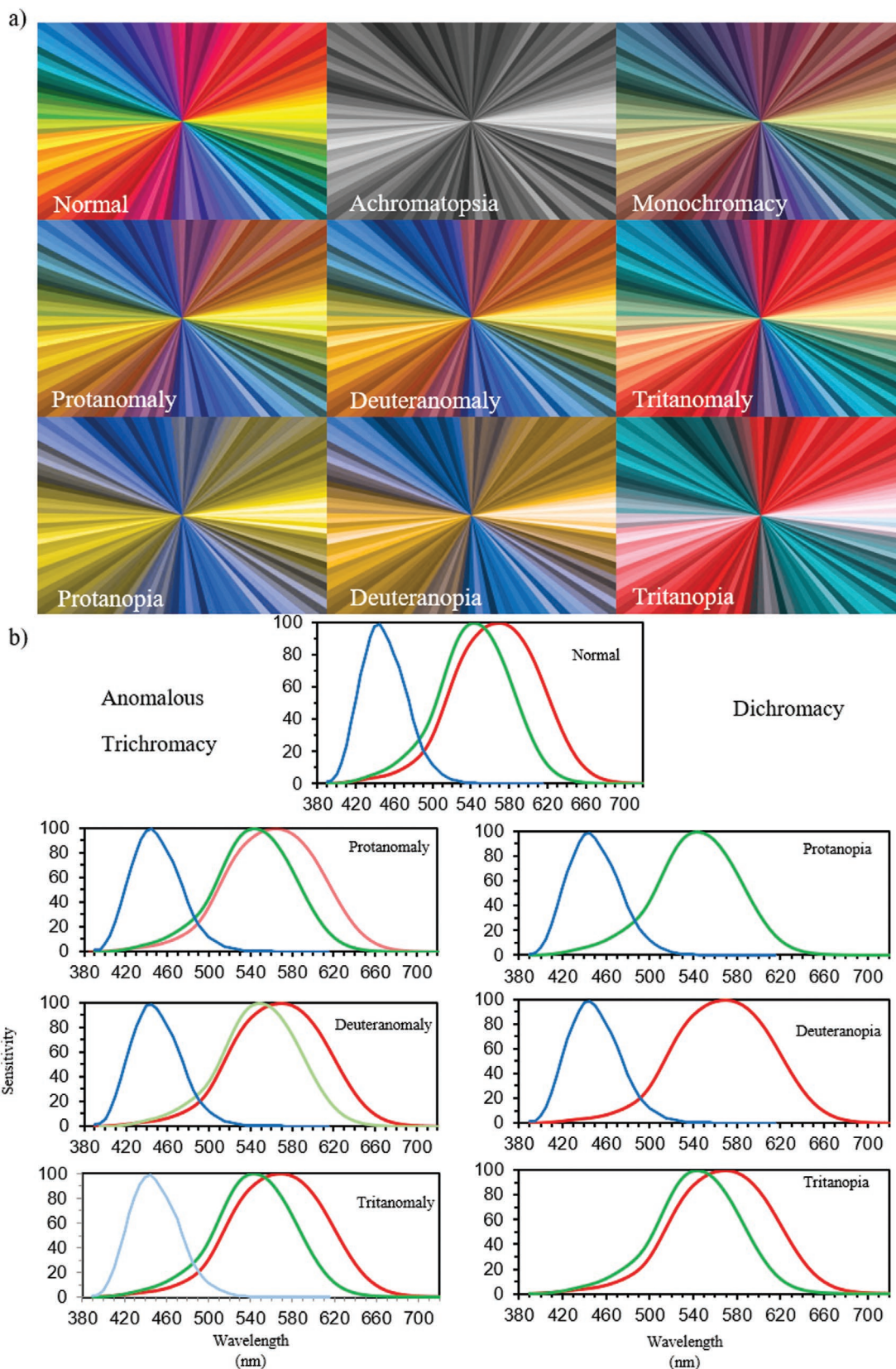


Figure 2. CVD color perception. a) Visual illustration of what is perceived by individuals having normal color sight and different types of CVDs. b) Sensitivity spectra of normal human vision and most common CVDs.

Table 1. Prevalence of CVD types.^[3a,14c,16]

CVD form	Type	Prevalence [%]
Monochromacy	Achromatopsia	0.003
	Blue cone monochromacy	0.001
Dichromacy	Protanopia	1.01
	Deuteranopia	1.27
	Tritanopia	0.2
Anomalous trichromacy	Protanomaly	1.08
	Deuteranomaly	4.63
	Tritanomaly	0.2

added. The work also discusses the limitations of using gene therapy to correct human color blindness.

Cornelissen et al. simulated how adding a photoreceptor cone to the retinas will affect the behavioral tests conducted by Mancuso and Neitz.^[24] Cornelissen argues that although the monkeys have become “three-photopigment individuals,” the gene therapy did not necessarily make them trichromatic beings. The claim is that these tests do not provide a conclusive evidence that gene therapy cures color blindness in primates and can treat human color blindness.^[24]

Gene therapy is yet to be applied on humans. The promising results are those of Mancuso et al. which showed that even two years after treatment, the monkeys did not show signs of serious complications. Moreover, as Cornelissen suggests, further simulations and tests need to be conducted to assess the effectiveness of the therapies conducted on mice and monkeys.

3.2. Glasses

Nowadays, one of the main wearable devices used to aid color blind people is a form of tinted glasses.^[25–35] The idea of using colored filters came from Seebeck in 1837.^[2,25] By using a red filter followed by a green filter, Seebeck noted that patients could differentiate between the relative brightness of different

shades of red and green. The red and green filters achieve the latter by blocking out wavelengths (540–580 nm), at which patients’ M-cone and L-cone overlap. After using the filters, both photoreceptor cells are activated individually depending on the wavelength of the incoming light. Moreover, the first pair of glasses, developed by Maxwell in 1857, was made of one lens dyed green and the other red. CVD subjects were able to discriminate between previously indistinguishable colors. From these results, Maxwell hypothesized that after prolonged exposure to the glasses, subjects were able to differentiate between more shades of red and green out of habit.^[25]

The current market leaders for color blind glasses are Enchroma (**Figure 3**). Enchroma glasses were first released in 2012.^[26] The glasses use multi notch filter to remove red and green overlapping regions of the optical spectrum.^[27] The tinting process of Enchroma utilizes the color filter concept developed by Seebeck. To absorb the desired wavelengths, dyes with narrow absorption bands are utilized; this is also done to avoid altering colors that can be rightly perceived by CVD patients. Moreover, the targeted absorption spectrum is selected based on the wavelengths in which the photoreceptor cones overlap.^[28] For instance, if a patient’s L-cone and M-cone overlap at 550 nm, a dye which has high absorbance at that wavelength is applied on the glass substrate. The degree of absorption would depend on the patient’s CVD severity. Moreover, the diffusion of the dye into the glass material occurs at a temperature below the boiling point of the solvent containing the dye, which is usually below 60 °C. The solvent forces the lens material to swell to allow diffusion of the dye into the material. The glass lens then retains its original shape, and the dye is trapped within the material.^[28] The lens material used in Enchroma glasses is Trivex, which is lighter, thinner, and stronger than the commonly used glass materials (CR-39 and polycarbonate).^[26]

