
Abstract
Because of the risk of thermal damage to the pulp, the temperature rise induced by light-curing units should not be too high. LED (light emitting diode) curing units have the main part of their irradiation in the blue range and have been reported to generate less heat than QTH (quartz-tungsten-halogen) curing units. This study had two aims: first, to measure the temperature rise induced by ten LED and three QTH curing units; and, second, to relate the measured temperature rise to the power density of the curing units. The light-induced temperature rise was measured by means of a thermocouple embedded in a small cylinder of resin composite. The power density was measured by using a dental radiometer. For LED units, the temperature rise increased with increasing power density, in a statistically significant manner. Two of the three QTH curing units investigated resulted in a higher temperature rise than LED curing units of the same power density. Previous findings, that LED curing units induce less temperature rise than QTH units, does not hold true in general.

Schlagwörter
Composite Resins; chemistry; radiation effects; Equipment Design; Humans; Lighting instrumentation; Materials Testing; Temperature; Thermometers

Boatright, Jeffrey H.; Moring, Anisha G.; McElroy, Clinton; Phillips, Michael J.; Do, Vi T.; Chang, Bo et al. (2007): Tool from ancient pharmacopoeia prevents vision loss. In: Molecular vision, Jg. 12, S. 1706–1714.

Abstract
PURPOSE: Bear bile has been used in Asia for over 3,000 years to treat visual disorders, yet its therapeutic potential remains unexplored in Western vision research. The purpose of this study was to test whether treatment of mice undergoing retinal degeneration with taoursodeoxycholic acid (TUDCA), a primary constituent of bear bile, alters the course of degeneration. METHODS: Two retinal degeneration models were tested: the rd10 mouse, which has a point mutation in the gene encoding the beta subunit of rod phosphodiesterase, and light induced retinal damage (LIRD). For LIRD studies, albino Balb/C adult mice were subcutaneously injected with TUDCA (500 mg/kg body weight) or vehicle (0.15 M NaHCO(3)). Sixteen h later, each mouse received repeat injections. Half of each treatment group was then placed in bright light (10,000 lux) or dim light (200 lux) for seven h. At the end of exposure, animals were transferred to their regular housing. Electroretinograms (ERGs) were assessed 24 h later, mice sacrificed, eyes embedded in paraffin and sectioned, and retina sections assayed for morphology and apoptosis by TUNEL and anti-active caspase-3 immunoreactivity via fluorescent confocal microscopy. A subset of mice were sacrificed 8 and 15 days after exposure and retina sections analyzed for morphology and apoptosis. For rd10 studies, mice were injected subcutaneously with TUDCA or vehicle at postnatal (P) days 6, 9, 12, and 15. At p18, ERGs were recorded, mice were euthanized and eyes were harvested, fixed, and processed. Retinal sections were stained (toluidine blue), and retinal cell layers morphometrically analyzed by light microscopy. Consecutive sections were analyzed for apoptosis as above. RESULTS: By every measure, TUDCA greatly slowed retinal degeneration in LIRD and rd10 mice. ERG a-wave and b-wave amplitudes were greater in mice treated with TUDCA compared to those treated with vehicle. Retinas of TUDCA-treated mice had thicker outer nuclear layers, more photoreceptor cells, and more fully-developed photoreceptor outer segments. Finally, TUDCA treatments dramatically suppressed signs of apoptosis in both models. CONCLUSIONS: Systemic injection of TUDCA, a primary constituent of bear bile, profoundly suppressed apoptosis and preserved function and morphology of photoreceptor cells in two disparate mouse models of retinal degeneration. It may be that bear bile has endured so long in Asian pharmacopoeias due to efficacy resulting from this anti-apoptotic and neuroprotective activity of TUDCA. These results also indicate that a systematic, clinical assessment of
TUDCA may be warranted.

Schlagwörter
Animals; Apoptosis drug effects; Bile chemistry; Blindness etiology prevention & control; Cyclic Nucleotide Phosphodiesterases, Type 6; Disease Models, Animal; Electroretinography; Injections, Subcutaneous; Light; Medicine, East Asian Traditional; Mice; Mice, Mutant Strains; Phosphoric Diester Hydrolases genetics; Photoreceptor Cells, Vertebrate drug effects pathology; Retinal Degeneration complicationsetiology genetics physiopathology; Taurochenodeoxycholic Acid administration & dosage pharmacology; Ursidae


Abstract
Phototherapy of newborn infants with blue or green light is the most common treatment of neonatal hyperbilirubinemia. Using bilirubin bound to human lymphoid and basal skin cells we obtained the green light dose dependency of the bilirubin phototoxicity to these cell types. Cells (3-5 x 10^6/mL) were incubated with bilirubin complexed to human serum albumin (final concentrations 340 microM bilirubin, 150 microM albumin). Under these conditions all cells showed maximum binding of bilirubin. Irradiation with broadband green light (lambda max = 512 nm) over 24 h led to a light dose-dependent population of cells, which contained no bilirubin on the cell membrane as determined by Nomarski interference microscopy. The light-induced mechanism of the disappearance of bilirubin caused lethal membrane damage to the cells (trypan blue exclusion test). The cell kill rate increased with the irradiation dose and with the fraction of cells with no bilirubin. When 90% of lymphoid cells were bilirubin free, 46% of them were dead (using 480 J cm^{-1} green light). Similar results were obtained with basal skin cells. In addition, bilirubin-induced damage of cell membrane and nuclear membrane was also shown by transmission electron microscopy. Bilirubin (340 microM) in the dark led to 5% of the cells being killed. Basal skin cells bind 2.5 times more bilirubin molecules than lymphoid cells and showed a different bilirubin disappearance. Irradiation of bilirubin in carbon tetrachloride with 514.5 nm laser light showed generation of singlet oxygen via its luminescence at 1270 nm. These results demonstrate that green light phototherapy of hyperbilirubinemia may cause both skin and immune system damage.

Schlagwörter
Bilirubin metabolism radiation effects; Cell Death radiation effects; Cells, Cultured; Humans; Light; Lymphocytes cytology metabolism radiation effects; Phototherapy adverse effects; Skin cytology metabolism radiation effects; Spectrophotometry


Abstract
BACKGROUND: Clinical evidence of injury to the retinal pigment epithelium is an important feature of age-related macular degeneration, but the mechanism of this injury is unknown. Blue-light-dependent activation of the blood-borne photosensitizer protoporphyrin IX is known to produce free radicals which may damage cells and tissues. This study was undertaken to determine the effect of blue light and protoporphyrin IX on retinal pigment epithelial cells in vitro.

METHODS: Third-passage porcine retinal pigment epithelial cells were plated in six-well culture plates at 100,000 cells/well and grown to confluence. Retinal pigment epithelial cells were then incubated in culture media with and without 35 micrograms/dl protoporphyrin IX and exposed to low intensity (118 microW/cm^2) blue, blue-free, or full-spectrum white light in an irradiating incubator for 16 h on/8 h off cycles for 7 days. Some of the wells were shielded from light (dark controls). Retinal pigment epithelial cells were examined by light microscopy and were trypsinized and counted after 7 days. RESULTS: White light with and without
protoporphyrin IX and protoporphyrin IX in dark conditions did not decrease the retinal pigment epithelial cell count significantly. Blue light alone and blue light with protoporphyrin IX decreased the cell count by 22 +/- 4% and 35 +/- 3% compared to the controls, respectively. CONCLUSION: Blue wavelength light without exogenous protoporphyrin IX has a cytotoxic effect on confluent cultures of retinal pigment epithelium, suggesting that endogenous photosensitizers may be present in retinal pigment epithelial cells. Protoporphyrin IX has an additive cytotoxic effect in the presence of blue light, suggesting that this photosensitizer is capable of mediating blue-light-induced retinal pigment epithelial damage. Since protoporphyrin IX is present in blood and tissue fluids, and the retina is chronically exposed to light, protoporphyrin IX-mediated free radical formation may occur in vivo and may play a role in retinal pigment epithelial changes that occur early in the pathogenesis of age-related macular degeneration.


Abstract

OBJECTIVE: To investigate the effect of blue light on apoptosis and mitochondrial permeability transition (MPT) of cultured human retinal pigment epithelium (RPE) cells in vitro. METHODS: Human RPE cells were exposed to blue light (wave length 470 -490 nm). The present study consisted of three parts. Part one studied the effect of various intensities of blue light on the RPE cells. Cells were irradiated with (500 +/- 100) lx (group 1) , (2000 +/- 500) lx (group 2) and (3000 +/- 500)lx ( group 3) blue light, and followed by 24 hours observation. Part two studied the effect of various duration of blue light at identical intensity on the RPE cells. For the study on various subtypes of RPE cells, cells were irradiated by blue light at (2000 +/- 500) x for 6, 12, and 24 hours. For the study of mitochondrial membrane potential, cells were irradiated for 3, 6, and 12 hours. Part three studied cells irradiated with blue light at identical intensity and duration, but with various prolongation of post-exposure culture. The prolongation of post-exposure culture was 6, 12, 24, and 36 hours. Phototoxicity was quantified at various periods after exposure by staining of the nuclei of membrane-compromised cells, by TdT-dUTP terminal nick-end labeling (TUNEL) of apoptotic cells and by Annexin V labeling for phosphatidylserine exposure. Transmission electronmicroscopy was used to determine the ultrastructure changes of RPE cells. Mitochondrial membrane potential ( deltaPsim ) was measured by rhodamine 123 staining and subsequent flow cytometry. Cytochrome C activity was assayed by ELISA. Caspase-3 was detected by colorimetric assay. RESULTS: TUNEL-positive labeling cells in first group of part two study showed cell shrinkage, membrane blebbing, apoptotic body, condensation and fragmentation of chromatin. Mitochondrial swelling, extinction of inner mitochondrial membrane ridge, dilation of rough endoplasmic reticulum and increase of the lysosome were also observed in transmission electronmicroscopy. Blue light at (500 +/- 100) x intensity did not induce damage to RPE cells, but decrease of deltaPsim was observed. A significant increase of apoptotic, apoptotic necrotic and necrotic percentages, as well as significant decrease of deltaPsim were observed at higher light intensity in part one study. Increase of apoptotic percentage was the main response to shorter exposure of blue light. Increase of apoptotic necrotic and necrotic percentage and pronounced decrease of deltaPsim occurred in cells irradiated by longer exposure in part two study. In part 3 study, apoptotic response was increased gradually during 6 and 12 hours prolongation of post-exposure culture, more apoptotic necrosis or necrosis were found after post-exposure 24 hours. Decrease of deltaPsim was observed in 6 hours prolongation of post-exposure culture and lasting for 48 hours. The concentration of cytochrome C
was significantly increased in post-exposure 24 and 36 hours, without any changes of Caspase-3 activity. CONCLUSIONS: Blue light exposure can induce damages to human RPE cells in vitro, which include apoptosis, apoptotic necrosis and necrosis. These changes are caused by triggering the mitochondrial permeability transition, which results in decrease of deltaPsim and release of cytochrome C. deltaPsim can be used as an earlier parameter of blue light-induced apoptosis.


Abstract

OBJECTIVE: To answer the question whether mitochondrial permeability transition (MPT) participates in blue light-induced damage to human retinal pigment epithelium (RPE) cells, this study was directed at assessing the effect of blue light on mitochondrial membrane potential (delta psi(m)) and cytochrome C (Cyt C) of cultured human RPE cells. METHODS: Human RPE cells were exposed to blue light (wave length 470-490 nm); delta psi(m) was measured by rhodamine 123 staining and subsequent flow cytometry. Three groups were investigated: Group A (exposure to different intensity of blue light); group B (exposure to identical intensity for different duration); group C (exposure to identical intensity and duration, different prolongation of post-exposure culture). Cyt C activity was assayed by ELISA. Caspase-3 was detected by colorimetric assay. In these aspects, two groups were investigated: Group I [(2000+/-500) 1x for 6 h]; Group II [(2000+/-500) 1x for 12 h]. RESULTS: When human RPE cells were exposed to blue light, the more pronounced decrease of delta psi(m) was consistent with the increase of light intensity in group A. Pronounced decrease of delta psi(m) was seen at 6 h and 12 h of exposure duration in group B. At 6 h prolongation of post-exposure culture in group C, the decrease of delta psi(m) was observed, lasting 48 h. The concentration of Cyt C was detected; no significant changes were found at 6 h and 12 h prolongation of post-exposure culture, but a significant increase was found at 24 h and 36 h post-exposure in the two groups. The increase was more significant in Group II than in Group I at 24 h post-exposure. The activity change of caspase-3 was not found in the two groups. CONCLUSION: Blue light exposure over threshold can induce damage to human RPE cells, probably by triggering the mitochondrial permeability transition, which results in the decrease of delta psi(m) and the release of cytochrome C.

