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FULL PAPER

Expression of superoxide dismutase-2 (SOD2) and catalase (CAT) in the lens epithelial cells of mice: A comparative study of UV blocking protection by uv blocking glasses and UV blocking contact lenses

Made Dessy Gangga Ayu Cinthiadewi[a] |Muhammad Firmansjah[a,*] |Nurwasis Nurwasis[a] |Djoko Legowo[b] |Ni Putu Ayu Reza Dhiyantari[a] |Rifat Nurfahri[a]

[a]*Department of Ophthalmology, Dr. Soetomo General Academic Hospital, Faculty of Medicine, Universitas Airlangga, Surabaya, 60132, Indonesia*

[b]*Department of Pathology Veterinary, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, 60132, Indonesia*

***Corresponding Author:**
Muhammad Firmansjah
Email: firmansjah.spm@gmail.com
Tel.: + 62818581925

Cataract is a leading cause of global blindness, often associated with long-term sunlight exposure and UV-B radiation. This study investigates the protective effects of anti-UV-B glasses and contact lenses on the expression of superoxide dismutase-2 (SOD2) and catalase (CAT) in mice lens epithelial cells. UV-B exposure is known to induce oxidative stress and cataract formation by disrupting the balance of oxidant and antioxidant enzymes. Our study evaluates the role of SOD2 and CAT expression in response to UV blocking glasses and contact lenses. Results demonstrate a significant reduction in ROS generation and DNA damage in epithelial cells, suggesting the protective efficacy of these UV-blocking interventions.

KEYWORDS

UV-B; SOD2; CAT; UV blocking glasses; UV blocking contact lenses; mice lens capsule epithelial cells.

Introduction

Cataracts represent a significant burden on global eye health, contributing substantially to visual impairment and blindness. While estimates vary, cataracts are widely recognized as a leading cause of visual impairment worldwide. The prevalence of cataracts may differ across regions and populations, influenced by factors such as age, genetics, and environmental exposures. While it is acknowledged that cataracts are a substantial public health concern, the exact proportion of global blindness attributed to cataracts may vary depending on the demographic and epidemiological context. Therefore, understanding the prevalence and impact of cataracts requires comprehensive and context-specific assessments [1]. In Indonesia alone cataracts are diagnosed in

210,000 people every year, or 0.1% of Indonesia's total population of 250 million [2]. The only currently available treatment for cataracts is surgery. Post-recovery vision surgery is advantageous for its high effectiveness and safety when conducted by a proficient and educated surgeon. Expensive surgery may not be universally accessible. 1.8 million cataract procedures in the United States annually account for about $4 billion, which is two-thirds of the overall vision health expense. Delaying the onset of cataracts for as long as possible is one way in which the process of equalization can be achieved [1].

Long-term exposure to sunshine is widely acknowledged to elevate the likelihood of developing mature cataracts in humans. Ultraviolet-B (UV-B) is associated with cortical cataract formation. High levels of UV-B radiation can harm the lens epithelium and disrupt ion balance, contributing to cataract formation in older individuals [1]. The loss of mitochondrial transmembrane potential and the formation of reactive oxygen species (ROS) lead to cell damage and death [3]. Oxidative stress caused by ROS has been reported in various diseases, especially age-related ones, such as cataracts. Aside from the direct interaction of small ROS molecules, the lens contains many antioxidant enzymes for ROS detoxification. Eukaryotic organisms utilize primary antioxidant enzymes like superoxide dismutase-2 (SOD2) and catalase (CAT) to convert ROS into stable molecules like water and oxygen through a sequence of processes. These enzymes can reduce oxidative stress by enhancing antioxidant defence systems that regulate the level of ROS using ROS-specific reducing agents to remove excess free radicals, therefore preserving the integrity of the lens [4].