Gómez-Robledo et al. evaluated the effectiveness of Enchroma glasses by firstly subjecting 48 CVD patients to Ishihara, Fansworth-Munsell Hue 100, and a subjective color naming test.^[29] The second approach involved modeling the spectral transmittance of the glasses and the stimulus of the patients wearing them. As for the subjective experiment,

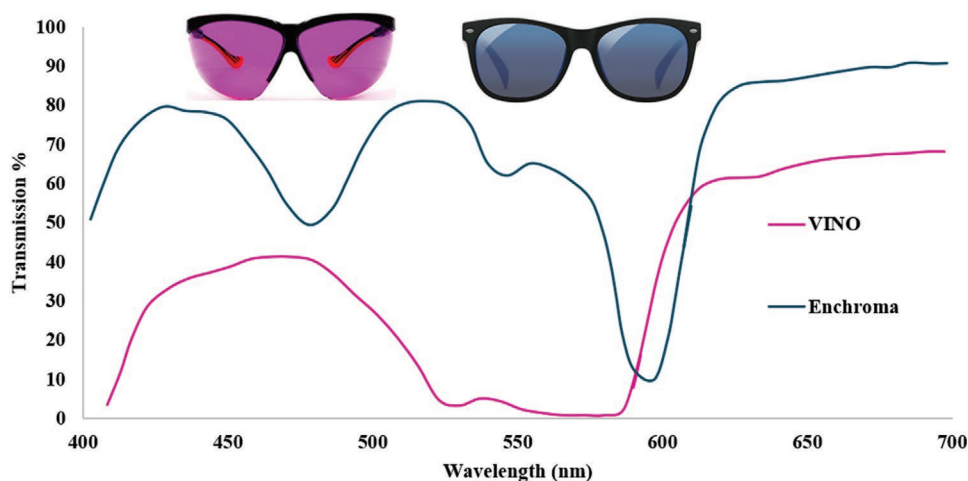


Figure 3. Spectral transmittance of VINO and Enchroma CVD glasses. Adapted with permission.^[32] Copyright 2019, The Optical Society.

the improvements in Ishihara (<5%) and the FM 100 (<9%) tests were insignificant. Similarly, the patients were not able to score higher in the color naming test after wearing the Enchroma glasses. Deuteranomaly and deuteranopia patients had even more fails in the test. Overall, only one female patient with severe deuteranomaly noticed an improvement in color perception. In the second approach, images were simulated as seen by mild, medium, and severe deutan and protan. The noticeable variation was in chroma values. Images with high blue hues had a decrease in chroma while images with low or negative blue hues had an increase in chroma.^[29] This can be seen from the spectral transmittance of Enchroma (Figure 3). Enchroma has a relatively high transmittance in the blue region of the optical wavelength spectrum. Enchroma glasses can only change few perceptive color attributes (chroma), but they do not enhance the scores in the color vision tests, nor they give the user a “normal color vision experience.”

Almutairi et al. also recruited 10 CVD individuals and tested Enchroma glasses on them using ColorDx software (digital version of Ishihara test) and FM Hue 100. Only two individuals, who were severe deutans and protans, scored higher in the ColorDx test, while wearing the Enchroma glasses. Also, Enchroma did not improve the subjects' score in the FM Hue 100 test.^[33]

The second brand of CVD glasses is VINO/O2Amp glasses, which were originally made to enhance the oxygen signal from the blood under the skin, but the product manufacturers claim that it “corrects” the red-green color deficiency (Figure 3).^[34] The glasses are priced at \$250.

Martinez et al. evaluated the VINO glasses by testing 52 CVD subjects for Ishihara, FM Hue 100, and a color naming test.^[32] The results indicate that the subjects were able to score better on the Ishihara test but have more errors in the other tests. A higher contrast would enhance the color distinction of the Ishihara plates. However, this does not represent the colors perceived by a normal color-sighted individual. This suggests that the VINO glasses do not correct the color vision of the CVD patient, but they only darken green color and increase the chroma for red color. The Enchroma glasses were also evaluated against the VINO glasses.^[32] Authors suggest that VINO glasses allowed the patient to score better in Ishihara test because they provided an increased color contrast, especially for deutans. The authors conclude that both Enchroma and VINO glasses do not fully correct color blindness, but they can improve color distinction for specific applications.

As shown in Figure 3, transmission spectra of Enchroma and VINO show that the former glasses block light in fewer regions of the spectrum as compared to the latter. Hence, VINO glasses alter more of the colors in the spectrum, and consequently colors that were correctly perceived by CVD patients might also shift. On the contrary, Enchroma blocks light only in the wavelengths that are problematic to the patients. For instance, in Figure 3, incoming light is only blocked (low transmittance) at 470 and 590 nm, while all other wavelengths remain unchanged.

Another company that manufactures CVD glasses is Colorlite.^[35] Klara Wenzel invented these glasses in 1998. Colorlite also utilizes the concept of filters to block light in specific regions of the spectrum. Similar to Enchroma and VINO, Colorlite claims that their glasses “correct red-green color vision

deficiency.”^[35] The company, recently, started manufacturing CVD contact lenses as well. Even though Colorlite is one of the oldest manufacturers of color blind glasses, clinical studies on its effectiveness are limited.

Overall, the reviewed studies show that these tinted glasses do not provide a “normal color vision experience,” as proclaimed by the companies. Another issue is that these glasses are used for all types of CVD although they are designed to block light in specific wavelengths, and as discussed in the introduction, these wavelengths would be different for every CVD type. Also, they are not selective in terms of color enhancement; they recolor the whole view of the patient.

3.3. Contact Lenses

In this subsection, contact lenses that were manufactured to aid CVD patients are discussed, and their effectiveness is evaluated. Most colorblind contact lenses use the same concept of glasses (i.e., colored filters to block certain wavelengths of the human's color vision spectrum). Since a contact lens is to be placed on the eye rather than to be resting in front of it, it has a stricter health and safety regulations. One of the first tinted lenses introduced to assist color blind patients is X-Chrom. X-Chrom lens is a monocular corneal contact lens manufactured by the X-Chrom Corporation. It is made of polymethyl methacrylate (PMMA) and red dye for wavelength filtering properties.^[36] This lens functions on the principle of a red filter, i.e., placing it on one eye would enhance the contrast for undistinguishable colors. The X-Chrom lens absorbs colors in the wavelength region of 500–570 nm.^[37] Siegel evaluated the effect of using the X-Chrom lens.^[38] Siegel refuted the claims of the manufacturers who said that the lens corrects the color defectiveness. He argued that protans and deutrans suffer from defective or missing red-green cone pigments, so inserting a red tinted lens on the eye would certainly not “correct” the deficiency. However, filters can only reduce the amount of absorbed light in specific regions of the wavelength spectrum. Siegel mentioned a study done by LaBissoniere, an optometrist, who also suffered from deuteranomaly.^[39] LaBissoniere experimented the lenses on defective subjects and used vision perception tests for assessment. The participants showed a score improvement in these tests. LaBissoniere further experimented the lenses on himself by wearing them for 50 h and assessing the vision discrepancies. He noted a decrease in color contrast, specifically red-orange and red-yellow, and his score in a hue discrimination test was 50% less than with the lens.^[38–39] X-Chrom lens aids in color perception but does not correct the deficiency, and patients should be aware of the adverse effects of wearing it.

