

Antimicrobial Blue Light

Mitochondrial Medicine
Mitochondrial Metabolism, Diseases, Diagnosis and Therapy

Anna Gvozijakova, editor
Medical Faculty, Comenius University, Bratislava, Slovakia

Springer
2008

"Polarized Light"
Chapter 22
Jan Palinkas and Alfonz Smola

"The actual development of polarized light application started after implementation of laser therapy in the 1960s of the 20th century,"

"Energy of photons as the smallest parts of light waves depends indirectly on the wavelength.

Photons with lower wavelengths have more energy than those with longer wavelengths.

So, photons of UV radiation are richer in energy than photons of visible light.

Photons of blue light have more energy than those of red light."

Lasers work through a "biostimulation effect."

The energy of red color "has the greatest ability of biostimulation."

"Red stimulates when there is lack of energy."

"With monochromatic polarized light of red color we can irradiate inflammations from the very beginning."

"Blue color: 400-490 nm. The light of this color has calming effects—blue is considered to be a cold color. It slows down pulse frequencies, helps the overloaded vessels get into normal state, acts as an antiseptic, kills pain and cools."

"For children, it is one of the best healing colors."

"Blue is very effective in combination with red."

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J *Hosp Infect.* 2014 Sep;88(1):1-11. doi: 10.1016/j.jhin.2014.06.004. Epub 2014 Jul 3.

405 nm light technology for the inactivation of pathogens and its potential role for environmental disinfection and infection control.

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Abstract

BACKGROUND: Although the germicidal properties of ultraviolet (UV) light have long been known, it is only comparatively recently that the antimicrobial properties of visible violet-blue 405 nm light have been discovered and used for environmental disinfection and infection control applications.

AIM: To review the antimicrobial properties of 405 nm light and to describe its application as an environmental decontamination technology with particular reference to disinfection of the hospital environment.

METHODS: Extensive literature searches for relevant scientific papers and reports.

FINDINGS: A large body of scientific evidence is now available that provides underpinning knowledge of the 405 nm light-induced photodynamic inactivation process involved in the destruction of a wide range of prokaryotic and eukaryotic microbial species, including resistant forms such as bacterial and fungal spores. For practical application, a high-intensity narrow-spectrum light environmental disinfection system (HINS-light EDS) has been developed and tested in hospital isolation rooms. The trial results have demonstrated that this 405 nm light system can provide continuous disinfection of air and exposed surfaces in occupied areas of the hospital, thereby substantially enhancing standard cleaning and infection control procedures.

CONCLUSION: Violet-blue light, particularly 405 nm light, has significant antimicrobial properties against a wide range of bacterial and fungal pathogens and, although germicidal efficacy is lower than UV light, this limitation is offset by its facility for safe, continuous use in occupied

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Toxicol In Vitro. 2016 Jun;33:54-62. doi: 10.1016/j.tiv.2016.02.011. Epub 2016 Feb 23.**ELSEVIER**
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Cytotoxic responses to 405nm light exposure in mammalian and bacterial cells: Involvement of reactive oxygen species.

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Abstract

Light at wavelength 405 nm is an effective bactericide. Previous studies showed that exposing mammalian cells to 405 nm light at 36 J/cm² (a bactericidal dose) had no significant effect on normal cell function, although at higher doses (54 J/cm²), mammalian cell death became evident. This research demonstrates that mammalian and bacterial cell toxicity induced by 405 nm light exposure is accompanied by reactive oxygen species production, as detected by generation of fluorescence from 6-carboxy-2',7'-dichlorodihydrofluorescein diacetate. As indicators of the resulting oxidative stress in mammalian cells, a decrease in intracellular reduced glutathione content and a corresponding increase in the efflux of oxidised glutathione were observed from 405 nm light treated cells. The mammalian cells were significantly protected from dying at 54 J/cm² in the presence of catalase, which detoxifies H₂O₂. Bacterial cells were significantly protected by sodium pyruvate (H₂O₂ scavenger) and by a combination of free radical scavengers (sodium pyruvate, dimethyl thiourea (OH scavenger) and catalase) at 162 and 324 J/cm². Results therefore suggested that the cytotoxic mechanism of 405 nm light in mammalian cells and bacteria could be oxidative stress involving predominantly H₂O₂ generation, with other ROS contributing to

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**Drug Resist Updat.** 2017 Nov;33-35:1-22. doi: 10.1016/j.drup.2017.10.002. Epub 2017 Oct 13.

