

# Using Visible and Near-IR Light to Facilitate Photobiomodulation: A Review of Current Research

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**Abstract:** This review article summarizes the work of our research team. We are engaged in efforts to evaluate the effect of visible and near-IR light on various biologic tissues. Much of our work has dealt with the antimicrobial effect of light. Those examples are discussed in the paper. We are also engaged in examining the use of light to positively address deficits associated with peripheral neuropathies and musculoskeletal injuries. This review article is not intended as a comprehensive treatment of low level light therapy, but rather is intended to summarize our research agenda. We hope this summary can serve as a part of the basic science foundation that will lead to effective use of light energies as an alternative, if not adjunctive, therapy to inhibit the growth of microorganisms that threaten human health and to assist in the management of pain and inflammation associated with soft tissue injury and peripheral neuropathy.

**Key Words** – Photobiomodulation, Antimicrobial, Visible and Near-IR Light

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## 1. Background / Introduction

*“The investigation of novel non-antibiotic approaches for the prevention of and protection against infectious diseases should be encouraged, and such approaches must be high-priority research and development projects [1].”* Non-pharmaceutical approaches to preventing and treating infection have formed the basis of a research agenda that we have pursued since 2006. Our primary focus has been to examine the degree to which visible and near infrared (near-IR) light energies could modulate the growth and replication of microorganisms *in vitro*. Our hope has been to lay a basic research foundation that might eventually lead to the development of clinical protocols to assist in the care of cutaneous ulcers.

After our research agenda related to microbial inhibition was established, we began examining the degree to which light energies might affect outcomes of patients

with various orthopedic and neurologic conditions. Whether in reference to microorganisms or human subjects with orthopedic / neurologic conditions, our purpose is to document photobiomodulation. We are interested in how biologic tissues respond to focused applications of visible and near-IR energies. The review that follows summarizes this work.

## 2. Antimicrobial Effect

Nussbaum et al. piqued our interest in the potential for light as treatment of microbial infections when their two works were published in 2002 and 2003 suggesting that near-IR wavelengths could inhibit *Staphylococcus aureus* and *Pseudomonas aeruginosa* [2, 3]. Menendez et al. demonstrated a related application for light in 2004 when they showed improved healing of wounded tissue following irradiation with red and near-IR wavelengths [4]. Gantz et al., in 2005, reported that *Helicobacter pylori* could be inhibited by light [5]. These observations stimulated our interest and led to our first two publications [6, 7]. We were

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able to demonstrate that (*in vitro*) 405nm light could produce a dose dependent bactericidal effect on *P. aeruginosa* and *S. aureus*. 470nm light was also effective on both organisms, but not as effective on *S. aureus*. The addition of 880nm energy to the 405nm energy similarly resulted in the inhibition of *P. aeruginosa* and *S. aureus*.

These positive indications that blue and near-IR wavelengths could inhibit common aerobes seemed to form a foundation for the potential application of light in the treatment of infected dermal ulcers. Citing our work, Dai et al. showed blue light to be effective in preventing septicemia in rats with burn wounds infected by *P. aeruginosa* [8]. Dai and his group also showed a similar outcome in rat wounds infected with methicillin-resistant *S. aureus* [9]. While neither our work, nor the work of Dai et al., involved human subjects, the evidence does suggest that blue light does inhibit certain microorganisms *in vitro* and *in vivo*.

Blue light (405nm) energy has proven inhibitory to *Mycobacterium smegmatis* [10]. Feese and Ghiladi showed photodynamic therapy, using a sensitizing dye, could effectively inhibit *M. smegmatis* [11]. Murdoch et al. demonstrated the same outcome in late 2012 without using sensitizing agents [12]. The issue that arose from this work was that the dose needed to inhibit this organism was quite high (in excess of 100 J/cm<sup>2</sup>). We set out to find techniques that might lower the dose needed to produce inhibition, while not including a sensitizing dye material. We were able to lower the dose needed to inhibit *M. smegmatis* by employing a near-IR wavelength (850nm) at 45 J/cm<sup>2</sup> [13]. In this case the near-IR energy was more effective in producing inhibition than was blue light or blue light in combination with near-IR.

*Klebsiella pneumoniae* is an organism that was recently placed on the "Urgent Threat" list by the Centers for Disease Control in the United States. Multi-drug resistant (MDR) strains of this organism have emerged recently. *K. pneumoniae* is a highly antibiotic resistant microbe and can carry the New Delhi Metallo-Beta-Lactamase-1 (NDM-1) gene on the plasmid, making transference of antibiotic resistance possible to same and similar organisms such as *Escherichia coli*. We were able to demonstrate (*in vitro*) that a combination of blue (464nm) and near-IR (850nm) energies could inhibit growth of *K. pneumoniae* when doses of 45 and 60 J/cm<sup>2</sup> were employed [14]. *M. smegmatis* and *K. pneumoniae* both have cell walls with a high lipid content that offers a protective advantage. A unique outer capsule is formed that protects the microbes from antibiotic entrance. Our experience suggests that organisms with this trait may be more effectively inhibited when near-IR energies are included. Lee et al. suggested this was the case in 2011 [15].