Unlike X-Chrom, which is a hard lens, ChromaGen are soft lenses that are made of Hioxifilicon A, copolymer of hydroxyethyl methacrylate and glycerol methacrylate. ChromaGen was introduced by an English optician David Harris.^[42] The tinted lenses were made for glasses and contact lenses, but the contact lenses form is more popular.^[42b] ChromaGen packaging and contact lens is shown in Figure 4c. A study tested the ChromaGen lenses on 14 young adults over a period of two weeks.^[43] Lenses tint depended on the patient's CVD

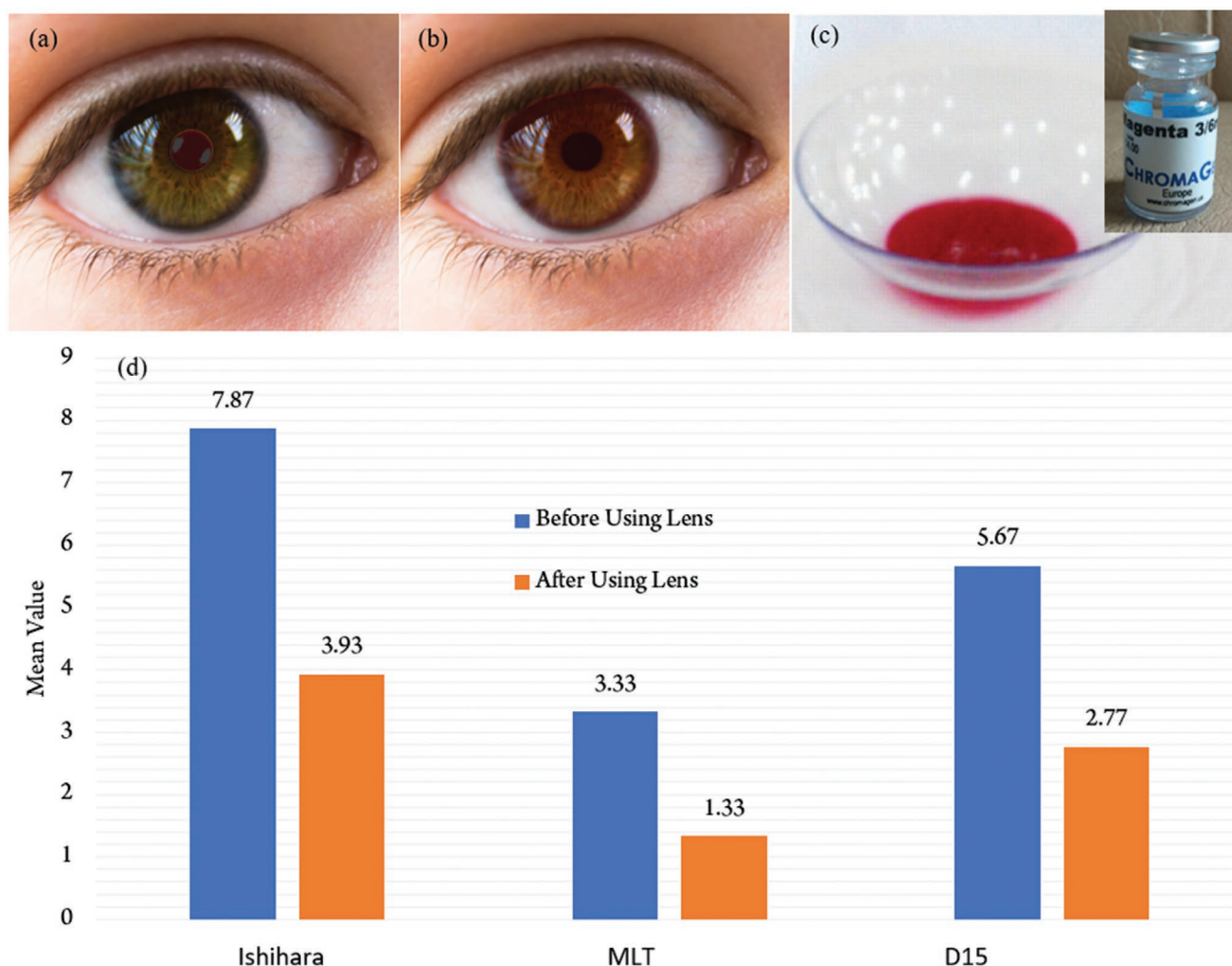


Figure 4. Use of commercial lenses to aid CVD patients. a) ChromaGen lens applied to the pupil. b) X-Chrom lens applied to the pupil and iris. c) ChromaGen lens. Inset shows the packaging of the lens. Reproduced with permission.^[40] Copyright ChromaGen. d) Effect of using red lens represented by error scores in diagnostic tests for 30 CVD patients.^[41]

type. Deuteranomaly and deuteranopia patients showed a vast improvement on the Ishihara test; protanomaly and protanopia patients' color perception improved also but to a smaller extent. As for the Farnsworth Lantern test, most patients did experience a better color perception. It can be asserted that ChromaGen lenses can improve the color perception in some cases but cannot help CVD patients in day-to-day chores.^[43] The main difference between the ChromaGen and X-Chrom lens is that ChromaGen covers only the pupil of the eye (Figure 4a) while X-Chrom covers the pupil and iris (Figure 4b).

Oli et al. also evaluated the effectiveness of a red contact lens, similar to ChromaGen, made of poly-2-hydroxyethyl methacrylate, using color vision tests.^[41] The tests were Ishihara, Farnsworth D-15, and Martin Lantern Test. 30 CVD patients were tested with and without the lenses, of which 18 had deuteranomaly, and seven suffered from protanomaly. Five people's CVD could not be identified. Results based on the three tests showed a reduction in error score when the lens was used.^[41] The mean error scores for the three tests are shown in Figure 4d. Discrepancies in individual improvement among

the patients were minor which confirms that almost all subjects benefited from the red lens.

Colormax or Color Correction System is another CVD contact lens manufacturer. Colormax also uses customized filters to alter the wavelengths of the colors perceived by the patients' eyes. The latter is designed uniquely as per the patient's CVD type and severity. Thomas Azman invented the Color Correction System in 1999. His company currently offers CVD contact lenses and glasses. Patients need to be diagnosed and have an appropriate lens prescribed to them. Diagnosis is done using Ishihara Test plates.

More recently, Badawy et al. developed and evaluated a cost-effective contact lens, dyed with fluorescent Atto dyes, to filter out the wavelength bands affected by red-green vision deficiency namely: deuteranomaly, deuteranopia, protanopia, and protanomaly.^[44] Customized lenses (made from poly 2-hydroxyethyl methacrylate (pHEMA)) and commercial contact lenses were dyed using two techniques. One involving adding drops of the dye solution onto the surface of the lens (Figure 5e) while in the second, the lens was dipped into the dye solution (Figure 5f).