Antimicrobial blue light inactivation of pathogenic microbes: State of the art.

[Wang Y¹](#), [Wang Y²](#), [Wang Y³](#), [Murray CK⁴](#), [Hamblin MR⁵](#), [Hooper DC⁶](#), [Dai T⁷](#).

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Abstract

As an innovative non-antibiotic approach, **antimicrobial blue light** in the spectrum of 400-470nm has demonstrated its intrinsic **antimicrobial properties** resulting from the presence of endogenous photosensitizing chromophores in pathogenic microbes and, subsequently, its promise as a counteractant of antibiotic resistance. Since we published our last review of **antimicrobial blue light** in 2012, there have been a substantial number of new studies reported in this area. Here we provide an updated overview of the findings from the new studies over the past 5 years, including the efficacy of **antimicrobial blue light** inactivation of different microbes, its mechanism of action,

PubMed antimicrobial blue light and normal flora

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Sci Rep. 2017 Jul 12;7(1):5225. doi: 10.1038/s41598-017-05706-1.



Antimicrobial effect of blue light using *Porphyromonas gingivalis* pigment.

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Abstract

The development of antibiotics cannot keep up with the speed of resistance acquired by microorganisms. Recently, the development of **antimicrobial** photodynamic therapy (aPDT) has been a necessary **antimicrobial** strategy against antibiotic resistance. Among the wide variety of bacteria found in the oral **flora**, *Porphyromonas gingivalis* (*P. gingivalis*) is one of the etiological **agents** of periodontal disease. aPDT has been studied for periodontal disease, but has risks of cytotoxicity to **normal** stained tissue. In this study, we performed aPDT using protoporphyrin IX (PpIX), an intracellular pigment of *P. gingivalis*, without an external photosensitizer. We confirmed singlet oxygen generation by PpIX in a **blue-light** irradiation intensity-dependent manner. We discovered that **blue-light** irradiation on *P. gingivalis* is potentially bactericidal. The sterilization mechanism seems to be oxidative DNA damage in bacterial cells. Although it is said that no resistant bacteria will emerge using aPDT, the conventional method relies on an added photosensitizer dye. PpIX in *P. gingivalis* is used in energy production, so aPDT applied to PpIX of *P. gingivalis* should limit the appearance of resistant bacteria. This approach not only has potential as an effective treatment for new periodontal diseases, but also offers potential antibacterial treatment for multiple drug resistant bacteria.

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Microbiology, 2016 Sep;162(9):1680-1688. doi: 10.1099/mic.0.000350. Epub 2016 Aug 11.

The effects of 405 nm light on bacterial membrane integrity determined by salt and bile tolerance assays, leakage of UV-absorbing material and SYTOX green labelling.

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Abstract

Bacterial inactivation by 405 nm light is accredited to the photoexcitation of intracellular porphyrin molecules resulting in energy transfer and the generation of reactive oxygen species that impart cellular oxidative damage. The specific mechanism of cellular damage, however, is not fully understood. Previous work has suggested that destruction of nucleic acids may be responsible for inactivation; however, microscopic imaging has suggested membrane damage as a major constituent of cellular inactivation. This study investigates the membrane integrity of *Escherichia coli* and *Staphylococcus aureus* exposed to 405 nm light. Results indicated membrane damage to both species, with loss of salt and bile tolerance by *S. aureus* and *E. coli*, respectively, consistent with reduced membrane integrity. Increased nucleic acid release was also demonstrated in 405 nm light-exposed cells, with up to 50% increase in DNA concentration into the extracellular media in the case of both organisms. SYTOX green fluorometric analysis, however, demonstrated contradictory results between the two test species. With *E. coli*, increasing permeation of SYTOX green was observed following increased exposure, with >500% increase in fluorescence, whereas no increase was observed with *S. aureus*. Overall, this study has provided good evidence that 405 nm light exposure causes loss of bacterial membrane integrity in *E. coli*, but the results with *S.*

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[Antimicrob Resist Infect Control.](#) 2017 Sep 29;6:100. doi: 10.1186/s13756-017-017-01Read free
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Assessment of the potential for resistance to antimicrobial violet-blue light in *Staphylococcus aureus*.