UV-B induced cataract

UV radiation, particularly UV-B, is the primary environmental element responsible for producing cataracts. Exposure to UV-B radiation triggers the production of reactive oxygen species and promotes cell death in the lens epithelium, resulting in the development of cataracts. Ultraviolet radiation (UVR) comprises wavelengths ranging from 100 to 400 nm and is categorized into three types: UVA (315-400 nm), UVB (280-315 nm), and UVC (100-280 nm). UV-B primarily targets deoxyribonucleic acid (DNA) [5]. UV-B radiation can penetrate through the stratum corneum. UV-B radiation is directly absorbed by the DNA in epidermal cells, specifically keratinocytes and Langerhans cells, leading to cytotoxic and mutagenic effects. This exposure primarily induces the formation of cyclobutane pyrimidine dimers (CPDs) and pyrimidone photoproducts. These photoproducts are recognized as common abnormalities resulting from UV-induced DNA damage. UV-B light is recognized as a potent generator of H_2O_2. UV-B radiation can cause a delayed oxidative reaction that continues even after exposure stops. However, there is no proof that this leads to delayed oxidative damage to cellular DNA [6] (Figure 1).

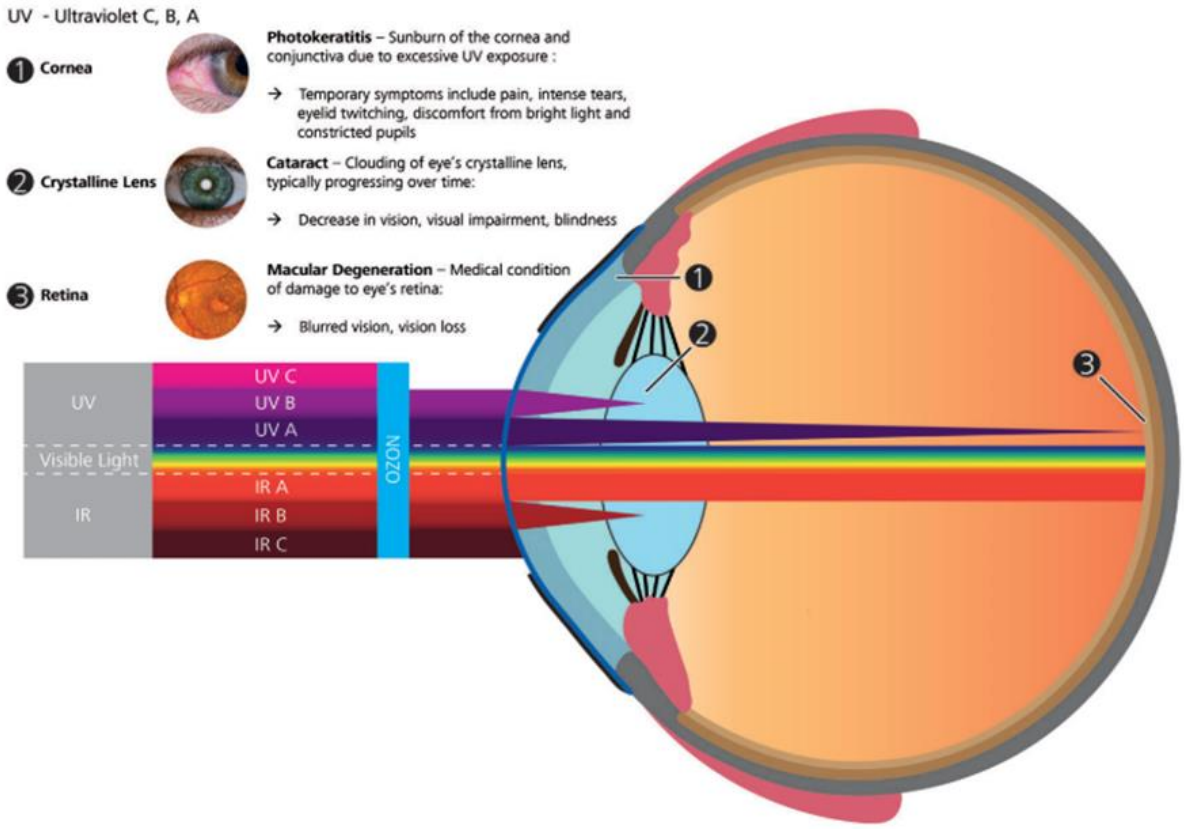

FIGURE 1 A schematic illustration illustrating the transmission of different optical radiation bands through the eye tissues [6]