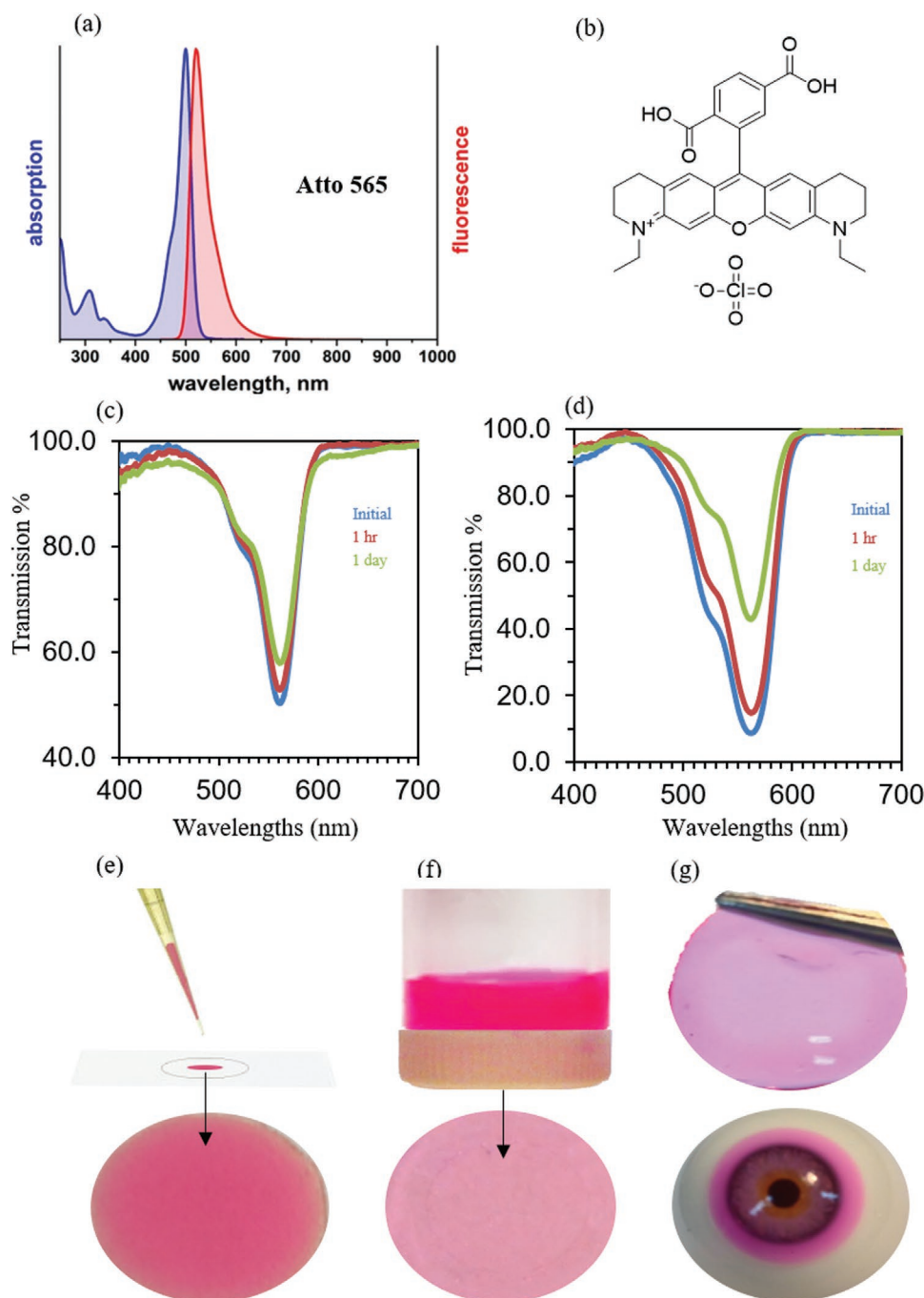


Figure 5. Atto dye use in contact lens. a) Spectral absorbance of Atto 565. b) Chemical composition of the dye. Lens' transmission spectrum and stability checked after one hour and after one day for c) dip method and d) drop method. Visual representation of e) the dip method and f) the drop method. g) Dyed lens on an artificial eye. Reproduced with permission.^[44] Copyright 2018, Wiley.

Initially, the drop method yielded better absorption properties, but the dip method provided better stability for the lenses over a one-day period as shown in Figure 5c,d. The contact lens's toxicity toward human corneal cells and response to eye tear was assessed. A phosphate buffered saline (PBS) solution was used to simulate the tear. As expected, the lens' absorption decreased as the lens was in contact with the PBS solution. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, commonly known as MTT assay, was carried out on

human corneal epithelial and fibroblast cell samples exposed to the dyed lenses. Toxicity was not observed, and cell viability remained at 99%.^[44]

The contact lenses have been tested on several individuals with and without CVD, using Ishihara test.^[44] Quantitative results have not been disclosed. Normal color vision subjects identified an enhancement in color contrast, but color perception improvement in CVD patients varied significantly. This might be due to some patients not knowing their CVD.

Since the lenses were designed to absorb the red-green wavelength overlap bands region (545–575 nm), they would not filter out wavelengths that might cause other CVD forms.

Similar to the commercially available glasses (Enchroma and VINO), tinted contact lenses improve the color perception in some cases (especially for severe deuterans and protans) and provide an enhanced color distinction experience, but they do not correct color blindness. Individuals can use the lenses in soft color related tasks. However, some people might use them to qualify for critical occupations (e.g., military) that are restricted for color blind.

Other concepts which utilize contact lenses, include the usage of nanoparticles. Gold and silver nanoparticles have been used in the biomedical sector, particularly, in sensing, drug delivery, cancer therapy, X-ray imaging, and optical processes.^[45] These nanoparticles, depending on their sizes, can absorb light in different regions of the wavelength spectrum. Smaller sized particles can absorb light in the blue region of the spectrum (400–450 nm). As the size of the particles increase, the absorption wavelength increases (shifts to red-green region).^[46] Gold and silver nanoparticles are highly effective in absorbing and scattering light. Surface plasmon resonance (SPR) is responsible for this optical property of the metallic nanoparticles. SPR refers to the collective oscillation of conduction electrons due to the electric field of the incident light.^[47] However, the absorption bands of these particles are relatively larger than dyes.^[47] Thus, they would also affect wavelengths that are not problematic for CVD patients. Also, the complexity of incorporating them into the lenses makes them less practical.

3.4. Dyes in Contact Lenses

In this subsection, the various types of dyes used in contact lenses to filter out certain colors of the visible light spectrum are discussed. Sulfur, vat, reactive, and Rhodamine dyes have been used in tinting contact lenses manufactured for CVD management.^[48] Generally, sulfur dye is the most common dye used in cotton clothes manufacturing, because of its cost-effectiveness (Figure 6).^[48a,49] This dye is water-insoluble; however, at high alkaline pH and high temperature, it becomes water-soluble in presence of a reducing agent.^[48d] Hence, it can be absorbed by the contact lenses matrices. Commonly, sodium sulfide or sodium hydrosulfide is used as a reducing agent for sulfur dyes.^[48a,50] Following the tinting process, the colored contact lenses are left to dry in air which oxidizes the sulfur dye regenerating the water-insoluble dye form.^[48d,50] The low water solubility of the dye coloring the contact lenses is the basis for prohibiting the dye leakage.^[50] Also, vat dye which is applied on cellulose fibers for coloring, has been employed for tinting commercial contact lenses.^[48e] High pH and a reducing agent are necessary for the tinting process. The reducing agent converts the dye into leuco form which is soluble in water.^[48b] Hence, the dye is attached to the contact lens, and the leuco form is oxidized due to the air exposure of the contact lenses. This results in the formation of an insoluble form of the dye.