Bacteria are not the only microbes that may be inhibited by light energies. *Candida albicans* appears to be susceptible to light energies. We have found red (624nm) light to be an effective inhibitor of this organism [16]. We have also found that combining near-IR (850nm) with red light can improve the level of inhibition obtained [17]. We are currently examining the degree to which light can inhibit the growth of other common fungal pathogens.

### 3. Resistance

The opening paragraphs of this paper suggested the primary reason for our work with light energy was the ever present threat of antibiotic resistance. Certainly this issue is an important part of what we do. We asked the question, "Are microbes able to develop resistance to the application of light energies?" While those who work with photodynamic therapy (application of photosensitizing dyes) have suggested resistance to light does not occur we still believed it was important to test this question. We have seen *S. aureus* demonstrate the ability to develop resistance to blue (405nm) light. After four to five generations, the effective inhibition of the light energy was seen to diminish [18]. We then sought to find ways to overcome this resistance. We were able to show that alterations such as slightly varying dose, rate of delivery and combination with near-IR energy would result in sustaining effective inhibition for seven or more generations of the organism [19].

### 4. Other Applications of Light Energy

There is some evidence that light can be used to promote repair in various musculoskeletal conditions [20 – 25]. We have examined the value of light in the treatment of plantar fasciitis. We found that 9 J/cm<sup>2</sup> of a combined red (625nm) and near-IR (850nm) energy can improve outcomes double those obtained by conventional physical therapy interventions [26]. Pain and function improvements were enhanced when light was combined with conventional therapy (heat, electrical stimulation, friction massage and stretching) and applied two times weekly for four weeks.

Hamblin has written extensively and compellingly about the connection between low level light therapy and nitric oxide [27]. Others have made similar suggestions [28 – 32]. We considered this work and believed that near-IR light might improve the status of patients with peripheral neuropathy. We recently published a case study demonstrating a very good clinical outcome in a patient with peripheral neuropathy. We treated this patient three times weekly for six weeks using near-IR (850nm) energy applied to the lumbosacral junction, the ankles and plantar surfaces of the feet. We saw significant improvements in sensation and function [33]. We are continuing to pursue this line of research. We have also added a patient group with restless leg syndrome.

### 5. Summary

In this review we have attempted to summarize the work our team is doing to evaluate the degree to which visible and near-IR light can be used to inhibit microbial growth, facilitate repair for musculoskeletal injury, and improve sensation loss associated with peripheral neuropathy. We have included certain works of other researchers as they have either laid the groundwork for our efforts and/or obtained similar outcomes in their research related to light energies. Tables 1 and 2 provide an overview of the work we have published.

This paper is not intended to be an exhaustive review. Our objective was to summarize the work associated with photobiomodulation we have undertaken. This work was begun in 2006 and continues to the present. Our current efforts include attempts to inhibit the growth of various microbes, but also to evaluate the effects light energies have on neurologic, circulatory, contractile and non-contractile tissues.

**Table 1.** Summary of Light Related Research on Microbes, Guffey et al.

Microbe	Light Energy Employed	Dose	% Inhibition
<i>P. aeruginosa</i>	405nm	10J/cm <sup>2</sup>	95.1
	470nm	5J/cm <sup>2</sup>	96.5
	405&880nm	20J/cm <sup>2</sup>	93.8
<i>S. aureus</i>	405nm	15J/cm <sup>2</sup>	87.9
	470nm	15J/cm <sup>2</sup>	62.0
	405&880nm	3J/cm <sup>2</sup>	72.3
<i>M. smegmatis</i>	405nm	120J/cm <sup>2</sup>	98.3
	464&850nm	45J/cm <sup>2</sup>	70.79
<i>K. pneumoniae</i>	464&850nm	60J/cm <sup>2</sup>	96.19
<i>C. albicans</i>	624&850nm	30J/cm <sup>2</sup>	76.23

nm = Nanometers

J/cm<sup>2</sup> = Joules per square centimeter

**Table 2.** Musculoskeletal and Neurologic, Guffey et al.

Condition	Light Energy Employed	Dose	Outcome
Plantar Fasciitis	624&850nm	9J/cm <sup>2</sup>	Decreased Pain and Improved Function
Peripheral Neuropathy	850nm	12J/cm <sup>2</sup>	Decreased Pain, Improved Function, Improved Sensation

nm = Nanometers

J/cm<sup>2</sup> = Joules per square centimeter

Many other researchers are engaged in efforts to explain the effects of light energy on biologic tissues. We are certainly supported and inspired by their efforts. We are particularly influenced by the work of Michael Hamblin and Tianhong Dai. Both these visionary researchers are from Massachusetts General Hospital and Harvard University. Their respective contributions far exceed those of our team. We encourage the reader to refer to their many published works to more fully appreciate the intricacies of photobiomodulation.

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Mr. Payne is Assistant Professor of Clinical Laboratory Science. He is a microbiologist by training and collaborates with Dr. Guffey on various microbiology related research.