Schlagwörter

Caspase 3; Caspasesmetabolism; Cells, Cultured; Cytochromes cmetabolismradiation effects; Humans; Light; Membrane Potentialsradiation effects; Mitochondriaphysiology; Pigment Epithelium of Eyecytologyradiation effects


Abstract

Clinical evidence indicates that phototherapy of hyperbilirubinaemia in newborn infants is a safe and efficient form of therapy. The short-term side effects are not serious and seem to be well controlled. There are few long-term follow-up studies of phototherapy-treated infants. Therefore one cannot completely exclude the possibility that side effects can be found in future studies. With this background we undertook the present study of possible genotoxic effects of phototherapy. Human cells of the established glioblastoma cell line TMG-1 were used. The cells were exposed to visible light in the presence of different concentrations of bilirubin or in the absence of bilirubin. DNA was unwound in alkaline solution and the induction of strand breaks was assayed by a method taking advantage of the fluorescence from the dye Hoechst 33258. Blue light induced single-strand breaks in the DNA of cells in culture in the absence of bilirubin. During irradiation of bilirubin solutions with blue and green phototherapy light, long-lived toxic photoproducts were formed under in vitro conditions. At high and clinically relevant bilirubin concentrations, the effects of
blue and green light were relatively similar. At low concentrations, there was a smaller effect of green light as expected from the absorption spectrum of bilirubin. It remains to be seen whether the genotoxic effect observed in the present studies can occur in vivo.

**Abstract**

The induction of single-strand breaks (SSB) and the kinetics of SSB repair were measured in two Chinese hamster ovary cell lines irradiated with monochromatic photons of near-visible radiation (405 nm) and blue light (434 nm). The radiosensitive and UV-A-sensitive mutant line EM9 is known to repair SSB induced by ionizing radiation or 365-nm UV-A more slowly than the parent line AA8. At the 10% survival level, EM9 cells were 1.7- and 1.6-fold more sensitive than AA8 cells to 405 and 434 nm radiation, respectively. This sensitivity was not due to differences in induction of SSB because AA8 and EM9 cells accumulated the same number of initial breaks when irradiated at 0.5 degrees C with either 405 nm (5.9 SSB per MJ/m2) or 434 nm (5.1 SSB per MJ/m2), as measured by alkaline elution. When the cells repaired these SSB at 37 degrees C in full culture medium, biphasic repair kinetics were observed for both cell lines. In both phases of repair, EM9 cells repaired breaks induced by both wavelengths more slowly than did AA8 cells. The t1/2 values for the repair phases for 405-nm-induced SSB were 3.8 and 150 min for EM9, and 1.5 and 52 min for AA8; the corresponding values for repair of 434 nm breaks were 3.7 and 39 min for EM9, and 2.0 and 30 min for AA8. Because of this slower repair, EM9 cells left more SSB unrepaired after 90 min than did AA8 cells for both wavelengths.(ABSTRACT TRUNCATED AT 250 WORDS)

**Schlagwörter**

Animals; CHO Cells; Cell Survival; DNA Repair; DNA, Single-Stranded; Light; Ultraviolet Rays


**Abstract**

The structural changes associated to non-photochemical quenching in cyanobacteria is still a matter of discussion. The role of phycobilisome and/or photosystem mobility in this mechanism is a point of interest to be elucidated. Changes in photosystem II fluorescence induced by different quality of illumination (state transitions) or by strong light were characterized at different temperatures in wild-type and mutant cells, that lacked polyunsaturated fatty acids, of the cyanobacterium Synechocystis PCC 6803. The amplitude and the rate of state transitions decreased by lowering temperature in both strains. Our results support the hypothesis that a movement of membrane complexes and/or changes in the oligomerization state of these complexes are involved in the mechanism of state transitions. The quenching induced by strong blue light which was not associated to D1 damage and photoinhibition, did not depend on temperature or on the membrane state. Thus, the mechanism involved in the formation of this type of quenching seems to be unrelated to the movement of membrane complexes. Our results strongly support the idea that the mechanism involved in the fluorescence quenching induced by light 2 is different from that involved in strong blue light induced quenching.

**Schlagwörter**

Cyanobacteria; Genetics; Metabolism; Fluorescence; Light; Oxidation-Reduction; Photosynthetic Reaction Center Complex Proteins; Metabolism; Phycobilisomes; Temperature; Thylakoid metabolism

Abstract
Why the leaves of many woody species accumulate anthocyanins prior to being shed has long puzzled biologists because it is unclear what effects anthocyanins may have on leaf function. Here, we provide evidence for red-osier dogwood (Cornus stolonifera) that anthocyanins form a pigment layer in the palisade mesophyll layer that decreases light capture by chloroplasts. Measurements of leaf absorbance demonstrated that red-senescing leaves absorbed more light of blue-green to orange wavelengths (495-644 nm) compared with yellow-senescing leaves. Using chlorophyll a fluorescence measurements, we observed that maximum photosystem II (PSII) photon yield of red-senescing leaves recovered from a high-light stress treatment, whereas yellow-senescing leaves failed to recover after 6 h of dark adaptation, which suggests photo-oxidative damage. Because no differences were observed in light response curves of effective PSII photon yield for red- and yellow-senescing leaves, differences between red- and yellow-senescing cannot be explained by differences in the capacities for photochemical and non-photochemical light energy dissipation. A role of anthocyanins as screening pigments was explored further by measuring the responses PSII photon yield to blue light, which is preferentially absorbed by anthocyanins, versus red light, which is poorly absorbed. We found that dark-adapted PSII photon yield of red-senescing leaves recovered rapidly following illumination with blue light. However, red light induced a similar, prolonged decrease in PSII photon yield in both red- and yellow-senescing leaves. We suggest that optical masking of chlorophyll by anthocyanins reduces risk of photo-oxidative damage to leaf cells as they senesce, which otherwise may lower the efficiency of nutrient retrieval from senescing autumn leaves.

Schlagwörter
Adaptation, Physiological; Anthocyanins; metabolism; radiation effects; Apoptosis; Carotenoids; metabolism; radiation effects; Chlorophyll; metabolism; radiation effects; Chloroplasts; physiology; radiation effects; Cornus; physiology; radiation effects; Darkness; Fluorescence; Light; Light-Harvesting Protein Complexes; Nitrogen metabolism; Oxidative Stress; Photosynthesis; physiology; radiation effects; Photosynthetic Reaction Center Complexes; Protein Complexes; Plant Epidermis; physiology; radiation effects; Plant Leaves; physiology; radiation effects; Seasons


Abstract
PURPOSE: Acute white-light damage to rods depends on the amount of rhodopsin available for bleaching during light exposure. Bleached rhodopsin is metabolically regenerated through the visual cycle involving the pigment epithelium, or photochemically by deep blue light through photoreversal of bleaching. Because photoreversal is faster than metabolic regeneration of rhodopsin by several orders of magnitude, the photon catch capacity of the retina is significantly augmented during blue-light illumination, which may explain the greater susceptibility of the retina to blue light than to green light. However, blue light can also affect function of several blue-light-absorbing enzymes that may lead to the induction of retinal damage. Therefore, this study was conducted to test whether rhodopsin and its bleaching intermediates play a role in blue-light-induced retinal degeneration.

METHODS: Eyes of anesthetized rats and mice that did or did not contain rhodopsin were exposed to green (550 +/- 10 nm) or deep blue (403 +/- 10 nm) light for up to 2 hours. Rats with nearly rhodopsinless retinas were obtained by bleaching rhodopsin in animals with inhibited metabolic rhodopsin regeneration—that is, under halothane anesthesia. In addition, Rpe6S(-/-) mice that are completely without rhodopsin were used to test the susceptibility to blue-light damage of a rodent retina.
completely devoid of the visual pigment. Effects of illumination on photoreceptor morphology were assessed 24 hours or 10 days thereafter by morphologic and biochemical methods. RESULTS: Exposure to blue light resulted in severe retinal damage and activation of the transcription factor AP-1 in rats. In contrast, green light had no effect. When rhodopsin was almost completely bleached by short-term green-light exposure while metabolic regeneration (but not photoreversal) was prevented by halothane anesthesia, blue-light exposure induced distinct lesions in rat retinas. When both metabolic rhodopsin regeneration and photoreversal of bleaching were almost completely inhibited, blue-light exposure caused only very moderate lesions. When mice without rhodopsin were exposed to blue light, no damage occurred, in contrast to wild-type control mice. CONCLUSIONS: Short time exposure to blue light has deleterious effects on retinal morphology. Because damage was observed only in the presence of the visual pigment, blue-light-induced retinal degeneration is rhodopsin mediated. Absorption of blue light by other proteins is not sufficient to induce light damage. Photoreversal of bleaching, which occurs only in blue but not in green light, increases the photon-catch capacity of the retina and may thus account for the difference in the damage potential between blue and green light.

Schlagwörter
Animals; DNA analysis; DNA Fragmentation; In Situ Nick-End Labeling; Light adverse effects; Male; Mice; Inbred C57BL; Mice, Knockout; Radiation Injuries, Experimental; etiologymetabolism; pathology; Rats; Rats, Sprague-Dawley; Retinametabolism; pathology; radiation; effects; Retinal Degeneration; etiology; metabolism; pathology; Rhodopsingenetics; metabolism; radiation; effects; Transcription Factor AP-1; metabolism

Abstract
Photoinhibition of PSII occurs at the same quantum efficiency from very low to very high light, which raises a question about how important is the rate of photosynthetic electron transfer in photoinhibition. We modulated electron transfer rate and light intensity independently of each other in lincomycin-treated pea leaves and in isolated thylakoids, in order to elucidate the specific effects of light and PSII electron transport on photoinhibition. Major changes in the rate of electron transport caused only small changes in the rate of photoinhibition, suggesting the existence of a significant photoinhibitory pathway that contains an electron-transfer-independent phase. We compared the action spectrum of photoinhibition with absorption spectra of PSII components that could function as photoreceptors of the electron-transfer-independent phase of photoinhibition and found that the absorption spectra of Mn(III) and Mn(IV) compounds resemble the action spectrum of photoinhibition, showing a steep decrease from UV-C to blue light and a low visible-light tail. Our results show that the release of a Mn ion to the thylakoid lumen is the earliest detectable step of both UV- and visible-light-induced photoinhibition. After Mn release from the oxygen-evolving complex, oxidative damage to the PSII reaction center occurs because the Mn-depleted oxygen-evolving complex cannot reduce P680+ normally.

Schlagwörter
Cucurbitametabolism; Electron Transport; physiology; Glyceraldehyde; Light; Manganese Compoundsmetabolism; Oxygenmetabolism; Peasmetabolism; Photochemistry; Photosynthesis; radiation; effects; Photosystem II Protein Complex; metabolism; radiation; effects; Thylakoids; metabolism

Abstract
Violet-blue light is toxic to mammalian cells, and this toxicity has been linked with cellular production of H2O2. In this report, we show that violet-blue light, as well as
UVA, stimulated H2O2 production in cultured mouse, monkey, and human cells. We found that H2O2 originated in peroxisomes and mitochondria, and it was enhanced in cells overexpressing flavin-containing oxidases. These results support the hypothesis that photoreduction of flavoproteins underlies light-induced production of H2O2 in cells. Because H2O2 and its metabolite, hydroxyl radicals, can cause cellular damage, these reactive oxygen species may contribute to pathologies associated with exposure to UVA, violet, and blue light. They may also contribute to phototoxicity often encountered during light microscopy. Because multiphoton excitation imaging with 1,047-nm wavelength prevented light-induced H2O2 production in cells, possibly by minimizing photoreduction of flavoproteins, this technique may be useful for decreasing phototoxicity during fluorescence microscopy.

Schlagwörter
3T3 Cells; Acyl-CoA Oxidase; Animals; Cell Line; Cercopithecus aethiops; Cytoplasm radiation effects; Enzyme Activation; radiation effects; Humans; Hydrogen Peroxide metabolism; Intracellular Membranes; radiation effects; Light; Mice; Microbodies; radiation effects; Mitochondria; radiation effects; Models, Chemical; Oxidoreductases metabolism; radiation effects; Rats; Recombinant Proteins; metabolism; radiation effects; Transfection; Ultraviolet Rays; Xanthine Oxidase metabolism; radiation effects


Abstract
Due to its function of light perception, the eye is exposed to high levels of radiation of the optical spectrum. Most of the ultraviolet and infrared radiation is absorbed in the cornea and lens, and mostly only radiation of the visible spectrum can reach the retina. Visible light can cause retinal damage by photomechanical, photothermal, and photochemical mechanisms. The most important mechanism of light damage to the retina under daily conditions or when using ophthalmologic light sources is the photochemical light toxicity caused by light-induced chemical reactions. The extent of damage depends on several factors, such as wavelength, exposure time, and irradiance. Particularly the shorter portion of the visible light spectrum (blue light) is responsible for photochemical damage to the retina.

Hwang, In-Yong; Son, Young-Ok; Kim, Ji-Hae; Jeon, Young-Mi; Kim, Jong-Ghee; Lee, Choon-Bong et al. (2008): Plasma-arc generated light inhibits proliferation and induces apoptosis of human gingival fibroblasts in a dose-dependent manner. In: Dental materials : official publication of the Academy of Dental Materials, Jg. 24, H. 8, S. 1036–1042. Online verfügbar unter doi:10.1016/j.dental.2007.11.018.

Abstract
OBJECTIVE: This study examined the effects of blue light exposure on the proliferation and cytotoxicity of human gingival fibroblasts (HGF). Cellular mechanism by which blue light causes cytotoxic effects was also investigated.

METHODS: HGF were exposed to the plasma-arc generated blue light with various energy densities ranging from 2 to 48J/cm(2). After light exposure of the cells, they were processed for analyzing tritium incorporation, succinate dehydrogenase (SDH) activity, trypan blue exclusion, and DNA fragmentation. In addition, possible mechanism of the light-mediated cytotoxicity was investigated through flow cytometric and Western blot analyses.