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Abstract

BACKGROUND: Antimicrobial violet-blue light in the region of 405 nm is emerging as an alternative technology for hospital decontamination and clinical treatment. The mechanism of action is the excitation of endogenous porphyrins within exposed microorganisms, resulting in ROS generation, oxidative damage and cell death. Although resistance to 405 nm light is not thought likely, little evidence has been published to support this. This study was designed to establish if there is potential for tolerance development, using the nosocomial pathogen *Staphylococcus aureus* as the model organism.

METHODS: The first stage of this study investigated the potential for *S. aureus* to develop tolerance to high-intensity 405 nm light if pre-cultured in low-level stress violet-blue light ($\leq 1 \text{ mW/cm}^2$) conditions. Secondly, the potential for tolerance development in bacteria subjected to repeated sub-lethal exposure was compared by carrying out 15 cycles of exposure to high-intensity 405 nm light, using a sub-lethal dose of 108 J/cm^2 . Inactivation kinetics and antibiotic susceptibility were also compared.

RESULTS: When cultured in low-level violet-blue light conditions, *S. aureus* required a greater dose of high-intensity 405 nm light for complete inactivation, however this did not increase with multiple (3) low-stress cultivations. Repeated sub-lethal exposures indicated no evidence of bacterial tolerance to 405 nm light. After 15 sub-lethal exposures 1.2 and 1.4 \log_{10} reductions were achieved for MSSA and MRSA respectively, which were not significantly different to the initial 1.3 \log_{10} reductions achieved ($P = 0.242$ & 0.116 , respectively). Antibiotic susceptibility was unaffected,

with the maximum change in zone of inhibition being ± 2 mm.

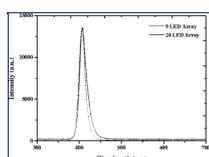
CONCLUSIONS: Repeated sub-lethal exposure of non-proliferating *S. aureus* populations did not affect the susceptibility of the organism to 405 nm **light**, nor to antibiotics. Culture in low-level violet-**blue light** prior to 405 nm **light** exposure may increase oxidative stress responses in *S. aureus*, however, inactivation still occurs and results demonstrate that this is unlikely to be a selective process. **These results demonstrate that tolerance from repeated exposure is unlikely to occur, and further supports the potential development of 405 nm light for clinical decontamination and treatment applications.**

KEYWORDS: 405 nm **light**; Bacterial resistance; Bacterial tolerance; EMRSA-15; *Staphylococcus aureus*

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Antimicrobial blue light inactivation of pathogenic microbes: State of the art.

[Wang Y¹](#), [Wang Y²](#), [Wang Y³](#), [Murray CK⁴](#), [Hamblin MR⁵](#), [Hooper DC⁶](#), [Dai T⁷](#).

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Abstract

As an innovative non-antibiotic approach, **antimicrobial blue light** in the spectrum of 400-470nm has demonstrated its intrinsic **antimicrobial** properties resulting from the presence of endogenous photosensitizing chromophores in pathogenic microbes and, subsequently, its **promise as a counteracter of antibiotic resistance**. Since we published our last review of **antimicrobial blue light** in 2012, there have been a substantial number of new studies reported in this area. Here we provide an updated overview of the findings from the new studies over the past 5 years, including the efficacy of **antimicrobial blue light** inactivation of different microbes, its mechanism of action,

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Recent Pat Antiinfect Drug Discov. 2017 Nov 7. doi: 10.2174/1872213X11666171108104104. [Epub ahead of print]

Recent Patents on Light-Based Anti-Infective Approaches.

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Abstract

BACKGROUND: Antibiotic resistance is one of the most serious health threats to modern medicine. The lack of potent antibiotics puts us at a disadvantage in the fight against infectious diseases, especially those caused by antibiotic-resistant microbial strains. To this end, an urgent need to search for alternative antimicrobial approaches has arisen. In the last decade, light-based therapy has made significant strides in this fight to combat antibiotic resistance among various microbial strains. This method includes utilizing antimicrobial blue light, antimicrobial photodynamic therapy, and germicidal ultraviolet irradiation, among others. Light-based therapy is advantageous over traditional antibiotic-based therapy in that it selectively eradicates microbial cells without harming human cells and tissues.

METHODS: This review highlights the patents on light-based therapy that were filed approximately within the last decade and are dedicated to eradicating pathogenic microbes.