Reactive dyes have been used in tinting cellulose fibers such as cotton and viscose. Advantageously, this dye can form a covalent bond between the contact lenses and its reactive group.^[52] Reactive dyes are soluble in water and can be used for dyeing

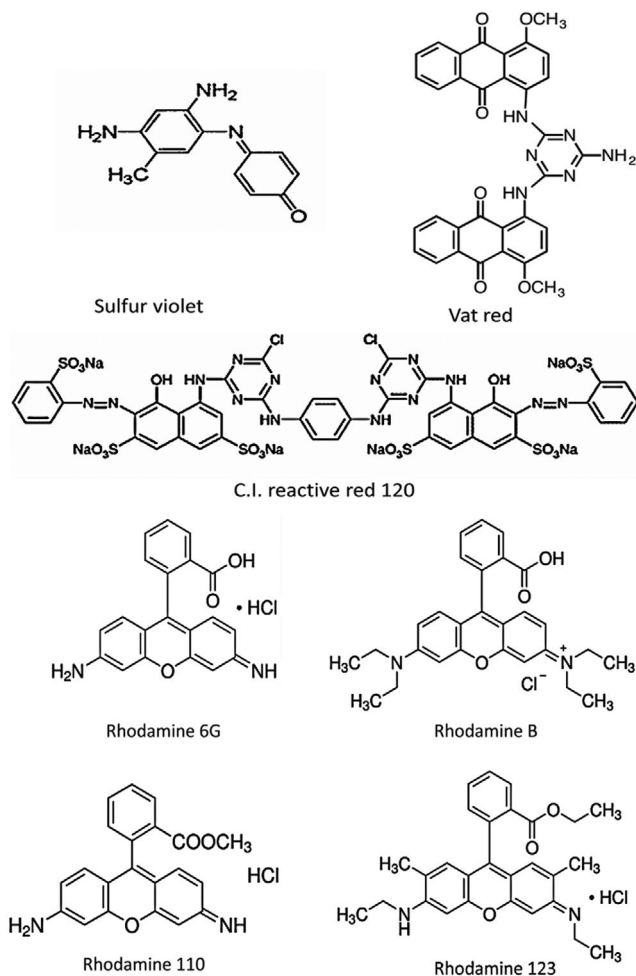


Figure 6. The chemical formulae for different types of dyes that have been used for tinting contact lenses for CVD treatment.

in cold or hot conditions. However, the tinting process of the contact lenses must be followed by the exposure to alkali. The lenses are then washed-off to remove the uncrosslinked dye.^[52b]

Recently, rhodamine dyes have been used for tinting contact lenses. Harding et al. tinted contact lenses using rhodamine 110, Rhodamine 123, rhodamine 6G, rhodamine 116, and rhodamine B (Figure 6).^[51] The dyeing was carried out through chemical cross-linking and spin coating for home-made soft contact lenses, hard contact lenses, and hybrid contact lenses. Alternatives to the rhodamine dyes include the Atto dyes, which have been recently used to tint CVD lenses. For instance, Badawy et al. used Atto 565 (chemical structure shown in Figure 5b) to tint the hydrogel contact lenses, where 565 represents the wavelength of the peak fluorescence of the dye (Figure 5a).^[44] The implementation of the dye on the lens was successful using the techniques illustrated in the previous subsection.

3.5. Optoelectronic Glasses

With the developments in the smart glasses and other head mounted wearables, the usage of such active optoelectronic

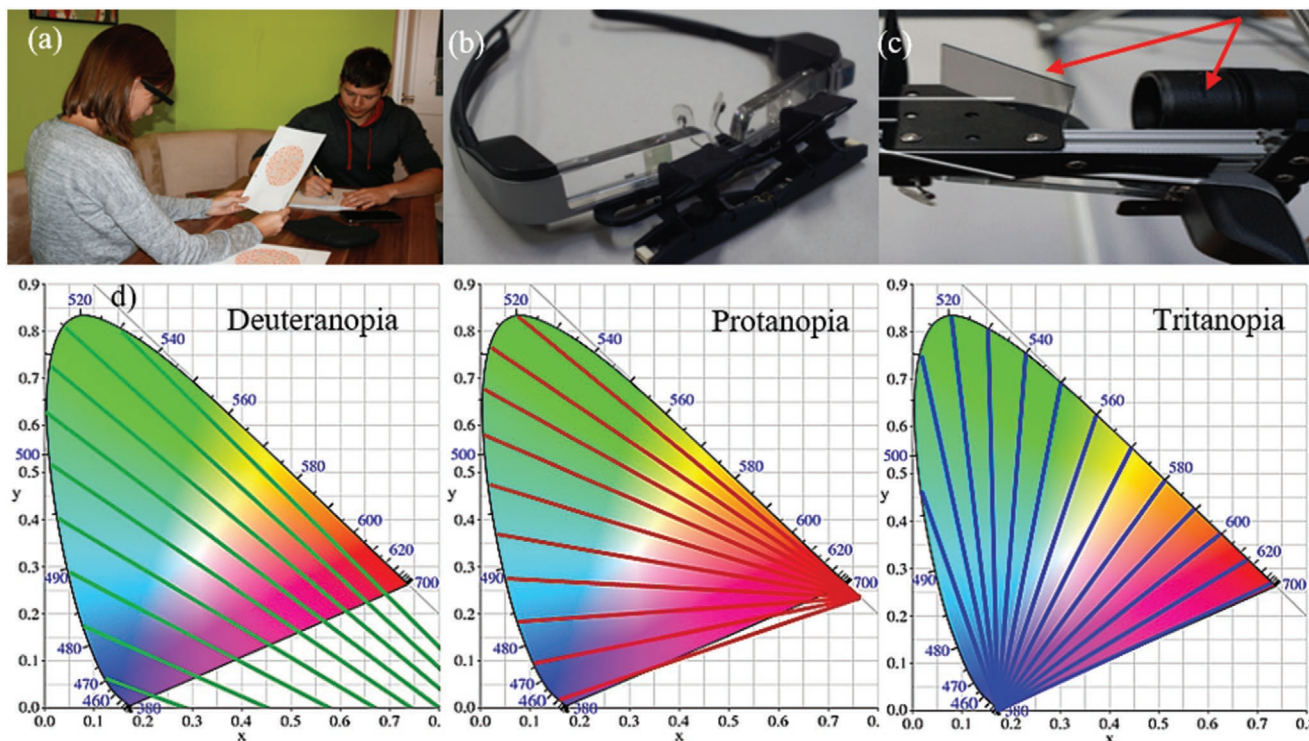


Figure 7. Incorporating optoelectronic glasses to aid CVD patients. a) Smart glasses in CVD diagnosis tests. Reproduced with permission.^[53] Copyright 2017, International Journal of Interactive Mobile Technologies. b) Attachment of external hardware to Epson smart glass. c) Closeup of the external attachment including the camera and beam splitter (red arrow). b,c) Reproduced with permission.^[58] Copyright 2018, Association for Computing Machinery. d) Confusion lines for deuteranopia, protanopia, and tritanopia. Adapted with permission.^[55a] Copyright 2010, Daltonize.