RESULTS: Blue light exposure significantly inhibited proliferation and SDH activity of HGF in a dose-dependent manner; exposure more than 12J/cm(2) had a toxic effect on the cells. The blue light-induced cytotoxicity of the cells resulted from apoptosis, as proven by the migration of many cells to the sub-G(1) phase of cell cycle and the appearance of DNA ladders. Additional experiments revealed that blue light induces apoptosis of HGF through mitochondrial stress and poly (ADP ribose) polymerase cleavage.

SIGNIFICANCE: This study suggests that plasma-arc generated blue light exerts some harm to cells, particularly damaging effect to DNA, and thus a long curing
Methylene blue plus light-induced lipid peroxidation in rat liver microsomes: inhibition by nicotinamide (vitamin B3) and other antioxidants. In: Chemico-biological interactions, Jg. 99, H. 1-3, S. 1–16.

Abstract

Methylene blue plus visible light, in the presence of oxygen, induced lipid peroxidation in rat liver microsomes, as assessed by the formation of thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides and the loss of membrane-bound enzymes. Peroxidation was enhanced by deuteration of the buffer and inhibited by scavengers of singlet oxygen (1O2) and superoxide (O2.-). The damage induced seemed to be mainly due to Type II involving 1O2 and to a lesser extent Type I reactions with O2.- and hydroxyl radical (.OH) as intermediates. Nicotinamide or vitamin B3, an endogenous metabolite occurring at high concentrations in tissues, had a relatively high rate constant of 1.8 × 10^8 M^-1 s^-1 with 1O2 and had a significant inhibitory effect on lipid peroxidation induced by photosensitization. This effect was both time- and concentration-dependent, high inhibition being associated with millimolar concentrations. Chemically related endogenous compounds like tryptophan and isonicotinic acid also had significant inhibitory properties. Similar protective effects were observed with natural antioxidants such as beta-carotene, canthaxanthin, lipoic acid, glutathione, alpha-tocopherol and to a lesser extent ascorbic acid. Nicotinamide was a more effective antioxidant than ascorbic acid. It also showed a similar inhibitory effect against NADPH-ADP-FE3(+) induced lipid peroxidation. Our results suggest that nicotinamide had significant ability to protect against photosensitization-induced cytotoxicity and cell damage and that it may do so by its ability to react with 1O2 and other reactive oxygen species.
darkness. RESULTS: Halothane anesthesia reversibly inhibited metabolic rhodopsin regeneration and thus prevented rhodopsin from absorbing high numbers of photons during light exposure. Consequently, photoreceptors of mice and rats anesthetized with halothane were completely protected against degeneration induced by white light. In remarkable contrast, however, halothane anesthesia did not protect against blue-light-induced photoreceptor cell death. CONCLUSIONS: After the initial bleach, halothane impeded photon absorption by rhodopsin by inhibiting metabolic rhodopsin regeneration. Apparently, the rhodopsin-mediated uptake of the critical number of photons to initiate white light-induced retinal degeneration was prevented. In contrast, halothane did not protect the retina against blue light. Blue light can efficiently restore functional rhodopsin from bleaching intermediates through a process termed photoreversal of bleaching. This process does not depend on the visual cycle via the pigment epithelium but nevertheless enables rhodopsin molecules to absorb the critical number of photons required to induce retinal degeneration.

Schlagwörter
Anesthesia, Inhalation; Anesthetics, Inhalationpharmacology; Animals; Apoptosisradiation effects; DNAanalysis; Halothane pharmacology; In Situ Nick-End Labeling; Mice; Mice, Inbred BALB C; Radiation Injuries, Experimental metabolismpathologyprevention & control; Rats; Rats, Sprague-Dawley; Regeneration drug effects; Retinophysiologyradiation effects; Retinal Degeneration metabolismpathologyprevention & control; Rhodopsinphysiology


Abstract

The possible involvement of Fe-S clusters in photodynamic reactions as endogenous sensitizing chromophores in cells has been investigated, by using an artificial non-heme iron protein (ANHIP) derived from bovine serum albumin and ferredoxins isolated from spinach and a red marine algae. Ferredoxins and ANHIP, when exposed to visible light, generate singlet oxygen, as measured by the imidazole plus RNO method. Irradiation with intense blue light of the ANHIP-entrapped liposomes caused severe membrane-damage such as liposomal lysis and lipid peroxidation. In the presence of ANHIP, isocitrate dehydrogenase and fructose-1,6-diphosphatase were photoinactivated by blue light. However, all of these photosensitized reactions were significantly suppressed by a singlet oxygen (1O2) quencher, azide, but enhanced by a medium containing deuterium oxide. Further, the Fe-S proteins with the prosthetic groups destroyed did not initiate the blue light-induced reactions. In addition, the action spectrum for 1O2 generation from ANHIP was very similar to the visible absorption spectrum of Fe-S centers. The results obtained in this investigation appear consistent with the suggestion that Fe-S centers are involved in photosensitization in cells via a singlet oxygen mechanism.

Schlagwörter
Animals; Cattle; Iron-Sulfur Proteins chemistryisolation & purification; radiation effects; Liposomes; Metalloproteins chemistryisolation & purification; radiation effects; Nonheme Iron Proteins; Oxygenradiation effects; Photochemistry; Radiationsensitizing Agents chemistry; Serum Albumin, Bovine chemistriyaradiation effects; Singlet Oxygen


Abstract

A2-PE is a pigment that forms as a byproduct of the visual cycle, its synthesis from all-trans-retinal and phosphatidylethanolamine occurring in photoreceptor outer segments. A2-PE is deposited in retinal pigment epithelial (RPE) cells secondary to phagocytosis of shed outer segment membrane and it undergoes hydrolysis to generate the RPE lipofuscin fluorophores, A2E, iso-A2E and other minor isomers of A2E. We have demonstrated that A2-PE can initiate photochemical
processes that involve the oxidation of A2-PE and that, by analogy with A2E are likely to include the formation of reactive moieties. We also show that potential sources of protection against the photooxidation of A2-PE are the lipid-soluble carotenoids zeaxanthin and lutein (xanthophylls), that constitute the yellow pigment of the macula. Irradiation of A2-PE in the presence of lutein or zeaxanthin suppressed A2-PE photooxidation and in experiments in which we compared the antioxidant capability of zeaxanthin and lutein to alpha-tocopherol, the carotenoids were more potent. Additionally, the effect with zeaxanthin was consistently more robust than with lutein and when alpha-tocopherol was combined with either carotenoid, the outcome was additive. Lutein, zeaxanthin and alpha-tocopherol were all efficient quenchers of singlet oxygen. We have also shown that lutein and zeaxanthin can protect against A2-PE/A2E photooxidation without appreciable consumption of the carotenoid by chemical reaction. This observation contrasts with the pronounced susceptibility of A2E and A2-PE to photooxidation and is of interest since lutein, zeaxanthin, A2E and A2-PE all have conjugated systems of carbon-carbon double bonds terminating in cyclohexenyl end-groups. The structural features responsible for the differences in quenching mechanisms are discussed. It has long been suspected that macular pigment protects the retina both by filtering high-energy blue light and by serving an antioxidant function. Evidence presented here suggests that the photochemical reactions against which lutein and zeaxanthin protect, may include those initiated by the A2-PE. Quantitative HPLC analysis revealed that in eyecups of C57BL/6J and BALB/cByJ mice, levels of A2-PE were several fold greater than the cleavage product, A2E. Taken together, these results may have implications with respect to the involvement of A2-PE formation in mechanisms underlying blue light-induced photoreceptor cell damage and may be significant to retinal degenerative disorders, such as those associated with ABCA4 mutations, wherein there is a propensity for increased A2-PE synthesis.

Schlagwörter

Animals; Chromatography, High Pressure Liquid; Light; Lutein; Pharmacology; Physiology; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Oxidation-Reduction Drug Effects; Pyridinium Compounds; Metabolism; Radiation Effects; Retinoids; Metabolism; Radiation Effects; Rod Cell Outer Segment; Metabolism; Xanthophylls; Pharmacology; Physiology


Abstract

Throughout the lifetime of an individual, light is focused onto the retina. The resulting photooxidative stress can cause acute or chronic retinal damage. The pathogenesis of age-related macular degeneration (AMD), the leading cause of legal blindness in the developed world, involves oxidative stress and death of the retinal pigment epithelium (RPE) followed by death of the overlying photoreceptors. Evidence suggests that damage due to exposure to light plays a role in AMD and other age-related eye diseases. In this work a system for light-induced damage and death of the RPE, based on the human ARPE-19 cell line, was used. Induction of mitochondria-derived reactive oxygen species (ROS) is shown to play a critical role in the death of cells exposed to short-wavelength blue light (425 +/- 20 nm). ROS and cell death are blocked either by inhibiting the mitochondrial electron transport chain or by mitochondria-specific antioxidants. These results show that mitochondria are an important source of toxic oxygen radicals in blue light-exposed RPE cells and may indicate new approaches for treating AMD using mitochondria-targeted antioxidants.

Schlagwörter

Aging; Radiation Effects; Antioxidants; Pharmacology; Apoptosis; Drug Effects; Radiation Effects; Cell Line; Electron Transport; Humans; Light; Mitochondriadru Drug Effects; Metabolism; Radiation Effects; Oxidative Stress; Radiation Effects; Pigment Epithelium of Eyem; Radiomembras; Metabolism; Radiation Effects; Ultrastructure; Reactive Oxygen Species; Antagonists & Inhibitors; Metabolism

Abstract

The ability of vanillin (4-hydroxy-3-methoxybenzaldehyde), a naturally occurring food flavouring agent, in inhibiting photosensitization-induced single-strand breaks (ssbs) in plasmid pBR322 DNA has been examined in an in vitro system, independent of DNA repair/replication processes. Photosensitization of DNA with methylene blue, visible light and oxygen, induced ssbs resulting in the production of open circular form (OC form) in a concentration-dependent manner. The yield of OC form induced by photosensitization was increased several-fold by deuteration of the buffer and was found to be inhibited by sodium azide, a scavenger of singlet oxygen \((1O(2))\). Vanillin, per se, did not induce but inhibited photosensitization-induced ssbs in plasmid DNA, at millimolar concentrations. The inhibitory effect of vanillin was both concentration- and time-dependent. On a molar basis, vanillin was, however, less effective than trolox, a water-soluble analogue of alpha-tocopherol. Photosensitization by methylene blue system generates singlet oxygen, as one of the major components of ROS. Therefore, interaction of singlet oxygen with vanillin was investigated. The rate constant of vanillin with \(1O(2)\) was estimated to be \(5.93 \times 10^{-7} \text{M}^{-1} \text{s}^{-1}\) and that of sodium azide as \(2.7 \times 10^{-8} \text{M}^{-1} \text{s}^{-1}\). The present investigations show that vanillin can protect against photosensitization-induced ssbs in the plasmid pBR322 DNA, and this effect may partly be due to its ability to scavenge \(1O(2)\).

Schlagwörter

Antioxidantspharmacology; Benzaldehydespharmacology; DNA Damage; Flavoring Agentspharmacology; Free Radical Scavengerspharmacology; Light; Methylene Bluetoxicity; Oxygenmetabolism; Photosensitizing Agentstoxicity; Plasmidsdrug effectsmetabolismradiation effects; Singlet Oxygen


Abstract

The present study was performed to investigate the effect of flavonols, namely myricetin and structurally related quercetin and kaempferol against A2E and blue light-induced photoreceptors death in primary retinal cell cultures. Primary retinal cell cultures were prepared from bovine retinas. Fourteen-day-old cultures were pretreated with different concentrations of myricetin, quercetin, kaempferol (1-40 microM) for 24 h, then treated with 30 microM of A2E or exposed to blue-actinic light for 20 h. Green nucleic acid stain assay was used to evaluate cell death. Photoreceptor and bipolar cells were immunolabeled with specific antibodies and were counted using automated microscope imaging and image-based cell counting software. Twenty hours exposure to blue light induced approximately 75% death of photoreceptors in bovine retinal cell cultures. Myricetin protected 100% of photoreceptors against blue-light-mediated damage in primary retinal cell cultures. Myricetin protected 100% of photoreceptors against blue-light-mediated damage with an EC(50) of 9+/1-0.7 microM. Quercetin resulted in a maximum of 15% protection against light damage, and kaempferol was inactive. A2E induced photoreceptor and bipolar cell death in a concentration-dependent manner with EC(50) of 25 microM for photoreceptors and 31 microM for bipolar cells. Myricetin, quercetin and kaempferol protected against A2E-induced photoreceptors and bipolar cells death with EC(50) values of 2+/1-0.3 microM, 2+/1-0.3 microM, 5+/1-0.9 microM and 0.8+/1-0.07 microM, 0.44+/1-0.06 microM, 1+/1-0.4 microM, respectively. Caspase-3 inhibitor (Z-DEVD-fmk) protected 42% photoreceptors and 57% bipolar cells from A2E toxicity. In contrast, this inhibitor had no effect against light-induced photoreceptor damage. Despite the poor activity of quercetin and the inactivity of kaempferol against blue light, myricetin, quercetin and kaempferol exhibited approximately 100% protection against A2E toxicity. This suggests that light- and A2E-induced cell deaths are mediated through different pathways. These results suggest that myricetin functions

**Abstract**

**PURPOSE:** The present study was performed to investigate the effect of crocin on blue light- and white light-induced rod and cone death in primary retinal cell cultures. **METHODS:** Primary retinal cell cultures were prepared from primate and bovine retinas. Fifteen-day-old cultures were exposed to blue actinic light or to white fluorescent light for 24 hours. Cultures were treated by the addition of different concentrations of crocin for 24 hours before light exposure or for 8 hours after light exposure. Cultures kept in the dark were used as controls. Green nucleic acid stain assay was used to evaluate cell death. Rods and cones were immunolabeled with specific antibodies and counted. TUNEL labeling was used to detect fragmented DNA in fixed cells after light exposure. **RESULTS:** Primary retinal cell cultures contained a mixture of retinal cells enriched in photoreceptors, bipolar cells, and Müller cells. Twenty-four-hour exposure to blue and white light induced death in 70% to 80% of the photoreceptors in bovine and primate retinal cell cultures. Crocin protected the photoreceptors against blue light- or white light-mediated damage in a concentration-dependent manner with an EC50 of approximately 30 microM. TUNEL assays confirmed that crocin protected photoreceptors from light damage. **CONCLUSIONS:** These results show that blue and white light selectively induce rod and cone cell death in an in vitro model. Crocin protects retinal photoreceptors against light-induced cell death.
cryptochrome functions in other dicots such as pea and tomato and lower plants including moss and fern. This review will focus on recent advances in functional and mechanism characterization of cryptochromes in plants. It is not intended to cover every aspect of the field; readers are referred to other review articles for historical perspectives and a more comprehensive understanding of this photoreceptor.

