Visible Blue Light is Capable of Inactivating *Candida albicans* and Other Fungal Species

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THE INEXORABLE ADVANCE of multidrug resistance occurring in a wide range of pathogenic microorganisms has alarmed the world in recent years. It has led to fears of the eventual emergence of “untreatable infections,” with huge death tolls and mind-boggling expense. In response to these concerns, new antimicrobial approaches are urgently being sought, to which it is expected that microbes will be unable to develop resistance. Prominent among these new approaches are light-based technologies.

It has been known for many years that visible light (particularly in the violet-blue region of the spectrum, between 400 and 490 nm) is capable of killing bacteria on its own. The mechanism is proposed to be the natural accumulation of photoactive metal-free porphyrins such as uroporphyrin, coproporphyrin, and to a lesser extent protoporphyrin. The light is absorbed by the Soret band of the porphyrins (around 405–420 nm) exciting them to the triplet state, where they can generate singlet oxygen, as is well known to occur in photodynamic therapy. There may be a secondary mechanism for longer wavelength blue light (440–490 nm), which hits flavin molecules that also occur in bacteria. This “antimicrobial blue light therapy” (aBLT) is attractive as it does not require any added photosensitizer, does not involve possibly harmful ultraviolet radiation, and kills microbial cells regardless of their antibiotic-resistance status. aBLT can be applied *in vivo* to treat bacterial infections caused by species such as methicillin-resistant *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, particularly in superficial lesions such as burns and skin abrasions.

What is not widely known, however, is whether aBLT can also be used to kill fungal species. We recently showed that the eukaryotic dimorphic yeast, *Candida albicans*, could be eradicated ($\sim 6\text{-log}_{10}$ of killing) by 70 J/cm^2 of 415 nm light under conditions in which human keratinocytes were hardly affected.¹ No resistance to the effects of aBLT was found after 10 repeated cycles of sublethal aBLT and subsequent regrowth. It was found that extracts of *C. albicans* cells contained fluorescence signatures attributed to free porphyrins, and also flavins. Importantly, we were able to show that aBLT could treat *Candida* infections in third-degree mouse burns. Using a genetically engineered bioluminescent *C. albicans* strain, we were able to use bioluminescence imaging to show that 324 J/cm^2 of 415 nm light almost

eliminated the signal from the mouse burns, and that the level of infection remained very low for 8 days compared with untreated controls.

Our findings are reinforced by the studies of other groups. It was documented by other laboratories that aBL successfully inactivated *C. albicans* planktonic cells and biofilms. In a study carried out by Gupta et al., 4.52-log_{10} inactivation of *C. albicans* in suspension was observed when 332.1 J/cm^2 aBL at 405 nm had been delivered.² Rosa et al. reported that 2.3-log_{10} inactivation of *C. albicans* in biofilms was observed after being exposed to 45.16 J/cm^2 aBL at 455 nm.³

In addition to *C. albicans*, aBLT has also demonstrated its efficacy against other fungal species, including dermatophytes, yeasts, and molds. For example, Moorhead et al. investigated the use of aBL for inhibiting the growth of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Aspergillus niger*.⁴ On agar plates, the growth of the microconidia of *T. rubrum* and *T. mentagrophytes* was completely inhibited after an exposure of 504 J/cm^2 aBL at 405 nm. *A. niger* conidia showed greater resistance, and colony growth developed after aBL exposure. In suspension, an exposure of 360 J/cm^2 resulted in complete inactivation of *T. rubrum* microconidia, whereas *A. niger* showed greater resistance. After an exposure of 1440 J/cm^2 , however, *A. niger* hyphae were completely inactivated, while only a 3-log_{10} reduction in a conidial suspension (initially 5-log_{10} CFU) was achieved.

In another study, 405-nm light was successfully applied for the inactivation of *Saccharomyces cerevisiae* and dormant or germinating conidia of *A. niger*.⁵ To achieve 5-log_{10} CFU/mL reduction in a fungal suspension, the required aBL exposure was 288 J/cm^2 for *S. cerevisiae*, but a much higher value of 2.3 kJ/cm^2 was required for dormant conidia of *A. niger*. Upon germination, the susceptibility of *A. niger* conidia to aBL significantly increased. The study also revealed that aBL inactivation of fungi involved an oxygen-dependent mechanism, as previously described in bacteria, and as is consistent with a photodynamic effect occurring.

Another application of aBL being explored is to treat postharvest spoilage in agricultural crops. It was found that aBL (410–540 nm) suppressed the growth of the blue mold (*Penicillium italicum*), green mold (*Penicillium digitatum*), gray mold (*Botrytis cinerea*), and stem end rot (*Phomopsis citri*), and significantly reduced postharvest spoilage.

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In addition, aBL was found to reduce the cell wall digestive enzyme activity of *P. digitatum*, and could also induce octanal production in citrus fruits, which is lethal to molds. aBL also increased the scoparone concentration and ethylene production in citrus fruits, which mediate resistance to mold infection.

In conclusion, it can be seen that contrary to some beliefs, fungal cells are indeed killed by the action of blue light alone, and this effect may have both medical and agricultural applications.

References

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