The role of ROS in UV-B-induced cataract

UV radiation generates ROS, contributing to the detrimental effects of UV light on health. Free radicals are compounds that have one or more unpaired electrons in their electron orbital. Electrons in pairs tend to be more stable, while free radicals are generally more reactive than those without unpaired electrons. Radicals can pair up their unpaired electrons through the creation of a covalent bond. Radicals can either donate electrons (reducing action), accept electrons from non-radical molecules (oxidizing action), or merge into non-radicals during interactions. Non-radicals can transform into radicals, leading to diverse impacts on physiology. Oxidative stress arises when the production of ROS exceeds the capacity of the body's antioxidant defences, resulting in a state of imbalance. Oxidative stress can cause cell damage, including lipid peroxidation and DNA fragmentation, which can result in apoptosis and cell death [15]. The body produces ROS continuously, which can originate from either external or internal sources. Mitochondria produce endogenous ROS by reducing oxygen to make adenosine triphosphate (ATP), a process that includes adding four electrons to create water as a byproduct. In the electron transport chain (ETC), the vast majority of oxygen undergoes reduction, a process that typically does not produce byproducts. However, around 5% of oxygen is reduced via a univalent pathway, which leads to the creation of free radicals. The ROS generation is influenced by some factors such as the composition of the mitochondrial membrane, species differences, and age. The primary activities within mitochondria are reduction-

oxidation (redox) reactions. These reactions promote electron transfer and movement, involving the enzyme cytochrome oxidase, which is solely responsible for reactions utilizing oxygen. It has been noted that redox reactions in the ETC predominantly generate superoxide (O_2^-), with the most significant production of ROS occurring at complex III, and to a lesser extent, complex I. Additionally, ROS formation also occurs in the endoplasmic reticulum (ER) and cellular peroxisomes. External or exogenous sources are plentiful and contribute significantly to the majority of ROS in the body [7].

Superoxide dismutase (SOD) was first identified by Irwin Fridovich in 1967, with significant contributions detailed by McCord and Fridovich in 1969. Humans possess three primary forms of SOD: Cu, Zn-SOD (SOD1), Mn-SOD (SOD2), and EC-SOD (SOD3), as noted in research by Matsuda *et al.* in 2018. SOD is predominantly found in the cytoplasm and is recognized as one of the most potent enzymes in neutralizing oxidative stress. It effectively catalyzes the dismutation of superoxide anion radicals into less reactive molecules. SODs have the capability to bind negatively charged anions, such as fluoride and azide, with different levels of affinity. The SOD function can be suppressed by certain copper chelators, including ethylenediaminetetraacetic acid (EDTA) and cuprizone. In particular, Mn-SOD (SOD2) is a homotetrameric enzyme that integrates manganese into its active site and is primarily found within the mitochondria. In the dismutation reaction, Mn ions transition from the stable oxidation state of Mn(III) to the stable oxidation state of Mn(II). Various triggers, such as inflammatory cytokines, alterations in redox equilibrium, and ionizing radiation, activate the Mn-SOD gene [8] (Figure 2).