Schlagwörter
Arabidopsis physiology; Arabidopsis Proteins metabolism; Circadian Rhythm genetics physiology; DNA Damage genetics physiology; Deoxyribodipyrimidine Photo-Lyase genetics metabolism; Dimerization; Flavoproteins genetics metabolism; Light; Photoreceptor Cell metabolism; Plant Physiological Phenomena; Signal Transduction physiology radiation effects; Ubiquitin-Protein Ligases metabolism


Abstract
Data from 3,087 persons age 45 or older in the National Health and Nutrition Survey, 1971-74, showed that subjects with lens opacifying disease had an increased odds for age-related macular degeneration (AMD) compared to those who had no lens opacities. The crude odds ratio for aphakic patients was 4.6 (95% CI = 2.5, 8.6). The association remained after controlling for age, sex, and systolic blood pressure (a common risk factor) in a logistic regression model. These data are consistent with the hypothesis that light-induced damage may contribute to both lens and retinal disease and suggest that cataract extraction without implantation of ultra-violet/blue light absorbing intraocular lens may place subjects at increased risk of AMD.

Schlagwörter
Aged; Aging pathology; Cataract complication epidemiology; Female; Health Surveys; Humans; Macular Degeneration complication epidemiology; Male; Middle Aged; Regression Analysis; Risk Factors; United States


Abstract
Incubation with 50 microM methylene blue (MB) and subsequent intense illumination resulted in abolition of the slow-wave activity in the submuscular interstitial cells of Cajal-circular muscle (ICC-CM) preparations of canine colon. This was often accompanied by a decrease in resting membrane potential. Repolarization of cells back to -70 mV did not restore the slow-wave activity, indicating that MB plus light directly interrupted the generation mechanism of slow waves. After MB incubation, a 2-min illumination consistently changed the mitochondrial conformation in ICCs from very condensed to orthodox, without inducing any obvious changes in smooth muscle cells. After 4- to 10-min illumination, ICCs became progressively more damaged with swollen and ruptured mitochondria, loss of cytoplasmic contrast and detail, loss of caveolae, and rupture of the plasma membrane. No damage was seen in smooth muscle cells or nerves. Gap junctional ultrastructure was preserved. Intense illumination without preincubation with MB left the slow waves and the ultrastructure of ICC-CM preparations unaffected. In CM preparations, without the submuscular ICC-smooth-muscle network, MB plus light induced no changes in electrical activity. We conclude that the correlation between selective damage to the submuscular ICCs (relative to smooth muscle) and selective loss of the slow-wave activity (relative to other electrical activity of the CM) strongly indicates that the ICCs play an essential role in the generation of slow waves.

Schlagwörter
Animals; Colonic drug effect pathology radiation effects; Dogs; Electrophysiology; Female; Gastrointestinal Motility drug effect radiation effects; Light; Male; Methylene Blue pharmacology; Microscopy, Electron; Muscle, Smooth drug effect pathology radiation effects
Ohnishi, Norikazu; Allakhverdiev, Suleyman I.; Takahashi, Shunichi; Higashi, Shoichi; Watanabe, Masakatsu; Nishiyama, Yoshitaka; Murata, Norio (2005): Two-step mechanism of photodamage to photosystem II: step 1 occurs at the oxygen-evolving complex and step 2 occurs at the photochemical reaction center. In: Biochemistry, Jg. 44, H. 23, S. 8494–8499. Online verfügbar unter doi:10.1021/bi047518q.

Abstract
Under strong light, photosystem II (PSII) of oxygenic photosynthetic organisms is inactivated, and this phenomenon is called photoinhibition. In a widely accepted model, photoinhibition is induced by excess light energy, which is absorbed by chlorophyll but not utilized in photosynthesis. Using monochromatic light from the Okazaki Large Spectrograph and thylakoid membranes from Thermosynechococcus elongatus, we observed that UV and blue light inactivated the oxygen-evolving complex much faster than the photochemical reaction center of PSII. These observations suggested that the light-induced damage was associated with a UV- and blue light-absorbing center in the oxygen-evolving complex of PSII. The action spectrum of the primary event in photodamage to PSII revealed the strong effects of UV and blue light and differed considerably from the absorption spectra of chlorophyll and thylakoid membranes. By contrast to the photoinduced inactivation of the oxygen-evolving complex in untreated thylakoid membranes, red light efficiently induced inactivation of the PSII reaction center in Tris-treated thylakoid membranes, and the action spectrum resembled the absorption spectrum of chlorophyll. Our observations suggest that photodamage to PSII occurs in two steps. Step 1 is the light-induced inactivation of the oxygen-evolving complex. Step 2, occurring after step 1 is complete, is the inactivation of the PSII reaction center by light absorbed by chlorophyll. We confirmed our model by illumination of untreated thylakoid membranes with blue and UV light, which inactivated the oxygen-evolving complex, and then with red light, which inactivated the photochemical reaction center.

Schlagwörter
Cyanobacteriametabolismradiation effects; Electron Transportradiation effects; Light; Oxygenmetabolismradiation effects; Photosystem II Protein Complexantagonists & inhibitorsmetabolismradiation effects; Thylakoidsmetabolismradiation effects


Abstract
Methylene blue (MB+) is a well-known dye in medicine and has been discussed as an easily applicable drug for the topical treatment during photodynamic therapy (PDT). The therapeutic response of MB+ was investigated in vivo by local injection of MB+ in a xenotransplanted subcutaneous tumor (adenocarcinoma, G-3) in female nude mice. MB+ in a concentration of 1% was applied both undiluted and diluted to 0.1 and 0.01% with isotonic sodium chloride. Treatment with 1% MB+ and subsequent irradiation at 662 nm with 100 J/cm² led to complete tumor destruction in 79% of the treated animals. A decrease of the fluence rate from 100 to 50 mW/cm² increased the phototoxic response as well as fractionated light application. Small sensitizer concentrations reduced the PDT effect significantly. It seems that the light induced reaction of MB+ could be correlated with the rapid production of reactive oxygen species. Below a threshold dose of MB+ oxidative damage of the tissue is prevented. However, above this dose, as a point of no return, MB+ acts as an extremely potent oxidant.

Schlagwörter
Adenocarcinomadrug therapy; Animals; Colorectal Neoplasmsdrug therapy; Disease Models, Animal; Female; Humans; Methylene Bluetherapeutic use; Mice; Mice, Nude; Photochemotherapymethods; Photosensitizing Agentstherapeutic use


Abstract
PURPOSE: To experimentally clarify the processes of the changes induced by blue light directly on the retinal pigment epithelium (RPE) before the formation of
phagosomes or the accumulation of lipofuscin. METHODS: We developed a new experimental method in which primary cultured cells of very young pigmented rats were exposed to several intensities and durations of blue light (wavelength = 440+/−10 nm). RESULTS: At 1.0 mW/cm², the damage was limited to mitochondria. At 2.0 mW/cm², the cytoplasm exhibited large whorls of membrane or whorled inclusions, which were consistent with autophagic vacuoles. At 4.0 mW/cm², the RPE cells showed lysis of the cytoplasm and a nucleus that was consistent with necrosis. CONCLUSIONS: Our results suggested that damage induced by blue light to cultured RPE cells may originate in the mitochondria and end in necrosis. The type of cell death induced in the RPE by blue light seems to be determined mainly by the intensity of the light, but is also related to the duration of exposure.

Schlagwörter
Animals; Cell Nucleus; radiation effects; ultrastructure; Cells, Cultured; Cytoplasm; radiation effects; ultrastructure; Light adverse effects; Mitochondria; radiation effects; ultrastructure; Phagosomes; radiation effects; ultrastructure; Pigment Epithelium of Eye; radiation effects; ultrastructure; Rats; Rats, Long-Evans


Abstract
The initial yields of DNA-to-protein crosslinks (dpc) caused by ionizing and nonionizing radiations were compared, with emphasis upon values within the biological dose ranges (D0). Induction of dpc in cold (0-0.5 degrees C) human P3 teratocarcinoma cells was measured by using alkaline elution techniques after exposure to monochromatic UVC (254 nm), UVB (313 nm), UVA (365 and 405 nm), and blue light (434 nm). UVC and UVB light induced detectable numbers (about 100 dpc per cell per D0). Monochromatic UVA radiations produced yields about 8 times higher than UVC or UVB (for 365 nm, about 1500 dpc per cell per D0) Similar results at low doses were obtained for measurements of single-strand breaks induced by the different radiations. The action spectra for dpc were closely similar. The biological significance of these relatively high numbers of DNA lesions caused by environmental nonionizing radiation that readily penetrates into human skin is not understood.

Schlagwörter
Cells, Cultured; DNA; radiation effects; DNA Damage; DNA Repair; Dose-Response Relationship; Radiation; Humans; Light adverse effects; Ultraviolet Rays; adverse effects; X-Rays; adverse effects


Abstract
The purpose of this study was to determine the role of epithelial melanin in blue light phototoxicity of the retina. The first manifestation of the phototoxicity has been shown to be a breakdown of the blood-retinal barrier at the retinal pigment epithelium. The blood-retinal barrier function of six New Zealand albino rabbits was compared to that of four pigmented chinchilla rabbits after exposure to broad-band blue light (400-520 nm). Additionally, the spectral sensitivity of blood-retinal barrier dysfunction was determined by exposing 15 New Zealand albino rabbits to narrow-band blue light with peak intensity at lambda = 408 nm, 418 nm, 439 nm, 455 nm and 485 nm (bandwidth: 11.7-13.5 nm). The blood-retinal barrier function was evaluated with vitreous fluorophotometry. Ultrastructural changes and permeability of the retinal pigment epithelium for horseradish peroxidase were evaluated in the albino rabbits with electron microscopy. Exposure to broad-band blue light up to 832 J cm-2 demonstrated the blood-retinal barrier of albino and pigmented rabbits to be equally sensitive. Electron microscopy of albino rabbits exposed to above-threshold energy demonstrated an increase of inclusion bodies in the retinal pigment epithelium and vacuolation of the cytoplasm. Transcellular passage of
intra-arterially administered horseradish peroxidase through the pigment epithelium into the subretinal space was seen. The narrow-band exposures demonstrated that light of 439 nm was more effective than the light of other wavelengths in inducing barrier dysfunction in albino rabbits. This implies that chromophores absorbing at 439 +/- 6 nm were responsible for the phototoxicity in albino rabbits. The results indicate that melanin does not have a damaging nor a protective role in phototoxicity since (1) the presence of melanin is not essential for blue-light-induced photochemical damage to the blood-retinal barrier at the retinal pigment epithelium, and (2) protection from this sort of damage is not greater in melanin containing epithelia than in non-melanin containing epithelia.

Abstract

The protective role of reactive oxygen scavengers against photodamage was studied in isolated photosystem (PS) I submembrane fractions illuminated (2000 microE x m(-2) x s(-1)) for various periods at 4 degrees C. The photochemical activity of the submembrane fractions measured as P700 photooxidation was significantly protected in the presence of histidine or n-propyl gallate. Chlorophyll photobleaching resulting in a decrease of absorbance and fluorescence, and a blue-shift of both absorbance and fluorescence maximum in the red region, was also greatly delayed in the presence of these scavengers. Western blot analysis revealed the light harvesting antenna complexes of PSI, Lhca2 and Lhca1, were more susceptible to strong light when compared to Lhca3 and Lhca4. The reaction-center proteins PsaB, PsaC, and PsaE were most sensitive to strong illumination while other polypeptides were less affected. Addition of histidine or n-propyl gallate lead to significant protection of reaction-center proteins as well as Lhca against strong illumination. Circular dichroism (CD) spectra revealed that the alpha-helix content decreased with increasing period of light exposure, whereas beta-strands, turns, and unordered structure increased. This unfolding was prevented with the addition of histidine or n-propyl gallate even after 10 h of strong illumination. Catalase or superoxide dismutase could not minimize the alteration of PSI photochemical activity and structure due to photodamage. The specific action of histidine and n-propyl gallate indicates that 1O2 was the main form of reactive oxygen species responsible for strong light-induced damage in PSI submembrane fractions.