glasses in CVD management has been explored by several researchers.^[53–62] Lauegger et al. introduced an experimental prototype of a Google Glass application, called Omnicolor, to help people with color deficiency.^[53] Google Glass, first manufactured in 2013, is a head mounted wearable device which is priced at \$1500. The glass has smartphone and laptops like features including CPU, camera, microphone, display unit, and a touchpad.^[54] Google Glass can be controlled either by the touchpad mounted on the right side of the device or by head gestures and voice input. It has a screen resolution of 640×360 pixels and a camera with 5 Megapixel resolution.^[53] Omnicolor allows the user to select the desired color vision deficiency and capture a picture. The application processes it based on the selected color vision deficiency. Omnicolor uses a modified version of the daltonization algorithm as its image processing technique. Daltonization algorithms aim to shift colors from the confusion lines of the patients to colors which they can see. Patients, depending on their CVD type, have different confusion lines (Figure 7d). Color blind people cannot distinguish colors along the same line.^[55] To evaluate the efficacy of Omnicolor, 14 CVD subjects were tested with and without the prototype. Overall, the CVD participants were able to score better when using Omnicolor.^[53]

Tanuwidjaja et al. also demonstrated the use of Google Glass to aid CVD patients, by developing an application named Chroma.^[59] Chroma permits patients to see a recolored filtered image in real-time based on their CVD type. It does the latter by asking the users to select the colors of their interest in a specific scene and filters the scene based on the colors chosen. The filter

attempts to map the selected colors to ones that are distant on the color spectrum and distinguishable for color blind patients. Similar to Omnicolor, the Chroma filter utilizes daltonization algorithms. To assess the prototype's efficacy, 23 CVD patients used the glasses and were subjected to two types of tests: general tests like Ishihara and occupation specific tests. Example of the latter is questioning the subjects on colors of pH strips. Results indicate that the severity of the patients' CVD reduced when using Chroma. However, limitations of the prototype include its low processing power, battery life, and camera's resolution.^[59]

Popletev et al. developed a smart glass application aimed to aid color blind patients in distinguishing problematic colors in daily life.^[60] Unlike the previous prototypes, the application was implemented on Epson Moverio BT200 smart glasses, which was first introduced in 2014. Epson smart glasses are priced at \$600. Since Epson smart glass is more affordable than the Google Glass, it has become more popular in research fields.^[61] The application developed^[60] improves the image for color blind people by processing the frames from a live video stream, altering the frames containing the indistinguishable colors for the color blind, and finally displaying the processed video. The application focuses on increasing contrast between red and green colors for which it utilizes two processing techniques. In the first approach, the image is enhanced by increasing the contrast among indistinguishable colors (like red and green) and producing a completely new image. The second technique improves only certain parts of the image which have the problematic colors. The application has not been tested yet.^[60]

Moreover, Langlotz et al. presented ChromaGlasses, a prototype of an optical head mounted display to aid color blind patients (Figure 7b). In contrast to the previous studies presented, these glasses allow the user to look directly in their line of sight rather than viewing the processed result through the periphery.^[58] Like Popleteev's application, an Epson Moverio smart glass was used for the system's processing. An external camera is attached to the smart glasses as shown in Figure 7c.^[58] The camera is used to capture the environment of the user, from his/her vision's axis. ChromaGlasses use the camera to map the user's view, find colors that are difficult to distinguish, and alternate these colors based on Daltonization algorithms. Langlotz et al. states that their feasibility, usability, and user feedback tests show that the ChromaGlasses enhanced the users' perception of colors "to the level that they cannot be detected as color blind."^[58] Further research needs to be done to improve issues like the latency, which is about 0.3 s.

Melillo et al. developed a real-time wearable augmented reality system.^[62] This prototype, unlike the ones in the previous studies, is not based on any commercial smart glass (Epson or Google); it is custom-made to aid CVD patients. The system consists of three main modules: acquisition, processing, and rendering. As for the acquisition module, an OVRVISION PRO camera with a resolution of 120 × 50 pixels was utilized, to capture the feed real-time. The processing module, which is customized per the CVD type, uses daltonization algorithms to implement the color remapping. The output is then displayed on a head mounted display. The performance of the prototype was evaluated by subjecting 24 patients to Ishihara and Farnsworth D15 tests. Although the results of the test show that the patients were able to identify more plates when using the wearable augmented system, the prototype is yet to be tested outdoors.^[62]

Even though the research on optoelectronic glasses for color blindness is limited, prototypes like the customized wearable augmented reality system and ChromaGlasses have the potential to help the CVD patients because they alter the specific colors that are problematic for them unlike the tinted glasses and lenses which modify their entire vision. **Table 2** summarizes the wearable devices that were reviewed in this paper along with the tests conducted and corresponding results.

3.6. Features in Smartphones and Computers

Companies like Microsoft, Google, and Apple have developed features in their operating systems to aid color blind patients. Microsoft added a color filter feature to Windows 10, in which CVD users can alter the color of the screen (windows and all programs) to enhance their color perception (**Figure 8a**). In the color filter feature, Windows 10 includes a color wheel, so users who are unaware of their CVD type will select the filter that improves color contrast. Similarly, Apple and Google have added this feature to IOS and Android, respectively (Figure 8b,c). The color filtering feature included the three different forms of CVD: protanopia, deuteranopia, and tritanopia.

4. Conclusion

Patients with CVD find difficulties perceiving shades of similar colors, which may hinder numerous aspects of their daily lives, like cooking, playing sports, driving, and watching TV. Critical occupations (military, navy, and few medicine specializations)

Table 2. Summary of the commercial and research based ocular wearables and their testing results.

Class	Wearable	Testing	Results
Tinted glasses	Enchroma	Ishihara, FM Hue 100, and subjective color naming test ^[29,32,33]	Insignificant improvements in all tests
	VINO/O2Amp	Ishihara, FM Hue 100, and color naming test ^[32]	Improved color contrast and fewer errors in Ishihara
	Colorlite	–	–
Tinted lenses	X-Chrom	Ishihara and HRR ^[38]	Better color contrast and fewer errors in both tests
	ChromaGen	Ishihara, Farnsworth D-15, and Farnsworth Lantern ^[43]	Improved color contrast and fewer errors in all tests
	Colormax	–	–
	Atto565 dyed lens	Ishihara ^[44]	Enhanced color contrast but inconsistent improvements in test scores
Optoelectronic glasses	Omnicolor ^{a)}	Ishihara ^[53]	Fewer error scores for all participants
	Chroma ^{a)}	Ishihara and occupation specialized tests ^[59]	Fewer error scores in Ishihara but inconsistent improvements in occupation related tests
	Colorizer ^{b)}	–	–
	ChromaGlasses ^{b)}	Ishihara ^[58]	Improved color perception and significant reduction in error scores for most participants
	Customized wearable augmented reality system	Ishihara and Farnsworth D-15 ^[62]	Fewer error scores in both tests

^{a)}Based on Google Glass; ^{b)}Based on Epson Moverio.