RESULTS: The treatments and devices discussed in this review are interestingly enough to be used in various different functions and settings, such as dental applications, certain diseases in the eye, skin and hard surface cleansing, decontamination of internal organs (e.g., the stomach), decontamination of apparel and equipment, eradication of pathogenic microbes from buildings and rooms, etc. Most of the devices and inventions introduce methods of destroying pathogenic bacteria and fungi without harming human cells.

CONCLUSIONS: Light-based antimicrobial approaches hold great promise for the future in regards to treating antibiotic-resistant infections and diseases.

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Antimicrobial Blue Light Therapy for Infectious Keratitis: Ex Vivo and In Vivo Studies

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PURPOSE. To investigate the effectiveness of antimicrobial blue light (aBL) as an alternative or adjunctive therapeutic for infectious keratitis.

METHODS. We developed an ex vivo rabbit model and an in vivo mouse model of infectious keratitis. A bioluminescent strain of *Pseudomonas aeruginosa* was used as the causative pathogen, allowing noninvasive monitoring of the extent of infection in real time via bioluminescence imaging. Quantitation of bacterial luminescence was correlated to colony-forming units (CFU). Using the ex vivo and in vivo models, the effectiveness of aBL (415 nm) for the treatment of keratitis was evaluated as a function of radiant exposure when aBL was delivered at 6 or 24 hours after bacterial inoculation. The aBL exposures calculated to reach the retina were compared to the American National Standards Institute standards to estimate aBL retinal safety.

RESULTS. *Pseudomonas aeruginosa* keratitis fully developed in both the ex vivo and in vivo models at 24 hours post inoculation. Bacterial luminescence in the infected corneas correlated linearly to CFU ($R^2 = 0.921$). Bacterial burden in the infected corneas was rapidly and significantly reduced ($>2\text{-log}_{10}$) both ex vivo and in vivo after a single exposure of aBL. Recurrence of infection was observed in the aBL-treated mice at 24 hours after aBL exposure. The aBL toxicity to the retina is largely dependent on the aBL transmission of the cornea.

CONCLUSIONS. Antimicrobial blue light is a potential alternative or adjunctive therapeutic for infectious keratitis. Further studies of corneal and retinal safety using large animal models, in which the ocular anatomies are similar to that of humans, are warranted.

Keywords: antimicrobial blue light, keratitis, *Pseudomonas aeruginosa*, mouse model, rabbit model, bioluminescence imaging

Infectious keratitis is a potentially blinding ocular condition of the cornea. According to a recent report released by the U.S. Centers for Disease Control and Prevention (CDC), each year in the United States there are approximately 1 million clinical visits for keratitis, translating into an estimated total cost of \$175 million per year.¹ The risk factors for infectious keratitis include ocular trauma, contact lens wear, recent ocular surgery, preexisting ocular surface disease, dry eyes, lid deformity, corneal sensation impairment, chronic use of topical steroids, and systemic immunosuppression.² The common causative pathogens of infectious keratitis are *Pseudomonas aeruginosa*,^{2–5} *Staphylococcus aureus*,^{2,5–7} *Streptococcus pneumoniae*,^{8,9} and *Fusarium solani*.^{10,11} Treatment of infectious keratitis must be rapidly instituted to minimize the destruction of corneal tissue, limit the extent of corneal scarring, and prevent vision loss. The current standard of care for the treatment of infectious keratitis is the use of topical or systemic antibiotics.^{12,13} However, the clinical management of keratitis has been significantly complicated by the increasing emergence

of multidrug-resistant pathogens.^{2–8,11,14} Pathogens replicate rapidly, and a mutation that helps a pathogen survive in the presence of antibiotic(s) will quickly become predominant throughout the microbial population, rendering infections that cannot be treated with available antibiotics. There is, consequently, a pressing need for the development of alternative treatment regimens to tackle drug resistance in infectious keratitis.

A novel light-based antimicrobial approach, antimicrobial blue light (aBL), has attracted increasing attention due to its intrinsic antimicrobial effect without the involvement of exogenous photosensitizers.^{15–17} It also appears that pathogens are less able to develop resistance to aBL than to traditional antibiotics due to the multitarget characteristic of aBL.^{15,18} The mechanism of action of aBL is still not fully understood. A common hypothesis is that aBL excites the naturally occurring endogenous porphyrins or/and flavins in microbial cells and subsequently leads to the production of cytotoxic reactive oxygen species (ROS).¹⁵ The transparency of the cornea and