Abstract

The tetraruthenated porphyrin, mu-[meso-5,10,15,20-tetrapyridyl]porphyrin[tetrakis[bis-(bipyridine) chloride ruthenium(II)]] (TRP) is a supramolecular cationic species. The aim of the present investigation was to evaluate the photodynamic properties of TRP and Zn-TRP to damage DNA with emphasis on the mechanistic aspects. The ability for tetraruthenated porphyrin derivatives to induce photosensitzation reactions has been determined using 2'-
deoxyguanosine as a DNA model compound. The main photooxidation products of the targeted nucleoside were identified and classified according to their mechanisms of formation, involving either a radical pathway (type I) or a singlet oxygen-mediated mechanism (type II). Quantification of the different oxidation products provides a means to evaluate the relative contribution of type I and type II pathways associated with the oxidative photosensitization of 2'-deoxyguanosine by tetraruthenated porphyrin derivatives. Results indicate that 1O2 plays a major role in the mechanism of photooxidation mediated by these porphyrin derivatives. In addition an increase of the photosensitizing effect in the presence of zinc is observed. For each sensitizer, the ratio between type II and type I photoproducts has been calculated and compared to that of other known dyes such as methylene blue and riboflavin.

Schlagwörter: DNA Damage; Deoxyguanosine; Chemistry; Radiation Effects; Guanosine Analogs & Derivatives; Chemistry; Light; Organometallic Compounds; Chemistry; Radiation Effects; Oxygen; Photochemistry; Photolysis; Photosensitizing Agents; Chemistry; Porphyrins; Chemistry; Radiation Effects; Singlet Oxygen


Abstract

Are observations on ultraviolet (UV) - and visible light-induced ocular changes in animals relevant for human pathology? Different conclusions are drawn by different groups, depending on their perspective: while in the epidemiologist's view the evidence for those lesions is mostly limited or insufficient, laboratory scientists continually extend observations on radiation damage in animals. Consequently, there are diverging views on the necessity and specifications for eye protection. In this review, problems of epidemiological surveys and observations in humans and animal studies are discussed, and natural and artificial protection of the eye is outlined. The human and animal eye has an inherent potential for photochemical lesions due to chromophores including the visual pigments that are present at birth. Lifelong light exposure gives rise to additional absorbing molecules. With decreasing wavelengths of the electromagnetic spectrum the number of absorbing molecules rises; therefore, the likelihood of a photochemical reaction grows. As the spectral energy is augmented, more damage will occur. In our view, the knowledge gained from laboratory studies is a significant component of the total evidence from different fields-epidemiology, clinical observations, model studies and theoretical calculations-that UV radiation and short-wavelength visible light can cause acute and chronic changes in ocular structures. Such changes may comprise irreversible damage. Following recently issued recommendations of the major visual health organizations in the United States, protection against UV and blue light should be incorporated into the spectrum of safety considerations for sunglasses.

Schlagwörter: Absorption; Animals; Eye; Radiation Effects; Humans; Light; Adverse Effects; Radiation Injuries; Epidemiology; Prevention & Control; Radiation Injuries, Experimental; Epidemiology; Prevention & Control; Ultraviolet Radiation; Adverse Effects


Abstract

Fluorescent material generated in the human retina accumulates within lipofuscin (HLF) granules of the retinal pigment epithelium (RPE) during aging. We have been investigating the possible light-induced contribution of these fluorophores to various diseases including age-related macular degeneration. Our studies have shown that some of the fluorescent components of HLF are products of the reaction of retinaldehyde with ethanolamine and that synthetic mixtures of this reaction can serve as a useful model for photophysical studies. Previous research by us has demonstrated that irradiation of either natural or synthetic lipofuscin resulted in the formation of a triplet state and possibly a free radical. Here EPR studies were
performed to verify the formation of that radical. The UV irradiation of either
synthetic or natural human retinal lipofuscin extracts in oxygen-free methanol led to
the formation of a 5,5-dimethylpyrroline-N-oxide (DMPO) spin-trapped carbon-
centered radical resulting from either hydrogen atom or electron abstraction from
solvent molecules. In the presence of oxygen superoxide was formed, which was
observed as a DMPO adduct. It is concluded that certain components of the
chloroform-soluble fluorophores of human RPE lipofuscin granules and the
fluorescent reaction products of retinaldehyde and ethanolamine are
photophysically similar but not the same. Electron or hydrogen abstraction from a
substrate by these fluorophores in vivo and the resulting radical products may
contribute to the age-related decline of RPE function and blue light damage in the
retina.

Schlagwörter
Adult; Electron Spin Resonance Spectroscopy; Humans;
Lipofuscinchemistryisolation & purification; Photochemistry; Pigment Epithelium of
Eyechemistrymetabolism

by anticancer agents. 11. Mechanisms of photosensitization of human leukemic cells by diaminoanthraquinones:
317–335.

Abstract
The synthesis of several aminoanthraquinone derivatives (AAQs), designed to
suppress the dark toxicity and to promote more efficient cancer cell
photosensitization for potential use in photodynamic therapy (PDT), is described.
The following AAQs were synthesized: 1-NH2-4,5-(MeO)2-AQ (1), 1,5-(NH2)2-4,8-
(MeO)2-AQ (2), 1,8-(NH2)2-4,5-(MeO)2-AQ (3), and 1,5-(NHPhMe)2-4,8-(MeO)2-
AQ (8). The agents exhibit strong absorption in the region 480-620 nm. Possible
mechanisms of photosensitization were studied by measuring 1O2
phosphorescence at 1270 nm, detecting superoxide radicals employing an electron
paramagnetic resonance (EPR)-spin trapping technique, and measuring oxygen
consumption during the photo-oxidation of a representative biological electron
donor, NADH. Strong phosphorescence from 1O2 was observed upon illumination
of 2 and 3 in C6H6 (quantum yield of 0.25 and 0.5 respectively), and in EtOH
(quantum yield of 0.23 and 0.34). The 1-amino-AQ (1) was the weakest 1O2
sensitizer, with quantum yield of 0.13 in benzene. No phosphorescence was
observed in EtOH. A superoxide radical was detected as a spin adduct of 5,5-
dimethyl-1-pyrroline-N-oxide (DMPO) in irradiated benzene solutions of 1, 2 or 3
and DMPO. AAQs 2 and 3 sensitized photo-oxidation of NADH in H2O/EtOH
mixture with the intermediacy of singlet oxygen as judged by the effect of sodium
azide on the photostimulated oxygen consumption. Evolution of O2 upon addition of
catalase to the illuminated solution confirmed the ultimate formation of hydrogen
peroxide. These findings suggested that the (di)amino-dimethoxyanthraquinones
might exert photosensitization via both Type I and Type II mechanisms. The AAQs
were tested for their ability to photosensitize K562 human chronic myeloid leukemic
cells in culture. Viability was measured using the 3,4,5-diethylthiazol-2,5-diphenyl
tetrazolium blue assay, and DNA and possible membrane damage were assessed.
The results from illuminating cells with light > 475 nm show that for the 1,5-
compounds, the presence of methoxy substituents at 4,8 positions reduces the dark
toxicity from ID50 of 23 to 250 microM and for the 1,8-compounds correspondingly
from ID50 of 53 to > 300 microM. In the 1,5-series this decrease of the dark toxicity
is accompanied by an increase in light-induced dose modification from 8.85 to 14.4.
Differences exist in the mechanisms of cytotoxicity between the prototype phenolic
AAQs and their methoxy counterparts. It appears that the cytotoxic action of the
latter causes cell damage by the formation of a high proportion of alkali labile sites
in addition to frank strand breaks.(ABSTRACT TRUNCATED AT 400 WORDS)

Abstract

Exposure of the eye to intense light, particularly blue light, can cause irreversible, oxygen-dependent damage to the retina. However, no key chromophores that trigger such photooxidative processes have been identified yet. We have found that illumination of human retinal pigment epithelium (RPE) cells with light induces significant uptake of oxygen that is both wavelength- and age-dependent. Analysis of photoreactivity of RPE cells and their age pigment lipofuscin indicates that the observed photoreactivity in RPE cells is primarily due to the presence of lipofuscin, which, under aerobic conditions, generates several oxygen-reactive species including singlet oxygen, superoxide anion, and hydrogen peroxide. We have also found that lipofuscin-photosensitized aerobic reactions lead to enhanced lipid peroxidation as measured by accumulation of lipid hydroperoxides and malondialdehyde in illuminated pigment granules. Hydrogen peroxide is only a minor product of aerobic photoexcitation of lipofuscin. We postulate that lipofuscin is a potential photosensitizer that may increase the risk of retinal photodamage and contribute to the development of age-related maculopathy.

Schlagwörter

Aged; Humans; Hydrogen Peroxidemetabolism; Light; Lipofuscinmetabolism; Middle Aged; Oxygen Consumption; Pigment Epithelium of Eyemetabolism; Reactive Oxygen Speciesmetabolism; Superoxidesmetabolism


Abstract

Accumulation of lipofuscin (LF) is a prominent feature of aging in the human retinal pigment epithelium (RPE) cells. This age pigment exhibits substantial photoreactivity, which may increase the risk of retinal photodamage and contribute to age-related maculopathy. In a previous study, we detected singlet oxygen generation by lipofuscin granules excited with blue light. In this paper we investigated the ability of hydrophobic components of lipofuscin to photogenerate singlet oxygen in non-polar environments. Singlet oxygen was detected directly by monitoring its characteristic phosphorescence at ca 1270 nm. The action spectrum of singlet oxygen formation indicated that this process was strongly wavelength-dependent and its efficiency decreased with increasing wavelength by a factor of ten, comparing 420 nm and 520 nm. The quantum yield of singlet oxygen increased with increasing concentration of oxygen. Using laser flash photolysis we studied the possible mechanism of singlet oxygen formation. The observed transient, with a broad absorption spectrum peaking at around 440 nm, was identified as a triplet with lifetime ca 11 microseconds. It was quenched by both molecular oxygen and beta-carotene with concomitant formation of a beta-carotene triplet state. These results indicate the potential role of hydrophobic components of lipofuscin in blue light-induced damage to the RPE.

Schlagwörter

Aged; Aged, 80 and over; Agingmetabolism; Energy Transfer; Free Radicalsmetabolismradiation effects; Humans; Lasers; Light; Lipofuscinmetabolismradiation effects; Middle Aged; Oxygenmetabolismradiation effects; Photochemistry; Photolysis; Pigment Epithelium of Eyemetabolismradiation effects; Retinametabolismradiation effects; Singlet Oxygen
Toward a better understanding of light-induced photoreceptor damage, the crystallin content of rat retina was examined following intense light exposure. Nine crystallin species were identified by mass spectrometric analysis of rat retina fractionated by 2D gel electrophoresis. The Coomassie blue staining intensity of all crystallin 2D gel components was 2- to 3-fold greater in light exposed than in control retinas. Following light exposure, anti-alphaB-crystallin immunoreactivity was increased in rod outer segments and retinal pigment epithelium. These findings support a possible role for crystallins in protecting photoreceptors from light damage.

Cyclobutane-type pyrimidine dimers generated by ultraviolet irradiation of DNA can be cleaved by DNA photolyase. The enzyme-catalysed reaction is believed to be initiated by the light-induced transfer of an electron from the anionic FADH-chromophore of the enzyme to the pyrimidine dimer. In this contribution, first infrared experiments using a novel E109A mutant of Escherichia coli DNA photolyase, which is catalytically active but unable to bind the second cofactor methenyltetrahydrofolate, are described. A stable blue-coloured form of the enzyme carrying a neutral FADH radical cofactor can be interpreted as an intermediate analogue of the light-driven DNA repair reaction and can be reduced to the enzymatically active FADH- form by red-light irradiation. Difference Fourier transform infrared (FT-IR) spectroscopy was used to monitor vibronic bands of the blue radical form and of the fully reduced FADH- form of the enzyme. Preliminary band assignments are based on experiments with 15N-labelled enzyme and on experiments with D2O as solvent. Difference FT-IR measurements were also used to observe the formation of thymidine dimers by ultraviolet irradiation and their repair by light-driven photolyase catalysis. This study provides the basis for future time-resolved FT-IR studies which are aimed at an elucidation of a detailed molecular picture of the light-driven DNA repair process.