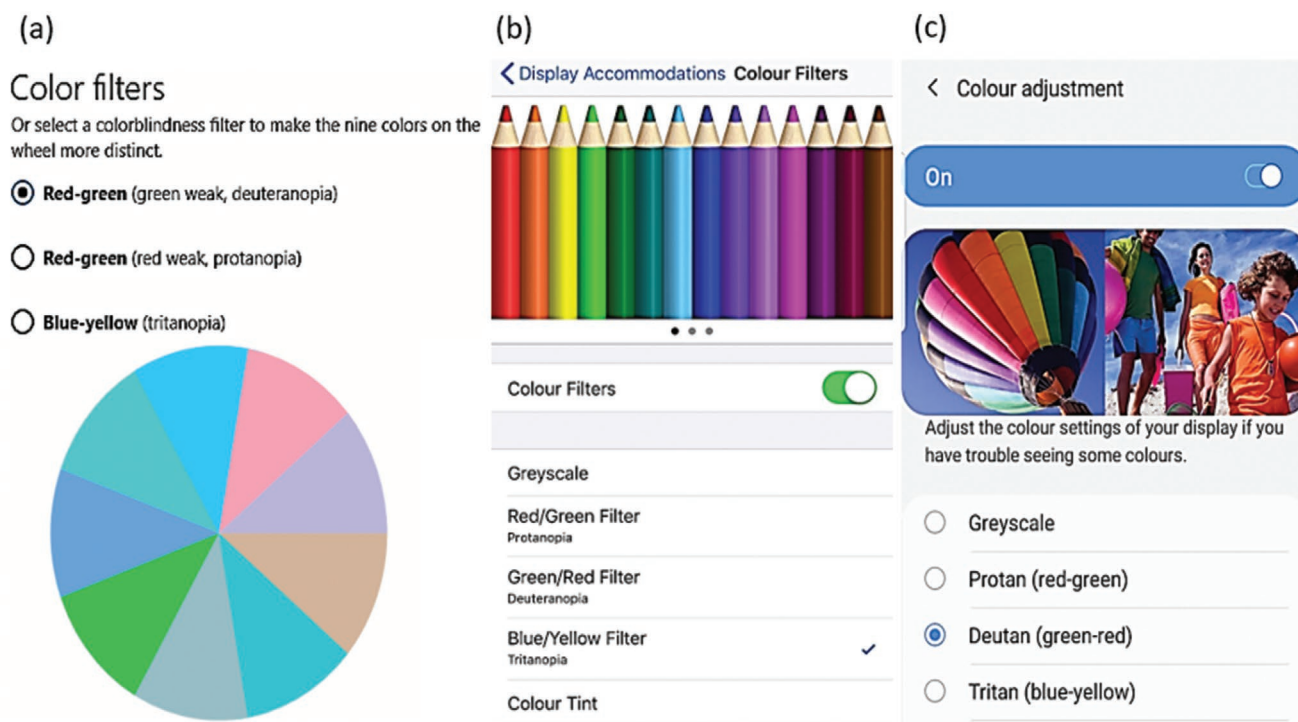


Figure 8. Advanced color filter features developed in smartphone and laptop operating systems to aid CVD individuals. a) Windows 10; b) iOS; c) Android.

are restricted for color blind people. To be able to discriminate between indistinguishable colors, CVD sufferers opt for the tinted lenses and glasses. Even though they do not provide a normal color vision experience, tinted lenses and glasses allow color blind individuals to distinguish between colors that previously appeared the same. Enchroma glasses and ChromaGen lens are the most used and effective for color blind patients. However, prospects for gene therapy and optoelectronic glasses are very promising, but both management techniques still require more research to be implemented.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

biomaterials, color blindness, contact lenses, ophthalmology, wearable electronics

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- [1] a) W. M. Hart, *Surv. Ophthalmol.* **1987**, 32, 10; b) M. P. Simunovic, *Surv. Ophthalmol.* **2016**, 61, 132.
- [2] L. T. Sharpe, H. Jägle, *Color Res. Appl.* **2001**, 26, S269.
- [3] a) M. P. Simunovic, *Eye* **2010**, 24, 747; b) Y.-C. Chen, Y. Guan, T. Ishikawa, H. Eto, T. Nakatsue, J. Chao, M. Ayama, *Color Res. Appl.* **2014**, 39, 234; c) J. Birch, *J. Opt. Soc. Am. A* **2012**, 29, 313.
- [4] S. Ahsana, R. Hussain, M. Fareed, M. Afzal, *Iran. J. Public Health* **2013**, 42, 16.
- [5] A. Tagarelli, A. Piro, G. Tagarelli, P. Lantieri, D. Risso, R. Olivieri, *Acta Ophthalmol. Scand.* **2004**, 82, 436.
- [6] a) E. Holroyd, D. Hall, *Child: Care, Health and Dev.* **1997**, 23, 391; b) R. A. Cronem, *Am. J. Ophthalmol.* **1961**, 51, 298.
- [7] a) J. A. B. Spalding, *Occup. Med.* **1999**, 49, 247; b) L. Ali, *J. Univ. Med. Dent. Coll.* **2012**, 3, 1.
- [8] L. Tocantins, H. Jones, *Am. J. Med. Sci.* **1933**, 185, 243.
- [9] W. D. Dannenmaier, *J. Exp. Educ.* **1972**, 41, 15.
- [10] R. Seales, World Cup 2018: Why millions of fans see the football like this, <https://www.bbc.com/news/world-44535687> (accessed: September, 2019).
- [11] UEFA, Helping colour blind people in football, <https://www.uefa.com/insideuefa/social-responsibility/news/newsid=2498333.html> (accessed: September, 2019).
- [12] J. Breech, *LOOK: Bills-Jets game is complete torture for color-blind people*, <https://www.cbssports.com/nfl/news/look-bills-jets-game-is-complete-torture-for-color-blind-people/> (accessed: September, 2019).
- [13] S. Pal, *Design of Artificial Human Joints & Organs*, Springer, Boston, MA **2014**, p. 219.
- [14] a) A. Tofts, *Focus: J. Res. Scholarly Output* **2007**, 2, 63; b) A. Stockman, L. T. Sharpe, *Vis. Res.* **2000**, 40, 1711; c) L. Sharpe, K. Gegenfurtner, *Color Vision*, Cambridge University Press, Cambridge **1999**.
- [15] L. M. Hurvich, *Color Vision*, Sinauer, Sunderland, MA **1981**.
- [16] L. Went, N. Pronk, *Hum. Genet.* **1985**, 69, 255.