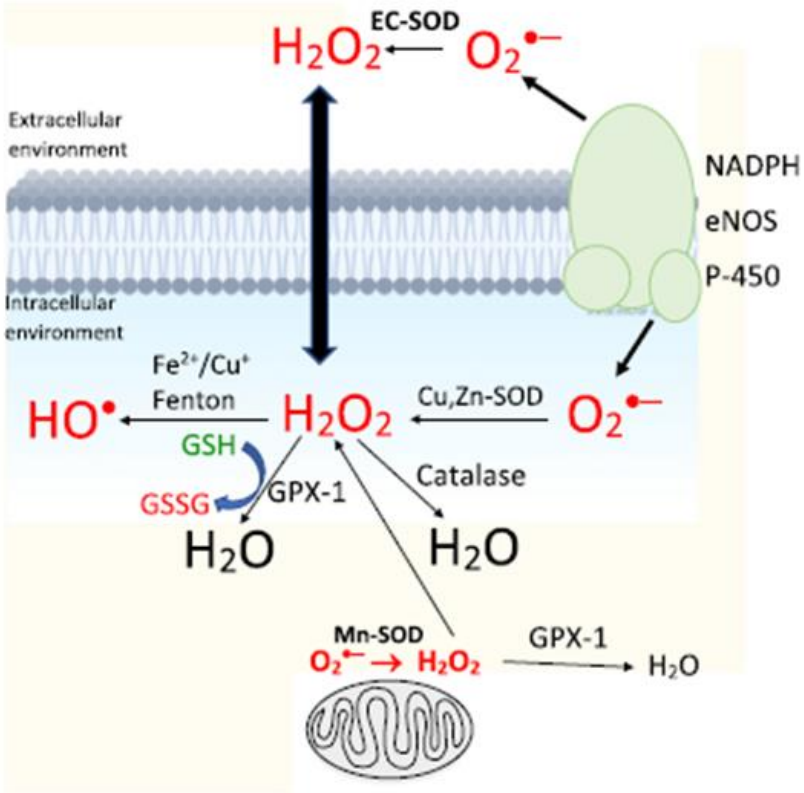

FIGURE 2 The role of SOD and CAT in the process of reducing free radical levels [8]

The role of SOD2 and CAT in oxidative stress process in lens epithelial

SOD is an enzyme that functions as an antioxidant by neutralizing superoxide radicals and transforming them into hydrogen peroxide. Two factors contribute to the decline in SOD levels: (i) When more ROS like O_2 are produced, SOD is used to convert O_2 into H_2O_2 and (ii) H_2O_2 also hinders the function of SOD [9]. Various kinds of SOD vary in their metal-binding capacity, cellular localization, and susceptibility to different chemicals. SOD catalyzes a dismutation reaction where one O_2 is oxidized to oxygen and another O_2 is reduced to hydrogen peroxide, removing O_2 in the process [10].

Antioxidant enzymes located in mitochondria collaborate with protein reduction and repair systems to protect against damage from ROS and prevent cell death in the eye. Specifically, SOD enzymes such as SOD1 and SOD2 are critical in safeguarding cells from oxidative harm. These enzymes efficiently neutralize ROS, thereby reducing the risk of oxidative stress-related cellular damage. SOD2 is particularly involved in the process of apoptosis. SOD2, located in the mitochondria, plays a vital role in converting superoxide radicals (O_2^-) produced by the ETC into hydrogen peroxide. This conversion is crucial for mitigating oxidative stress within cells. The SOD2 regulation, both up-regulation and down-regulation, has been demonstrated to be essential in protecting lens epithelial cells from oxidative stress, highlighting its significance in maintaining cellular health and preventing damage. Increased expression of SOD2 throughout the lens has been shown to decrease H_2O_2-induced harm to the lens, thereby lowering the occurrence of cataracts [11]. The impact of SOD2 on cell death was studied in cultured human lens epithelial cells. Cells with elevated levels of this enzyme showed increased resilience to the harmful effects of H_2O_2, O_2^-, and UV-B exposure. Furthermore, the lack of SOD2 led to significant mitochondrial damage, the release of cytochrome C, the activation of caspase 3, and a rise in apoptotic cell death [12].

Hydrogen peroxide is converted to water and oxygen by CAT. The primary site of CAT activity is within peroxisomes, which are subcellular organelles. Galactosylation facilitated the specific transportation of catalase to the liver, resulting in the inhibition of liver metastasis and a reduction in matrix metalloproteinase activity. In contrast, a drop in catalase levels was found to be associated with the development of malignant characteristics in mouse keratinocytes induced by carcinogens. CAT further reduced the expression of matrix metalloproteinase and the deposition of collagen, both in the basal state and in a manner reliant on manganese superoxide dismutase (MnSOD) [13].

The CAT enzyme catalyses the decomposition of two molecular byproducts of hydrogen peroxide into two water molecules and one oxygen molecule. The reaction takes place in two distinct phases. In the initial step, the first H_2O_2 molecule is reduced, resulting in the formation of oxyferryl species (FeIVO). During the following stage, the FeIVO complex undergoes reduction by two H_2O_2 molecules, leading to the formation of O_2 and H_2O. CAT plays a crucial role in the development of oxidative stress-related illnesses, including inflammation, mutagenesis, and inhibition of apoptosis. A deficiency in CAT is associated with a wide range of diseases, including neurological conditions like Alzheimer's disease, Parkinson's disease, schizophrenia, and bipolar disorder; metabolic disorders such as diabetes, hypertension, and insulin resistance; and other serious health issues including cancer, anemia, and asthma. CAT holds promise as a treatment option for diseases related to oxidative stress [14].