OBJECTIVE: To observe the internalization of A2E by human retinal pigmented epithelial (hRPE) cells and study whether the lipofuscin fluorophore A2E (N-retinylidene-N-retinylethanolamine) participates in blue light-induced damage to hRPE cells. METHODS: A mixture of all-trans-retinal and ethanolamine was used to produce A2E in one step. A2E granules were delivered to medium of cultured hRPE cells for internalization. Confluent cultures were subsequently exposed to 450 nm (blue) light for 20 minutes with or without A2E (25, 50, 100 micromol/L). The light
intensity was 70 mW/mm\(^2\). Phototoxicity was quantified at 12, 24, 36, and 48 h after exposure by CCK-8 of viable cells. Apoptosis of cells was detected by Hoechst 33342 DNA staining and flow cytometry. RESULTS: The reaction of all-trans-retinal (100 mg) and ethanolamine (9.5 mg) produced 53.8 mg A2E in one step. When A2E was delivered to hRPE cells in culture, it accumulated intracellularly. Internalized A2E presented as autofluorescent granules having a perinuclear distribution. As shown by CCK-8 analysis, the A2E-fed hRPE cell viability reduced with duration after 450 nm light exposure. Conversely, blue light-exposed hRPE cells that did not contain A2E showed less loss of cell viability. The percentage of hRPE cell apoptosis with 25 micromol/L A2E 12, 24, 36 and 48 h after blue light exposure was (12.11 +/- 2.32)\%, (31.21 +/- 3.72)\%, (64.23 +/- 3.53)\% and (58.71 +/- 3.48)\% respectively. Conversely, the apoptosis was less than 5\% in other hRPE cells. CONCLUSIONS: A2E is essential to blue light-induced hRPE cell damage. Only blue light exposure and without A2E lead to little cell injury. hRPE cells in old people which contain much lipofuscin are sensitive to blue light injury.


Abstract

It has been shown that illumination of rod outer segment suspension in the presence of photosensitizers (methylene blue lambda greater than or equal to 620 nm; retinal 370 less than or equal to lambda less than or equal to 390 nm) results in chemical modification of the lipid and protein components of the photo-receptor membranes. This modification can be registered by accumulation of lipid peroxidation (LPO) products as well as oligomerization of rhodopsin and a decrease of rhodopsin thermal stability. These effects are prevented by 'O2-quenchers and free radical scavengers. It has been found that the electric activity (ERG) of isolated frog retina is inhibited due to photosensitized generation of 'O2 which can be overcome by preliminary addition of 'O2-quenchers and free radical scavengers to the incubation medium. The LPO products are accumulated in the retinae of rats exposed to high intensity light in vivo. It is concluded that 'O2 and LPO are involved in light-induced damage of the retina.


Abstract

Lycopene, lutein, and zeaxanthin are major carotenoids in human blood and tissues but unlike beta-carotene do not contribute to vitamin A supply. These carotenoids are efficient antioxidants quenching singlet molecular oxygen which is formed in photooxidative processes and thus may contribute to the prevention of light-exposed tissue, skin and eyes, from light-induced damage. Increasing lycopene intake by daily consumption of tomato paste over a period of ten weeks provides protection against erythema formation following UV-irradiation. Lycopene and other carotenoids may be used as oral sun protectants and contribute to the maintenance of skin health. The yellow color of the macula lutea is due to the presence of the carotenoid pigments lutein and zeaxanthin. These macula carotenoids are suggested to play a role in protection against light-dependent damage. Filtering of blue light and scavenging of reactive intermediates generated in photooxidation are considered to be the underlying protective mechanisms. Epidemiological studies provide evidence that an increased consumption of lutein is associated with a lowered risk for age-related macular degeneration, a disease with increasing incidence in the elderly.
The neurosensory retina is a highly specialized sense organ that is subjected to constant exposure of systemic toxins, oxidative stress and focused light rays. Important advances have been made in recent decades in unravelling a myriad of defence mechanisms against such insults and consequently in improving the understanding of the principles underlying various drug- and light-induced disease processes. To defend against circulating toxins, the retina possesses a specialized blood-retinal barrier (BRB) that tightly regulates the transport of substances across the functional boundaries of the retina at the retinal capillaries and the retinal pigmented epithelium. An endogenous cytochrome p450 system is strategically located within the retina to neutralize agents that can diffuse through the BRB. The biooxidation effect of light is prevented by a wide array of unique antioxidant mechanisms in the retina. Nonetheless, pathological processes may evolve when these different lines of defence are overwhelmed by various xenobiotics, environmental agents such as cigarette smoke and excessive light exposure, particularly of short wavelength high frequency blue light and ultraviolet light. Latest research using transgenic models has revealed novel apoptotic pathways implicated in acute phototoxicity, in particular blue light damage, and provides important clues for further understanding the risks of high-frequency light exposure to human retinopathy. This review article summarizes the basic scientific principles of these different defence mechanisms and discuss the implications in pathophysiology and treatment.
presence of caspase-3 inhibitor and in A2E-loaded RPE cells that had been stably transfected with Bcl-2. CONCLUSIONS. Blue light illumination of RPE in the setting of intracellular A2E initiates a cell death program that is executed by a proteolytic caspase cascade and that is regulated by Bcl-2.

Schlagwörter
Apoptosis, drug effects, radiation effects; Blotting, Western; Caspase 3; Caspases, antagonists & inhibitors; metabolism; Cell Survival, physiology; Genes, bcl-2; genetics; Humans; In Situ Hybridization; In Situ Nick-End Labeling; Light; Lipofuscin, metabolism; Oligopeptides, pharmacology; Pigment Epithelium of Eye, drug effects; metabolism; pathology; Proto-Oncogene Proteins c-bcl-2, metabolism; RNA, Messenger, metabolism; Transfection


Abstract
PURPOSE: To determine whether the lipofuscin fluorophore A2E participates in blue light-induced damage to retinal pigmented epithelial (RPE) cells. METHODS: Human RPE cells (ARPE-19) accumulated A2E from 10, 50, and 100 microM concentrations in media, the levels of internalized A2E ranging from less than 5 to 64 ng/10⁵ cells, as assayed by quantitative high-performance liquid chromatography (HPLC). Restricted zones (0.5-mm diameter spots) of confluent cultures were subsequently exposed to 480 +/- 20-nm (blue) or 545 +/- 1-nm (green) light for 15 to 60 seconds. Phototoxicity was quantified at various periods after exposure by fluorescence staining of the nuclei of membrane-compromised cells, by TdT-dUTP terminal nick-end labeling (TUNEL) of apoptotic cells and by Annexin V labeling for phosphatidylserine exposure. RESULTS: Nonviable cells were located in blue light-exposed zones of A2E-containing RPE cells, whereas cells situated outside the illuminated areas remained viable. As shown by fluorescence labeling of the nuclei of membrane-damaged cells and by the presence of TUNEL-positive cells, the numbers of nonviable cells increased with exposure duration and as a function of the concentration of A2E used to load the cells before illumination. The numbers of blue light-induced TUNEL-positive cells also increased in advance of the increase in labeling of membrane-compromised cells, a finding that, together with Annexin V labeling, indicates an apoptotic form of cell death. Conversely, blue light-exposed RPE cells that did not contain A2E remained viable. In addition, illumination with green light resulted in the appearance of substantially fewer nonviable cells. CONCLUSIONS: These studies implicate A2E as an initiator of blue light-induced apoptosis of RPE cells.

Schlagwörter
Annexin A5, metabolism; Apoptosis, drug effects; Cells, Cultured; Chromatography, High Pressure Liquid; DNA, radiation effects; DNA Damage; Humans; Light; Lipofuscin; Microscopy, Fluorescence; Pigment Epithelium of Eye, metabolism; pathophysiology; Pyridinium Compounds, metabolism; Retinal Pigments; Retinoids, metabolism

Sparrow, Janet R.; Zhou, Jilin; Ben-Shabat, Shimon; Vollmer, Heidi; Itagaki, Yasuhiro; Nakanishi, Koji (2002): Involvement of oxidative mechanisms in blue-light-induced damage to A2E-laden RPE. In: Investigative ophthalmology & visual science, Jg. 43, H. 4, S. 1222–1227.

Abstract
PURPOSE: The lipofuscin fluorophore A2E is known to be an initiator of blue-light-induced apoptosis in retinal pigment epithelial cells (RPE). The purpose of this study was to evaluate the role of oxidative mechanisms in mediating the cellular damage. METHODS: Human RPE (ARPE-19) cells that had accumulated A2E were exposed to blue light in the presence and absence of oxygen, and nonviable cells were quantified. Potential suppressors (histidine, azide, 1,4-diazabicyclooctane [DABCO], and 1,3-dimethyl-2-thiourea [DMTU]) and enhancers (deuterium oxide [D(2)O] and 3-aminotriazole [3-AT]) of oxidative damage, were also screened for their ability to modulate the frequency of nonviable cells. A2E in PBS, with and without an oxygen-depleter or singlet-oxygen quencher and A2E-laden RPE, were
exposed to 430-nm light and examined by reversed-phase high performance liquid chromatography (HPLC) and fast atom bombardment mass spectrometry (FAB-MS). RESULTS: The death of blue-light-illuminated A2E-laden RPE was blocked in oxygen-depleted media. When A2E-laden RPE were transferred to D(2)O-based media and then irradiated (480 nm), the number of nonviable cells was increased, whereas the latter was decreased in the presence of histidine, DABCO, and azide. Conversely, no effect was observed with 3-AT and DMTU. When A2E, in either acellular or cellular environments, was irradiated at 430 nm, FAB-MS revealed the generation of a series of higher molecular mass derivatives of A2E. The sizes of these species increased by increments of mass 16. The generation of these photo-products was accompanied by the consumption of A2E, the latter being diminished, however, when illumination was performed after oxygen depletion and in the presence of a singlet-oxygen quencher. CONCLUSIONS: The augmentation of cell death in the presence of D(2)O and the protection afforded by quenchers and scavengers of singlet oxygen, indicates that the generation of singlet oxygen may be involved in the mechanisms leading to the death of A2E-containing RPE cells after blue light illumination. The finding that irradiation also produces oxygen-dependent photochemical changes in A2E, indicates that the effects of singlet oxygen may be mediated either directly or through the generation of reactive photo-products of A2E.

Schlagwörter
Apoptosis; Cells, Cultured; Chromatography, High Pressure Liquid; DNA Damage; Humans; Light; Oxidation-Reduction; Oxygenmetabolism; Pigment Epithelium of Eyemetabolismpathologyradiation effects; Pyridinium Compoundsmetabolismradiation effects; Retinoidsmetabolismradiation effects; Spectrometry, Mass, Fast Atom Bombardment


Abstract
Fowlpox virus (FPV), a pathogen of poultry, can persist in desiccated scabs shed from infected hosts. Although the mechanisms which ensure virus survival are unknown, it is likely that some type of remedial action against environmentally induced damage is required. In this regard, we have identified an open reading frame (ORF) coding for a putative class II cyclobutane pyrimidine dimer (CPD)-photolyase in the genome of FPV. This enzyme repairs the UV light-induced formation of CPDs in DNA by using blue light as an energy source and thus could enhance the viability of FPV during its exposure to sunlight. Based on transcriptional analyses, the photolyase gene was found to be expressed late during the FPV replicative cycle. That the resultant protein retained DNA repair activity was demonstrated by the ability of the corresponding FPV ORF to complement functionally a photolyase-deficient Escherichia coli strain. Interestingly, insertional inactivation of the FPV photolyase gene did not impair the replication of such a genetically altered virus in cultured cells. However, greater sensitivity of this mutant than of the parental virus to UV light irradiation was evident when both were subsequently photoreactivated in the absence of host participation. Therefore, FPV appears to incorporate its photolyase into mature virions where the enzyme can promote their survival in the environment. Although expression of a homologous protein has been predicted for some chordopoxviruses, this report is the first to demonstrate that a poxvirus can utilize light to repair damage to its genome.

Schlagwörter
Amino Acid Sequence; Animals; Cell Line; DNA Repair; Deoxyribodipyrimidine Photo-Lyasechemistrygeneticsmetabolism; Fowlpoxvirology; Fowlpox virusesenzymologygeneticsphysiologyradiation effects; Molecular Sequence Data; Mutation; Poultry; Pyrimidine Dimersmetabolism; Sequence Alignment; Ultraviolet Rays; Virus Replication

The yellow color of the macula lutea is due to the presence of the carotenoid pigments lutein and zeaxanthin. In contrast to human blood and tissues, no other major carotenoids including Beta-carotene or lycopene are found in this tissue. The macular carotenoids are suggested to play a role in the protection of the retina against light-induced damage. Epidemiological studies provide some evidence that an increased consumption of lutein and zeaxanthin with the diet is associated with a lowered risk for age-related macular degeneration, a disease with increasing incidence in the elderly. Protecting ocular tissue against photooxidative damage carotenoids may act in two ways: first as filters for damaging blue light, and second as antioxidants quenching excited triplet state molecules or singlet molecular oxygen and scavenge further reactive oxygen species like lipid peroxides or the superoxide radical anion.


Abstract

Intense ultraviolet (UV) and blue stimulation photolyses rhodopsin through a fluorescent metarhodopsin (M') in the predominant photoreceptor type, R1-6, of the compound eye of white eyed Drosophila melanogaster. We investigated the associated retinal degeneration using High Voltage Electron Microscopy (HVEM). The threshold for UV induced damage was about 19 log quanta/cm² while for blue, the threshold was about 20. These intensities are toward the upper level of the dynamic range for rhodopsin photolysis. Thus, there is a sensitization for near UV induced degeneration as had been found for photolysis of the visual pigment. Vitamin A deprivation protects against light elicited retinal degeneration, particularly in the UV. Since vitamin A deprivation eliminates the blue absorbing rhodopsin and a UV sensitizing pigment in R1-6, the degeneration is likely mediated through quantal absorption through these photoexcitation pigments. Intense light converts the microvilli of the rhabdomeres (the photopigment containing organelles) into dense strands and the cytoplasm fills with a dense reticulum. Such damage is elicited shortly after stimulation and is permanent. Under most conditions, the second order interneurons are spared. These results are discussed in the context of other animal models of intense light retinal degeneration.