- [17] M. Rodriguez-Carmona, in *Encyclopedia of Color Science and Technology* (Ed: R. Luo), Springer, Berlin **2014**, p. 1.
- [18] S. Ishihara, *Test for Colour-Blindness*, Kanehara, Tokyo, Japan **1987**.
- [19] L. H. Hardy, G. Rand, M. C. Rittler, *J. Opt. Soc. Am.* **1945**, *35*, 268.
- [20] a) D. Farnsworth, *J. Opt. Soc. Am.* **1943**, *33*, 568; b) N. R. Council, *Procedures for Testing Color Vision: Report of Working Group 41*, National Academies Press, Washington, DC **1981**.
- [21] K. Mancuso, W. W. Hauswirth, Q. Li, T. B. Connor, J. A. Kuchenbecker, M. C. Mauck, J. Neitz, M. Neitz, *Nature* **2009**, *461*, 784.
- [22] J. J. Alexander, Y. Umino, D. Everhart, B. Chang, S. H. Min, Q. Li, A. M. Timmers, N. L. Hawes, J.-j. Pang, R. B. Barlow, *Nat. Med.* **2007**, *13*, 685.
- [23] M. Neitz, J. Neitz, *Cold Spring Harbor Perspect. Med.* **2014**, *4*, a017418.
- [24] F. W. Cornelissen, E. Brenner, *J. Vis.* **2015**, *15*, 22.
- [25] a) P. Lanthony, C. Mailer, *The History of Color Blindness*, Wiley-VCH Verlag, Weinheim, Germany **2013**; b) A. Seebeck, *Ann. Phys. Chem.* **1837**, *118*, 177.
- [26] EnChroma, <https://enchroma.com/> (accessed: September, 2019).
- [27] a) R. Mastey, E. J. Patterson, P. Summerfelt, J. Luther, J. Neitz, M. Neitz, J. Carroll, *Invest. Ophthalmol. Visual Sci.* **2016**, *57*, 192; b) A. W. Schmeder, D. M. McPherson, *Google Patents*, **2018**.
- [28] D. McPherson, *Google Patents*, **2020**.
- [29] L. Gómez-Robledo, E. M. Valero, R. Huertas, M. A. Martínez-Domingo, J. Hernández-Andrés, *Opt. Express* **2018**, *26*, 28693.
- [30] A. Sciacca, *Growing vision firm is bringing color to the colorblind* <http://www.startribune.com/growing-vision-firm-is-bringing-color-to-the-colorblind/379276511/> (accessed: September 2019).
- [31] P. Schneider, O2Amp Colorblind Correction Glasses [Review], <https://churchm.ag/o2amp-colorblind-correction-glasses/> (accessed: September, 2019).
- [32] M. A. Martínez-Domingo, L. Gómez-Robledo, E. M. Valero, R. Huertas, J. Hernández-Andrés, S. Ezepeleta, E. Hita, *Opt. Express* **2019**, *27*, 17954.
- [33] N. Almutairi, J. Kundart, N. Muthuramalingam, J. Hayes, K. Citek, S. Aljohani, *Assessment of Enchroma Filter for Correcting Color Vision Deficiency*, College of Optometry, Pacific University, Oregon **2017**, pp. 15–25.
- [34] VINO, Color-Enhancing and Colorblindness Protective Glasses, <https://www.vino.vi/> (accessed: October, 2019).
- [35] W. Li, D. R. Flatla, presented at *The 21st Int. ACM SIGACCESS Conf. on Computers and Accessibility*, Pittsburgh, PA, USA **2019**.
- [36] a) H. Zeltzer, *J. Am. Optom. Assoc.* **1971**, *42*, 933; b) H. I. Zeltzer, *Google Patents*, **1971**.
- [37] A. Evans, *Color is in the Eye of the Beholder: A Guide to Color Vision Deficiency and Colorblindness*, CVD Pub., Auburn, CA **2003**.
- [38] I. M. Siegil, *Surv. Ophthalmol.* **1981**, *25*, 312.
- [39] P. LaBissoniere, *Int. Contact Lens Clin. Q.* **1974**, *4*, 48.
- [40] ChromaGen, Worldwide producer and supplier of Chromagen Lenses for Color Blindness and Dyslexia, <https://www.chromagen.us/> (accessed: October, 2019).
- [41] A. Oli, D. Joshi, *Med. J. Armed Forces India* **2019**, *75*, 458.
- [42] a) D. Harris, *ChromaGen Clinical Procedures*, Cantor & Silver Ltd, Northants **1998**; b) D. A. Harris (ChromaGen Vision LLC), *US Patent: US7931369B2*, **2007**.
- [43] H. A. Swarbrick, P. Nguyen, T. Nguyen, P. Pham, *Ophthalmic Physiol. Opt.* **2001**, *21*, 182.
- [44] A.-R. Badawy, M. U. Hassan, M. Elsherif, Z. Ahmed, A. K. Yetisen, H. Butt, *Adv. Healthcare Mater.* **2018**, *7*, 1800152.
- [45] V. Amendola, R. Pilot, M. Frascioni, O. M. Maragò, M. A. Iati, *J. Phys.: Condens. Matter* **2017**, *29*, 203002.
- [46] a) S. Link, M. A. El-Sayed, *J. Phys. Chem. B* **1999**, *103*, 4212; b) X. Huang, M. A. El-Sayed, *J. Adv. Res.* **2010**, *1*, 13.
- [47] M. A. Garcia, *J. Phys. D: Appl. Phys.* **2011**, *44*, 283001.
- [48] a) P. Gregory, *Kirk-Othmer Encyclopedia of Chemical Technology*, John Wiley & Sons, Inc., New York **2000**, p. 1; b) D. R. Waring, G. Hallas, *The Chemistry and Application of Dyes*, Springer Science & Business Media, Berlin **2013**; c) W. M. Hung, K. C. Su, *Google Patents*, **1990**; d) C. W. Neefe, *Google Patents*, **1986**; e) K. Niwa, Y. Taniyama, N. Iwata, Y. Yokoyama, *Google Patents*, **1996**.
- [49] M. Mohsin, A. Rasheed, A. Farooq, M. Ashraf, A. Shah, *J. Cleaner Prod.* **2013**, *53*, 341.
- [50] W. Bauer, H. Kruse, G. Nagl, J.-H. Mast, L. Schlosser, *Google Patents*, **1993**.
- [51] B. T. Harding, S. Li, A. Mochizuki, *Google Patents*, **2014**.
- [52] a) K. C. Su, *Google Patents*, **1984**; b) J. W. Wittmann, J. M. Evans, *Google Patents*, **1990**.
- [53] G. Lausegger, M. Spitzer, M. Ebner, *Int. J. Interact. Mobile Technol. (ijIM)* **2017**, *11*, 161.
- [54] O. J. Muensterer, M. Lacher, C. Zoeller, M. Bronstein, J. Kübler, *Int. J. Surg.* **2014**, *12*, 281.
- [55] a) Daltonize, There is not just one color blindness, <http://www.daltonize.org/search/label/Color%20Blindness> (accessed: October, 2019); b) C.-N. Anagnostopoulos, G. Tsekouras, I. Anagnostopoulos, C. Kalloniatis, presented at *Int. Conf. on Computer Vision Systems: Proc.*, Bielefeld, Germany **2007**.
- [56] Google Glass (2019). Description of Google's Smart Glass, <https://www.google.com/glass/start/> (accessed: October, 2019).
- [57] C. d. Looper, Hands on: Epson BT-300 <https://www.digitaltrends.com/virtual-reality/epson-bt-300-hands-on/> (accessed: October, 2019).
- [58] T. Langlotz, J. Sutton, S. Zollmann, Y. Itoh, H. Regenbrecht, presented at *Proc. of the 2018 CHI Conf. on Human Factors in Computing Systems*, Montreal, QC, Canada **2018**.
- [59] E. Tanuwidjaja, D. Huynh, K. Koa, C. Nguyen, C. Shao, P. Torbett, C. Emmenegger, N. Weibel, presented at *Proc. of the 2014 ACM Int. Joint Conf. on Pervasive and Ubiquitous Computing*, Seattle Washington, USA **2014** (UbiComp 2014).
- [60] A. Popleteev, N. Louveton, R. McCall, in *Proc. of the 2015 Workshop on Wearable Systems and Applications (WearSys'15)*, ACM, New York **2015**, pp. 7–8.
- [61] L. Qian, A. Barthel, A. Johnson, G. Osgood, P. Kazanzides, N. Navab, B. Fuerst, *Int. J. Comput. Assist. Radiol. Surg.* **2017**, *12*, 901.
- [62] P. Mellillo, D. Riccio, L. D. Perna, G. S. D. Baja, M. D. Nino, S. Rossi, F. Testa, F. Simonelli, M. Frucci, *IEEE J. Transl. Eng. Health Med.* **2017**, *5*, 1.