The initial process to be addressed is the ROS generation produced by UV radiation

through the enzyme CAT. CAT may decompose hydrogen peroxide into water and oxygen by the catalytic reaction $2H_2O_2 \rightarrow 2H_2O + O_2$. CAT enzyme has peroxidatic activity at low concentrations of hydrogen peroxide (H_2O_2). UV-B radiation leads to elevated levels of ROS in keratinocytes, particularly in cells deficient in glutathione. Subsequent tests revealed that the protein's oxidant generator was CAT [15].

UV-B light affects CAT activity in a pH-sensitive and oxygen-dependent manner. The intracellular level of oxidants influences whether the CAT reaction to UV radiation is harmful or beneficial. Shortwave UV light is believed to change the H_2O_2 binding site on the catalase enzyme, enabling water molecules to reach heme iron. This enables the water molecule to serve as a proton production source. These protons can combine with diatomic oxygen to produce ROS such as peroxides. The enzyme's charge relay network was determined to have a crucial role in the UV light-induced effects on CAT. UV-B light affects CAT activity in a pH-sensitive and oxygen-dependent manner. The intracellular level of oxidants influences whether CAT activity in response to UV radiation is harmful or beneficial [16].

UV-B Protection with UV Blocking Glasses and UV Blocking Contact Lenses

Glasses and contact lenses are tools that have been proven to protect the lens by reducing UV-B radiation. The reflective film coating on eyeglass lenses offers numerous optical advantages to the wearer. Eyeglass lenses coated with UV-absorbing or UV-reflective monomers reflect UV wavelengths outside the visible spectrum, limiting UV transmission to the eye [17]. Multiple investigations offered a clinical understanding of safeguarding the visual system from UV wavelengths and evaluated the UV-blocking characteristics of two types of spectacle lenses: one with a UV400 coating and one with a photochromic coating. Eyeglass lenses coated with anti-UV protection can prevent UVB-induced damage to the eyes' surface. No histologic abnormalities were seen under the microscope [18].

Research has demonstrated that soft contact lenses can decrease the level of UV radiation that reaches the front part of the eye and are suggested as a way to shield the eye from the harmful effects of UV light. Soft contact lenses with their large diameter can cover the cornea and perilimbal around the conjunctiva, which greatly protects the ocular surface [19]. UV absorption or transmission levels vary significantly across different brands of these contact lenses. UV-blocking contact lenses are recommended for those with hypersensitivity to UV light, aphakia, or professionals who are regularly exposed to high levels of UV light in their work. Contact lenses provide augmented defence against UV radiation by enveloping the cornea and blocking reflected and dispersed rays. Yet, the majority of commercial contact lenses do not offer complete protection against UV rays [20]. A grading system is implemented to quantify the UV-blocking efficacy of contact lenses. Class I lenses effectively filter out 90% of UV-A light in the range of 316-380 nm and 99% of UV-B light in the range of 280-316 nm. On the other hand, Class II lenses block 70% of UV-A light and 90% of UV-B light. ACUVUE brand lenses are the only commercially available lenses that have Class I blocking, notwithstanding the issuance of several patents for anti UV-B contact lenses [21].

Conclusion

UV-B radiation has been demonstrated in numerous investigations to induce alterations in the expression of SOD2 and CAT. Measuring SOD2 and CAT expression can potentially indicate the effectiveness of protective equipment and demonstrate that UV-B radiation triggers the intrinsic mechanism of oxidative stress.

UV-B radiation-induced cataract have become more common in recent times. Protective equipment like spectacles and contact lenses are frequently used to minimize the impact of UV-B radiation. The utilization of these protective equipment is highly beneficial, particularly in regions with intense UV-B exposure, such as the equatorial zone.

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***Orcid*:**

Made Dessy Gangga Ayu Cinthiadewi:
https://orcid.org/0009-0004-4408-4485
*Muhammad Firmansjah *:*
https://orcid.org/0009-0009-9063-0906
Nurwasis Nurwasis:
https://orcid.org/0000-0001-8302-729X
Ni Putu Ayu Reza Dhiyantari:
https://orcid.org/0000-0001-8527-3072
Rifat Nurfahri:
https://orcid.org/0000-0002-5238-0362

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