Abstract

Intense ultraviolet (UV) and blue stimulation decreases visual pigment concentration and increases long wavelength fluorescent emission in R1-6 photoreceptors in the white eyed fruit fly Drosophila melanogaster. We used microspectrophotometry to show that the threshold for visual pigment decrease is about 1 log unit lower for UV than for blue light (18.7 vs approximately 19.9 log quanta/cm² respectively). UV and blue stimuli about 0.2 log units brighter had been shown to cause structural degeneration. Above the threshold for structural damage, visual pigment is decreased permanently while below this level, a recovery of visual pigment was achieved within several hours. Microspectrofluorometric data are partially consistent with the hypothesis that the visual pigment is converted into a fluorescent product which had been named M'. M' had been proposed to be a new form of metarhodopsin which absorbs chiefly in the yellow and which has a
fluorescent emission in the red; long wavelength stimulation had been reported to regenerate the native visual pigment from M'. Our data suggest that the situation is significantly more complex than this simple model. For instance, we report that long wavelength stimulation regenerates only a small fraction of the visual pigment which had been decreased by UV or blue stimulation. Furthermore, several lines of evidence suggest that other fluorescent products are also created by intense UV and blue stimulation. We were particularly interested in the lower damage threshold for UV light because of the hypothesis that UV visual sensitivity is mediated by a sensitizing pigment which absorbs UV light and transfers its energy to the blue absorbing rhodopsin. Our data suggest that the UV light decreases the rhodopsin without preferentially decreasing the sensitizing pigment.

Schlagwörter: Animals; Drosophila melanogasterradiation effects; Electrophysiology; Electroretinography; Fluorometry; Lightadverse effects; Retinaradiation effects; Retinal Pigmentsbiosynthesismetabolismradiation effects; Spectrophotometrymethods; Time Factors; Ultraviolet Rayselectroretinographyadverse effects


Abstract

PURPOSE: Sonic hedgehog (Shh) signaling is essential for photoreceptor differentiation and retinal cell survival in embryonic zebrafish. The study was conducted to determine whether adult heterozygous carriers of mutant alleles for the shh gene display retinal abnormalities. METHODS: Retinal cryosections from young, middle-aged, and senescent wild-type and sonic-you(+/-) (syu(+/-)) zebrafish were probed with retinal cell type-specific markers. Contralateral retinal flatmounts from these fish, and from adult albino zebrafish subjected to light-induced photoreceptor damage followed by regeneration, were hybridized with blue cone opsin cRNA for quantitative analysis of the blue cone pattern. Retinal expression of shh mRNA was measured by quantitative RT-PCR. RESULTS: Regions of cone loss and abnormal cone morphology were observed in the oldest syu(+/-) zebrafish, although no other retinal cell type was affected. This phenotype was age-related and genotype-specific. Cone distribution in the oldest syu(+/-) zebrafish was predominantly random, as assessed by measuring the short-range pattern, whereas that of wild-type fish and the younger syu(+/-) zebrafish was statistically regular. A measure of long-range pattern revealed atypical cone aggregation in the oldest syu(+/-) zebrafish. The light-treated albino zebrafish displayed random cone patterns immediately after light toxicity, but showed cone aggregation on regeneration. Retinas from the syu(+/-) fish showed reduced expression of shh mRNA compared with those of wild-type siblings. CONCLUSIONS: The syu(+/-) zebrafish presents a model for the study of hereditary age-related cone abnormalities. The syu(+/-) retinas most likely experience progressive cone photoreceptor loss, accompanied by cone regeneration. Shh signaling may be required to maintain cone viability throughout life.

Schlagwörter: Agingphysiology; Alleles; Animals; Cell Death; Cell Proliferation; Fluorescent Antibody Technique, Indirect; Gene Expressionphysiology; Hedgehog Proteinsgenetics; In Situ Hybridization; In Situ Nick-End Labeling; Light; Microscopy, Fluorescence; Mutation; RNA, Messengermetabolism; Radiation Injuries, ExperimentalitoIogygeneticspathology; Retinaradiation effects; Retinal Cone Photoreceptor Cellsmetabolismpathology; Retinal Degenerationiologystveygeneticspathology; Reverse Transcriptase Polymerase Chain Reaction; Rod Opsinsmetabolism; Zebrafishgenetics; Zebrafish Proteinsgenetics


Abstract

An earlier mechanistic phase of iron toxicity in photosynthetic cells was interpreted...
in terms of enhanced photodynamic action by the cytochrome b6/f complex (Cyt b6/f) via singlet oxygen (1O2) on the photosystem II complex (PS II). Iron excess was induced in hydroponically cultured pea (Pisum sativum L.) plants, and its effect on the function of PS II in vivo as well as in vitro was studied under high-irradiance conditions. Iron excess in plants gave rise to a significant increase in Cyt b6/f content of thylakoids. It appeared that the larger the content of Cyt b6/f, the more susceptible PS II was to photoinhibition, and the higher the rate of 1O2 photoproduction in thylakoids was. The action spectrum for degradation of the D1 protein in thylakoids revealed that photosensitization by nonporphyrin chromophore(s) was apparently associated with near UV to blue light-induced deterioration of PS II. The results are pertinent to the concept that photodegradation of PS II, exacerbated by iron accumulation in thylakoid membranes in the form of Cyt b6/f, is involved in the mechanism of iron toxicity in leaf cells.


Abstract
Recently, a yellow intraocular lens (IOL) was developed for the purpose of reducing potential blue light-induced retinal damage after cataract surgery. However, the effect of yellow filters on retinal protection remains to be clarified. To test the protective effects of yellow filters on blue light-induced retinal damage, a yellow and a clear soft acrylic filter were attached to the right and left eyes, respectively, of albino rats and exposed to 4.5 k lux blue fluorescent lights with peak wavelength at 420 nm (ranging 380-500 nm; short blue) or 446 nm (ranging 400-540 nm; long blue) for 6h. To assess retinal damage, the electroretinogram (ERG) was recorded at 7 days, outer nuclear layer (ONL) thickness and area were measured at 7 days, apoptosis was analyzed by TUNEL staining at 24 h, and the level of lipid peroxidation in retinas was assessed by Western dot blots using specific antibodies against 4-hydroxynonenal (4-HNE) and carboxyethylpyrrole (CEP)-modified proteins immediately after light exposure. After short blue light exposure, a- and b-wave ERG amplitudes and the ONL thickness at 1-2.5 mm inferior and 0.5-2.5 mm superior to optic nerve head (ONH) were significantly reduced. TUNEL staining in the ONL at 0-2 mm inferior and 1-2 mm superior to the ONH, and retinal levels of 4-HNE- and CEP-modified proteins were significantly increased in the clear filter-covered eyes compared to yellow filter-covered eyes. After long blue light exposure, the only difference seen was a greater ONL thickness at 1.5 mm superior to the ONH in yellow filter-covered eye. Transmission of light through the yellow filter was 58% for short blue and 89% for long blue compared to the clear filter. The ONL area was not different between clear filter-covered and -uncovered eyes after exposure to short or long blue light. Given the results, yellow IOL material protects the retina against acute shorter wavelength blue light exposure more effectively than the clear IOL material.

Abstract

In vitro photosensitization by visible light in the presence of methylene blue (MB-light) produces lesions in M13mp18 lacZ phage DNA, the lethal and mutagenic potential of which was analyzed after transfection into various bacterial hosts. Mutagenesis was determined with a forward mutation assay using the lacZ gene of M13mp18 as a target. When, MB-light-treated double-stranded (ds) M13mp18 DNA was used to transfect wild-type cells which were not induced for SOS functions, a fivefold increase in mutation frequency was observed at 10% survival compared to that observed with untreated DNA. Mutation frequency obtained with MB-light-treated ds M13mp18 DNA was greater when transfected into the uvr A fpg-1 double mutant than that seen in uvr A, fpg-1, or umuC single mutants or in the wild-type. Sequence analysis shows that in the wild-type strain, MB-light treatment of ds M13mp18 DNA results mostly in single base substitutions. The most frequent base change is the GC-->TA transversion. MB-light treatment of single-stranded (ss) M13mp18 DNA also results in an increased mutation frequency after transfection into the wild-type strain, yielding mostly G-->T transversions. Our results show that MB-light-induced mutagenesis is at least partially independent of the induction of SOS functions in Escherichia coli. The mutation spectra suggest that 8-oxo-7,8-dihydroguanine is the major promutagenic lesion in DNA.

Schlagwörter

Bacteriophage M13; drug effect; genetics; radiation effects; Base Sequence; DNA Damage; DNA Repair; DNA, Viral drug effect; genetics; radiation effects; Enzyme Induction; Escherichia coli; drug effect; genetics; radiation effects; Frameshift Mutation; Free Radicals; Genes, Bacterial; genetics; Guanine analogs & derivatives; Light; Methylene Blue; pharmacology; Molecular Sequence Data; Mutagenesis; Photosensitivity Disorders; Point Mutation; SOS Response (Genetics); Sequence Analysis, DNA; Transfection; beta-Galactosidase biosynthesis


Abstract

The light-induced reactions of methylene blue and related phenothiazinium dyes with biological substrates are described. The properties of the excited states of the dyes, their reactions with nucleic acids and their photosensitised chemical modifications of nucleic acid bases are examined. Reports on phenothiazinium dye-induced damage to proteins, lipids, biological membranes, organelles, viruses, bacteria, mammalian cells and carcinomas are reviewed.

Schlagwörter

Animals; Bacteriadrug effect; Cell Line; DNA chemistry; Eukaryotic Cells drug effect; Humans; Lipids chemistry; Mammals; Membrane Lipid chemistry; Methylene Blue analogs & derivatives; Light; Methylene Blue pharmacology; Molecular Sequence Data; Mutagenesis; Photosensitivity Disorders; Point Mutation; SOS Response (Genetics); Sequence Analysis, DNA; Transfection; beta-Galactosidase biosynthesis


Abstract

The purpose of this study was to determine the threshold energy for light-induced functional damage of the retinal pigment epithelium after light-induced damage. In: Microscopy research and technique, Jg. 36, H. 2, S. 77–88. Online verfügbar unter doi:10.1002/(SICI)1097-0029(19970115)36:2<77::AID-JEMT1>3.0.CO;2-S.

Abstract

The purpose of this study was to determine the threshold energy for light-induced functional damage of the retinal pigment epithelium at various wavelengths. Retinas of 58 pigmented and 21 albino rabbits were exposed to low intensity broadband blue light (400-520 nm), yellow light (510-740 nm), and narrowband blue light (408, 417, 439, 455, 485, 501 nm, respectively; delta lambda = 10-13 nm). The intensity values were 50, 280, and 5 mW x cm^-2, respectively, and the illumination time was 0.5 up to 5 h. The cumulative dose of light energy was calculated from these data (J x cm^-2). The blood-retinal barrier dysfunction was evaluated in vivo using fluorophotometry to measure the leakage of fluorescein into the vitreous after intravenous injection and in vitro using light and electron microscopy after an in vivo
The threshold energy for fluorescein leakage was 50 J x cm(-2) for blue light and 1,600 J x cm(-2) for yellow light. After broadband blue light exposure, the HRP reaction product was seen in the cytoplasm of the retinal pigment epithelium (RPE) cells and in the subretinal space but only if fluorescein leakage had been observed. Threshold energy and fluorescein leakage as a function of light energy were similar for albino and pigmented rabbits (P > 0.5). Only after yellow light exposure in excess of 3,700 J x cm(-2) was fluorescein leakage found. In that case complete disruption of the RPE was seen, but no HRP was observed in the RPE cytoplasm. Of the narrow-band blue light exposures, only that at lambda = 418 nm caused a significant increase in fluorescein leakage; the threshold energy was 18 J x cm(-2). Blue light was found to be at least 30 times more efficient than yellow light in causing dysfunction of the blood-retinal barrier. The most efficient wavelength was 418 nm, corresponding with the absorption spectrum of cytochrome c oxidase. Melanin seemed to play no role. The presence or absence of melanin in the RPE appeared to have no influence on the threshold energy.

Schlagwörter
Animals; Blood-Brain Barrierphysiology; Cytoplasmmetabolism; Electron Transport Complex IVmetabolismphysiology; Fluorophotometry; Horseradish Peroxidasepharmacokinetics; Humans; Lightadverse effects; Melaninsmetabolismphysiology; Microscopy; Microscopy, Electron; Pigment Epithelium of Eyeinjuriesphysiologyultrastructure; Rabbits; Retina inuriesradiation effectsultrastructure


Abstract
OBJECTIVE: To investigate the effect of lutein on rat retina blue light damage. METHODS: Sprague-Dawley rat were randomly separated into 6 groups: normal control, model control, solvent control, low-dose, media-dose, and high-dose. The concentration of lutein solution in the low-dose, media-dose, and high-dose groups are 0.5 mg/ml, 1.0 mg/ml, 2.0 mg/ml respectively. Mix sodium chloride and Tween 80 together at the ration of 1:9 as the solvent. Solvent and lutein solution were injected into rats' vitreous body of the solvent group and the lutein groups respectively (the injection volume is 5 microl), dark adaptation 24h, then the rats exposed to the blue light equipment 2h to set up the light-damage animal model. After light exposure, the rats were raised in darkness for 72 hours. Then the rats were killed, the eyes were removed and were processed to paraffin section for microscopy, then we observed the changes of retina morphous, measured the thickness of the outer nuclear layer (ONL thickness), and counted the number of apoptotic photoreceptors to compare the effect of lutein on light-damage of retina among different dosages. RESULTS: Comparing with the model-control group, the rats of lutein group had more clearly demarcated retina structure and more ordered cells. After detected under microscopy, we found that the ONL thickness (40 x 10 times, mm) of the rats of normal control group was 21.25 +/- 1.04. And the ONL thickness of the rats of lutein groups were 15.00 +/- 5.58, 11.75 +/- 4.20 and 14.75 +/- 3.96, from low dosage to high dosage, which was significantly (P < 0.01) higher than those of the rats of model control group (3.25 +/- 1.48) and solvent control group (3.25 +/- 0.89). Compare the number of apoptotic photoreceptors, there is no significant differences among groups. CONCLUSION: In the experiment conditions, the effect of prevention of lutein on retina light damage was significant. The result provided an important base on the application of lutein on crowd.
The photo-oxidation of A2E, a constituent of RPE lipofuscin, leads to the sequential addition of up to nine oxygen atoms and/or the addition or loss of two hydrogen atoms. These photo-oxidations were investigated in the presence and absence of either calf or human RPE melanin in A2E-laden RPE cells. It was found that calf melanin was protective against the photo-oxidation of A2E, with an inhibition of oxidation of up to 50% in the case of the addition of two oxygen atoms. Calf melanin was also protective against blue light-induced damage to RPE cells. In addition this ability appears to decrease in humans as they grow older. With aging, a melanin-lipofuscin complex called melanolipofuscin forms. It is suggested that the oxidation or photo-oxidation of A2E in vivo may contribute to the age-related deterioration of the anti-oxidant role of RPE melanin and lead to various retinal disorders, such as age-related macular degeneration.


Abstract

One of the most important functions of blue light (BL) is to induce chloroplast movements in order to reduce the damage to the photosynthetic machinery under excess light. Hydrogen peroxide (H(2)O(2)), which is commonly generated under various environmental stimuli, can act as a signalling molecule that regulates a number of developmental processes and stress responses. To investigate whether H(2)O(2) is involved in high-fluence BL-induced chloroplast avoidance movements, a laser scanning confocal microscope and a luminescence spectrometer were used to observe H(2)O(2) generation in situ with the assistance of the fluorescence probe dichlorofluorescein diacetate (H(2)DCF-DA). After treatment with high-fluence BL, an enhanced accumulation of H(2)O(2), indicated by the fluorescence intensity of DCF, can be observed in leaf cells of Arabidopsis thaliana. Exogenously applied H(2)O(2) promotes the high-fluence BL-induced chloroplast movements in a concentration-dependent manner within the range of 0-10(-4) M, not only increasing the degree of movements but also accelerating the start of migrations. Moreover, the high-fluence BL-induced H(2)O(2) generation and the subsequent chloroplast movements can be largely abolished by the administration of the H(2)O(2)-specific scavenger catalase and other antioxidants. In addition, in-depth subcellular experiments indicated that high-fluence BL-induced H(2)O(2) generation can be partly abolished by the addition of diphenyleneiodonium (DPI), which is an NADPH oxidase inhibitor, and the blocker of electron transport chain dichlorophenyl dimethylurea (DCMU), respectively. The results presented here suggest that high-fluence BL can induce H(2)O(2) generation at both the plasma membrane and the chloroplast, and that the production of H(2)O(2) is involved in high-fluence BL-induced chloroplast avoidance movements.


Abstract

The lipofuscin fluorophore A2E has been shown to mediate blue light-induced damage to retinal pigmented epithelial (RPE) cells. To understand the events that
lead to RPE cell apoptosis under these conditions, we explored signaling pathways upstream of the cell death program. Human RPE cells (ARPE-19) that had accumulated A2E were exposed to blue light to induce apoptosis and the involvement of the transcription factors p53 and c-Abl and the mitogen activated protein kinases p38 and JNK were examined. We found that A2E/blue light caused upregulation and phosphorylation of c-Abl, and upregulation of p53. Pretreatment with the c-Abl inhibitor STI571 and transfection with siRNA specific to c-Abl and p53 prior to irradiation reduced A2E/blue light-induced cell death. Gene and protein expression of JNK and p38 was upregulated in response to A2E/blue light. Treatment with the JNK inhibitor SP600125 before irradiation resulted in increase in cell death whereas inhibition of p38 with SB203580 had no effect. This study indicates that c-Abl and p53 are important for execution of the cell death program initiated in A2E-laden RPE cells exposed to blue light, while JNK might play an anti-apoptotic role.


Abstract
BACKGROUND: Excessive generation of free radicals due to light absorption is proposed as the most likely mechanism for photochemical retinal damage. The observed reduction of green light-induced retinal injury after ascorbate treatment is believed to be an antioxidative effect. The aim of the present study was to evaluate the possible protection of ascorbate against blue light-induced photoreceptor damage.
METHODS: Cyclic light-reared albino rats were injected intraperitoneally with either ascorbate (1 mg/g body weight) or, as placebo, physiological saline 24 h before and just prior to exposure to blue light. After 20-22 h of dark adaptation, two groups of the rats were exposed to the blue light (400-480 nm) for 6 h at an average irradiance of 0.7 W/m² in the cage. Six days after light exposure, all rats were killed and retinal samples were analyzed.
RESULTS: Diffuse blue light irradiation resulted in an uneven distribution of damage in the retina. As judged from the pathological changes in the retina irradiated, no microscopic difference was observed between the two groups. The preserved thickness of the outer nuclear layer was on average 61.3% in the ascorbate-treated and 66.4% in the placebo-treated group. The photoreceptor loss was not significantly different between the two groups. CONCLUSION: The ascorbate did not protect the retina from blue-light induced damage. This favors the assumption that the mechanisms for blue light-induced retinal damage might differ from that for green light.

Schlagwörter
Animals; Ascorbate Oxidasepharmacology; Disease Models, Animal; Female; Injections, Intraperitoneal; Lightadverse effects; Photoreceptor Cells, Vertebrate drug effectsradiation effects; Radiation Injuries, Experimentaletiologypathologyprevention & control; Rats; Rats, Sprague-Dawley; Retinal Diseasessetiologypathologyprevention & control; Treatment Failure


Abstract
PURPOSE: To explore cell death in blue light induced retinal damage. METHODS: Sprague-Dawley rats reared under cyclic light were exposed continuously to diffuse blue light (400-480 nm) at 0.64 W/m² for 3 or 6 h after 22 h of dark adaptation. The rats were kept in darkness and killed immediately, 8, 16 and 24 h following light exposure. The retinal damage by the blue light was examined with a transmission electron microscope. The cell death was characterised by in situ terminal dUTP nick end labelling (TUNEL) and gel electrophoresis. RESULTS: During the 24 h following light exposure, photoreceptor cell death was characterised by progressive condensation and margination of the chromatin, shrinkage or convolution and fragmentation of the nucleus, condensation of the cytoplasm, and formation of apoptotic bodies along with rapid removal of dying cells from damaged areas in the
absence of inflammatory response. The TUNEL-positive nuclei were scattered individually in the outer nuclear layer just after light exposure. A wave of massive TUNEL labelling of photoreceptor nuclei peaked at 8-16 h and dropped at 24 h following light exposure. The distribution of TUNEL-positive nuclei was located predominantly at the upper temporal region of the retina, which was the most sensitive area to the damage caused by blue light. Furthermore, the multiples of internucleosomal cleavage of 180-200 base pairs were demonstrated at corresponding time points. CONCLUSION: Photoreceptor cell apoptosis is seen early after the retina is damaged by blue light.


Abstract

PURPOSE: To investigate the protective effect of a blue-light filtering intraocular lens (yellow IOL) (YA60BB, Hoya) and an ultraviolet (UV)-absorbing IOL (VA60BB, Hoya) on light-induced phototoxicity to retinal pigment epithelial (RPE) cells laden with the lipofuscin fluorophore A2E and on the production of vascular endothelial growth factor (VEGF) after light exposure. SETTING: University of Tokyo, Tokyo, Japan. METHODS: The A2E-laden ARPE-19 cells were exposed to white light and a UV-absorbing IOL or a blue-light filtering IOL was placed over the light beam. After 48 hours of irradiation, the viability of the cells was determined with WST-1 (a sodium salt of 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate) assay, and the secreted protein level of VEGF was determined by enzyme-linked immunosorbent assay. RESULTS: Without an IOL, the white-light exposure decreased cell viability to 28% of the nonirradiated control. Although the UV-absorbing IOL tended to reduce light-induced cell death, the decrease was not significant. However, the presence of the blue-light filtering IOL significantly attenuated light-induced cell damage, increasing cell viability to 42%. The secreted VEGF protein level increased 3.2-fold after the A2E-laden RPE cells were exposed to white light. In the presence of the UV-absorbing IOL, the VEGF protein level decreased, but not significantly. The presence of the blue-light filtering IOL significantly attenuated the upregulated VEGF expression compared to upregulation without an IOL. CONCLUSION: This study supports the theory that a blue-light filtering IOL may be more protective against A2E-induced photochemical damage and inhibit more light-induced VEGF production than a conventional UV-absorbing IOL.


Abstract

PURPOSE: To investigate whether photoreceptor ellipsoids generate reactive oxygen species (rOx) after blue light illumination. METHODS: Cultured salamander photoreceptors were exposed to blue light (480 +/- 10 nm; 10 mW/cm²). The light-induced catalytic redox activity in the culture was monitored with the use of 3,3'-diaminobenzidine (DAB). Tetramethylrhodamine ethyl ester (TMRE) and 2',7'-dichlorodihydro-fluorescein acetate (DHF-DA) were used as probes to measure the mitochondrial membrane potential and intracellular rOx, respectively. RESULTS: A significant deposit of DAB polymers was found in the culture after exposure to blue
light. Basal levels of rOx were observed in photoreceptor ellipsoids when cells were stained with DHF-DA. This staining colocalized with TMRE. After exposure to blue light, a sharp increase of rOx immediately occurred in the ellipsoids of most photoreceptors. When the light intensity was reduced, the response kinetics of rOx generation were slowed down; however, comparable amounts of rOx were generated after a standard time of exposure to light. The production of rOx in photoreceptors was markedly decreased when an antioxidant mixture was included in the medium during exposure to light. Rotenone or antimycin A, the respiratory electron transport blockers at complex I and III, respectively, significantly suppressed the light-evoked generation of rOx. CONCLUSIONS: A robust amount of rOx is produced in the ellipsoid when photoreceptors are exposed to blue light. This light-induced effect is antioxidant sensitive and strongly coupled to mitochondrial electron transport. The cumulative effect of light on rOx generation over time may implicate a role for mitochondria in light-induced oxidative damage of photoreceptors.

Zhou, Jian Wei; Ren, Guo Liang; Zhang, Xiao Ming; Zhu, Xi; Lin, Hai Yan; Zhou, Ji Lin (2004): [Study of blue light induced DNA damage of retinal pigment epithelium(RPE) cells and the protection of vitamin C]. In: Shi yan sheng wu xue bao, Jg. 36, H. 5, S. 397–400.

Abstract
To evaluate protection of vitamin C on blue light-induced DNA damage of human retinal pigment epithelium (RPE) cells. The cultured RPE cells were divided into 3 groups: Control group (no blue light exposure), blue light exposure group (blue light exposure for 20 minutes) and blue light exposure + vitamin C group (blue light exposure + 100 mumol/L vitamin C). Travigen's comet assay kit and Euclid comet assay software were used to assay the DNA damage levels. The DNA percentage in the tail of electrophoretogram in the three groups were 18.44%, 54.42% and 32.43% respectively (p < 0.01). Tail moments were 8.2, 48.3, and 18.4 respectively (p < 0.01). Blue light could induce DNA damage to RPE cells but vitamin C could protect the RPE cells from the blue light-induced DNA damage.


Abstract
The following review outlines the mechanisms of phototoxicity that are known so far, how they develop, which risk factors are involved, and what the consequences are for ophthalmology. It is necessary to differentiate between photochemical and thermal damage as they differ with regard to etiology and course. Photochemical damage in the lens originates from the absorption of UV-A light; damage caused by oxidation can cause nuclear cataract. Photochemical damage of the retina occurs typically after a longer interval and is mainly due to short-wavelength visible light ("blue light damage"); it entails destruction of membranes of the photoreceptor outer segments and finally photoreceptor death. There are indications that age-related macular degeneration can be accelerated by photochemical light damage. Lipofuscin, photo-sensitizing drugs and prolonged exposure, as well as aphakia and pseudophakia, can increase the risk. Thermal injury is caused mainly by absorption of longer-wavelength light by the retinal pigment epithelium; the effects are usually immediate. The amount of light that can cause threshold damage by common light sources and ophthalmological instruments is given in relation to wavelength, area, and the period of exposure. This information provides the criteria for optimal light-
protection glasses. Phototoxic damage can be avoided by awareness, measurement and corresponding action, including the development of better industrial standards for sunglasses and light-emitting devices.

Schlagwörter

- Eyeradiation effects
- Eye Burnsetiology
- Humans
- Lens, Crystallineradiation effects
- Lightadverse effects
- Photoreceptor Cellsradiation effects
- Radiation Injuriesetiology
- Retinaradiation effects